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Principles and Practice of Geriatric Surgery

Third Edition

Springer

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Editors

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With 261 Figures and 155 Tables

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Dedicated to our children and grandchildren, who will not only be taking care of us, but will lead the charge in improving the care of the next generation of vulnerable older adults across the healthcare continuum.

Preface to the Third Edition

In 2012 the first baby boomer turned 65, and now every day 10,000 people in the United States turn 65. By the end of the current decade, one in five people will be over age 65, and by 2050, there will be nearly 20 million over age 85. As we know, many of the diseases that surgeons treat, such as cancer, cardiac diseases, and musculoskeletal disorders, are diseases of aging. All of us, except perhaps our pediatric surgery colleagues, are seeing more and more, older and older patients in our practices every day. As we do, we increasingly realize that older adults have unique medical, surgical, and psychosocial care needs that must all be addressed if high-quality surgical care that is consistent with each patient's health goals is to be consistently achieved.

We are now very pleased to present the third edition of our book: *Principles and Practice of Geriatric Surgery*. This has been a work of love for us, and we are so pleased to help this unique field of surgical care grow over 20 years. When the first edition of this book was published in 2001, only a few surgeons pursued Geriatric Surgery as an academic niche interest or as a personal mission or both (some of us for 15–20 years before that). Twenty years later, it is a core value of surgeons in every field. We have all become Geriatric Surgeons, and to borrow the words of an American College of Surgeons (ACS) promotional video, "Care has come of age."

We have had wonderful partners in this journey. In the early days, interest in the field was more grassroots than organized. In 1995, the American Geriatrics Society with support of the John A. Hartford Foundation established the Geriatrics for Specialists Initiative. This eleven-specialty collaborative developed novel programs, such as the Jahnigen Research Scholarship and the Geriatrics Education for Specialty Residents grants, designed to encourage young surgeons to pursue a career in geriatric surgery. In 2008, the American College of Surgeons established the Geriatric Surgery Task Force which led educational and clinical awareness initiatives. This evolution culminated into evidence-based clinical initiatives, when in 2015 the American College of Surgeons, again with the generous support of the John A. Hartford Foundation, assembled a coalition of 58 national stakeholder organizations. Representatives of older adults, their families and caregivers, medical and surgical specialties, nurses, allied health professionals, insurers, and regulators convened to identify the requirements for providing high-quality, patient-centered care to senior citizens. Over a 4-year period, this Coalition for Quality in Geriatric Surgery defined a group of 30 evidence-based or consensus-derived (where evidence was lacking) standards that were both valid and feasible for hospitals to adopt. These standards address how to assure truly shared surgical decision-making and how to identify and plan for optimizing the vulnerabilities that aging has imposed on each individual, throughout the surgical care continuum.

These standards have formed the foundation for the development of the American College of Surgeons Geriatric Surgery Verification Program, which was introduced in July of 2019 and began taking applications in October 2019. This quality program is based on the same four pillars as all ACS quality programs:

1. Identify the standards for quality care.
2. Define the infrastructure needs.
3. Collect appropriate data to allow for measurement of improvement.
4. Verify that the standards are in fact being met to assure the public.

The hope is that this program will be adopted by all hospitals across the country where surgical care of older adults takes place and thereby raise the bar for the care of all hospitalized older adults.

But no program will be successful without healthcare providers who are familiar with the differences between older and younger adults. Older adult patients are unique. It is the purpose of this text to bring the latest scientific, clinical, and social information on the changes in aging, and their impact on the conduct of all aspects of surgery, to all healthcare providers.

2020 Ronnie A. Rosenthal
Michael E. Zenilman
Mark R. Katlic

Preface to the Second Edition

It has been a decade since the first edition of this textbook came to press, and the field of geriatric surgery is growing. Over the last decade, Geriatrics has been recognized as a distinct aspect of surgery by leadership in our field and others. The American College of Surgeons established the Task Force for Geriatric Surgery, a Geriatrics Section in the Surgical Forum, and a community for Geriatric Surgery on the ACS Web portal. The American Geriatrics Society created the Jahnigan Scholars Program to expand geriatric clinical and basic research in the surgical disciplines as part of its Geriatrics-for-Specialists Initiative. Recently, the American Board of Surgery and Surgical Residency Review Committees expanded the requirements for working knowledge of the geriatric patient, most notably using the ABS Surgical Council on Resident Education (SCORE) curriculum project, which now includes a Geriatric module. Evidence of the growing interest in geriatric aspects of surgery can be found in the rapidly growing literature and in the numerous panels, discussions, and presentations at local and national meetings. One of the most notable of these was the panel at the 2009 American College of Surgeon's Clinical Congress entitled "She's 92, what do I do?" The audience was standing room only; the questions were thoughtful and nearly unending; there is obvious hunger for knowledge by surgeons from all practice venues. Most importantly, in 2008 the Institute of Medicine published a 250-page report on "Retooling for an Aging America: Building the Health Care Workforce." In it, the Committee on the Future Health Care Workforce for Older Americans clearly outlined the population statistics, described the prevalence of chronic disease in the elderly population, and predicted the resource challenges for our health-care system. The report suggested a three-pronged program to meet these challenges: (1) to enhance the competencies of all practitioners in geriatric care, (2) to increase the recruitment and retention of geriatric specialists, and (3) to redesign models of care and broaden provider and patient roles to achieve greater efficiencies. Surgery will be an integral part of the care for this population, and this textbook provides the foundation of knowledge for the teams that will be caring for these patients. In this edition of *Principles and Practice of Geriatric Surgery*, we have kept the same format as the last edition, with each section preceded by an invited commentary from a well-known and widely respected senior member of each discipline. The opinion pieces submitted are all highly relevant and informative. For the chapters, we chose authors who are recognized leaders in their fields, and were gratified with their enthusiasm and high quality of the submissions. We added a number of new chapters to enhance the focus on the latest topics of interest such as frailty (Chap. 9), geriatric models of care (Chap. 21), unique complications (Chap. 29), oral cavity (Chap. 41), and dysphagia (Chap. 44). Another new chapter addresses geriatric surgical education and provides links and information for a number of additional educational resources (Chap. 15). The final addition provides a hard look in our own mirror as surgeons, with an excellent discussion of the effects of age on surgeon performance (Chap. 18).

Also new to this edition, the physiology chapters begin with a table that summarizes the key points regarding changes in physiologic function with age. The clinical chapters contain an illustrative clinical vignette designed to drive home the critical learning points for each topic. As you will see, a simple example makes a seemingly complex topic manageable. The passion for bringing this book to completion was palpable from our first informal editorial lunch in New York in the spring of 2007 to the present volume in your hands. The editors have become close friends and greatly appreciate the hard work done by all the authors. On the editorial side, Portia Bridges, our development editor from Springer was as dedicated as we. She was professional, persistent, and relentless in the pursuit of fresh ideas, manuscript deadlines, quality figures, and simple excellence (we have several thousand emails from Portia in our archives, etc.). We have all been through a lot over the last few years and hope this book symbolizes both the deep affection we have for each other and the commitment we have to improve the quality of care for older surgical patients. We each would like to thank our families, coworkers, and patients for their patience and support in creating this textbook. They all understand that Geriatric Surgery is a real discipline and have lived with our enthusiasm to bring this field to the forefront of surgery. Maybe the next edition will start off with a chapter whose title is borrowed from the pediatricians: "Your geriatric patient is not just an 'older human,' s/he has specific needs."

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Preface to the First Edition

More than two decades ago, in response to the special healthcare needs of the aging American population, interest in the field of geriatric medicine began to grow and blossom in the United States. In 1984 and 1985, under the editorial leadership of Christine K. Cassel and William R. Hazzard, respectively, two major textbooks devoted to the medical care of aged patients were published. These scholarly, comprehensive texts provided insight into the principles of aging and guidance in the care of the geriatric patient. Three editions later, the need to understand the special issues involved in the medical care of the elderly is widely accepted by internists, primary care providers, and medical specialists. For the editors of this book, the special issues involved in the surgical care of the elderly have been apparent for nearly as long. Although there have been a few scholarly texts on the subject, including one in 1990 by Mark R. Katlic, general acceptance of the concept of geriatric surgery by our surgical and medical colleagues has, however, lagged. This is not the result of a proportionately smaller number of older patients with surgical disease, because cancer, cardiovascular disease, and orthopaedic problems are diseases, of the aged. It is rather the result of uncertainty about the value of surgery in the elderly and concerns about the risks of operations. In the past, such concerns prevented primary care givers from referring patients for surgical care and prevented surgeons from agreeing to operate. With the improvements in technology, monitoring, and anesthesia, we are now able to safely operate on most older patients, based on indications that are determined by the disease and the patient's overall health rather than by age. Since 1980, the percentage of operations performed in which the patient was over age 65 has nearly doubled to almost 40%. It is now estimated that approximately half of the patients in most general surgery practices, and even higher percentages in most cardiac and vascular surgery practices, are 65 years of age or older. This recent rapid increase in the elderly surgical population has increased the awareness that older surgical patients are different from younger surgical patients and therefore require special consideration. In 1995, shortly before this text was conceived, the American College of Surgeons, with input from three well-respected senior surgeons, George E. Block, Ben Eiseman, and Gerald O. Strauch, added a panel on Surgery in the Elderly to that year's program at the Annual Clinical Congress. Similar programs have since been presented at each of the last three Clinical Congresses. Also in 1995, the American Geriatrics Society in association with the Hartford Foundation began a program to increase geriatric expertise in nonprimary care specialties, including general surgery, orthopedics, urology, and gynecology. As part of this program, Drs. Walter Pories and Sherralyn Cox developed a geriatric syllabus that has now been added to the Surgical Resident Curriculum of the Association of Program Directors in Surgery. The field of "Geriatric Surgery" has begun to emerge. Our goal in developing the present book was not to form the basis for a new surgical specialty because most surgeons, with the exception of our podiatric colleagues, will need to be "geriatric surgeons" soon. It was rather to provide a comprehensive collection of information that would allow all providers of healthcare to the elderly to understand the issues involved in choosing surgery as a treatment option for their patients. We have, by now, shown that we can operate on the elderly, the question is often whether we should. To help answer this question, we have divided the book into two parts. Part I, General Principles, describes general aspects of the physiology of aging and gives an overview of surgical management and important ethical considerations. Part II, Specific Issues, is organized by organ system. The first chapter in each section details the physiologic changes of that organ system with age. The subsequent chapters describe the pathophysiology, surgical treatment, and outcome of treatment for the disease of that organ system that are commonly encountered in elderly patients. With this information in hand, geriatricians, internists, and other primary care providers can better decide which of their patients will benefit from surgical referral; surgeons, surgical residents, and students can better understand how aging changes the assessment of risks, the choice of operation, the perioperative management, and treatment outcome. Each section is also preceded by an invited commentary from well-known and widely respected senior members of each discipline. We have asked them to reflect on the changes they have seen in their area of expertise over the course of their careers and to comment on how they feel these changes have influenced the care of the elderly. We are extremely grateful to them for graciously agreeing to share their thoughts. The road from concept to reality of this book has been long and somewhat bumpy, but throughout, there has been a genuine commitment to the importance of such a book by all involved. We are most grateful to our editor at Springer-Verlag, Laura Gillan, and her assistants for maintaining the high level of enthusiasm for the topic and commitment to the quality of the work. It has been a great pleasure to work with, and learn from, someone who understands so well why we embarked on this kind of journey and who so clearly shares our goal. Without her help, it would not have happened. We also thank Barbara Chernow and her associates for the very skillful copyediting done under considerable pressure. Finally we are extremely grateful to all of our authors, who have given so generously of their valuable time and effort to produce outstanding chapters in an era when rewards for such efforts are primarily internal. It is our belief that the information they have so carefully provided will bring significant improvements to the overall healthcare of our elderly patients.

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About the Editors

Ronnie A. Rosenthal M.D., is a graduate of the SUNY Downstate College of Medicine, where she also did her general surgery residency training and had her first faculty position. She is currently Professor of Surgery and Geriatrics at Yale University School of Medicine and is in her 21st year as Chief of Surgery at the VA Connecticut Healthcare System. She also serves as the Chief Surgical Consultant for VA New England Healthcare System (VISN 1). She is Chair of the ACS Geriatric Surgery Task Force and Co-Director of the ACS NSQIP Geriatric Surgery Pilot. Currently, she is the Co-PI on the "Coalition for Quality in Geriatric Surgery" grant with Dr. Clifford Ko, Director of Quality Programs for the ACS. Through this 4-year national grant, funded by the John A. Hartford Foundation (JAHF), she has worked with 60 stakeholders to develop a set of standards for the surgical care of older adults, which has culminated in the creation of the ACS Geriatric Surgery Verification Program.

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Michael E. Zenilman, M.D., graduated college at State University of New York at Stony Brook and received his medical degree from SUNY Downstate Medical School in Brooklyn in 1984. He served as Clarence Dennis Professor and Chair of Surgery at SUNY Downstate, Brooklyn, NY, for 10 years. From 2011 to 2016, Dr. Zenilman led the integration of surgical care between the community hospitals and main campus as the inaugural Regional Director of Surgery for the Johns Hopkins Health System. He is currently doing similar work for Weill-Cornell and the NewYork-Presbyterian healthcare network.

An established clinician, teacher, and researcher, Dr. Zenilman has published extensively on pancreatic disease and geriatric surgery and served on the editorial board of *JAMA Surgery* and the *American Journal of Surgery*. He remains clinically active and has mentored over 100 surgical residents and over 50 students, fellows, and junior faculty.

Mark R. Katlic is a Phi Beta Kappa graduate of Washington and Jefferson College and an Alpha Omega Alpha graduate of the Johns Hopkins University School of Medicine. He completed residencies in Surgery and Cardiothoracic Surgery at the Massachusetts General Hospital. A practicing thoracic surgeon since 1984, Dr. Katlic also earned a Master of Medical Management degree from the John Heinz School of Public Policy and Management at Carnegie Mellon University in 1999.

Dr. Katlic has had a special interest in caring for the elderly for over 35 years. His paper, “Surgery in Centenarians,” was published in the *Journal of the American Medical Association* in 1985, and he went on to publish seven textbooks and to lecture frequently on this subject. As a thoracic surgeon, Dr. Katlic has pioneered video-assisted thoracic surgery (VATS) under local anesthesia and sedation, with results of 576 cases published in 2017.

Dr. Katlic is presently Chairman of the Department of Surgery and Surgeon-in-Chief of Sinai Hospital in Baltimore, Maryland. He also directs the Sinai Center for Geriatric Surgery. In 2014, Dr. Katlic established The Aging Surgeon Program, a comprehensive, objective evaluation of a surgeon’s cognitive and physical faculties, at Sinai Hospital of Baltimore. He was named Maryland Innovator of the Year in 2013 and Maryland Physician of the Year in 2019. In his free time he trains for triathlons.

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Part I

Principles

1 Principles of Geriatric Surgery

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Contents

Abstract

The world population is aging and the conditions that require surgery – atherosclerosis, cancer, arthritis, prostatism, cataract, pelvic floor disorders, and others – increase in incidence with increasing age. What do we know about surgery in the elderly that will help us improve our care of these conditions? Six general principles are useful for teaching purposes. These include the fact that the clinical presentation of surgical problems may be subtle or different from that of the general population; the elderly handle stress well but not severe stress due to lack of reserve; preoperative preparation and attention to detail are crucial; when these are lacking, as in emergency surgery, risk dramatically increases; and the results of elective surgery in the elderly are good in many centers and do not support prejudice against advanced age. Surgeons must become students of the physiologic changes that occur with aging and, guided by these few principles, apply this knowledge to daily clinical care. We owe it to our elders to become good geriatric surgeons and in so doing we will become better surgeons to patients of all ages.

Keywords

Geriatric · Elderly · Geriatric surgery · Preoperative · Perioperative · Ageism · Complications

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Introduction

With a few obvious exceptions, those of us who are surgeons must become geriatric surgeons. The population as a whole is aging, with the most explosive growth in the over 85 year group, and the conditions that require surgery (atherosclerosis, cancer, arthritis, prostatism, cataract, pelvic floor disorders, and others) increase in incidence with increasing age. Improving our care of the elderly surgical patient will become progressively more important to all of us.

Admittedly, surgeons have always cared for the elderly, but the definition of "elderly" has changed. A threshold of 50 years was chosen for the 167 patients described in a paper in 1907 [1], and 20 years later influential surgeons still wrote that elective herniorrhaphy in this age group was not warranted [2]. Now, though, we are performing complex operations in octogenarians, nonagenarians, and occasionally centenarians [3–8]. In addition, the salutary results of such surgery can even influence general sentiment about medical care of the elderly. Linn and Zeppa's study [9] of junior medical students reported that the surgery rotation, in contrast to other clerkships, positively influenced the students' attitudes about aging regardless of the students' career choices, as the elderly surgical patients were admitted and treated successfully.

Surgery therefore has much to offer the geriatric patient, but that patient must be treated with appropriate knowledge and attention to detail. Discussions of physiologic changes in the elderly and results of specific operations comprise the bulk of this book and are not presented here. The authors' three decade study in this area, in addition to caring for an elderly oncology population, has led to a distillate of several general principles (Table 1) which are relevant to all who care for the aged. These principles are worthwhile chiefly for teaching purposes, as they cannot apply to every patient or every clinical situation. Some principles also apply to surgery in the young patient, but the quantitative differences in the elderly are significant enough to approach qualitative status. Risks of many emergency operations in the young, for example, are indeed greater than the risks of similar elective operations, but the differences are small compared to the threefold increase in the elderly. With respect to these principles, the elderly need not be treated as a separate species but perhaps as a separate genus or order within the same larger group of surgical candidates.

Table 1 Principles of geriatric surgery

I.	The *clinical presentation* of surgical problems in the elderly may be subtle or somewhat different from that in the general population. This may lead to delay in diagnosis
II.	The elderly handle stress satisfactorily but handle severe stress poorly because of *lack of organ system reserve*
III.	Optimal *preoperative preparation* is essential, because of Principle II. When preparation is suboptimal, the perioperative risk increases
IV.	The results of elective surgery in the elderly are excellent in some centers; the results of emergency surgery are poor though still better than nonoperative treatment for most conditions. The risk of *emergency surgery* may be many times that of similar to elective surgery because of Principles II and III
V.	Scrupulous *attention to detail* intraoperatively and perioperatively yields great benefit, as the elderly tolerate complications poorly (because of Principle II)
VI.	A patient's age should be treated as a *scientific fact, not with prejudice*. No particular chronologic age, of itself, is a contraindication to operation (because of Principle IV)

Although our results have generally improved over the years [10–12] (Fig. 1), this improvement has not been universal [13, 14] (Fig. 2) and emergency surgery is still risky. Understanding these six general principles may help us improve our care of the elderly patient who requires surgery.

Principle I: Clinical Presentation

The clinical presentation of surgical problems in the elderly may be subtle or somewhat different from that in the general population. This may lead to delay in diagnosis.

Classic symptoms of appendicitis are present in a minority of elderly patients, as few as 26% in Horattas' series over 20 years [15] (Table 2). Rebound tenderness was present in fewer than

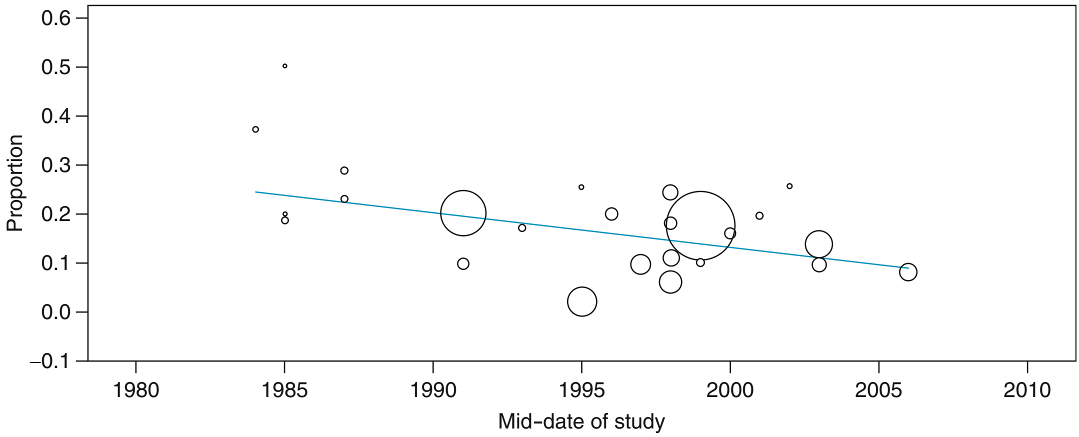


Fig. 1 Operative mortality for mitral valve surgery in octogenarians has improved over time. Scatter plot depicting odds ratios of operative mortality from mid-date of studies. (From Biancari [11], with permission)

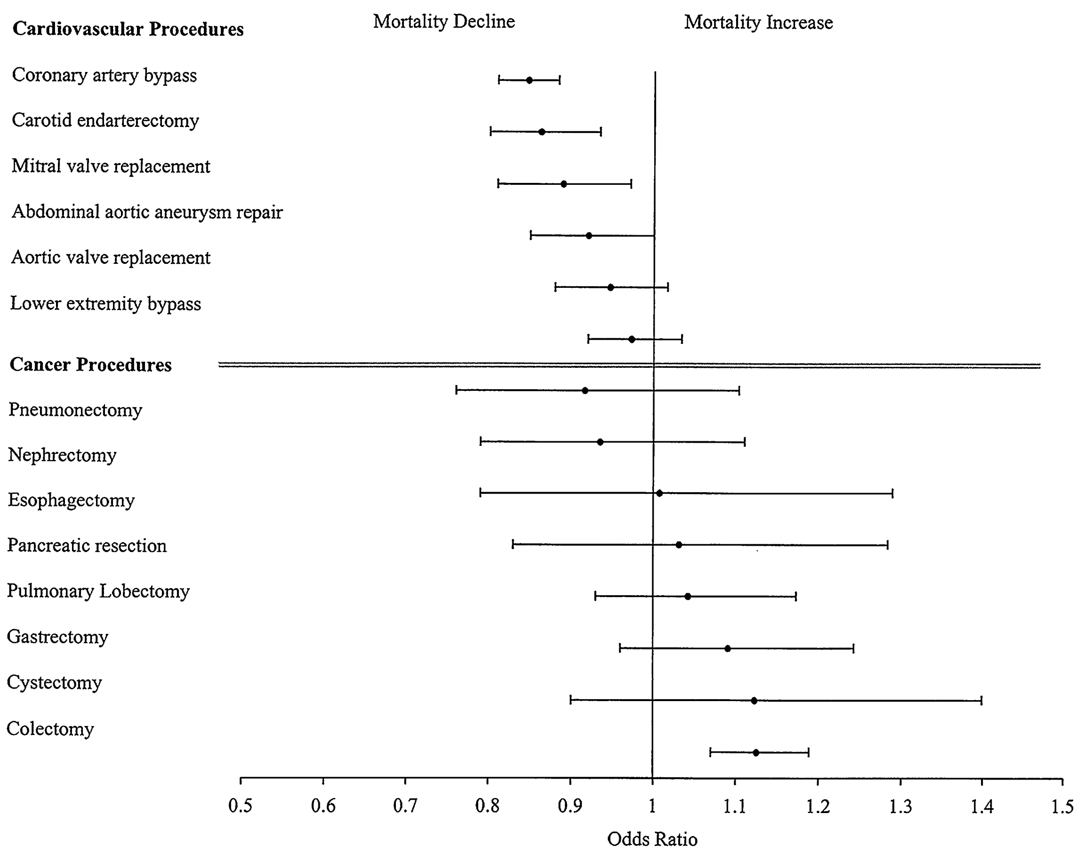


Fig. 2 Operative mortality in the Medicare population has declined for some, but not all, procedures. (From Goodney [13] with permission)

Table 2 Subtle sx, appendicitis

Twenty-year comparison and compilation			
Characteristic	1978–1988 ($n = 96$)	1988–1998 ($n = 113$)	1978–1998 ($n = 209$)
Classic presentation	(19) 20%	(36) 30%	(55) 26%
Delayed presentation (>48 h)	(32) 33%	(36) 30%	(68) 33%
Imaging			
AAS	(81) 84%	(86) 76%	(167) 80%
Sensitivity	(22) 27%	(22) 25%	(44) 26%
CT		(50) 44%	
Sensitivity		(45) 90%	
Correct admitting diagnosis	(49) 51%	(52) 46%	(101) 48%
Surgery within 24 h	(80) 83%	(97) 85%	(177) 85%
Perforation	(60) 72%	(58) 51%	(127) 61%
Complications	(30) 32%	(24) 21%	(54) 26%
Those with perforation	(25) 83%	(15) 72%	(40) 76%
Deaths	(4) 4%	(4) 4%	(8) 4%

half the patients in another [16] and leukocytosis in only 42.9% in another [17]. Clouding the picture further, objective tests may suggest alternative diagnoses: one in six patients has an elevated bilirubin and one in four has signs of ileus, bowel obstruction, gallstones, or renal calculus on abdominal radiographs [18]. Even astute diagnosis may not prevent perforation, present in 42–60% of elderly patients despite operation within 24 h of symptom onset [15, 17].

Biliary tract disease is the most common entity requiring abdominal surgery in the elderly, yet the diagnosis is often delayed. More than one-third of patients with acute cholecystitis are afebrile, one-fourth are nontender, and one-third are without leukocytosis [19–22]. Cholangitis may appear only as fever of unknown origin or as confusion [23]. Consequently, the elderly predominate in series of patients with complications of biliary disease (gallbladder perforation, empyema, gangrene, gallstone ileus, cholangitis) [24], and the complication may result in the first apparent symptom [21, 25]. Saunders [26] reported that abdominal pain was a less prominent symptom and that the bilirubin level was nearly double in elderly patients presenting with bile duct carcinoma, compared to the findings in young patients seen during the same time period.

Peptic ulcer disease may present as confusion, malaise, anemia, or weight loss as opposed to pain [27]; even with perforation pain may be absent or minimal. Rabinovici [28] found a discrepancy between "severe intraoperative findings" and preoperative objective findings such as heart rate (mean 88/min), temperature (37.2 °C), and white blood cell count (10,900/dl). Some have suggested that the elderly and possibly their physicians become tolerant over the years to abdominal pain, loss of energy, and other symptoms, resulting in a delay in diagnosis or an emergency presentation [29]. In Mulcahy's [30] series of patients with colorectal carcinoma, for example, elderly patients were nearly twice as likely (18%) as younger patients (11%) to present emergently. Elderly patients with perforated diverticulitis are three times more likely to have generalized peritonitis at operation than young patients [31].

Gastroesophageal reflux disease in the elderly is less likely to cause heartburn and more likely to cause regurgitation or cough ($p = 001$) [32]. In Pilotto's study of 840 consecutive patients [33], typical heartburn/acid reflux, pain, and indigestion were more likely in the young ($p < 0.001$); older patients more often experienced dysphagia, anorexia, anemia, or vomiting ($p < 0.001$ each) or weight loss ($p < 0.007$).

Head and neck disease may also present differently in the elderly. Sinusitis may lead to subtle signs such as delirium or fever of unknown origin [34, 35], and head and neck cancers are less likely to be associated with smoking ($p < 0.01$) [36] and alcohol use ($p < 0.001$) [36, 37]. Hyperparathyroidism is more likely to cause dementia or skeletal complaints and less likely to cause renal stones [38]. In Thomas and Grigg's series [39] of patients with carotid artery disease, stroke was the most common indication for surgery in octogenarians and was the least common indication in younger patients. Unstable angina is as likely to present with dyspnea, nausea, or diaphoresis as it is with classic chest pain [40]. Cioffi's group found that normal presenting vital signs are unreliable in elderly patients admitted for blunt trauma [41].

Even the eureka moments that keep us energized as diagnosticians [42] may be "subtler and less electric" [43] in the elderly.

The clinician who understands that classic presentations of surgical disease occur in a minority of elderly patients will maintain the high index of suspicion needed to minimize delay in diagnosis.

Principle II: Lack of Reserve

The elderly handle stress satisfactorily but handle severe stress poorly because of lack of organ system reserve.

Functional reserve may be considered the difference between basal and maximal function; it represents the capacity to meet increased demands imposed by disease or trauma. Although there is variability among individuals, this organ system reserve inexorably declines in one's 70s, 80s, and 90s. With excellent anesthetic and perioperative care, the aged patient may tolerate the stress of even complex surgery – particularly if elective – but not the added stress of exceptional or emergency surgery.

The elderly patient with lung cancer, for example, can undergo routine pulmonary lobectomy with results nearly indistinguishable from those of the general population [44, 45], but the added stress of concomitant chest wall resection leads to a disparate increase in risk. In Keagy's series [46], the one death and two of the three respiratory failures were in patients who underwent the *en bloc* chest wall resection. An elderly patient, entering the operating room with decreased chest wall compliance and strength and decreased elastic recoil as a baseline, may tolerate lung resection but lacks the reserve to tolerate an extended operation. Other researchers have reported increased mortality in septuagenarians and octogenarians following pneumonectomy, especially right pneumonectomy or completion pneumonectomy [47–49].

On the other side of the spectrum, more limited procedures, such as video-assisted thoracic surgery, may decrease stress further by preserving respiratory muscle strength [50–53]. Yim [53] reported no deaths or pulmonary complications following thoracoscopic surgery in 22 patients over age 75 years, five with major resections, and Jaklitsch [51] found decreased mortality, length of hospital stay, and postoperative delirium after 307 video-assisted procedures in patients aged 65–90 compared to that associated with open thoracotomy. Video-assisted pulmonary lobectomy in half of a group of elderly lung cancer patients resulted in fewer complications ($p = 0.04$) and decreased length of stay ($p < 0.001$) compared to the half who underwent open (thoracotomy) lobectomy [54]. Patel [55] reported shorter hospitalization and similar late outcomes following endovascular thoracic aortic procedures in patients greater than 75 years, compared to open procedures. Endovascular repair of abdominal aortic aneurysm in the elderly had decreased all-cause and aneurysm-related mortality compared to open repair [56]. Partial as compared to radical nephrectomy resulted in improved survival in elderly patients who were candidates for either procedure [57].

Left ventricular functional reserve assumes critical importance in elderly patients undergoing cardiac surgery. In general, results in the elderly diverge from those of young age groups only in the worst functional classes. Bergus et al. [58], for example, found that length of stay following aortic valve replacement was significantly longer ($p < 0.05$) in septuagenarians in New York Heart Association class IV but not in class III, compared to patients under age 70. Patients over age 75 in Salomon's large series [59] had significantly higher mortality after coronary artery

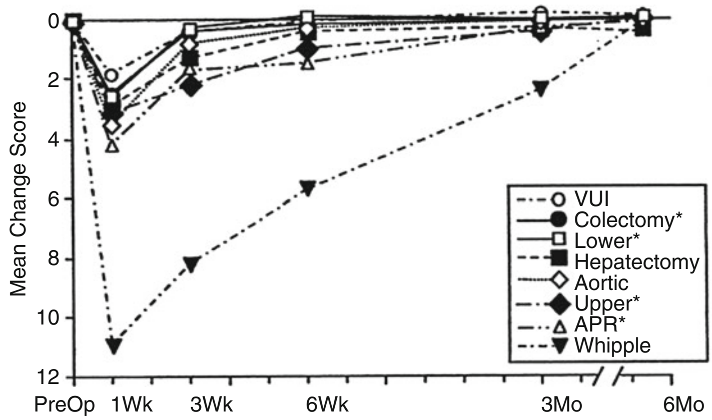


Fig. 3 Return to Activities of Daily Living after major surgery (function returns rapidly after stressful operations but not the most stressful, speaking to lack of reserve). (From Lawrence [72] with permission)

bypass grafting if they had suffered a myocardial infarction less than 3 weeks preoperatively compared to more than 3 weeks (14.1% vs. 5.2%); there was much less difference in patients younger than age 75 (3.5% vs. 2.3%). When patients over age 70 years undergo a third coronary reoperation, only those in the worse Canadian Functional Class experience increased mortality, an increase not seen in young patients in a similar class [60]. Elayda [61] reported that mortality for isolated aortic valve replacement in patients over age 80 was acceptable (5.2%), but addition of concomitant procedures increased this figure significantly (27.7%). In cardiac surgery, too, a lesser procedure may be just as good in the elderly: contrary to a younger population, limited coronary revascularization appears to be acceptable in the high-risk elderly [62, 63].

Similar findings pertain to major abdominal surgery. Fortner and Lincer [64] found that the increased number of deaths among elderly patients undergoing hepatic resection for liver cancer were nearly all in the extended-resection group (i.e., extended right hepatectomy or trisegmentectomy), among whom 60% of deaths were due to hepatic insufficiency. In another group of hepatic resections done for metastatic colon cancer, where cirrhosis and functional hepatic reserve are less important factors, there was no difference in mortality between young and old patients [65]. Even the addition of common duct exploration to open cholecystectomy significantly increased mortality in the elderly (3.5% vs. 1.8%, $p < 0.05$) [66]. For some oncology cases (e.g., gastric cancer, lung cancer), a more limited operation in the elderly need not decrease survival [67–70].

The elderly can return to normal function after stressful operations (such as colectomy and hepatectomy), but after the most stressful operations (such as Whipple pancreaticoduodenectomy) it will take longer [71, 72]. (Fig. 3)

With modern anesthetic and critical care management, an elderly patient can tolerate the stress of even complex operations. However, if the most extended procedures are contemplated, a comprehensive preoperative evaluation of functional reserve is recommended.

Principle III: Preoperative Preparation

Optimal preoperative preparation is essential because of Principle II. When preparation is suboptimal the perioperative risk increases.

A patient's advanced age is immutable, but some factors can be improved preoperatively, with benefits in excess of those to a younger patient. No universal threshold of blood hemoglobin applies to every patient, but correction of anemia and dehydration do assume greater importance in the elderly because of their general lack of reserve and particularly the physiology of the aged heart and kidney. Among the predictors of an overall good postoperative course in Seymour's series of

288 elderly general surgery patients were a hemoglobin level of more than 11.0 g/dl and absence of volume depletion [73]. Contrary to this, Dzankic found that routine blood testing in the elderly surgical patient rarely showed abnormal results and even when abnormal did not correlate with adverse postoperative outcome [74].

Few would argue that pulmonary problems are among the most common perioperative complications in the elderly, in part due to decreased respiratory muscle strength. Nomori [52] showed that following thoracotomy patients older than 70 years experience significant reductions in both maximum inspiratory and expiratory pressures, unlike their younger counterparts; this effect persists for 12 weeks (Fig. 4). Although few data exist to support the routine use of preoperative pulmonary conditioning or rehabilitation, most authors strongly advocate smoking cessation [75] and treatment of bronchitis and reactive airways disease such as asthma [76, 77]. Prophylaxis against deep vein thrombosis (DVT), clearly a risk in the elderly [78], and against pulmonary embolism should be routine [79].

Another unsettled issue concerns the value of aggressive preoperative screening for coronary and carotid artery disease, particularly in patients scheduled for peripheral vascular surgery. Leppo [80] considered age over 70 years one of several risk factors (the others being a history of angina, congestive heart failure, diabetes mellitus, prior myocardial infarction, and ventricular ectopy), which should trigger further cardiac assessment. Echocardiogram and dobutamine stress testing have been shown to bear incremental value over clinical evaluation [81].

There is some evidence that performance testing may hold value. Maximal oxygen consumption (VO2 Max) tests [82] may not be readily available in all hospitals, but reasonable surrogates – stair climbing [83–85], shuttle walk [86], long distance corridor walk [87], gait speed [88, 89], metabolic equivalent (MET) – have been shown to correlate. Weinstein [90] reported prolonged length of stay following thoracic cancer surgery in those patients with METs ≤4 (equating to calisthenics or walking briskly). The International Society of Geriatric Oncology has studied a standardized Preoperative Assessment in Elderly Cancer Patient (PACE); postoperative complications were associated with poor preoperative performance status and lower score on Instrumental Activities of Daily Living, but major complications correlated only with American Society of Anesthesiologists (ASA) Physical Status ≤2 [91] (Table 3). However, as Internullo recently concluded, "a practical and

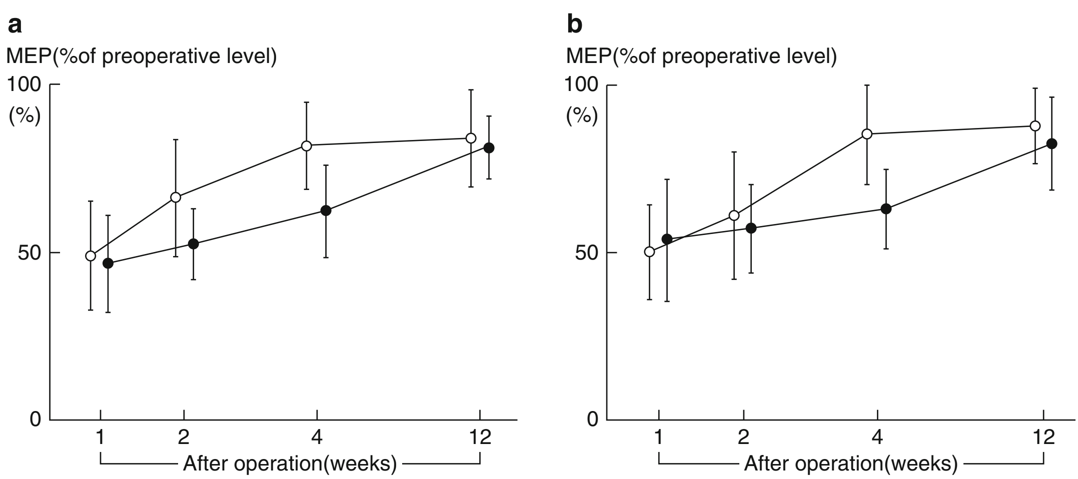


Fig. 4 Postoperative changes in mean (**a**) maximum inspiratory pressure (MIP, percent of preoperative level) and (**b**) maximum expiratory pressure (MEP, percent of preoperative level) following pulmonary resection in 36 patients younger than 69 years (open circles) and 12 patients older than 70 years (closed circles). (From Nomori [52] with permission)

Table 3 Univariate association between components of PACE with 30-day morbidity (any and major complication) adjusted for age, sex, type, and stage of cancer and severity of surgery

Component of PACE	Any complication RR[a]	95% CI	Major complication RR[a]	95% CI
MMS abnormal (<24)	1.23	0.81–1.88	1.08	0.48–2.44
ADL dependent (>0)	1.41	0.95–2.10	1.87	0.95–3.69
IADL dependent (<8)	***1.43***	1.03–1.98	1.65	0.88–3.08
CDS depressed (>4)	1.30	0.93–1.81	1.69	0.93–3.08
BFI mod/severe fatigue (>3)	***1.52***	1.09–2.12	1.24	0.67–2.27
ASA abnormal (≥2)	1.00	0.73–1.38	***1.96***	1.09–3.53
PS abnormal (>1)	***1.64***	1.07–2.52	1.97	0.92–4.23
Satariano's index (1)	1.11	0.78–1.59	1.29	0.68–2.44
Satariano's index (2+)	1.58	0.88–2.85	1.95	0.74–5.18

[a]Bold italics: significant relationship ($p < 0.05$)

reliable individual risk assessment tool is still lacking" [92]. We have termed this simple, reliable test to assess perioperative risk the Holy Grail of Geriatric Surgery [93].

Preoperative antibiotics are not necessary for every type of elective surgery, but researchers agree that advanced age is a risk factor for nosocomial infection. Iwamoto [94] studied 4380 patients who underwent general anesthesia for thoracic, abdominal, or neurologic surgery and concluded that advanced age is a risk factor for nosocomial pneumonia, especially after thoracic surgery. Age greater than 70 years has been shown to be a risk factor for both positive bile cultures ($p < 0.001$) [95] and septic complications of biliary surgery compared to younger patients [96]; antibiotic prophylaxis can reduce these complications [97].

Efforts to improve our elderly patients' preoperative nutritional state would seem desirable – even active, community-dwelling older adults manifest impaired recovery of strength after major surgery [98] – but it is unclear how to do this. Low levels of serum albumin, for example, correlate strikingly with postoperative problems [99] (Fig. 5) but cannot be improved to a great degree preoperatively. Souba [100] reviewed the literature on nutritional support and concluded that preoperative support should be reserved for severely malnourished patients scheduled to undergo major elective surgery and then should be provided for no more than 10 days.

In addition to those already cited, a number of surgeons have attributed their improved results in elderly patients to compulsive preoperative preparation. Bittner [101] believed that the significant decrease in mortality after total gastrectomy in septuagenarians (32.0% in 1979 to 4.4% in 1996) was the result of standardized perioperative antibiotics, thromboembolic prophylaxis, "a systemic analysis of risk factors and their thorough preoperative therapy," and nutritional support for the malnourished.

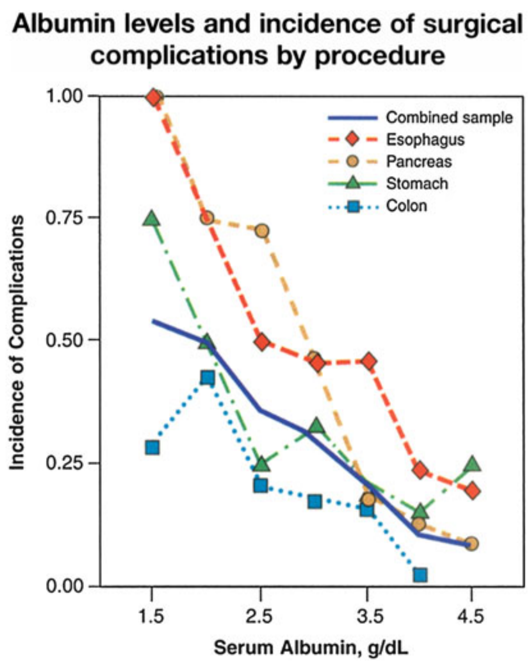


Fig. 5 Preoperative albumin level and major postoperative complications. (From Kudsk [99] with permission)

Hypovolemia is tolerated poorly by the elderly patient and it must be corrected. Smoking should be stopped. Treating other correctable aberrations such as anemia, bronchitis, and hypertension preoperatively increases the elderly patient's chance for a smooth postoperative course.

Principle IV: Emergency Surgery

The results of elective surgery in the elderly are excellent in some centers; the results of emergency surgery are poor though still better than non-operative treatment for most conditions. The risk of emergency surgery may be many times that of similar elective surgery because of Principles II and III.

Many centers have been able to achieve excellent results for elective surgery in the elderly, results indistinguishable from those in younger counterparts [102–104]. Coyle [105] reported the results of carotid endarterectomy in 79 octogenarians and summarized the results of five other series (634 total patients); mortality and morbidity were similar to those in a younger cohort. Maehara [106] had 0% operative mortality in 77 patients over age 70 who underwent resection of gastric carcinoma, and Jougon's [107] results for esophagectomy in 89 patients aged 70–84 years were identical to those in 451 younger patients. An 85-year-old patient with lung cancer could anticipate mortality and survival after pulmonary lobectomy statistically identical to that of younger patients with similar stage disease [76, 102, 108–110].

Identical operations performed emergently in the elderly, however, carry at least a threefold (and as much as a tenfold) increased risk [111] (Table 4). Keller [112], for example, reported 31% morbidity and 20% mortality in 100 patients over age 70 who underwent emergency operations, which is significantly more ($p < 0.0005$) than the 6.8% morbidity and 1.9% mortality following elective operation in 513 similar patients. Elective cholecystectomy can be performed in young and old with the risk of death approaching 0% [25, 113, 114]; the risk of mortality for emergency cholecystectomy increases somewhat in the younger group (1–2%) but increases greatly in the elderly (5–15%) [25]. Surgical priority clearly affects cardiac surgery risk [115, 116]. Elective operative mortality for colorectal surgery is as low as 1.5–3.0%, rising to over 20% for emergency operation [117, 118]. Nearly all of the deaths following paracolostomy hernia repair in Gregg's series were in patients older than 70 years who required emergency surgery [119].

Table 4 Emergency surgery

80–103 Years of age		
Predictive factors	Odds ratio (95% CI)	*p* Value
Emergency operation	11.4 (4.7–27.5)	<0.0001
ASA classification: 1, 2	0.1 (0.03–0.7)	0.0134
ADL impairment	3.2 (1.3–8.1)	0.0116
–	–	–
–	–	–
RVU	1.06 (1.009–1.103)	0.0176
Operative duration	1.17 (1.05–1.3)	0.0039
Hypertension	0.3 (0.1–0.6)	0.0019
–	–	–
–	–	–
–	–	–

A patient's advanced age therefore weighs in favor of commencing rather than deferring needed elective surgery.

Principle V: Attention to Detail

Scrupulous attention to detail intraoperatively and perioperatively yields great benefit, as the elderly tolerate complications poorly (because of Principle II).

Perioperative blood loss is the *bete noire* of geriatric surgery, as the elderly lack the responsive compensatory mechanisms necessary to restore equilibrium. Fong [65] reported that the only independent predictor of postoperative complications in 138 patients over age 70 who underwent pancreatic resection was intraoperative blood loss exceeding two liters. This finding has been mirrored in reports from cardiac surgery and neurosurgery. Sisto [120] reported that six of 23 octogenarian coronary bypass patients who required reexploration for tamponade died;

Logeais [121] found that reoperation for tamponade following aortic valve replacement placed the elderly patient at high risk for mortality ($p < 0.001$). Hemostasis is exceptionally important in the elderly craniotomy patient, possibly because the elderly brain is less likely to expand to obliterate dead space: Maurice-Williams [122] reported that postoperative bleeding following resection of meningioma occurred in 20% of 46 elderly patients and 0% of 38 young patients ($p < 0.05$).

Meticulous surgical technique is important in any patient, but it becomes crucial in those of advanced age. Anastomotic leak after esophageal or gastric resection, a dreaded complication in any patient, embodies an exceptional risk of mortality in the elderly [123]; yet this complication can be minimized by careful technique [124, 125]. Only one of Bandoh's [126] elderly patients who underwent gastrectomy for cancer experienced a leak, as did only 2 of 163 patients over age 70 in Bittner's series [101]. Despite having significantly greater preoperative co-morbidity, the elderly patients undergoing gastrectomy in Gretschel's series experienced no greater postoperative morbidity [68]. The elderly cardiac surgery patient may benefit from extra care when they have a calcified aorta (e.g., intraoperative ultrasound or modified clamping and cannulation technique) or a fragile sternum (e.g., additional or pericostal wires) [127]. Operative speed is less important than technique: in Cohen's series of 46 nonagenarians undergoing major procedures [7], the duration of operation did not correlate with mortality.

Perioperative monitoring is more important in the elderly, since they may manifest few signs or symptoms of impending problems (see section "Principle I: Clinical Presentation"). Bernstein [128] credits intensive hemodynamic monitoring in his lack of mortality among 78 patients over age 70 who underwent abdominal aortic aneurysmectomy. Such monitoring and intensive care were also emphasized by Alexander [3], who reported excellent results for 59 octogenarians having major upper abdominal cancer operations, and by Lo [129] for 85 elderly patients undergoing adrenal surgery at the Mayo Clinic. Giannice [130] credits attention to perioperative care (DVT prophylaxis, antibiotics, monitoring, respiratory care, pain management, early mobilization) for his group's improved recent results in gynecologic oncology patients. Adequate resources such as skilled nursing facilities for the more complex patients are important [131].

Table 5 Complications

Multivariate analysis of failure to return to premorbid function		
All cases	Odds ratio	95% Confidence interval
Emergency operation	2.7	0.99–7.24
ASA III or IV	1.0	0.29–3.56
Comorbidity index >5	1.8	0.48–6.66
Dependence on activities of daily living	1.8	0.42–7.73
Preexisting cardiac disease	1.9	0.69–5.44
Preexisting chronic pulmonary disease	2.0	0.54–7.47
Preexisting cerebrovascular disease	2.0	0.43–9.06
Development of postoperative complications	**24.5**	**3.08–194.88**
Elective cases only		
Comorbidity index >5	**11.2**	**1.08–116.26**
Development of postoperative complications	**10.6**	**3.08–194.88**

We may continue to teach the surgical aphorism, "Elderly patients tolerate operations but not complications" (Table 5).

Principle VI: Age is a Scientific Fact

A patient's age should be treated as a scientific fact, not with prejudice. No particular chronologic age, of itself, is a contra-indication to operation (because of Principle IV).

Great biologic variability exists among the elderly, with some octogenarians and nonagenarians proving to be healthier than their sons and daughters. Even an 85-year-old patient has a life expectancy exceeding 5 years [132, 133], so why not offer him resection of his lung cancer? No other treatment is likely to give him those 5 years. Yet even in 2005 this does not always happen: prejudice against the elderly, so-called "ageism" exists.

Despite the fact that elderly patients treated for lung cancer have survival equal to their younger matched counterparts, Nugent [134] found that patients older than 80 years were significantly less likely ($p < 0.05$) to be treated surgically. In England, the elderly are less likely to have histologic confirmation of their lung cancer and less likely to undergo anticancer treatment [135], although resection rates are increasing [136]. Kuo [137] also reported that octogenarian patients with lung cancer were more likely ($p < 0.01$) to receive only palliative care; when offered, they tolerate chemotherapy [138].

Elderly patients with ovarian cancer are less likely to undergo aggressive chemotherapy and surgery [139, 140] despite results equal to the young [141]. This has been reported with adjuvant treatment following pancreatic resection as well [71]. Older women with breast cancer were less likely to have had screening mammograms [142, 143] and were more likely to present in advanced stages than younger women [143]; once diagnosed, they tolerated surgery well [144, 145]. Guadagnoli [146] presented evidence against ageism in the treatment of early breast cancer, but Herbert-Croteau [147] found that only tamoxifen use was similar in women over and under age 70 ($p < 0.41$), while all other treatments (breast-conserving surgery, radiotherapy, axillary node dissection, chemotherapy) differed significantly ($p < 0.0001$). When elderly patients do receive chemotherapy for breast cancer, they tolerate it [148] and they benefit from it [149]. Elderly patients with colon cancer are less likely to undergo extensive lymph node dissection ($p < 0.0001$) [150]. Fewer than one in ten eligible older patients, with a low cardiac ejection fraction following myocardial infarction, received an implantable cardioverter-defibrillator [151]. Selection bias in the elderly may also lead to delay in referral for abdominal aortic aneurysm surgery [152] and coronary artery bypass surgery [153].

When patients are denied surgery they often do poorly. In Pierard's [154] study of 163 octogenarians with severe aortic stenosis and clear indication for operation according to established guidelines, 40% either refused or were denied operation; this resulted in twofold excess mortality even after adjustment for co-morbidities (Fig. 6). In a study of pancreatic cancer patients across the United States, those undergoing resection, regardless of age group into the 80s, were less than half as likely to die as the youngest group of unresected patients [155]. Owonikoko [156] noted, "Published evidence suggests that elderly patients are denied potentially beneficial treatment and participation in clinical trials solely because of chronologic age and because of physician perception that they are too frail to withstand treatment."

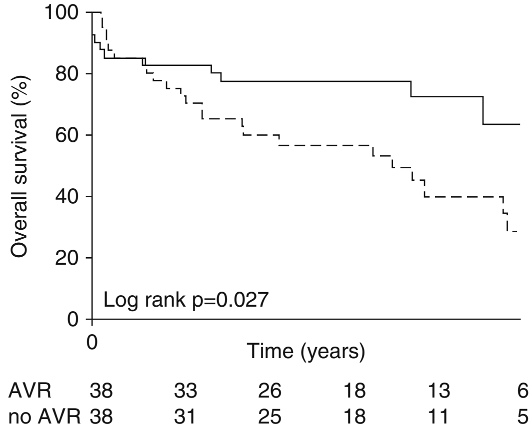


Fig. 6 Propensity score matched patients who refuse or are denied surgery for aortic valve diseased (dashed line) have decreased survival compared to those who undergo aortic valve replacement (solid line). (From Pierard [154], with permission)

Some studies do report increased operative mortality [14, 111, 157–159] (Fig. 7), increased complications [160, 161] (Fig. 8), and increased lengths-of-stay in the elderly [162–167], but overall results in many centers do not differ from the young for a wide variety of procedures: neurosurgery [122, 168]; head and neck surgery [36, 169, 170]; carotid endarterectomy [171, 172]; cardiac surgery [61, 127, 153, 173–177]; esophagectomy [92, 107, 124, 178–180] (Fig. 9); gastrectomy [3, 106, 181–183] (Fig. 10); colectomy [184–186] (Fig. 11); hepatectomy [65, 187–190] (Fig. 12); pancreaticoduodenectomy [65, 71, 191, 192]; radical hysterectomy [193]; total knee/hip replacement [194–196]; microvascular free tissue transfer [197]; cardiac transplant [198–200]; lung

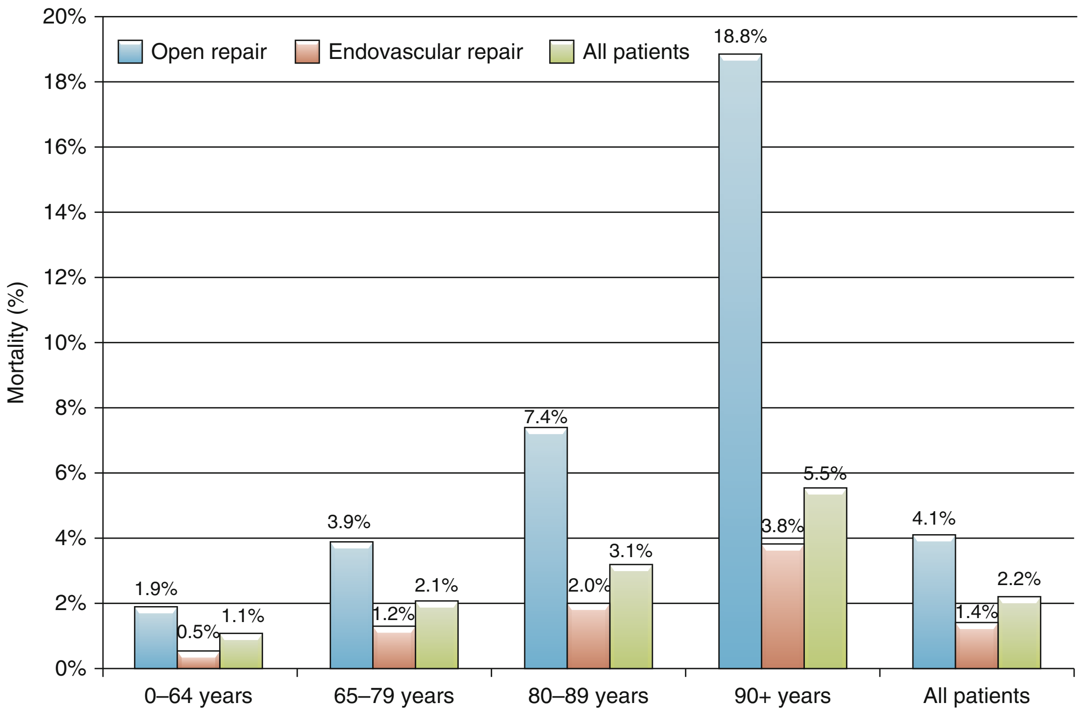


Fig. 7 Increased mortality by age of aortoiliac aneurysm repair. (From Talliniparis [220], with permission)

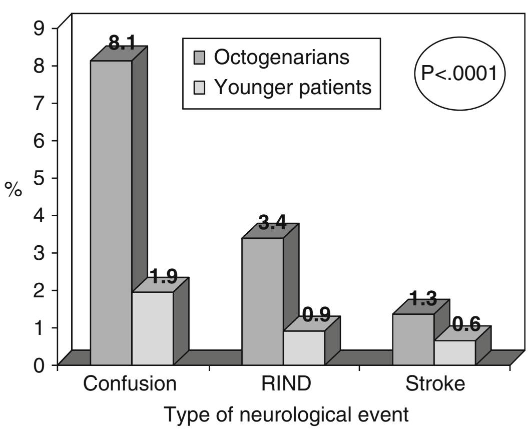


Fig. 8 Early postoperative neurologic complications after coronary artery bypass surgery and valve surgery in octogenarians (RIND = reversible ischemic neurological deficit). (From Ngaage [160] with permission)

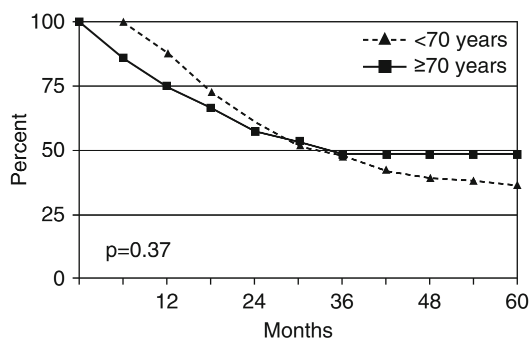


Fig. 9 Esophagectomy following neoadjuvant chemoradiation. Kaplan-Meier survival curves (including postoperative deaths) plotted for patients age < 70 years versus ≥ 70 years. (From Ruol [180] with permission)

transplant [201]; endovascular surgery [202]; gastric bypass [203]; laparoscopic colectomy [204]; and hernia [205]. Return to preoperative quality of life (QOL) is gratifying after elective surgery for gastric or colorectal surgery [206], joint replacement [196], thoracic aneurysm [207] (Fig. 13), and aortic valve replacement [208, 209].

For most patients, general medical condition and associated medical problems are more important than age. Dunlop [210] studied 8889 geriatric surgical patients in Canada and concluded that severity of illness on admission was a much better predictor of outcome than was age; Akoh [211] had similar findings in 171 octogenarians undergoing major gastrointestinal surgery. Co-morbidities were a greater influence on survival than age in several series of elderly patients with lung cancer [44, 45, 212]. Mehta [213] reported that separation of mitral valve replacement patients into low, medium, and high risk medical groups was more important than stratification by age within these three groups. Within the American Society of Anesthesiologists (ASA) Physical Status system [214], the ASA status influences results more than age. For elderly patients undergoing surgery for cancer, the stage of the malignancy also influences outcome more than age [45, 215–218].

Ageism may even be detrimental for the ageist [219].

Many geriatric surgery patients, including nonagenarians, have survival rates equal to those expected in the general population; even the sobering results of emergency surgery in the elderly are better than the results of nonoperative treatment for the same conditions. A patient's age should therefore be considered but not feared.

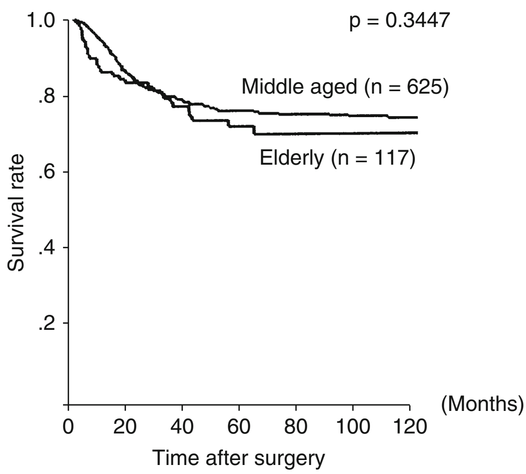
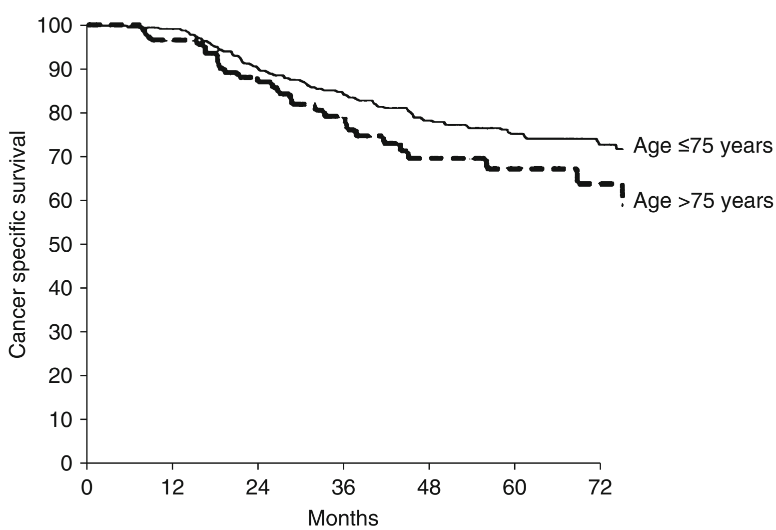


Fig. 10 Surgical outcome in elderly (≥75 years) and middle-aged (45–65 years) patients with gastric cancer. (From Kunisaki [182] with permission)

Conclusion

Surgical problems abound in the elderly and the numbers of elderly are increasing worldwide. Surgeons must become students of the physiologic changes that occur with aging and, guided by a few general principles, apply this knowledge to daily clinical care. The results of surgery in the elderly do not support prejudice against advanced age. We owe it to our elders to become good geriatric surgeons and in so doing we will become better surgeons to patients of all ages.

Fig. 11 Cancer-specific survival of elderly and younger patients treated for mid to distal colorectal cancer ($p = 0.061$), n = 612. (From Law [186] with permission)



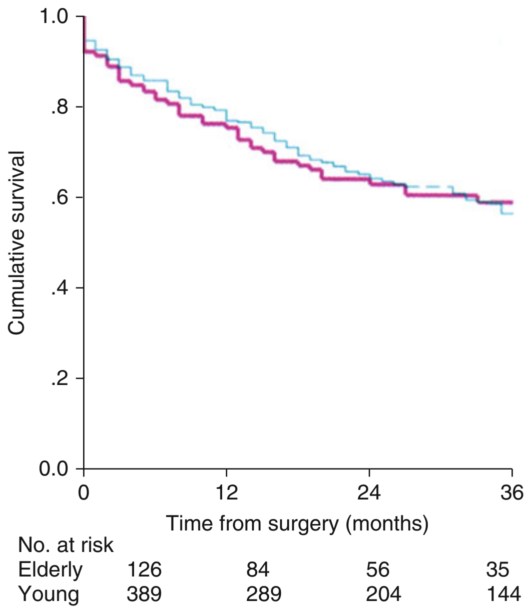


Fig. 12 Major hepatectomy. Overall survival for patients $\geq$70 years (solid line) and $<$ 70 years (dashed line), $p = 0.89$; n = 517. (From Menon [190] with permission)

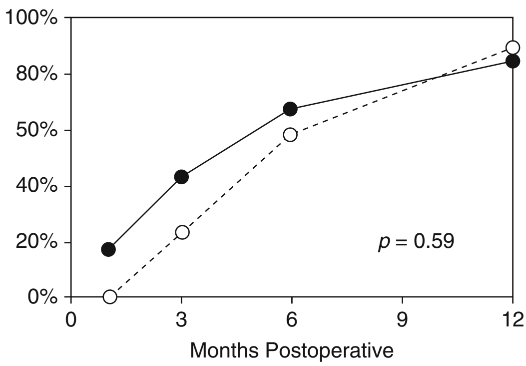


Fig. 13 Return to normal functional activity after thoracic aneurysm repair depending on age: <70 years (solid circles) and $\geq$ 70 years (open circles); n = 110. (From Zierer [207] with permission)

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Defining Quality of Care

2

Jill Klausner and Marcia McGory Russell

Contents

Abstract

The aging of the US population will place significant stress on the current health-care system. The impact of the aging population on the surgical disciplines is especially apparent given the inherent risks of undergoing surgery. It is essential that we develop strategies to deliver high quality and patient-centered care for this vulnerable population. Quality of care in surgery dates back to the early 1900s when Ernest Amory Codman was among the first to systematically measure, analyze, and compare patient care and outcomes. However, only recently has quality of care in geriatric surgery received systematic attention. For example, there have been efforts from the Institute of Medicine, American College of Surgeons, and American Geriatrics Society to improve the quality of care in this population. Using the Donabedian model of quality evaluation (e.g., structure, process, and outcomes), it is clear that there have been marked improvements within five domains important in the perioperative care of geriatric patients: cognitive impairment, functional status, frailty, medication management, and patient

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goals and preferences. Quality improvement in the relatively young field of geriatric surgery is progressing at a rapid rate and beginning to gain the national attention needed to optimize care for this unique patient population.

Keywords

Geriatric surgery · Quality of care · Quality improvement

Impact of the Aging Population

The aging of the US population will place significant stress on the current health-care system. Baby boomers began turning 65 in 2011 and life expectancy has also significantly increased [1]. As a result, the growth rate of the elderly population (aged 65 and older) exceeds the growth rate of the population as a whole. The elderly population currently represents 15% of the total population, but is expected to increase to 21% by 2030 [2]. By 2050, this population is expected to reach 83.7 million individuals, and the population of even older individuals (over age 85) is predicted to reach 18 million [1].

It logically follows that the elderly population is responsible for a disproportionate amount of health-care utilization and cost. In 2007, patients aged 65 years and over represented 37% of hospital discharges and 43% of hospital days, even though this age group only accounted for 13% of the population at that time [3]. Patients aged 65 years and over also stay in the hospital for longer, with an average length of stay of 5.6 days, compared to 5.1 in 45–64 year olds and 3.7 days in 15–44 year olds [3]. Greater than one third of all patients aged 85 and older were discharged to a long-term care facility, compared to less than 25% of their younger elderly counterparts. It has long been known that the aging of the population will affect the overall allocation of health care resources. However, the impact on the surgical disciplines is especially apparent given the inherent risks of undergoing surgery.

As our surgical expertise grows and less invasive operations become more widespread, it is not surprising that the threshold for performing surgery in the elderly has decreased. Older patients now consume a great proportion of surgical care. Patients aged 65 and older account for 36% of all inpatient operations in the USA [3] and more than half of all general surgery, orthopedic, and urological surgical procedures [4]. These numbers are expected to increase 31% by 2020 [4]. Given this significant increase in demand for surgical services in the elderly population, it is essential that we develop strategies to deliver high quality and patient-centered care for this vulnerable population.

Quality of Care in Surgery

The history of quality of care in surgery dates back to the early 1900s when Ernest Amory Codman founded the End-Result Hospital where he was among the first to systematically measure, analyze, and compare patient care and outcomes. He later published his work in an article titled *A Study in Hospital Efficiency* [5]. Decades later, it was clear that despite Codman's efforts and contributions, there was still much work to be done. In the 1980s, the US Congress brought into question the quality of surgical care provided by the Department of Veterans Affairs (VA) hospitals. Congress was concerned that operative mortality rates were inappropriately high – above the national average. Unfortunately, the "national average" was unknown at this time because this data did not exist. In response, the VA began collecting data on pre- and intraoperative variables and outcomes and the VA Surgical Quality Improvement Program (VASQIP) was established in 1994. After the introduction of this program, outcomes at VA hospitals significantly improved. By the year 2000, there was a 27% decrease in 30-day postoperative mortality and a 45% decrease in 30-day morbidity [6]. With the addition of private hospitals and academic centers, the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) was born, and has been named the best in the nation for measuring and reporting surgical quality and outcomes by the Institute of Medicine (IOM). Today there are almost 700 hospitals participating in ACS NSQIP, and the program continues to grow.

The past few decades have been marked with great improvements in the quality of care in surgery, but it is difficult for one database alone to cater to all subpopulations of patients. In addition to ACS NSQIP, organizations, initiatives, and coalitions have formed, each with a more narrow focus. Most relevant for this chapter, elderly surgical patients have recently been recognized as a unique population and there are ongoing efforts to identify factors most important to this population in order to improve care. The IOM addressed the health-care issues of our aging population through the Committee on the Future Healthcare Workforce for Older Americans in a 2008 report entitled *Retooling for an Aging America: Building the Healthcare Workforce* [7]. The committee proposed three mechanisms for improving the ability of our health-care system to care for older Americans: (1) enhance the competence of all individuals in the delivery of geriatric care, (2) increase the recruitment and retention of geriatric specialists and caregivers, and (3) redesign models of care and broaden patient and provider roles to achieve greater flexibility. More recently the ACS NSQIP and ACS Geriatric Surgery Task Force initiated the ACS NSQIP Geriatric Surgery Pilot Project to assess the value of adding geriatric-specific variables to the NSQIP database with the ultimate goal of using this data to evaluate interventions for improving outcomes in the elderly population. Data collection began in January 2014 and data has now been collected on more than 30,000 patients [8]. The variables collected fall into the following elderly specific domains: function, mobility, cognition, and healthcare goals. Additionally, the Coalition for Quality in Geriatric Surgery (CQGS) is a project supported by the John A. Hartford Foundation and the ACS that aims to set standards for geriatric care, verify these standards, develop patient-centered geriatric measures, and educate patients and providers over a 4-year grant period (2015–2019) [8]. These efforts specific to older adults are timely given the aging of the population and the emerging body of research suggesting that novel ways of providing surgical care to this population are needed.

Until recently, no guidelines existed for the perioperative care of older adult patients. Motivated by the projected growth of the over-65 age group and the increasing demand for surgical services from this population, in 2009, McGory et al. identified 91 valid quality indicators for elderly patients. Of note, 78% of these indicators were not routinely used in the assessment or management of younger patients, underscoring the uniqueness of this population and the importance of developing similarly unique quality indicators [9]. This work laid the foundation for the ACS NSQIP/American Geriatrics Society (AGS) Best Practices Guidelines published in 2012 and 2016. The 2012 ACS NSQIP/AGS Best Practices Guidelines: Optimal Preoperative Assessment of the Geriatric Surgical Patient provided guidelines within nine categories: cognitive/behavioral disorders, cardiac evaluation, pulmonary evaluation, functional/performance status, frailty, nutritional status, medication management, patient counseling, and preoperative testing [10]. In 2016, the ACS NSQIP/AGS published a comprehensive set of guidelines for the perioperative management of geriatric patients, also based upon the quality indicators developed by McGory et al. These guidelines addressed issues in the immediate preoperative period (e.g., preoperative fasting antibiotic prophylaxis, venous thromboembolism prevention), the intraoperative period (e.g., anesthesia, analgesia, perioperative nausea and vomiting), and the postoperative period (e.g., delirium, pulmonary complications, fall prevention, functional decline) [11]. The development of clinical practice guidelines was an important step toward improving the quality of care, but a multifaceted systems-based approach will likely be necessary to optimize the care of older adults undergoing surgery.

Quality of Care Definitions

The conceptual framework driving quality improvement is based on the Donabedian model of quality evaluation, where care can be categorized into three types: structure, process, and outcomes [12]. As shown in in Fig. 1, structural items

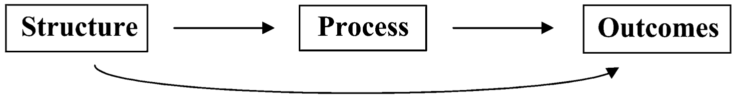

Fig. 1 Donabedian model of quality of care

are thought to influence both process and outcomes. Specifically, structural items include characteristics of the clinician (e.g., board certification), hospital (e.g., staffing patterns, procedure volume), and patients (e.g., insurance type, severity of comorbidities). Process refers to whether the medically appropriate decisions are made and whether care is provided in an effective and skillful manner. Process items are the activities that occur between the patient and practitioner (e.g., diagnosis, treatment, patient education). Outcomes data apply directly to patients and include mortality, morbidity, functional status, and quality of life. With respect to quality of care in geriatric surgery, examples of structural items include presence of a hospital ward designed for elderly patients or presence of a geriatric care coordinator. Examples of process items unique to geriatric surgery may include co-management of a geriatric surgery patient by a geriatrician or internist, and preoperative completion of a comprehensive geriatric assessment. Examples of outcomes unique to the geriatric surgery population may include postoperative delirium, change in functional status, and discharge to a skilled nursing facility.

We will now address five domains important in the perioperative care of older adult patients: cognitive impairment, functional status, frailty, medication management, and patient goals and preferences. There are current efforts to improve quality in each of these domains, and we will highlight examples of improvement in structure, process, and outcomes in each section.

Cognitive Impairment

Preoperative cognitive impairment has been shown to predict worse postoperative outcomes, and thus is an important domain to target in order to improve quality of care. Older adults with cognitive impairment have higher rates of postoperative pneumonia, renal insufficiency, urinary tract infections, venous thromboembolism, increased length of hospital stay, discharge institutionalization, and death when compared to matched counterparts without impaired cognition [13, 14]. Preoperative cognitive impairment also strongly predicts postoperative delirium [15], which in itself is associated with poor outcomes [16].

Early studies suggested that prevention of delirium is likely to have the most favorable impact on outcomes, so one focus of quality improvement in this domain is primary prevention [20]. Programs such as the Hospital Elder Life Program (HELP) and Nurses Improving Care for Healthsystem Elders (NICHE) have improved the quality of geriatric care in many ways, including a reduction in the incidence of delirium [17, 18]. HELP targets the processes of care and is specifically designed to reduce cognitive and functional decline during hospitalization by utilizing a skilled interdisciplinary team to implement targeted interventions [19]. The program screens patients for specific risk factors such as cognitive impairment, sleep deprivation, immobility, dehydration, and vision or hearing impairment and then implements targeted interventions (e.g., daily visitor/orientation, early mobilization, oral volume replacement, sleep enhancement) [19]. NICHE, on the other hand, targets both structure and process. Structural components of NICHE include the use of the Geriatric Resource Nurse model and the Acute Care for Elders (ACE) model, as well as an enhanced physical environment with flooring, furniture, fixtures, and beds adaptable to age-related changes. Process elements of NICHE include the use of a geriatric institutional assessment profile, staff development tools (e.g., use of a 5-part NICHE Introduction to Gerontology learning program), and the use of research-based clinical protocols (e.g., improving detection and management of delirium) [17].

The prevention and treatment of delirium in older adults differs from that in younger adults, and must be addressed as well. The AGS published clinical practice guidelines for postoperative delirium in older patients in 2015, emphasizing eight strong recommendations to assist providers in preventing and treating postoperative delirium (see Table 1) [20]. This is an example of process improvement – ensuring that medically appropriate decisions are made. Delirium in older adults is still incompletely understood and research further investigating risk factors and outcomes is ongoing. One current project underway is the Successful Aging After Elective Surgery Study (SAGES), which is a long-term prospective cohort study and an ongoing effort to examine novel biomarkers, neuroimaging markers, and long-term outcomes associated with delirium [21].

Table 1 Summary of strongly recommended AGS clinical practice guidelines for postoperative delirium in older adults

Recommendation
1) Healthcare systems should implement formal educational programs for healthcare professionals on delirium in older surgical adults
2) Healthcare systems should implement nonpharmacologic intervention programs for the entire hospitalization in at-risk older adults undergoing surgery
3) The healthcare professional should evaluate for and treat underlying contributors to delirium after an older adult has been diagnosed with postoperative delirium
4) Healthcare professionals should optimize postoperative pain control, preferably with nonopioid medications
5) Prescribing practitioners should avoid medications that induce delirium postoperatively (e.g., benzodiazepines, anticholinergics, diphenhydramine, meperidine)
6) Prescribing practitioners should not newly prescribe cholinesterase inhibitors perioperatively to prevent or treat delirium
7) Prescribing practitioners should not use benzodiazepines as a first-line treatment of postoperative delirious patients threatening substantial harm to self and/or others. Treatment with benzodiazepines should be at the lowest effective dose for the shortest possible duration and employed only if behavioral measures have failed or are not possible. Ongoing use should be evaluated daily
8) Prescribing practitioners should not prescribe any antipsychotic or benzodiazepine for the treatment of older adults with postoperative delirium who are not agitated or threatening substantial harm to self or others

Functional Status

Functional status is both a predictor of postoperative outcomes and an important patient-centered outcome itself. There are a variety of assessments used to classify functional status, including independence in activities of daily living (ADLs), walking speed, and the timed up and go test. Studies have used each of these measures and have clearly shown that impaired functional status is related to poor postoperative outcomes. One study showed that having a timed up and go test score >20 s is an independent risk factor for postoperative delirium [22]. A study of patients undergoing elective general and vascular surgery showed that patients who require any assistance from another person for activities of daily living have 75% greater odds of mortality and 51% greater odds of major morbidity postoperatively than matched functionally independent patients [23].

Berian et al. used data from the ACS NSQIP Geriatric Surgery Pilot Project to show that older patients are more likely than their younger counterparts to experience loss of independence (LOI) after surgery. LOI was defined as a decline in function, increased care needs, or discharge to a post-acute care facility. LOI occurred in more than half of elderly surgical patients, and the risk of LOI increased with age, to 84% in patients 75 years and older [24]. In addition to the direct negative effect LOI has on quality of life for the elderly, it was also shown to increase the risk of readmission by 70% and the risk of death after discharge by 6.7-fold [24].

Quality improvement in this domain initially started with addressing structure, which secondarily improved process. Several programs emerged in the 1990s that restructured the hospital environment in an attempt to improve the care delivered to elders and thus improve outcomes, most notably the ACE model [25]. The ACE unit was developed with the goal of lessening functional decline in elderly hospitalized patients. ACE units are equipped with elderly friendly elements such as carpeted floors, handrails, uncluttered hallways, and adequate space for visitors in dining rooms and patient rooms. They also employ the use of protocols to assess medications, review plans for medical care and procedures, and prepare early for discharge from the hospital [25]. Randomized controlled studies showed great efficacy of ACE units in preventing functional decline and long-term institutionalization, specifically by using a change in structure to affect change in processes and outcomes [26]. Unfortunately, ACE units are not currently the standard of care, likely because of high initiation cost, scarcity of geriatricians, and a perception that benefits are limited to a small population within each hospital.

Because ACE units have not been widely adopted, efforts have been made to disseminate ACE concepts to hospitals that do not have ACE units or geriatricians by teleconferencing and a software program called the ACE Tracker. The ACE tracker uses data from the electronic health record to generate a daily report of elderly specific information for all patients aged 65 and older in the hospital [27]. Examples of data included in this report include history of cognitive impairment, assessment for delirium, use of restraints, total number of prescribed medications, recent use of high-risk medications, fall risk, activities of daily living, and whether physical and occupational therapy assessment has been ordered. The goal is that this report serves as a guide to enable the multidisciplinary team to review multiple older patients in an efficient and effective manner. The HELP, NICHE, ACE, and the ACE Tracker models of care are all currently implemented and successful at select hospitals, but the next step in quality improvement will involve broad dissemination of these programs or at least their core concepts.

More recently, the idea of prehabilitation for elderly surgical patients has emerged as a potential intervention to improve postoperative outcomes. Prehabilitation programs aim to enhance the preoperative condition of a patient by improving functional capacity, and have been implemented in multiple surgical fields including orthopedic surgery, bariatric surgery, cardiac surgery, and colorectal surgery. There is wide variation in the composition of prehabilitation programs and the outcome measures used to evaluate their impact, and many studies are small in size and poor in quality, making it difficult to show that such programs can improve postoperative outcomes [28, 29]. However, some studies have shown good outcomes, including one randomized controlled trial in colorectal surgery in which postoperative functional capacity improved after implementation of a prehabilitation program consisting of aerobic exercise, nutritional counseling, and relaxation exercises [30].

Frailty

Frailty is defined as a “biologic syndrome of decreased reserve and resistance to stressors” and has recently emerged as a geriatric-specific preoperative variable strongly associated with adverse surgical outcomes including postoperative complications, increased length of stay, discharge to a post-acute care facility, readmission, and both short- and long-term mortality [31–33]. There is universal agreement on the broad concept of frailty, the general predisposition of frail individuals toward poor outcomes, and the potential of frailty as a powerful tool to help guide patient-centered perioperative care. However, there are more than 70 tools available to measure frailty and there is currently no consensus on which tools are best used in clinical practice [34]. Frailty assessment tools range from single item surrogate assessments such as gait speed or timed up-and-go score to the FRAIL scale (Fatigue, Resistance, Ambulation, Illness, and Loss of weight) to phenotypic frailty, to the deficit accumulation frailty index, and many others.

Quality improvement in this domain is related to improving process, as the assessment of frailty is performed by the provider and helps guide clinical management. The use of frailty assessments will aid in improving patient-centered outcomes in several ways. Most simply, physical frailty itself as a medical condition can be treated with modalities such as exercise, nutritional supplementation, and reduction of polypharmacy. As a more complex example, a high frailty score may prompt a goals-of-care discussion between the surgeon and patient that leads to a less aggressive surgical approach which ultimately leads to an outcome that is better-aligned with the patient’s wishes.

Medication Management

Medication use is common in older patients. More than 80% of elderly patients take one or more prescription medications, and the majority of patients aged 60 years or older take multiple medications and supplements [35]. The management of medications in older individuals in the perioperative period is multifaceted and includes stopping nonessential medications, continuing essential medications, planning for the resumption of medications postoperatively, minimizing polypharmacy, adjusting dosages for renal function, and avoiding potentially inappropriate medication use. A critical first step in this process is obtaining an up-to-date list of the patient's current medications, which may be difficult in the cognitively impaired older patient [10].

Quality improvement in this domain is focused on both structure and process. In order to ensure adequate preoperative review of medications and counseling regarding medication adjustments perioperatively, the healthcare system must be structured to provide a time and infrastructure for this. Although not primarily designed to minimize inappropriate medication use, geriatric models of care such as ACE units and HELP likely reduce inappropriate medication use during inpatient hospitalization given the intimate involvement of geriatricians and pharmacists in the care of these patients.

Process items have also been directly targeted to improve quality of care in the form of published criteria to ensure that practitioners do not prescribe inappropriate medications to elderly patients. In 1991, Dr. Mark Beers created the Beers Criteria for determining inappropriate medication use in nursing home residents [36]. These criteria have been updated a number of times and now take into consideration patients' comorbidities and renal function as well as potential drug-drug interactions that have been shown to harm older adults [37].

Despite these well-delineated guidelines, practitioners still frequently prescribe inappropriate medications to elderly patients. A national study of medication use in elderly surgical patients found that one in four patients received a potentially inappropriate medication (PIM) during their admission [38]. One common example is the use of Benadryl, despite moderate evidence to support avoiding the use of first-generation antihistamines in older adults. Some practitioners may be unaware that the use of Benadryl is not recommended in older adults and has been shown to increase the risk of cognitive decline. Additionally, Benadryl is frequently included within patient-controlled anesthetic order sets and thus may inadvertently be administered. Another example is the use of benzodiazepines in older adults with agitation. There is moderate evidence to avoid the use of benzodiazepines in older adults because it has been shown to increase the risk of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes in the elderly [37].

Avoiding the use of PIMs will likely involve both practitioner education and structural changes. There is evidence of a relationship between polypharmacy and potentially inappropriate prescribing which supports reconciling medications at both hospital admission and discharge. Hudhra et al. evaluated the relationship between polypharmacy and potentially inappropriate prescribing (as measured by the Beers criteria and other similar guidelines) based on medications prescribed at hospital discharge [39]. Potentially inappropriate prescribing was higher in patients taking more than 12 medicines and each additional medication increased the odds of potentially inappropriate prescribing by 14–15%. The authors concluded that patients taking more than six medications at discharge should undergo medication review. With regards to how best to perform this type of medication reconciliation, Poudel et al. reviewed the literature to develop an algorithm for medication review in frail older adults [40]. The algorithm consists of the following four steps: (1) identify a high-risk medication; (2) determine the current indications for the medication and assess their validity; (3) assess if the drug is providing ongoing symptomatic benefit; and (4) consider stopping, changing, or continuing the medication. Sonnichsen et al. seek to evaluate the impact of the "Polypharmacy in chronic diseases-Reduction of Inappropriate Medication and Adverse drug events in older populations" (PRIMA), an electronic decision support consisting of an indication check and recommendations for the reduction of polypharmacy and inappropriate prescribing based on systematic reviews and guidelines [41]. The authors are planning a cluster randomized controlled trial with the principal hypothesis that reducing polypharmacy and inappropriate medication use can improve the clinical composite outcome of hospitalization or death. This study will not only help determine if reducing polypharmacy improves clinical outcomes, but it will also assess whether or not providers are willing to follow the recommendations of the decision support tool. Despite robust guidelines for medication management in older adults, quality improvement in this domain will require changes in both structure and process to assist practitioners in complying with these guidelines.

Patient Goals and Preferences

Advance care planning is another topic especially pertinent to elderly patients undergoing surgery. Studies have shown that surgeons do not routinely discuss patient goals preoperatively and that elderly patients undergoing surgery rarely have an advance directive in the medical chart [42, 43]. It is especially important for surgeons to speak with patients about treatment preferences and expected outcomes given the high risk of functional decline and discharge to a nonhome location in elderly patients undergoing surgery. Studies have found that a variety of factors are related to failure in communication that leads to nonbeneficial emergency surgery in elderly patients, including time constraints, uncertainty about prognosis, patient and surrogate fear of inaction, inadequate provider communication, and inadequate advance care planning [44]. While surgeons are trained extensively in surgical treatments for disease, they are not necessarily well-trained in communicating with patients about nonsurgical alternatives.

Quality improvement in this domain requires structural changes that will improve processes and communication between surgeon and patient. First, it is essential to ensure that surgeons are trained in basic palliative care and communication about patient goals and preferences. Opportunities for education exist – there are courses in palliative care available through the ACS and other organizations, and over 100 Accreditation Council for Graduate Medical Education-accredited Hospice and Palliative Medicine fellowship programs exist. However, there are fewer than 100 surgeons with this subspecialty board certification [45]. More importantly, there is no training requirement during residency, so it is no surprise that many practicing surgeons have had no training in this area. Strategies such as case-based palliative care workshops and didactic sessions have been found to improve surgical residents' attitudes and knowledge and may be one element of a solution [46, 47]. Additionally, providing a concrete framework for communication with patients about goal-concordant care has been explored in the emergency surgery field. Cooper et al. has proposed a structured approach to communication that includes nine elements: (1) formulating prognosis, (2) creating a personal connection, (3) disclosing information regarding the acute problem in the context of the underlying illness, (4) establishing a shared understanding of the patient's condition, (5) allowing silence and dealing with emotion, (6) describing surgical and palliative treatment options, (7) eliciting patient's goals and priorities, (8) making a treatment recommendation, and (9) affirming ongoing support for the patient and family [48]. Kruser et al. designed the Best Case/Worst Case framework which uses both narrative description and a graphic aid to help promote shared decision making in high-stakes acute surgical scenarios [49]. With this framework, the surgeon must (1) break bad news; (2) identify two clear treatment options; (3) create a graphic aid that illustrates the range of outcomes; (4) use storytelling to describe the best, worst, and most likely outcomes; (5) elicit preferences; and (6) make a recommendation. Using this framework has been successful in shifting conversations from having a surgical focus to including a broader discussion about treatment alternatives and outcomes. While these frameworks are designed for critically ill patients in the acute setting, variations on these frameworks may also be beneficial for surgeons communicating with elderly patients about elective surgery.

Secondly, we must ensure that there is structural support for the discussion and documentation of advance care planning prior to surgery. The ACS NSQIP/AGS Best Practice Guidelines have emphasized the importance of documentation of advance directives and health care proxy information in the patient's medical chart [10, 11]. An ideal time to address or revisit patient goals and preferences is during the preoperative clinic visit. This is a time during which the surgeon and patient can discuss the operation, alternatives, and predicted outcomes including the possibility of discharge to a nonhome location.

The Coalition for Quality in Geriatric Surgery (CQGS)

As discussed in each of the sections above, the health care community has begun to develop tools and strategies to improve the quality of care of geriatric surgical patients in many ways. However, a collaborative effort is necessary to affect meaningful change. The CQGS Project is a quality improvement program supported by the ACS and the John A. Hartford Foundation that seeks to define the processes, resources, and infrastructures necessary to provide optimal care to the older surgical patient. The CQGS is comprised of a team of surgeons, nurses, geriatricians, ACS staff, and research scholars and is supported by over 50 diverse organizations representing surgical specialties, anesthesiology, geriatrics, nursing, pharmacy, social work, physical therapy, advocacy, and patients. The goals of this 4-year initiative are to set standards, engage key stakeholders, develop measures that matter, develop the verification process to ensure delivery of high-quality care, educate patients and providers, pilot the program, and launch the Geriatric Surgery Quality Campaign. Work from this project will be relevant and generalizable to all health care centers that provide surgical care to older adults.

The Project began on July 1, 2015, and since then, over 300 preliminary standards have been drafted and rated for validity and feasibility. The CQGS Stakeholders rated 99% of standards as valid and 94% as feasible for improving the quality of care provided to elderly surgical patients [50]. The next steps will be to develop a data registry to track and measure geriatric-specific elements, and to better understand and address challenges to implementation of the standards. The CQGS Project builds on the work done by individual researchers and organizations in years past to provide a contemporary, comprehensive set of standards, processes of care, data collection system, and measurement of outcomes to systematically optimize the surgical care for older adults.

Conclusion

Just as pediatric surgery became a specialty unto itself, the expanding and aging population has created a potential niche for the specialty of geriatric surgery at the opposite end of the age spectrum. The field of geriatric surgery may indicate a focus on elderly patients for the surgeon, but more importantly the specialty of geriatric surgery represents a multidisciplinary collaboration between surgeons, geriatricians, internists and many other health-care providers who together will address the complex issues unique to the growing elderly surgical patient population. Progress has been made over the past few decades, with the establishment of guidelines and quality indicators, as well as a focus on collecting data and measuring outcomes specifically relevant to geriatric surgical patients. The CQGS Project represents a significant milestone in defining quality of care in geriatric surgery, as it will for the first time provide a unified set of standards that all hospitals caring for elderly surgical patients should uphold. Despite this progress, there continue to be significant hurdles to overcome in order to optimize care for this vulnerable patient group. Even once standards are set and important geriatric patient-specific outcomes are established, the implementation of necessary interventions and structural elements will pose a new challenge. Nonetheless, quality improvement in the relatively young field of geriatric surgery is progressing at a rapid rate and beginning to gain the national attention needed to eventually optimize care for this unique patient population.

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3 Biology of Aging

Daniel Parker and Mitchell Heflin

Contents

Abstract

Principles distilled from geroscience, the scientific study of aging, can facilitate surgical decision making by identifying appropriate surgical candidates, anticipating surgical complications, and predicting functional outcomes. Theories of aging can be divided into program theories that emphasize genetically driven limits on lifespan and stochastic theories that focus on the accumulation of "wear and tear" with age. These changes lead to distinct patterns of dysfunction in intracellular processes and intercellular communication that culminate in organ system-specific alterations, which are reviewed here. The inter-related concepts of frailty and resilience synthesize these diverse changes into a unified conceptual framework that can be used to support surgical decision making. Frailty, which is defined as increased vulnerability to stress, is a risk factor for surgical complications and poor outcomes. Conversely, resilience is the ability to resist functional decline following health stressors. The assessment of frailty and resilience can be integrated into pre-surgical evaluation to gauge risk, support shared decision-making, and improve patient outcomes.

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Geroscience and the Surgical Patient

Over a third of surgeries occur in people over 65. Providing high quality care for this population in the perioperative period requires a deeper understanding of expected age-related changes at the cellular, physiologic, and phenotypic levels. These changes have important implications at the individual level for effective completion of the surgery itself and a safe and efficient postoperative recovery. Moreover, the population of older adults is remarkably heterogeneous with respect to health and ability and, as a result, decisions regarding candidacy for any given surgery may differ dramatically between people of the same age.

Aging is the decline in physiologic function that increases an organism's susceptibility to disease and ultimately leads to death. Aging is the predominant risk factor for neurodegenerative disease, diabetes, cardiovascular disease, and most cancers [1]. Advances in aging research, hereafter referred to as *geroscience*, have elucidated some of the molecular and cellular changes associated with aging. These changes span core systems regulating genomic stability, protein homeostasis, energy dynamics, and stem cell function (Fig. 1). They eventually culminate in impaired tissue and organ function through loss of functional parenchyma and the acquisition of a maladaptive cellular phenotype, a state referred to as *senescence*. Eventually, the series of changes, like falling dominos, results in impaired resilience to stress, increased susceptibility to disease and, in many cases, the clinical syndrome of *frailty*.

Many of the advances in geroscience have emerged through exploration of interventions that extend lifespan or decrease the incidence of aging-associated diseases, i.e., enhance health span. While multiple interventions using model organisms have achieved success in these twin aims, only caloric restriction and exercise have demonstrated efficacy in humans. Understanding how these age-related changes in fundamental biological processes translate into decreased resilience and frailty and the available interventions to modify them can inform clinical decision making. In this chapter, we relate these concepts to the care of the older surgical patient, exploring how biological aging leads to decline in resilience and the development of frailty. Finally, we describe the differential impact of aging on organ systems. These changes are summarized in Table 1.

Theories of aging fall into two camps, program theories, and damage-accumulation theories.

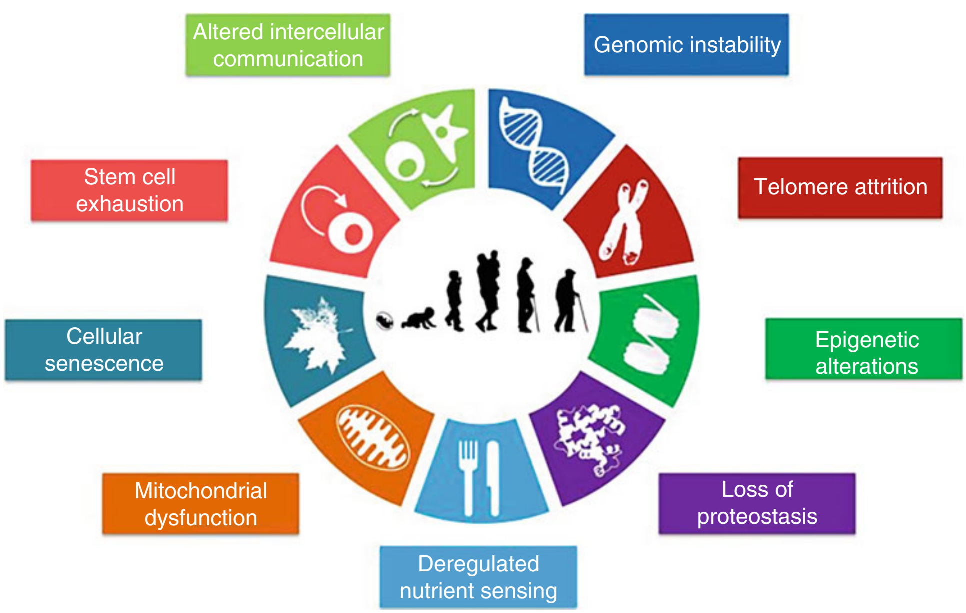

Fig. 1 Hallmarks of aging (Cell. 2013 Jun 6; 153(6):1194–1217. doi:10.1016/j.cell.2013.05.039)

Table 1 Summary of age-related changes by organ system

Organ system	Age-related changes	Clinical implications
Immune system	↑ Basal inflammation (inflamm-aging) ↓ Adaptive immune response	↑ Susceptibility to infections and sepsis ↓ Responsiveness to vaccination ↓ Wound healing
Hematologic	Hemostatic balance → thrombosis ↓ Platelet responsiveness to NO	↑ Risk of thrombotic complications
CNS	↓ Brain volume ↑ In neurodegenerative pathology	↑ Susceptibility to delirium
Cardiovascular	↑ Arterial stiffness leading ↑ Left ventricular hypertrophy ↑ Peripheral vascular resistance ↑ Myocardial fibrosis	↓ Organ perfusion ↓ Compensatory response to acute fluid shifts ↑ Risk of atrial arrhythmias
Gastrointestinal	↑ Oropharyngeal muscle loss ↑ Gastric contact time with noxious agents ↓ Hepatic drug clearance ↓ Gastric transit	↑ Dysphagia, aspiration, and malnutrition ↑ Susceptibility to adverse effects of medications ↑ Constipation
Endocrine	↑ Use of exogenous glucocorticoids ↓ Renin-angiotensin-aldosterone activation	↓ Compensatory response to hypovolemia ↓ Insulin sensitivity
Renal	↓ Renal blood flow and GFR	↓ Renal drug clearance ↑ Sensitivity to renal hypoperfusion

Program theories emphasize evolutionarily conserved genetic limits on lifespan. Damage or stochastic theories emphasize the effects of accumulated damage and environmental stressors.

Research in comparative biology supports evolutionarily conserved limits on lifespan. Maximum lifespans vary greatly by species, but show little variation among members of the species. The jellyfish *Turritopsis dohrnii* has evolved replicative immortality by reverting to a less mature developmental stage [2], but other phylogenetically related jellyfish have much shorter lifespans.

Telomeres are sequences of repetitive nucleotide sequences capping chromosomes that progressively shorten with each mitosis eventually triggering replicative senescence. Studies of their relationship to age-related disease provide additional support for programmed aging. Telomere-determined limitations on the number of cellular divisions, termed the Hayflick limit, may serve as a check on cancer. Indeed, most cancers demonstrate constitutive activation of telomerase, the enzyme responsible for maintenance of telomere length [3]. Conversely, telomere dysfunction that leads to premature telomere shortening causes premature aging syndromes like dyskeratosis congenita [4]. However, these observations, drawn from disease states, fail to establish a causal link between telomeres and normal aging.

Genome-wide association studies (GWAS) in humans have revealed allelic variants that enhance longevity through reduction in mortality due to diabetes, cancer, and coronary artery disease. Studies of the genetics of longevity suggest a contribution to lifespan variance of 20–30% [5]. This is despite long-lived families carrying a similar number of disease causing allelic variants [6], suggesting that enhanced longevity comes from genetic variants that delay aging or protect from disease. However, GWAS studies in different populations have identified conflicting candidate genes, suggesting that the contribution of any single nucleotide polymorphism (SNP) to longevity is small with difficult to predict effects in diverse groups [7, 8].

Unlike genetic contributions to aging, stochastic drivers of aging are better understood and potentially more amenable to intervention. Stochastic theories encompass many avenues of inquiry including metabolism, macromolecular damage, epigenetics, inflammation, adaptation to stress, proteostasis, and stem cells and regeneration. The most studied of these interventions is caloric restriction, which prolongs lifespan in organisms from yeast to mammals through activation of a conserved starvation response pathway.

Caloric restriction, which is defined as limiting energy intake while preserving essential nutrients, increases longevity and delays the onset of age-related diseases in many animal models including rhesus monkeys. The effects of caloric restriction on humans are unknown and difficult to study given the length of human lifespans, but a 2-year study of caloric restriction in young- and middle-aged healthy adults demonstrated significant reductions in cardiometabolic risk factors including LDL, systolic and diastolic blood pressure, and glucose control [9].

In model organisms, caloric restriction activates multiple, inter-related programs that vary based on the content of the diet. Accumulating evidence supports an integrative effect of caloric restriction on pathways that enhance mitochondrial function, decrease production of reactive oxygen species (ROS) and pro-inflammatory cytokines, and improve insulin sensitivity. These changes in cellular bioenergetics lead to decreased white adipose tissue mass and reduced systemic inflammation.

In aged animals, caloric restriction prevents downregulation of nuclear-encoded genes of the mitochondrial electron transport system (ETS), thereby preserving the integrity of mitochondrial energy metabolism. Caloric restriction also stimulates autophagy, an evolutionarily conserved mechanism for degrading and recycling intracellular proteins and organelles that is essential to mitochondrial health. Muscle biopsies from calorically restricted humans show increased expression of autophagy-associated genes and protein levels [10]. Normal aging is associated with decreases in autophagy, and autophagy of mitochondria, referred to as mitophagy, is required for production of new mitochondria. In humans, autophagy is essential to the adaptations of skeletal muscle in response to endurance exercise [11].

How do age-related changes at the cellular level impact function of the organism? Normal aging is characterized by both a loss of functional parenchyma, which is driven by stem cell exhaustion, and the accumulation of cells within tissues expressing a maladaptive phenotype known as senescence. Apoptosis of aged or damaged cells coupled with stem cell exhaustion leads to an imbalance between cellular loss and replenishment that reduces the functional capacity of organ systems. This manifests as decreased glomerular filtration rate (GFR) and maximum heart rate seen in normal aging. In addition to the loss of functional tissue, senescent cells can impair the function of remaining healthy cells and secrete pro-inflammatory factors that contribute to the development of age-related disease.

Cellular senescence was first described as a tumor suppression mechanism and is universal to all eukaryotic cells. Unlike apoptosis, or programmed cell death, which leads to rapid cell clearance, senescent cells acquire a unique phenotype with an associated secretome, referred to as the senescence associated secretory phenotype (SASP) that negatively impacts the surrounding microenvironment. Senescent cells accumulate in tissues with age and eventually, through the actions of the SASP, negatively impact the function of the whole organism [12, 13].

Multiple factors including telomere shortening, ROS-associated damage, and irreparable DNA damage trigger the acquisition of the senescent phenotype. The SASP is composed of multiple pro-inflammatory factors including IL-1 and IL-6, growth factors, and proteases that modify the tissue microenvironment [12]. Transfusion of blood from aged to young mice resulted in poorer performance on tests of strength, endurance, and learning; decreased hippocampal neurogenesis; and decreased hepatogenesis. These effects are likely related, at least in part, to factors produced by the SASP [14].

Progress in geroscience has demonstrated that the mechanisms underlying aging are multiple, complex, and interrelated. This complexity explains, in part, the dramatic variation in the observable biologic features of aging in patients of the same chronological age. Geroscience allows us to translate this observation into clinically relevant tools for use in surgical practice, particularly in the determination of surgical risk versus clinical benefit and overall fitness for surgery.

These clinical tools are built on the inter-related concepts of frailty and resilience. Frailty is defined as a physiologic vulnerability to stressors and is an important prognostic indicator for functional decline and death (Fig. 2) [15]. Conversely,

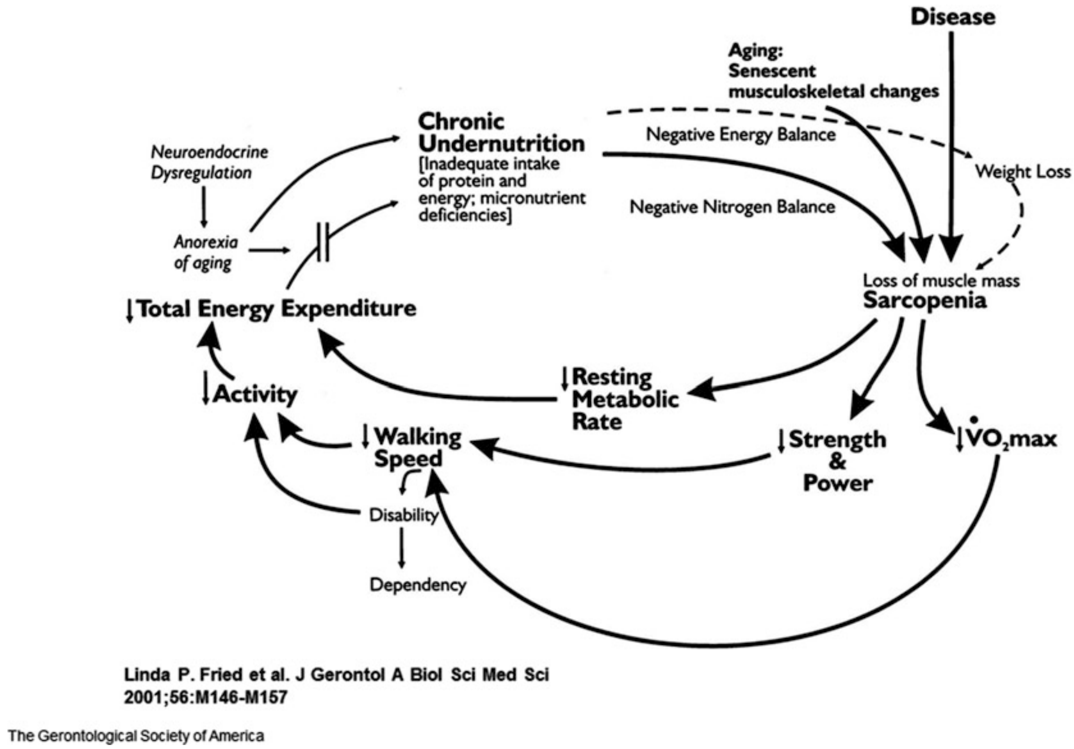

Fig. 2 Cycle of frailty hypothesized as consistent with demonstrated pairwise associations and clinical signs and symptoms of frailty [15]

physical resilience is the ability to resist or recover from functional decline following health stressors [16]. Multiple environmental and host factors contribute to physical resilience, but age-associated physiologic changes eventually erode an individual's capacity to recover from stress. When an individual's physical resilience has declined beyond a certain threshold, they may present with weight loss, weakness, exhaustion, slowness, and low activity, which define the phenotypic characteristics of frailty [15]. The incidence of frailty, defined by the presence of three of the five phenotypic characteristics, increases from 5 to 10% of adults over 65 to 30% of those over 80 [15, 17]. Chronologic age offers only a rough approximation of the equipoise between frailty and resilience.

Frailty has already demonstrated utility as a predictor of surgical outcomes. A systematic review of cohort studies evaluating the association of frailty with outcomes after cardiac surgery found that frailty predicted mortality 6 months after major and minimally invasive cardiac surgery [18]. This review also suggested frailty assessment was predictive of functional decline, lack of symptomatic benefit, and decreased quality of life after minimally invasive procedures. These findings emerged despite the heterogeneity of the frailty assessment tools used, some of which only measured a single frailty domain. Another study in 351 patients undergoing major abdominal surgery found that frailty was associated with 30-day morbidity and mortality [19].

Frailty is defined as both a characteristic, i.e., decreased reserve in response to stressors, and a measurable phenotype, i.e., three of the five objective findings described above. While the phenotypic definition is helpful in identifying those most likely to experience poor outcomes, frailty is only definitively assessed after exposure to a significant health stressor. This gap between phenotypic frailty and increased susceptibility to poor outcomes drove the development of physical resilience as a complementary parameter.

Research is currently underway to develop biomarkers and noninvasive "stress tests" to measure physical resilience in patients who are not phenotypically frail, but may be at higher risk of adverse outcomes following stressors such as surgery [16].

Immunosenescence and Inflammaging

Dysregulation of the immune response, particularly the development of chronic inflammation, is one of the hallmarks of aging. The immune system can be divided into an innate or nonspecific response, driven by macrophages, neutrophils, monocytes, and dendritic cells and an adaptive response, governed by B and T lymphocytes. Immunosenescence, or aging of the immune system, is associated with a decline in the adaptive immune response and an increase in basal activation of the innate immune system, characterized by a chronic pro-inflammatory state, referred to as "inflammaging."

Immunosenescence of the adaptive immune system is characterized by decline in the population of naïve T-lymphocytes and decreased antibody production. The decline in naïve T-lymphocytes is due to lifelong thymic involution coupled with shifts in T-lymphocyte subsets to an effector phenotype directed against chronic subacute infections, most commonly cytomegalovirus (CMV) and Epstein-Barr virus (EBV) [20]. As T-cells are activated and expand, but are unable to clear their target, some resist apoptosis and become senescent. These senescent immune cells inhibit clonal expansion of naïve cells and contribute to the pro-inflammatory state. This increases vulnerability to new bacterial and viral infections as well as cancerous cells. In centenarians, the pool of naïve lymphocytes, while still functionally capable of activation and proliferation [21], is almost completely lost [22].

As the adaptive immune system wanes, the innate immune system exhibits chronic low-level activation that leads to a pro-inflammatory milieu with systemic consequences [23]. Inflammation is defined as a tissue-remodeling state that occurs in response to traumatic stimuli, but inflammation is also an essential response to exercise, trauma, and maintenance of normal physiologic function.

The systemic inflammatory response seen in response to surgery is characterized by the same elevation in pro-inflammatory cytokines seen in inflammaging. IL-6 and C-reactive protein (CRP) increase in an age-dependent manner even in the absence of age-related diseases and IL-6 levels are 10-fold greater in centenarians compared to young adults [24, 25]. In surgical patients, IL-6 production peaks 18–24 h after surgery and is correlated with the invasiveness of the surgical procedure [26]. The key difference between pathologic and physiologic inflammation is the duration of the response, with concurrently activated anti-inflammatory mechanisms tempering the pro-inflammatory response under normal conditions. The dysregulated inflammation associated with aging is well established as a risk factor for development and accelerated progression of age-related diseases including cardiovascular disease, diabetes, and cancer.

Immunosenescence, through waning of the adaptive immune response and the development of chronic inflammation, accounts for the decreased responsiveness to vaccination, delayed wound healing, and the increased incidence of sepsis in older adults. As one might expect, inflammaging may contribute to the development of frailty. A meta-analysis comparing frail and prefrail individuals with robust individuals found that C-reactive protein, IL-8, and IL-6 were significantly elevated in frail and prefrail states [27]. This relationship was moderated by age and BMI, an expected finding given that both age and obesity are associated with elevated inflammatory markers. Higher inflammatory markers were also associated with decreased muscle strength, osteoporosis, mortality, hospitalization, and development of co-morbid diseases in older adults [28–30]. Experiments in mice disrupting pro-inflammatory signal transduction led to preserved skeletal muscle strength and mass suggesting a direct link between chronic inflammation and impaired muscle function, one of the core components of frailty [31]. Interestingly, exercise may attenuate immunosenescence and aging more generally by generating an acute pro-inflammatory response that increases the susceptibility of senescent cells to apoptosis [32]. As described below, immunosenescence is also implicated in the higher rates of postoperative complications seen in older adults.

Hemostasis

Age-related changes in hemostasis are likely driven by inflammaging, the chronic low-level inflammatory state associated with normal aging. Inflammation is tightly coupled with hemostasis through the complement and coagulation cascades. As IL-6 and other pro-inflammatory markers increase with age, so do coagulation factors. This general increase in the quantity of circulating coagulation factors interacting with an aging endothelium explains the age-related increase in the rates of arterial and venous thrombosis. This is reflected clinically in the recent adoption of age-adjusted cutoffs for d-dimer, a product of fibrin degradation, for the diagnosis of venous thromboembolism [33]. Levels of von Willebrand Factor (vWF), the multimeric glycoprotein that binds platelets to damaged endothelium, increase with age so much so that patients with mild von Willebrand disease who are generally prone to bleeding, may achieve normal hemostasis with age. Platelet function changes with age, with decreased production and responsiveness to nitric oxide, a potent vasodilator and inhibitor of platelet activation [34].

In addition to an increase in pro-thrombotic factors, advanced age is associated with downregulation of the fibrinolytic system. This is due, in part, to increased levels of plasminogen activator inhibitor-1 (PAI-1), an important regulator of fibrinolysis. Interestingly, increased PAI-1 is not just associated with an increased incidence of thrombotic diseases, but also obesity, type 2 diabetes, and inflammation [35]. This occurs through shared promoter response elements that link expression of PAI-1 to expression of other pro-inflammatory cytokines, providing another intersection between inflammation and pro-thrombotic states [36]. Data also suggest that PAI-1 is a component of the SASP and capable of inducing the senescent phenotype [37].

Delirium

Neurologic complications are the leading cause of morbidity in geriatric surgical patients [38]. Of these, delirium is the most common, affecting between 10 and 20% of geriatric surgical patients [39]. Delirium is defined by the DSM-V as an acute impairment in attention and cognition. Delirium has been shown to double the average length of stay and add an average of $2,500 to the cost of hospitalization [40]. The development of delirium also has significant deleterious effects on long-term morbidity and mortality. In patients with preexisting dementia, the development of delirium may accelerate cognitive decline [41, 42]. Advanced age and preexisting cognitive impairment are the two biggest risk factors for delirium with metabolic derangements, uncontrolled pain, sleep-wake cycle disruption, and adverse medication effects also contributing. In elderly ICU patients, for every year over age 65, the risk of developing delirium increases by 2% [43].

The pathophysiology of delirium is poorly understood but, like its precipitants, is probably multifactorial. Delirium may be due to neurotransmitter dysregulation, excess inflammation, and sleep-wake cycle disruptions. Delirious patients demonstrate cerebral hypoperfusion in frontal, temporal, and parietal regions on PET imaging [44]. Alterations in neurotransmitters in delirium are well documented, including increases in dopamine and serotonin and decreases in levels of acetylcholine. The latter likely explains the tendency of anticholinergic medications to precipitate delirium in susceptible patients.

Alterations in neurotransmitters leading to delirium may be precipitated by the acute inflammatory state in postoperative patients. As aging is associated with increased permeability of brain blood barrier (BBB), rendering the CNS more susceptible to the negative effects of systemic inflammation. Many of the direct and indirect physiologic consequences of surgery such as blood loss, use of anesthetic agents, tissue trauma, hypoxia, and ischemia are independently associated with delirium, independent of the additional stress of surgery.

Hospitalized delirious patients demonstrate higher levels of CRP, IL-6, TNF-α among other pro-inflammatory cytokines [45]. Inflammation leads to changes in CNS microvasculature that predispose to ischemic injury and dysregulated neurotransmitter production. When microglia, the resident macrophages of the CNS, are exposed to the pathologic protein aggregates associated with dementia, they demonstrate greater activation in response to systemic inflammatory signals. Thus, the increased risk of delirium in patients with dementia may be due to a lower threshold for microglial activation in response to systemic pro-inflammatory signals. This heightened inflammatory response, in conjunction with reduced cognitive reserve, may overwhelm the homeostatic mechanisms maintaining normal cognition.

Delirium, through the process described above, may also potentiate the inflammatory response to the neurodegenerative pathology, thereby contributing to accelerated progression of cognitive impairment after an episode of delirium. In a prospective matched controlled cohort study of older adults undergoing hip surgery, postoperative delirium doubled the risk of subsequent MCI or dementia [46].

Cardiovascular

Cardiovascular disease dramatically increases with age and is a major cause of morbidity and mortality in the elderly [47]. Eighty-two percent of all cardiovascular deaths in the United States occur in patients over 65 years old [48]. A high prevalence of hypertension and diabetes mellitus among older adults leads to high rates of coronary artery disease and stroke, which can, in turn, complicate recovery from major surgery. This sequence of events results, in part, from cellular and structural changes in heart and peripheral vasculature, leading to impairment of the body's normal hemodynamic compensatory mechanisms.

Over time, large arteries stiffen and thicken resulting in a critical loss of normal elasticity and a functional decrease in luminal diameter. This phenomenon is a result of accumulated fragmentation in elastin fibers, increased crosslinking of collagen in the subendothelium, and progressive calcification. Arterial wall rigidity leads to an increase in arterial systolic pressure and greater impedance to left ventricular outflow, which over time can stimulate ventricular hypertrophy. Systolic blood pressure increases steadily with age and, along with a leveling or decrease in diastolic blood pressure, results in a widening of the pulse pressure.

Similar to large arteries, the walls of the small arteries thicken and the luminal diameter decreases, causing increased impedance in the periphery and transmission of elevated pressures to end organs. Additionally, in small arteries, advancing age is associated with a decrease in the basal level of nitric oxide as well as a muted response to this intrinsically potent vasodilator [49]. An increase in impedance along with a decrease in vascular conductance leads to greater peripheral vascular resistance. At the capillary level, age-related increased peripheral vascular resistance has been associated with decreased perfusion during times of stress like ischemia, infection or surgery. At the venous level, the age-related decline in response to nitric oxide is thought to be responsible for the inability of older adults to respond to hypovolemic circulatory stress [50].

Like the vasculature, the heart undergoes structural changes with age. Myocytes hypertrophy but decrease in number. In addition, the heart becomes more fibrotic as collagen filaments, fibronectin, and integrins increase. Sympathetic as well as parasympathetic neurons decrease in number with age and valves calcify and stiffen. At rest, these structural changes may be inconsequential. However, under conditions which increase the work demanded of the heart, there can be significant compromise. Worsening fibrosis and hypertrophy impair the heart's ability to comply and contract. Loss of innervation leads to decreased neuromuscular control. Consequently, the heart is unable to meet increased demands needed during times of stress or even routine exercise.

Given the changes described above, fluid shifts associated with surgery present particular difficulty for the older patient. Increases in antidiuretic hormone secretion and renin-angiotensin-aldosterone system activation with stress result in retention of sodium and water with a tendency toward volume overload. Increased fluid retention (often compounded by administration of intravenous fluids and blood products) combined with ventricular hypertrophy and increased vascular resistance can predispose the older patient to increases in systolic blood pressure and a greater tendency for heart failure [51].

In addition to problems with pressure and volume, older adults appear to be uniquely susceptible to atrial arrhythmias in the postoperative period [52]. Estimates of the incidence of postoperative atrial fibrillation range from 15% in noncardiac surgery to over 30% in cardiothoracic procedures. The aging atrium, like the rest of the heart, often enlarges and undergoes fibrotic changes which can result in slowed conduction and a propensity to atrial arrhythmias. In the postoperative period, inflammatory changes and increases in adrenergic stimulation related to pain, fever, and hypovolemia are common triggers. The onset of atrial fibrillation with rapid ventricular response in the acute postoperative period can exacerbate the already tenuous balance of ventricular hypertrophy and decreased end diastolic volume by reducing filling time. This can be an important trigger for heart failure [53].

Gastrointestinal

Aging-related changes in the gastrointestinal tract can have critical implications for preparation for and recovery from surgery. A broad range of biologic factors can have direct bearing on nutrition, hydration, and recovery of bowel function in the postoperative period. This section provides a brief end-to-end overview of these changes. In the mouth, teeth discolor and become more likely to fracture as dental pulp recedes from the crown and the root canal narrows. Muscles of the tongue, like other skeletal muscles, decline in mass. Fat and fibrous tissue replace up to 25% of the secretory parenchyma of the salivary glands [54]. Compensatory mechanisms minimize the impact of these changes such that swallowing and phonation are not clinically diminished in the healthy elderly patient. However, if patients have a comorbid neurologic or muscular illness like Parkinson disease, stroke, diabetic neuropathy, myasthenia gravis, amyotrophic lateral sclerosis or polymyositis, the age-associated oropharyngeal changes predispose to dysphagia, aspiration, and malnutrition. Age-related declines in appetite and thirst can further impede intake as can the tendency for dry mouth, often exacerbated by anticholinergic medications.

Findings associated with "presbyesophagus" include decreased amplitude of peristaltic contractions, incomplete sphincter relaxation, delayed esophageal emptying, frequent tertiary contractions, and esophageal dilatation. These changes seem to be strongly associated with comorbid illness, including neurologic conditions and diabetes mellitus. More likely, esophageal dysmotility is a result of underlying chronic diseases like diabetes mellitus or side effects of medications rather than just normal aging.

Aging-related changes in the stomach include impairments in emptying and acid production. In the stomach, decline in motility and emptying is caused by age-related autonomic nervous system dysfunction and decreased compliance in the gastric wall [54]. In addition, the elderly often take anticholinergic or opioid medications, which further contribute to delayed emptying. This prolongs the "gastric contact time" of noxious agents, like nonsteroidal anti-inflammatory drugs (NSAIDs). Age-related gastric luminal changes include decreased prostaglandin and bicarbonate secretion, slowed mucosal cell proliferation, and impaired gastric blood flow. These changes collectively decrease the gastric mucosal defense against injury. On the other hand, there seems to be a higher incidence of achlorhydria in the elderly, which can impede effective digestion and absorption of nutrients. All these changes can also contribute to slowed emptying which can worsen the anorexia of aging and be particularly difficult to manage in the postoperative period with concurrent administration of medications like anticholinergics and opioids.

The liver, gallbladder, and pancreas all have an age-related decline in organ size, blood flow, and cell proliferation. Between age 70 and 90, the liver decreases from 2.5% of body weight to 1.6% as the overall number of hepatocytes decrease [55]. Cytochrome p450 activity decreases with age, contributing to a slower metabolism of certain drugs. Thus, caution must be used while prescribing hepatically cleared medications in the elderly.

Little evidence exists of major changes in small bowel structure or function with aging. The colon, on the other hand, undergoes changes that have implications for function and quality of life. Colonic transit time increases with age as a result of decreased peristaltic activity. This is likely a result of a decline in number and function of enteric neurons in the colon with a resultant decrease in critical neurotransmitters, particularly acetylcholine and nitric oxide. These changes can have important implications in the postoperative period, with increased rates of constipation. This may be a particular concern in those who remain immobile and dehydrated and on medications that further slow transit time. Eventually, this can also have adverse effects on resumption of oral intake and enteric nutrition [56].

Metabolic and Endocrine

The aging endocrine system presents an intriguing model for the overall changes in homeostatic regulation described earlier [57]. In a normal, unstressed state in the disease-free individual, little change is evident, particularly in the levels and activity of most hormones. However, with illness or surgery, abnormalities become obvious and important. Another key concept is that clinical presentations of endocrine disorders may be atypical, blunted, or even undetectable when compared with those of younger persons. Several examples of these principles are detailed below.

Hypothalamic-pituitary-adrenal axis function appears to be well preserved with normal aging. Prolonged elevation of glucocorticoid secretion with stress may have adverse effects, ultimately, on immune function and glucose metabolism. While primary Cushing syndrome is relatively rare in older adults, chronic administration of exogenous glucocorticoids is common. The ravages that steroids cause to the entire body are particularly severe and debilitating in older adults, including osteoporosis, glucose intolerance, neuropsychiatric symptoms, cataracts, glaucoma, and myopathy. Likewise, the most common cause of adrenal insufficiency in older adults is the suppression of normal adrenal function due to chronic glucocorticoid administration. The presentation of this syndrome can be nonspecific, including generalized weakness, weight loss, dizziness, falls, or overall failure to thrive. In the perioperative setting, systematic reviews of randomized controlled trials demonstrate no advantage to using supplemental (or "stress dose") corticosteroids in the perioperative period for those taking maintenance dose steroids for a medical condition. On the other hand, if a person is taking replacement doses for disorders of the hypothalamic pituitary axis, then supplemental dosing should be given [58].

In terms of the sympathetic nervous system and adrenal medulla, levels of norepinephrine and epinephrine increase with age, primarily due to a rise in secretion. However, the resultant physiologic response is muted due to decreased receptor and postreceptor activation despite increased circulating hormone levels. The clinical implication may be a less pronounced response to stimuli such as hypoglycemia, hypoxia, or systemic infection. The renin-angiotensin-aldosterone system also changes significantly with age. Decreased baseline levels of renin contribute to lower levels of aldosterone, which in turn leads to an increased propensity for salt-wasting among older adults. This phenomenon has important implications. Along with impaired thirst and antidiuretic hormone (ADH) response, older adults may become volume depleted more rapidly and have a greater propensity to develop hyperkalemia. This risk of dehydration and electrolyte imbalance, coupled with the tendency toward volume overload due to the changes in the cardiovascular system described above, illustrates a common "narrow therapeutic margin" in the clinical management of the older adult in the postoperative period. Effective clinical management requires careful continuous assessment and vigilance by all team members.

Decline in growth hormone (GH) is also observed with aging, such that about half of those over age 75 have negligible GH secretion. This may contribute to changes in body composition, including decreased muscle mass and strength, further increasing the risk of falls and fractures. Lower levels of testosterone among older men may contribute to changes in cognition, libido and sexual function, and loss of bone and muscle mass.

With respect to thyroid function, circulating triiodothyronine (T3) and thyroxine (T4) levels remain essentially normal with aging, but with acute illness, the levels of both are lower and, in particular, the conversion of T4 to T3 is impaired and results in a marked decline in the latter – this condition is often referred to as sick euthyroid. Thyroid disorders are common among older adults, but often difficult to diagnose. The presentation can be nonspecific with weight loss, apathy, and weakness as possible clinical manifestations of both hypo- and hyperthyroidism [59].

Alterations in glucose metabolism among older adults are primarily manifested with stress. In normal older adults versus younger controls, glucose tolerance testing reveals a higher elevation in serum glucose levels. Obesity, decreased activity, comorbid illness, and medication may all contribute to the impaired response to endogenous insulin observed with aging. Of course, a critically important consequence is the much higher incidence of diabetes mellitus – found in up to 20% of adults over age 65. The implications of this diagnosis for overall health, including vision, renal function, cardiovascular disease, cognition, and disability, are well described.

Finally, aging results in a number of important changes in calcium metabolism causing reduced bone mass and an increase in fracture risk among older adults. Decreased intake and impaired absorption of calcium and a high prevalence of vitamin D deficiency leads to lower levels of serum calcium in older adults. Most often, the body adjusts by increasing secretion of parathyroid hormone (PTH). This homeostatic mechanism, however, results in an increase in bone demineralization and a resultant reduction in bone mass.

Renal

The prevalence of chronic kidney disease (CKD) rises with age in the USA and may affect up to half of adults over age 70 [60]. Aging of the renal system is characterized by structural changes in the renal vasculature, tubules, and glomeruli. These changes manifest as an age-related decline in renal blood flow and impaired glomerular filtration. With age, the renal arteries undergo wall thickening much like the cardiovascular and pulmonary arteries. The smaller renal arteries become more tortuous, leading to increased vascular resistance. Simultaneously, there is a steady decline in the total number of nephrons starting at age 40. By the fifth decade, light microscopy reveals sclerotic glomeruli with focal sclerosis and partial thickening of the glomerular basement membrane [61]. With the loss of glomeruli, the attached renal tubules degenerate and become replaced by connective tissue.

Along with increased renal vascular resistance in both the afferent and efferent arterioles, there is an overall average decrease in renal blood flow of about 10% [61]. This leads to a decline in renal efficiency for handling fluids and electrolytes. This latter point has particularly important implications for the older adult undergoing surgery. Careful fluid management is warranted in the intraoperative and immediate postoperative period to avoid exacerbating renal function while avoiding fluid overload. Age-related changes in the glomerular filtration rate seem to be variable despite the gradual decline in renal blood flow. A systematic review of longitudinal studies examining changes in renal function with aging revealed heterogeneity in the estimates of age related loss of GFR. The best estimate of average decline in GFR was approximately 0.75 ml/min/year [62]. However, up to one-third of participants had no discernible change in renal function. Comparing and combining these studies was confounded by use of different formulas for estimating GFR. Current choices include those that utilize age, creatinine, and body mass, such as Cockcroft-Gault, the Modification of Diet in Renal Disease (MDRD), and the Chronic Kidney Disease Epidemiology (CKD-EPI) formula.

MDRD and CKD-EPI provide accurate and comparable measures among older adults. The latter may have some advantage in those with normal or near normal values [63]. Newer measures include the use of cystatin C, a protease inhibitor, along with creatinine. The accuracy and utility of this measure, however, may be confounded by the lack of specificity of changes in cystatin C given its association with comorbid conditions, including atherosclerosis, obesity, and inflammation. The variability in glomerular filtration rate also suggests that drug dosing, fluid replacement, or electrolyte correction need careful consideration in the elderly. In particular, health care providers must be cognizant of the route of clearance of medications and familiarize themselves with those drugs eliminated principally or exclusively by the kidneys. Many of these drugs are taken by elderly patients undergoing surgery and present a real risk to the health of the patient.

Summary

Geroscience has advanced beyond the basic biology of aging to provide a useful framework for assessing surgical risk. The conceptual framework of frailty and resilience provides surgeons with an opportunity to individualize the assessment of surgical benefit and risk of complications. Insights from the basic biology of aging are driving the development of biomarkers to assess biologic age and resilience as well as interventions that target the aging process itself. As this work advances, the growing population of geriatric patients will benefit from better informed decision making and surgical outcomes.

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Surgery in Centenarians

4

Mark R. Katlic and Joann Coleman

Contents

Abstract

Surgical problems do not cease on a person's centennial, and as our overall population ages, physicians will see increasing numbers of these most senior citizens requiring surgery. All that has been learned about surgery in the elderly – including compulsive preoperative preparation and scrupulous perioperative attention to detail – should be applied to the centenarian. It is not unreasonable, however, to speculate that the 100-year-old who has not already succumbed to a myocardial infarction or pulmonary embolus is unlikely to do so, even during the perioperative period. Survival to the centenary indicates that one has been tested by life and has been found exceptionally fit. Elective surgery should not be deferred nor emergency surgery denied the centenarian on the basis of chronologic age.

Keywords

Centenarian · Nonagenarian · Longevity · Elderly · Geriatric surgery

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Introduction

Ninety years is old, but 100 is news. Belle Boone Beard [1]

The 100th anniversary of an individual's birth still bestows an aura, a mystique, as the centenarian is as close to immortality as a human can be. This special prestige has been afforded the imprimatur of scientific study by Baker [2], who found that centenarians represented a striking exception to the inverted U curve of status across the life-span in Western culture. Baker's data, derived from factorial survey analysis, fit the postulate that there is an "American arc of life" that gives maximum prestige to middle age and least prestige to young and old persons. Centenarians, however, were given unique status nearly equal to that of middle-aged individuals (Fig. 1), because "like four leaf clovers or quintuplets, centenarians are rare."

Even those who care for centenarians are affected. Nishikawa et al. [3] found that family members who care for centenarians had a lower accumulated fatigue level, despite being older themselves and despite their subjects' worse performance status, than those who cared for individuals aged 70–90 years. Webb and Williams described a case of acute tenosynovitis of the right wrist and hand (centenarian hand syndrome) resulting from the congratulatory handshakes of many friends and relatives on a man's 100th birthday [4].

We have an inherent curiosity about our oldest old. What does he eat? What is her secret? Can it be bottled and sold? Decades ago one entrepreneur, Dr. Marie Davenport, became a professional centenarian, offering to teach her secrets of longevity to others for a fee [1]. Jeanne Calment, the world's presumed oldest person when she died at 122 years, was interviewed weekly by the foreign press who sought her out in Arles, France [5]. In 1997 a popular magazine devoted its cover story to "How to Live to 100." [6]

The mystique may wane, however, as more of us reach this milestone. The present paucity

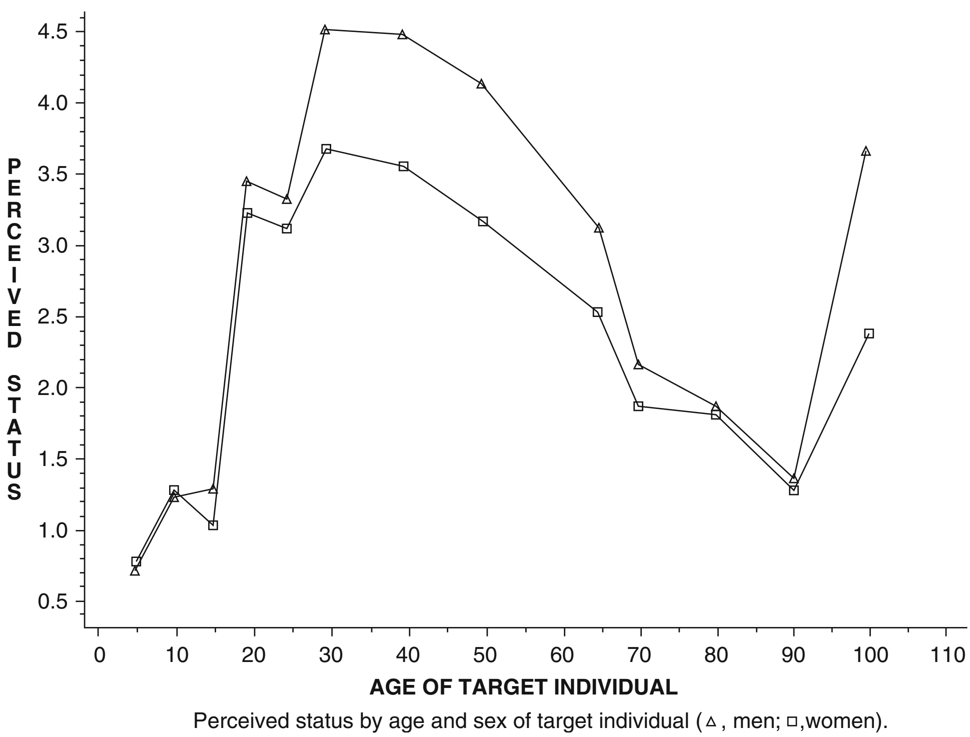


Fig. 1 Perceived status by age and sex of target individual. Triangles, men; squares, women. (From Baker [2], with permission)

of centenarians results from high mortality rates and a much smaller overall population a century ago. Over the past 40–50 years, the number of centenarians has nearly doubled every decade, owing chiefly to improved survival from age 80 to 100 years [7]. When Beard began her monumental, sedulous study of centenarians in 1940, there were 3700 possible subjects living in the United States; when she ended it during the late 1970s, there were at least 14,000 [8]. This number had reached 50,000 by the year 2000 [9], and 72,000 by 2014, an increase of 44% in 14 years [10]. Hallmark sold 85,000 "Happy 100th Birthday" cards in 2008 [11]. Centenarians may number 200,000 in 2020 and 500,000 to 4 million in 2050 [12].

Some authors argue that even these projections are too conservative because they discount the possibility of future baby booms and assume slow rates of mortality decline and low levels of immigration [13]. Vaupel and Gowan calculated that if mortality is reduced 2% per year, by the year 2080 the number of centenarians in the United States would approach 19 million [14].

Surgical problems do not end on a person's centennial. Surgeons will become increasingly familiar with these most senior citizens.

History

Surgeons have written with increasing frequency about operations in the elderly, but the definition of "elderly" has changed. A report in 1907 listed 167 operations performed on patients older than 50 years [15], and even 20 years later, Ochsner taught that "an elective operation for inguinal hernia in a patient older than 50 years was not justified" [16]. Brooks used a limit of 70 years as "advanced age" in his series of 293 operations reported in 1937 [17], and over the next few decades, most authors considered patients above age 60–70 years to be elderly. More recent studies show that good results can be expected in octogenarians and nonagenarians [18, 19], even in those undergoing complex vascular [20, 21], cardiac [22], and cancer operations [23].

An occasional centenarian is included in these series, but most papers devoted to centenarians per se are case reports, some written 50 years ago. Welch and Whittemore [24] in 1954 presented a 100-year-old woman who recovered well from abdominoperineal resection of the rectum for carcinoma. The next year Maycock and Burns [25] discussed prostate surgery in two patents in this age group, and in 1957 Childress [26] successfully treated three femoral fractures under spinal anesthesia. In 1971 isolated cases of pacemaker placement [27] and below-knee amputation [28] were reported. A basket-size ovarian leiomyoma was excised from a 103-year-old woman because of bowel obstruction in 1979, allowing her to live at least two additional years [29]. Six patients aged 100–106 underwent pacemaker procedures with good results in the 1989 report of Cobler et al. [30].

During the 1990s greater numbers of patients were reported. There were three deaths (12.5% mortality) in McCann and Smith's series of 24 patients undergoing a variety of operations, such as colon resection, ruptured aortic aneurysm repair, and hip prosthesis placement [31]. Cogbill et al.'s 1992 series of 16 patients reported perioperative mortality of 6% and a 1-year survival of 69% after a variety of small operations [32].

In 1998 Warner et al. [33] reported 42 procedures in 31 patients aged 100–107 years. There was one major complication (3%) and no mortality within 48 hours of operation; 30-day mortality was 16.1%, none directly related to the operative procedure or perioperative morbidity. Subsequent mortality of these patients equaled that of matched peers from the general population (Fig. 2). Grey and Keggi [34] reported a case of revision total hip arthroplasty, Lath et al. [35] an open abdominal aortic aneurysm repair, and Kent et al. [36] 24 centenary trauma patients. One chapter author (M.R.K.) reported a series of major and minor procedures in 6 patients aged 100–104 years, all of whom survived (Table 1) [37]. The illustrative cases below are from that series.

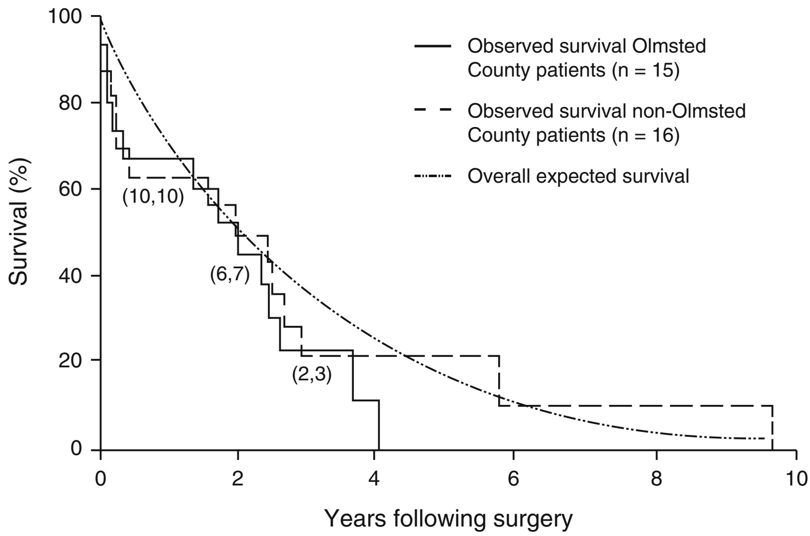


Fig. 2 Survival following surgery for patients ≥100 years of age. Numbers in parentheses represent number of patients alive and followed at yearly intervals during the first 3 years after surgery. (From Warner [33], with permission)

Case Studies

Case 1

A 100-year-old woman fractured her right hip in a nursing home fall. She had a history of myocardial infarction, congestive heart failure, aortic stenosis, arthritis, and hiatal hernia. She had previously undergone cataract surgery, cystocele repair, and open reduction/internal fixation of a left hip fracture. Open reduction/internal fixation of her new fracture was performed under general anesthesia. During her second postoperative week, she developed acute gangrenous cholecystitis, requiring emergency cholecystectomy. This episode was complicated by left lower lobe pneumonia, which resulted in antibiotic treatment, and a localized intraabdominal abscess, successfully treated with percutaneous drainage and antibiotics. Six weeks after admission, she returned to her nursing home. Protruding Enders rod pins in her right leg led to pin removal under local anesthesia 8 months later. At 101 years of age, she underwent elective endoscopic resection of a rectal villous adenoma containing carcinoma in situ. Postoperative bleeding from the resection site mandated suture ligation under general anesthesia. She returned to her nursing home, where she lived for two more years. She died 2 weeks before her 103rd birthday.

Case 2

A 100-year-old retired laborer was ambulatory at his nursing home until his toes became painful. He had a history of hypertension, chronic lung disease, and severe peripheral vascular disease and had undergone prostatectomy. On examination, he had a gangrenous right foot with *Proteus* cellulitis extending to the calf and an absence of leg pulses below the femoral arteries. He underwent amputation of the right leg above the knee while under general anesthesia (spinal anesthesia was aborted because of the patient's agitation) and was discharged 11 days later. He had one later 4-day admission for bronchitis and died at age 101 years of "old age."

Case 3

A 101-year-old woman was ambulatory and independent at home but suffered from a large right inguinal hernia. Her past history included congestive heart failure, atrial fibrillation, type 2 diabetes mellitus, blindness, and a resected basal cell carcinoma of the face. Elective right inguinal herniorrhaphy was completed under local anesthesia in the outpatient surgical unit. Postoperatively, stating that she would "rather wear out than rust out," she took a 3-month cruise around the

Table 1 Clinical summary of centenarians undergoing an operation. (Source: Katlic [37], with permission)

Patient No./sex	Age (years)	Medical problems	Operation	Status	Anesthesia	Complications	Death	Follow-up
1/M	100	Old MI, sick sinus syndrome with pacemaker, CHF, prostatectomy, cataract extraction, gout, arthritis, chronic renal failure	Pacemaker generator replacement	Urgent	Local	None	No	Died, age 102 years of CHF
2/F	100	Old MI, left radical mastectomy (13 years), arthritis	Excision of right femoral head, cemented Moore prosthesis	Urgent	General	None	No	Died, age 102 years of cerebrovascular disease
3/M	100	Hypertension, severe peripheral vascular disease, prostatectomy, chronic lung disease	Above-knee amputation	Urgent	General	None	No	Died, age 101 years of "old age"
4/F	100	Old MI, CHF, aortic stenosis, cataract extraction, cystocele repair, left hip open reduction internal fixation, arthritis, hiatus hernia	Open reduction, internal fixation of right hip fracture Cholecystectomy Removal of Enders rod pins	Urgent Emergency Elective	General General Local	Acute gangrenous cholecystitis, protruding Enders rod pins Pneumonia, resolved; abdominal abscess, percutaneously drained None	No	Died, age 102 years of "old age"

(continued)

Table 1 (continued)

Patient No./sex	Age (years)	Medical problems	Operation	Status	Anesthesia	Complications	Death	Follow-up
	101		Colonoscopic resection of villous adenoma Suture ligation of bleeding rectal polypectomy site	Elective Emergency	Local General	Bleeding at excision site None		
5/F	101	CHF, atrial fibrillation, blind, basal cell carcinoma of face excised, adult-onset diabetes	Right inguinal herniorrhaphy	Elective	Local	None	No	Died, age 102 years of CHF
6/M	104	Squamous cell carcinoma of neck excised, basal cell carcinoma of nose excised and irradiated	Gastroscopy with biopsy	Emergency	Local	None	No	Died, age 105 years of gastric carcinoma

MI myocardial infarction, *CHF* congestive heart failure world and later lectured at a local college geriatric course. On the penultimate day of her life, she completed a political poll. She died of congestive heart failure at age 102.

Discussion

> The first hundred years are the hardest—Wilson Mizner [38]

Centenarians recover surprisingly well from surgery, leading one to speculate that the 100-year-old patient who has not already succumbed to a myocardial infarction or pulmonary embolus is less likely to do so, even in the perioperative milieu. The Mayo Clinic study of surgery in nonagenarians supports this finding, as neither pneumonia nor atherosclerosis with myocardial infarction was a major cause of postoperative death [15].

Longer length of stay and higher costs, however, are likely [39].

Certainly all that has been learned about surgery in the elderly should be applied to the centenarian. Clinical presentation of surgical problems may be subtle, preoperative preparation is essential, and scrupulous attention to detail intraoperatively and perioperatively yields great benefit. Virtually all studies of surgery in the elderly have also shown an almost threefold greater risk for emergency surgery than elective surgery. The worst complications in the author's series, pneumonia and intraabdominal abscess, did occur after emergency surgery, but the patients generally tolerated even urgent operations well.

Centenarians may be considered a natural model of successful aging. What is it about the 100-year-old that allowed him or her to enter this select age group?

Physiologic Changes in Centenarians

The oldest old manifest low frequencies of the E4 form of gene coding for apolipoprotein E, a protein linked to an increased risk of acquiring Alzheimer's disease. Among healthy subjects age 90–103 years, 14% had at least one E4 gene, in contrast to 25% of subjects younger than age 65 [12]. It may be that many of those with E4 suffer early Alzheimer's disease and do not survive to become centenarians. This *cohort effect* may explain some of the other physiologic and pathologic changes in centenarians described below. Silver et al. found that dementia is not inevitable with aging and that dementia in centenarians is often not attributable to Alzheimer's disease [40–42].

Morphologic changes occur in the brain with age – decreased brain weight, atrophy of the cerebral hemispheres, and fall in the number of Purkinje cells in the cerebellum – but healthy aged subjects show little difference from young adults with respect to cerebral blood flow and oxygen uptake [43]. Hubbard et al. studied electroencephalograms in centenarians and found slowing of the posterior dominant rhythm, but there was no evidence of a progressive decrease in frequency between the ages of 80 and 100 years [44]. Well-preserved mucociliary clearance in the lung of a centenarian was documented by Pavia and Thomson despite 80 years of smoking history [45].

An even more paradoxical finding was described by Mari et al. group [46]. They found that a high proportion of 25 healthy centenarians had laboratory evidence of activation of the coagulation system, shown by high levels of enzymes, activation peptides, and enzyme–inhibitor complexes. Levels of factor X activation peptide were equal to those found in patients with disseminated intravascular coagulation. Even procoagulant proteins such as fibrinogen and factor VIII – predictors of cardiovascular disease in young adults – were elevated in centenarians; yet these individuals had no current or past thrombotic events. The authors concluded that significant alterations of these markers are still compatible with health and long life. A more recent study by this group found that the 4G allele and 4G/4G genotype associated with elevated levels of plasminogen activator inhibitor 1 (PAI-1), which predicts recurrence of myocardial infarction in young men, were even more frequent in centenarians than young adults.

The homozygous genotype for the deletion of polymorphism of the angiotensin converting enzymes, which predisposes to coronary artery disease, is also paradoxically more frequent in centenarians than in adults age 20–70 years [47]. Mannucci et al. speculated that occult factors compensate for these putatively unfavorable genotypes in centenarians (e.g., linkage disequilibrium with a locus counteracting the bad effect of elevated PAI-1 levels offsets the risk of hypofibrinolysis). It may be that if an elderly person has already escaped thrombotic disease, it is advantageous to have decreased fibrinolysis [48]. A different genetic finding in centenarians – decreased frequency of the E4 allele of the gene, which encodes apolipoprotein E – would go along with decreased risk of ischemic heart disease [47].

Laboratory values in healthy centenarians may differ even from those of younger elderly adults: widening of the range for sodium levels to 132–146 mmol/L; slightly higher potassium and chloride; decreased total calcium; slight increase in ionized calcium; increased blood glucose; increased alkaline phosphatase and lactate dehydrogenase; slightly decreased bilirubin and total protein; increased amylase likely due to decreased renal function; increased serum urea nitrogen and slightly increased creatinine; increased urinary albumin; elevated urate; decreased albumin; elevated carcinoembryonic antigen; decreased cholesterol and triglycerides; decreased vitamin B_{12}; decreased zinc; slightly decreased thyroxine; increased prolactin; no change in corticotropin; decreased testosterone and estradiol; marked decrease in dehydroepiandrosterone; decreased progesterone; unchanged cortisol; slightly higher gastrin; lower erythrocyte, leukocyte, and platelet counts; and slight decreases in hemoglobin, hematocrit, and iron [49]. Neutrophil function is preserved [50]. Higher functioning centenarians appear to have higher levels of serum albumin [51]. Discussion of possible mechanisms for these findings is beyond the scope of this chapter.

Franceschi et al. asserted that a complex remodeling of the immune system occurs in healthy centenarians in contrast to the presumed progressive deterioration (especially with the T cell branch) [52, 53]. Peripheral blood T cells and major T cell subsets are only slightly decreased despite age-related thymic involution. B lymphocytes are deceased despite data that several immunoglobulin classes are elevated in the serum. Interestingly, peripheral blood lymphocytes in centenarians appear resistant to the oxidative stress that causes irreversible cell damage in younger individuals; such stress may retard entrance into the cell cycle rather than cause permanent damage [54].

Centenarians are more likely to have low body weight [55, 56], possibly due to loss of muscle and fat [57]; a number of investigators have reported short stature even when the effects of aging are considered. Decreased bone mass, however, is not universally present [58]. Both male and female centenarians are more likely to have feminine or androgynous personality traits rather than masculine ones and are more likely to have a type B behavior pattern (easygoing) [59].

Centenarians use fewer drugs than the elderly in general and fewer inappropriate drugs [60].

Pathology in Centenarians

Although atherosclerosis has been found in coronary, cerebral, femoral, and abdominal aortas of centenarians [61], the ascending aorta may be spared [55, 62]. Myocardial fibrosis is located chiefly in the left ventricle and septum, and cardiac amyloid deposition is characteristic [61]. Coronary disease at autopsy is common [63, 64], though perhaps less so in Japanese centenarians [65]. Pneumonia was found in 15 of 23 patients in Ishii and Sternby's series and was also the most common cause of death [61]. Alveolar ectasia and decreased elastic fiber were also seen in the lungs. Interestingly, recent or old thromboembolism in the pulmonary arterial tree was common at autopsy despite the absence of clinical pulmonary emboli during life [61].

In the kidney, chronic pyelonephritis and atherosclerosis are usually pronounced; and the testes, ovaries, and uterus show atrophic changes [66]. In the gastrointestinal tract, the liver also shows atrophy, and colonic diverticula are common. Gallstones are common (13/23 patients), and peptic ulcer is rare [66]. Osteoporosis is common [67], but not universal [58]. Similarly, in the brain, changes of Alzheimer's disease are common but not universal; when present these may not correlate with clinical neurologic findings [68, 69].

Cancer as a cause of death was unusual in Ishii and Sternby's autopsy series [67]; it represented 7.1% of Stanta et al.'s 99 autopsies in centenarians [70], and 31% of Klatt and Meyer's 32 patients [62]. The 7.1% rate in Stanta et al. series was significantly different ($p < 0.001$) from that in age groups 75–90 years (25%) and 95–99 years (9.5%). Metastases in this series were found in 23.5% of the centenarians with cancer and 63.2% of those 75–90 years old; local infiltration did not differ among groups. Many of the cancers in centenarians (70%) were undiagnosed during life, a fact that may explain the exceptionally low incidence of cancer (4%) as a cause of death in epidemiologic studies [71]. Of all the types of cancer, only the prevalence of gallbladder adenocarcinoma was increased in Stanta's series [70]. Germ-line polymorphisms may play a role in the decreased susceptibility of centenarians to cancer [72]. In exploring an animal model of extreme longevity, Cooley found that only 19% of extreme aged dogs died of cancer versus 82% of dogs with usual longevity ($p < 0.0001$) [73] (Fig. 3). In summary, cancer in the oldest old is less frequent and less aggressive.

Centenarians, like younger individuals, die of specific organ failure, not "old age" [74]. Berzlanovich et al. [75] reviewed autopsy records of 40 Austrian centenarians, 60% of whom had been described as healthy before death; all had a specific cause of death, including cardiovascular in 68%, respiratory 25%, gastrointestinal 5%, and cerebrovascular 2%.

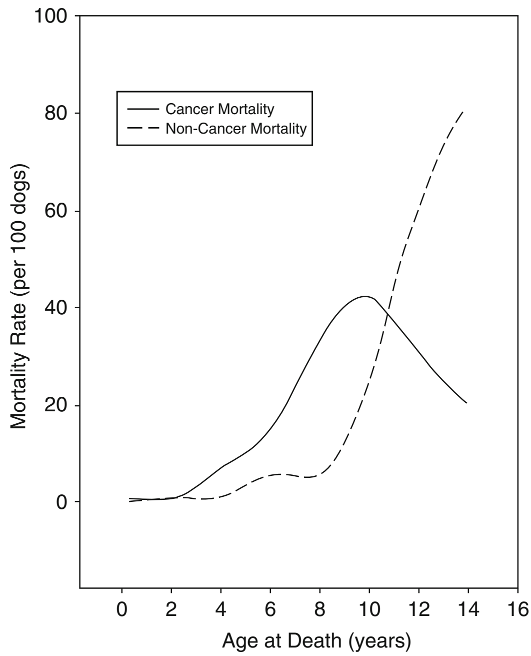


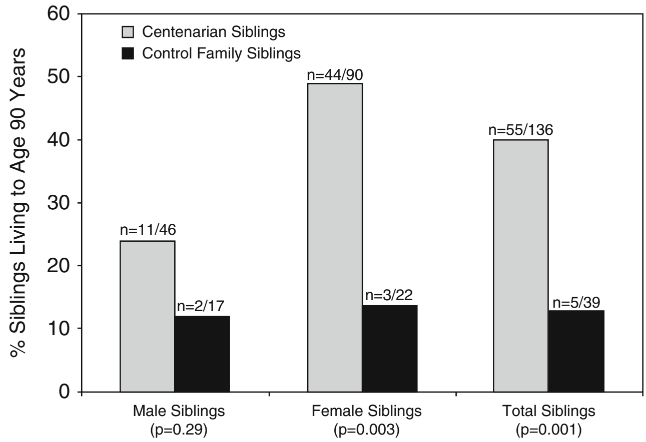
Fig. 3 Comparison of age-specific cancer and noncancer mortality for 345 Rottweiler dogs. Age-specific cancer and noncancer mortality rates were calculated at 2-year intervals from 0–14 years of age and expressed as the number of cancer or noncancer deaths per 100 dogs that entered the interval. (From Cooley [73], with permission)

Determinants of Extreme Longevity

Despite our fascination with centenarians, little is known about the influences – genetic, environmental, and medical – on their longevity. Herskind et al., in extensive studies of nearly 3000 Danish twin pairs born during 1870–1900, estimated the heritability of longevity to be 0.26 for men and 0.23 for women; the sex difference resulted from the greater impact of unshared environmental factors in women [76]. Other family studies have shown weak correlations for lifespan between parents and offspring (0.01–0.05) and somewhat higher correlations between siblings (0.15–0.35) [77, 78] (Fig. 4) suggesting either that the genetic factors are nonadditive (genetic intralocus interaction) or there is a higher degree of shared environmental influences among siblings than parents. The offspring of centenarians nevertheless manifest less cardiovascular disease than the general population at similar age [79–81] and, in one study, less cancer-specific mortality [81, 82].

Several specific genetic factors have been associated with extremely long life [83]. In a study of Japanese centenarians, Takata et al. [84] showed a significantly lower frequency of HLA-DRw9 and a higher frequency of HLA-DR1 among centenarians compared to younger adults; these antigens

Fig. 4 Percentage of siblings of centenarians and controls who reached age 90 years, when controlling for extrinsic or unknown causes of mortality. (From Willcox [78], with permission)



are negatively associated with autoimmune diseases in Japan, suggesting mediation of the genetic influence through a lower incidence of disease. The low prevalence of the E4 allele of apolipoprotein E (APOE) and increased prevalence of the DD genotype for angiotensin-converting enzyme (ACE) have been mentioned above [48]; neither of these, however, was associated with longevity in a Korean study [85]. Puca et al. reported evidence for a specific locus (D451564) on chromosome 4 associated with longevity in a sibling pair linkage study [86]. The role of inherited and somatic mutations of mitochondrial DNA (mtDNA) in centenarians remains unclear [87]. Short chromosomal telomeres have been associated with increased mortality in persons over the age of 60 [88], but this has not held true for the oldest old [89, 90]; nevertheless, Terry et al. [91] found healthy centenarians have significantly longer telomeres than unhealthy centenarians (Fig. 5).

Sebastiani et al. [92] studied 1055 centenarians and 1267 controls, building a genetic model which could predict exceptional longevity with 77% accuracy. Their data suggested that enrichment of longevity-associated variants "counter the effect of disease-risk alleles and contribute to the compression of morbidity and/or disability towards the end of very long lives." The model's limitations, however, confirm that lifestyle factors also contribute.

The mediation of genetic influences on longevity via genetic influences on smoking and body mass index – two factors associated with longevity in epidemiologic studies –was disproved by Herschind et al. [93] Even smoking status has shown no definite association with extreme longevity, nor has alcohol consumption, diet, or exercise [94]. Such "lifestyle" factors may, however, influence one's functional status at the age of 100 [51]. Environmental factors such as socioeconomic status and early life nutrition appear to have little influence [95]. Hagberg and Samuelson [96] demonstrated the importance of stochastic determinants (physiological reserve, present health and functional state, and chance) as opposed to programmed factors (family longevity). Although no "fountain of youth" medicine has been discovered, the inverse correlation of blood levels of dehydroepiandrosterone (DHEA) with mortality has prompted ongoing clinical trials of its administration [97], not all of them salutary [98].

Some environments, e.g., Sardinia and Okinawa, appear to be conducive to extreme longevity as do personal factors such as activity, discipline, altruism, spiritual faith [99], musical instruments, and humor. Even personality may be important [100, 101]. In a study of 483 Italian centenarians, 88.6% had never smoked cigarettes [102]. Centenarians themselves attribute their longevity to God, singing, pickled herring, shochu (sugar cane liquor), honey, port, abstinence, boiled onions, whiskey, red wine, fish, luck, chocolates, olive oil, weakness for women (or men), and more. Fifty percent of centenarians walk or hike; nine percent practice yoga or Tai Chi [103].

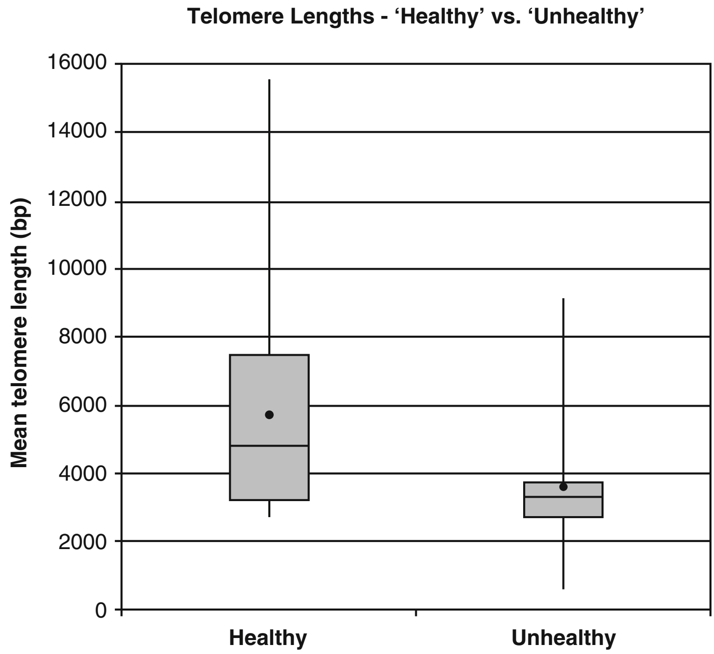


Fig. 5 Mean telomere length measured in base pairs (bp) in 19 healthy versus 19 unhealthy centenarians. Bars, interquartile ranges (Q75%–Q25%) of telomere length. Diamonds, mean; horizontal line within bars, median telomere lengths. Vertical lines, overall range of telomere lengths. (From Terry [91], with permission)

Table 2 Determinants of extreme life-span in the industrialized world

Genetics: genes coding for
Human leukocyte antigens HLA-DR (?)
Apolipoprotein E (?)
Angiotensin-converting enzyme (ACE) (?)
Environment
Year of birth
Smoking (?)
Alcohol (?)
Diet (?)
Locale (?) cf. Sardinia, Okinawa
Medicine
Dehydroepiandrosterone (DHEA) (?)
Other Long-lived sibling Long-lived parent (?)

In summary, it is likely a large number of factors interact to determine longevity, three-fourths of them environmental (Table 2). The involvement of a number of genes, each contributing a little, might influence longevity directly or, more likely, through determining susceptibility to disease at different ages. Willcox et al. [104] reviewed the determinants of longevity in 2008.

Selective Survival Hypothesis

> A 100-year-old is as likely to survive surgery as are his sons and daughters, and one may speculate that he is even more likely to do so. The man or woman who has endured ten decades of life's labors enters a select group whose physiological resilience is greater than that of many who are chronologically younger. M.R. Katlic, 1985 [37]

This selective survival concept was discussed by Thomas Perls, principal investigator with the New England Centenarian Study [12]. Perls postulated, supported by his research and that of others, that certain individuals are resistant to the diseases that cripple and kill most people before age 90. These individuals – although 95% have some form of chronic disease [105], including cardiovascular disease [106] – not only live longer lives, they also live relatively free of debilitating infirmities.

Mortality rates for centenarians, for example, are lower than would be anticipated by extrapolating the death rates of younger adults. Mortality can be reasonably predicted up to approximately age 80, but the linear decline in health not only slows at advanced age but varies more among individuals, thus selecting the most fit [107]. Selection is more than sufficient to overcome the effects of aging and is greater in men, probably because of their higher mortality at younger ages [108, 109]. This "gender crossover" resulting from the selection of fit men can be seen as early as age 80 but is more evident in centenarians: men make up 20% of 100-year-olds and 40% of 105-year-olds. Female-to-male ratios, however, may range from 2:1 to 7:1 in different provinces within the same country [110]. Possibly related, there are anatomic and functional gender differences in the heart in centenarians as well [111]. Age 95–97 years appears to be the age at which a person's chance of dying increases in a linear rather than an exponential manner with time (Fig. 6) [12]. Carey et al. [112] found the same phenomenon in medflies.

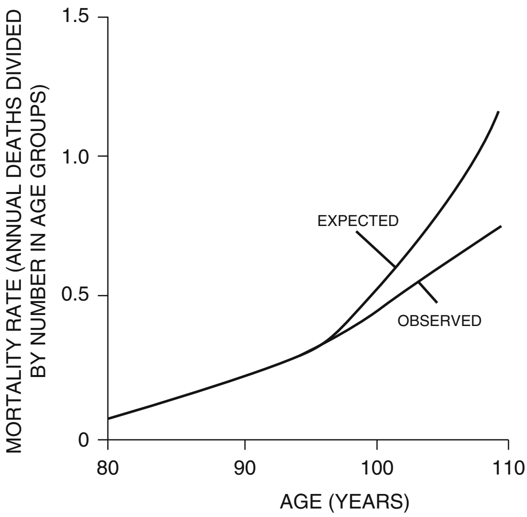


Fig. 6 Observed mortality rate slows after age 97 years compared to the expected mortality rate. (From Perls [12], with permission)

Whether due to compositional change in the cohort (selection of the fittest) or better intrinsic cellular defense mechanisms, the very old have a higher threshold for acquiring disease and a decreased mortality rate, allowing them not only to survive but to do so in relatively good health (Fig. 7). In 1990 the Medicare cost for those who died at age 70 was $6475 during each of the last 5 years of life compared to $1800 per year for those who died at age 100 [113]. In 1995 medical expenses for the last 2 years of life average $22,600 for people who died at age 70 and $8300 for those who died after

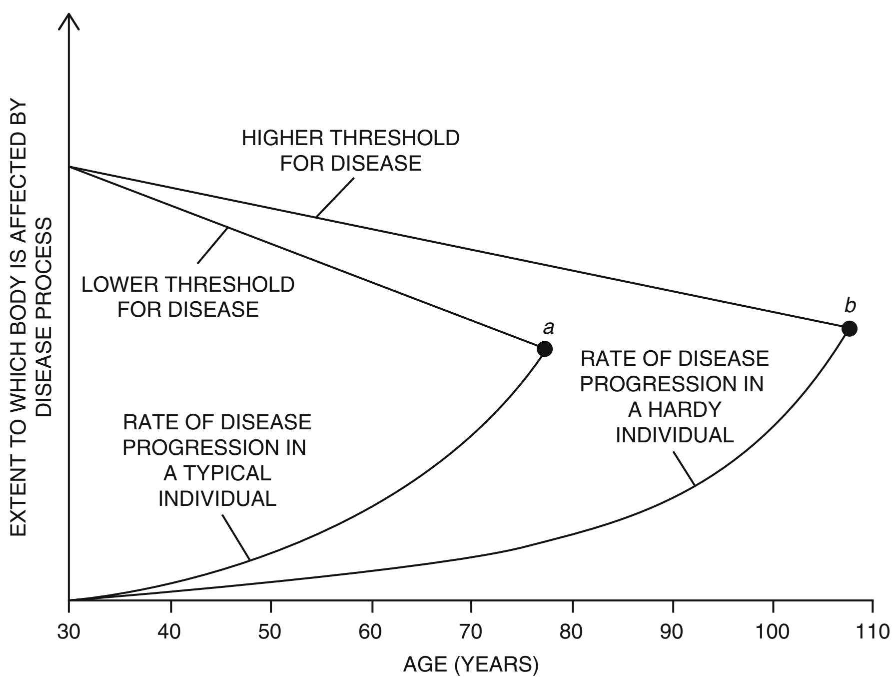


Fig. 7 High threshold for acquiring disease and slow aging process may promote survival because of the good health of centenarians. (From Perls [12], with permission)

age 100 [6]. Caregiver burden does not necessarily increase in this group [114].

Everts et al. have described three morbidity profiles for centenarians [115]. *Survivors* had an age-associated illness prior to age 80 years (24% of men, 43% of women); *Delayers* experienced an age-associated illness after 80 years (44% of men, 42% of women); *Escapers* reached age 100 without a diagnosis of common age-associated illness (32% of men, 15% of women). With respect to the most lethal diseases – heart disease, cancer, stroke – 87% of male centenarians and 83% of female centenarians either delayed or escaped [115]. Motta et al. [116], who studied 602 Italian centenarians, write that even those who are free of disease, autonomous, and bright should not be considered prototypes of "successful aging," as they have not maintained any social or productive activities. Most consider centenarians to be models of healthy aging from which we can learn, in order to improve the health of all elderly [117].

Supercentenarians

Supercentenarians, those aged 110 years or more, likely number less than 500 worldwide; most are women [118]. Schoenhofen et al. [119] studied 32 such individuals, 84% of them are women. Cardiovascular disease and stroke were rare, Parkinson's disease absent, and cancer successfully treated in 25%; 41% were independent or required minimal assistance. In the Okinawa Centenarian Study, supercentenarians had little clinical history of cardiovascular disease and no history of cancer or diabetes (in a different study, even centenarians with diabetes had few clinical problems related to the disease [120]); the authors called this "an elite phenotype" [121]. The parents and siblings of supercentenarians also manifest a survival advantage [122].

Conclusions

All that has been learned about surgery in the elderly should be applied to the centenarian: clinical presentation of surgical problems may be subtle, preoperative preparation is essential, emergency surgery carries high risk compared to elective operation, and scrupulous attention to detail intraoperatively and perioperatively yields great benefit. It is not unreasonable to speculate that the 100-year-old who has not already succumbed to a myocardial infarction or pulmonary embolus is unlikely to do so, even during the perioperative period. Survival to the centenary indicates that one has been tested by life and has been found exceptionally fit. Elective surgery should not be deferred nor emergency surgery denied the centenarian on the basis of chronologic age.

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Geriatric Syndromes

5

J. Macias and Michael Malone

Contents

Abstract

Older adults are the fastest growing segment in the USA. This aging segment of our population brings a significant number of older adults with multiple comorbidities. Older adults aged 65 and older represent approximately 15% of the total US population and they account for 36% of hospital admissions. They are responsible for approximately 44% of hospital charges [1]. This context has created a need for geriatrics expertise and new challenges for clinicians, hospitals, and health care organizations. Older adults in the USA undergo 20% of all surgical procedures while making up of 15% of the total US population; hence, these statistics suggest how relevant it is to understand the needs of older adults in the perioperative period. It is estimated that by 2030, about

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20% of Americans will be older than 65. Twenty-one percent of those over the age of 60 will undergo surgery and anesthesia, as compared with only 12% of those aged 45 to 60 years. These estimates emphasize the importance of identifying and screening geriatric syndromes to lower perioperative complications in older adults [7].

Keywords
Geriatric syndromes · Delirium · Frailty · Dementia · Acute care for elders

Introduction

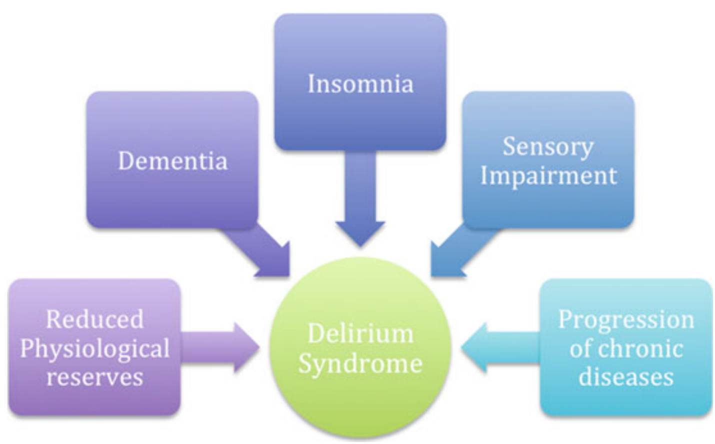
Older adults are at risk for certain adverse events with serious consequences in the acute care setting, including hospitalization-associated disability (HAD), delirium, falls, pressure ulcers, hospital acquired infections, and institutionalization. The increased rates of older adults with complex comorbidities across the care continuum have triggered different initiatives to increase expertise and knowledge in the care of older adults among other specialties. More surgical and related medical specialists are integrating geriatrics principles into their practices to improve their ability to care for vulnerable hospitalized older adults.

There are a number of physiological changes that occurred with aging. Changes in volume of distribution, bioavailability, and receptor sensitivity lead to alterations in the pharmacodynamics of most drugs prescribed to older adults. Poor renal clearance and changes in hepatic function require paying close attention to dosages of medications. Older adults have impairments in thermoregulation. Further, there may be impaired responsiveness in situations of hypotension. Ventilatory responses to hypoxia and hypercarbia are reduced, increasing the risk of postoperative respiratory complications in elderly patients [7]. These biologic changes and the progression of common diseases create a diminished physiological reserve in older adults, which results in a weak compensatory mechanism during stress or an acute illness.

According to the National Institute of Aging, about 80% of seniors have at least one chronic health condition and 50% have at least two chronic health conditions. Arthritis, hypertension, heart disease, diabetes, and respiratory disorders are some of the leading causes of activity limitations among older people. Further, heart disease and cancer are the leading causes of death within this population, with death rates varying by age, sex, and race [8].

In the context of diminished physiological reserves and the progression of common chronic diseases in older adults, the authors frame a discussion of geriatric syndromes. Geriatric syndromes are clinical conditions that share underlying causative factors and involve multiple organ systems [2, 3, 29]. Delirium is an example of a common geriatric syndrome as noted in Fig. 1.

Fig. 1 The interaction of multiple risk factors, which culminates in delirium



Other examples of geriatric syndromes include incontinence, cognitive impairment, falls, pressure ulcers, pain, weight loss, anorexia, frailty, functional decline, depression, and multimorbidity [4]. These geriatric syndromes are more prevalent with advancing age. They are associated with adverse outcomes and increased mortality. Therefore, their recognition and management is key when caring for a vulnerable hospitalized older adult [5]. Geriatric syndromes are often under-recognized in hospitalized older adults and may go unaddressed in the postacute care setting. The challenge in the surgical setting is that the surgical team is often focused on the acute injury and illness of the patient and then the surgical needs of the individual after a procedure. The geriatric syndromes of the patient may have been the context of the patient's acute illness/ injury and may be less apparent in the setting of other acute problems which need to be addressed.

Assessment of the Geriatric Surgical Patient

Hospitalized older adults, despite proper treatments, are prone to hospitalization associated disability (HAD) and other complications with serious consequences – if not identified in the acute care setting. This condition is a common outcome of many complications of medical and surgical care of acutely ill older patients. It appears that surgical patients are more likely to bounce back from their illness than medical patients, as described by a study of the recovery of each cohort of patients. Much of the decline in the function of vulnerable older adults may have to do with our systems of caring for these patients. Strategies that promote early mobilization and efforts to promote functional independence decrease the chances of hospitalization-associated disability. Caring for older patients requires: (1) knowledge of the presentation and management of common diseases in older adults and (2) taking into consideration theories of aging and physiological changes of aging of each organ system to appropriately prescribe and develop treatment plans. This topic has been nicely outlined in the ACS NSQIP/ AGS Best Practice Guidelines: Optimal Perioperative Assessment of the Geriatrics Surgical Patient [30]. Multiple models of care have developed to address the need of hospitalized older adults and minimize potential complication during hospitalization.

The Acute Care for Elders model of care was developed as a multicomponent intervention specially designed to address hospital-acquired dysfunction and systematically identify vulnerable adults. An ACE unit is a medical surgical nursing unit which focuses on improving the management of acutely ill older adults [6].

A model of care for older patients which is *not* unit-based is the Hospital Elder Life Program (HELP). This geriatrics "best-practice" strategy is designed for the prevention of delirium-targeting risk factors for delirium: cognitive impairment, hearing or visual impairment, sleep deprivation, immobility, and dehydration.

Deploying geriatrics models of care in the inpatient setting like the ACE unit or HELP along with geriatric education programs, it is fundamental to improve the care of older patients with geriatric syndromes (Table 1).

Common Geriatric Syndromes in the Setting of Surgical Care

Frailty

Frailty is a syndrome that represents vulnerability in the setting of a stress. Key clinical features include low level of physical activity, self-reported exhaustion, generalized weakness, impaired physical function, and unintentional weight loss. Frailty has been reported to be a predictor of mortality and functional limitations in older adults.

Various measurements exist for assessing frailty. One is the Fried Frailty Index (FFI), [9], which classifies frailty according to the presence of three or more of the following items: unintentional weight loss, low physical activity, low hand grip strength, slow walking speed, and exhaustion. A combination of these findings can

Table 1 Checklist to improve the hospital care of the older surgical patient

Delirium	Screen regularly using the b-CAM or Confusion Assessment Method or similar tools Initiate multicomponent strategies to mitigate delirium risk (Hospital Elder Life program) Minimize medications associated with delirium Remove unnecessary catheters Assess and effectively manage pain
Immobility/ falls	Screen with: Timed up and go test and "Have you fallen in the past year?" Low-bed/ alarms for high-risk patients Early PT/OT assessment Avoid pharmacologic and physical restraints Discontinue IV lines ASAP Use early and regular ambulation strategies
Undernutrition	Screen with Body Mass Index, weight loss, perhaps serum albumin Monitor daily nutritional intake Assist with meals and simplify meal tray where appropriate
Disability	Screen by assessing baseline and current activities of daily living Avoid bed rest unless medically necessary Raise activity level as tolerated

increase the individuals' subsequent risk during an acute injury or acute illness.

Handgrip strength can predict accelerated decline in activities of daily leaving and disability, which can contribute to dependency. In addition, a rapid decline in walking speed has been associated with a high risk of all mortality and impaired mobility. Physical inactivity has been shown to predict dependence and death [10–12]. Unintentional weight loss is a predictor of higher morbidity and mortality. The CSHA Frailty Index Scale, described by Rockwell and his colleagues, is a global clinical assessment of the older individual which defines the patient in one of seven clinical frailty scores. With each increasing scale from 1 to 7, patients had an increasing risk of death within about 6 years or of institutionalization. This CSHA Frailty Index Scale seems very easy to determine. The tool can assist the surgical teams with a global assessment of the older patients' vulnerability.

A screening for frailty should be a core part of the preoperative surgical assessment of an older adult. Understanding such vulnerability can help the surgeon and the patient better understand the risks of the procedure in the context of the overall health of the patient. This will better frame the decision-making and hence the patients' preferences. The management of frailty should include identifying any modifiable precipitating causes. The clinical team should minimize risk factors and stressors that can precipitate complications in hospitalized older adults during the acute illness or in the perioperative period. Likewise, the clinicians should encourage mobility and optimize nutrition. An interdisciplinary approach and comprehensive geriatric assessment is needed to appropriately manage vulnerable older patients with frailty.

Delirium

The most current definition of delirium was recently published in the 5th edition of the DSM and includes a disturbance in attention and awareness; a change in cognition that is not better accounted for by a preexisting, established, or evolving cognitive disorder. The disturbance develops over a short period and tends to fluctuate during the course of the day. The delirium is often a direct physiological consequence of a general medical condition, an intoxicating substance or withdrawal, medication use, or more than one etiology [13].

Delirium is a clinical diagnosis. The Confusion Assessment Method (CAM) is a screening tool commonly used in hospital settings. It provides an overall sensitivity from 94% to 100% with a specificity form 90% to –95% [15]. Recent studies have described a strategy to more easily implement the CAM at the bedside. Many hospitals have started to shift their efforts towards using other tools to screen for delirium, using a RASS score. The main point for the surgical team is to take the time to assess the older patients' ability to shift and sustain their attention. A nice clinical approach is to ask open-ended questions regarding the patient's hospital admission and then to ask the patient (in a reassuring manner) to say the days of the week or the month of the year backwards. Also, the surgical team should define the patients' baseline cognition. Likewise, the surgical team should ask the nursing staff to define any signs or symptoms of delirium.

Delirium is often multifactorial and is the result of the combination of predisposing factors and precipitating factors. Older adults who are admitted to the hospital for a surgical procedure might already have certain factors which increase their risk of delirium. These predisposing factors include cognitive impairment, male, and sensory impairment. The interaction of these vulnerabilities with precipitating factors (sleep deprivation, acute illness, high-risk medication) can result in delirium.

Delirium in older adults has major implications for the patient and the family caregivers. Delirium can be life-threatening. It is the most common postoperative complication in older adults. Delirium occurs in 5% of cases in low-risk patients with low risk procedures and up to 40% in high-risk patients with high-risk operations. Delirium is associated with major postoperative complications such as prolonged hospitalization, loss of functional independence, reduced cognitive function, incomplete recovery, delayed rehabilitation, and death [14]. In short, efforts to help older patients with the most advanced surgical procedures can "fall apart" when the patient develops the complication of delirium.

Delirium is commonly described as hyperactive, hypoactive, or mixed delirium. In the hyperactive type, the patient is agitated and combative. For hypoactive delirium, the patient is usually drowsy, or lethargic. This type of delirium is often unrecognized. The older patient with mixed delirium has a combination of clinical features of both hypoactive delirium and hyperactive delirium. In the hyperactive type, agitation and behavioral disturbances (aggression or combativeness) can be distressing to the patient, their families, and the professional caregivers.

Once delirium is diagnosed, the underlying causes should be treated and target laboratory assessment should be ordered based on clues from a history and physical exam. Neuroimaging should be obtained if the patient has had a history of trauma or if there are clinical findings to suspect a localizing condition. An electroencephalogram is not a part of the initial evaluation, but may be warranted if clinical features are consistent with seizure or if the patient's condition does not improve. Management of an older patient who has delirium includes nonpharmacologic interventions and pharmacologic interventions. This topic has been nicely described in recent guidelines released by the American College of Surgeons and the American Geriatrics Society. Nonpharmacologic interventions focuses on encouraging mobility, avoiding use of physical restraints, addressing sensory impairment ensuring that the patient has glasses, and hearing aids and dentures. Assessment of medications and reduction of psychoactive drugs is essential in the management of delirium [17].

The authors of several high-quality systemic reviews have concluded that the evidence to justify the use of antipsychotics for prevention or treatment of delirium is insufficient [16]. Pharmacologic interventions or use of antipsychotics are reserved for severe agitation, aggression, or combative behaviors that impair essential medical therapy (e.g., intubation). Haloperidol is the most studied of the medications used to treat older patients with delirium. A key clinical point for the surgeon is to use dosages of haloperidol which are low and to carefully reassess the patient's response to the treatment. Use of benzodiazepines in older adults is recommended only in alcohol or benzodiazepine withdrawal. Quetiapine is the drug of choice for patients with Lewy body dementia or Parkinson's disease.

As noted above, American Geriatric Society and the American College of Surgeons recently published clinical practice guidelines for postoperative delirium in older adults. These recommendations were made based on studies that included both surgical and nonsurgical patient cohorts. The guidelines address the prevention and treatment of postoperative delirium.

Key take home messages from these recommendations include: (1) multicomponent nonpharmacologic interventions should be administered to at-risk older adults to prevent delirium; (2) ongoing educational programs regarding delirium are important; (3) medical evaluation should be performed to identify and manage underlying contributors to delirium; (4) pain management (preferably with nonopioid medications) should be optimized to prevent post-operative delirium; and (5) Antipsychotics (e.g., haloperidol, risperidone, olanzapine, quetiapine, or ziprasidone) may be considered, at the lowest effective dose for the shortest possible duration to treat delirious patients who are severely agitated or distressed or who are threatening substantial harm to self and/or others [14].

Previous studies have shown that about 30–40% of delirium is preventable. This understanding is important to a surgical team. The Hospital Elder Life Program (HELP) is an evidence-based medicine program designed to decrease delirium and functional decline in hospitalized older adults. This program is essentially a prevention strategy. The premise of this program is to identify vulnerable older adults with certain risk factors and to deploy delirium prevention strategies.

Dementia

Dementia is a chronic and progressive decline in one or more cognitive domains (learning, memory, complex attention, language, visual-spatial skills, executive function) sufficient to affect daily life. Alzheimer's disease (AD) is the most prevalent cause of dementia (50–75%). Other common types of dementia include vascular dementia (20–30%), dementia with Lewy bodies (10–25%), Parkinson dementia, frontotemporal dementia (10–15%), and mixed dementia [18, 19].

Behavioral and Psychological Symptoms of Dementia (BPSD) is common as dementia progresses [20]. BPSD is present in approximately 60% of community dwelling patients and 80% in long-term care facility residents. Hence, many of the older patients who receive care on hospital surgical units have co-morbid dementia.

In the inpatient setting, it can be difficult to clearly differentiate dementia, delirium, and BPSD. Careful assessment, including obtaining baseline information from the family or the long-term care facility, is important to be able to discern these geriatric syndromes (Table 2) [31]. When evaluating individuals with dementia, it is important to identify reversible or treatable medical conditions such as depression, hypothyroidism, or vitamin B12 deficiency. The Mini-Cog screening tool helps the clinician define those who have cognitive impairment. This five-question screen uses three questions of short term recall and two questions posed to have the older patient draw the face of a clock and place the hands to depict a time (e.g., "ten minutes past ten"). Further assessment tools include the Mini-Mental State Examination (MMSE) or similar more detailed tools, which can assist clinicians to determine changes in cognition over time. The key point is to carefully follow up these patients after their hospital assessments to

Table 2 Discerning dementia from delirium and delirium superimposed on dementia

Features	Dementia	Delirium	Delirium superimposed on dementia
Onset	Insidious	Acute	Abrupt/acute
Course	Gradual deterioration	Fluctuating	Fluctuating
Awareness	Affected in late stages	Impaired	Severely impaired
Attention	Affected in late stages	Disturbed	Disturbed
Memory	Port short-term memory	Affected immediate recall	Impairment in multiple cognitive domains
Delusion	Fixed	Short in duration	Varies
Sleep disturbances	Sleep-wake reversal	Fragmented sleep	Fragmented sleep
Chronic cognitive symptoms	Yes	No	Yes

define if there cognitive assessments improve over time. Physical and neurologic examinations along with functional assessment are important steps in the initial evaluation of dementia. Neuroimaging is warranted in most all cases, especially those with unexplained focal neurologic signs or symptoms. Neuroimaging is particularly deemed necessary in cases of early onset dementia or an abrupt onset or rapid decline in cognition.

The primary goal of treating individuals with dementia is to improve quality of life, maximize function, and improve cognition, optimize mood, and address behavioral challenges. Supporting the family caregiver is likewise essential when delineating a treatment plan for older persons with dementia. Medications used to treat those with dementia (e.g., donepezil, rivastigmine, memantine) have demonstrated to slow cognitive decline and improve quality of life. These medications should be promptly resumed in the older surgical patient.

Recent efforts have been made to improve the management of behavioral and psychological symptoms of dementia (e.g., delusions, visual hallucinations, auditory hallucinations, agitation, irritability, wandering, psychomotor hyperactivity) because in unique situations, antipsychotics are prescribed to manage behavioral disturbances. The United Kingdom's National Institute for Health and Care Excellence (NICE), the American Psychiatry Association, and the American Geriatrics Society all recommend non-pharmacologic behavioral strategies as a first line strategy to manage BSPD.

Pharmacologic treatment of BPSD is considered as adjuvant in certain situations such as depressed mood, anxiety during times of transition, psychosis with potential for self-harm or others [20].

Nonpharmacologic strategies focus on addressing unmet needs like fear, hunger, toilet needs, sensory deficits, and improving communication (e.g., use a calm voice, limit choice, and keep interactions simple). In patients with a history of dementia or cognitive impairment, it is important to determine if the patient has the capacity to make medical decisions. Awareness of the patient's ability to understand information is important when obtaining consent for upcoming procedures. Physicians should assess patient's ability to understand information about treatment, their ability to appreciate how that information applies to their situation, their ability to reason with that information, and their ability to make a choice and express it [21].

Depression

Depression is common in older adults, often under-diagnosed and undertreated. Older adults may complain of lack of energy or pleasure and mistakenly attribute this to concurrent medical conditions. Older patients will neglect to mention such symptoms to healthcare professionals.

Older adults with depression are at an increased risk of functional impairment. Depression can precede cognitive impairment and malnutrition. It increases morbidity and mortality in medical conditions including cancer, diabetes stroke, and myocardial infarction. When depression is suspected in older adults, consider screening with patient health questionnaire (PHQ-2). Those older patients with a positive screen should be assessed by a behavioral health liaison to further evaluate and address their needs.

The DSM-V criteria for major depressive disorder indicate that five or more of the following criteria have to be present during the same 2-week period and represent change from previous functioning, at least one of the symptoms is ether depressed mood or loss of interest. Symptoms are not a direct result of a medical condition. The criteria includes: depressed mood, loss of interest, weight loss, decrease or increase in appetite, insomnia or excessive sleeping, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness, diminished ability to think or concentrate, and recurrent thoughts of death or suicidal ideation [22].

SSRI antidepressants are usually the first-line agents for the treatment of depression in older adults. Follow-up of the patient for hyponatremia is a part of standard care. Treatment with antidepressant should be continued for at least 6–12 months after remission. Counseling and support is also an effective treatment strategy, alone or in combination with medication management. If remission is not achieved with a first agent, consider switching to a different SSRI or a second-line agent (mirtazapine, duloxetine) or psychiatric consult might be needed. Clinicians should be cautious when combining antidepressants to prevent potential adverse effects.

Falls

Falls are the leading cause of unintentional injury and death in the older adult. Falls are a common problem for older adults. Approximately 30% of people aged 65 and older, and 50% of those aged 80 and older, have fallen at least once during the prior year [23]. Almost a third of older adults who fall experience an injury and some of the consequences of falls can be catastrophic. Accidental and incidental injuries are the fifth leading cause of death in older adults and falls comprise two-thirds of those events. Half of all older adults hospitalized for hip fracture never return to prior level of functional mobility [24]. The best screen for falls in older patients is to simply ask the individual: "Have you fallen in the past year?" The best screening examination tool for assessing ambulatory older patients is the Timed Up and Go Test. Falls in older adults are often multifactorial and are the result of a complex interaction of predisposing factors and precipitating factors. Multiple causes can lead to falls in older adults: for example, poor balance, weakness, sensory impairment, cognitive impairment, and multiple comorbidities. The interaction of these factors with polypharmacy (benzodiazepines, antipsychotics, antihypertensive medications, and skeletal muscle relaxants) and environmental factors can increase vulnerability and hence increase risk of falls in older adults.

Assessment of older patients with history of falls is very important and includes an evaluation of functional gait, balance, and mobility assessment. Assessing risk for falls is key in the acute care setting and usually requires an interdisciplinary approach, (physical therapist, occupational therapist, physicians, nurses, and pharmacist).

Simplifying psychotropic medications is important. Also the clinician must optimize medical treatment of the patients' chronic illnesses like Parkinson's disease, depression, dementia, and orthostatic hypotension. Addressing multiple risk factors by using an interdisciplinary approach is the key message in preventing falls. Other strategies that can assist to improve the risk for falls includes: balance and exercise programs, vitamin D supplementation, home safety evaluations (e.g., lighting, flooring, home adaptive equipment), encouraging the use of ambulatory assistive devices, and treating sensory impairments. Evidence-based falls prevention programs can help as well.

Hearing Impairment

Hearing impairment is common in older adults and increases with advancing age. The consequences of hearing loss in older adults may include: depression, social withdrawal, and decreased quality of life. Hearing impairment is classified as conductive hearing loss, sensorineural hearing loss, retro-cochlear, and mixed hearing loss [25]. Simple whisper test seems to be a clinically feasible screen for busy clinicians. Audiometry assessment can determine the severity of hearing loss as well as the type of impairment.

Mixed hearing disorders are common in older persons. Presbycusis affects about 30–50% of older adults. Some of these individuals have a combined cause of hearing impairment with conductive hearing loss, such as cerumen impaction. The surgical team should be aware of hearing impairment in the context of their instructions during the perioperative care of vulnerable older patients. Voice amplifier devices can help those with hearing impairment in the setting of a hospital nursing unit and in a specialists' office. These inexpensive devices should be a part of the standard tools which a surgical team can use to improve communication with older patients.

Visual Impairment

Visual loss is common in older adults. The Snellen acuity test is the most appropriate screen. The most common causes of visual impairment in an elderly person are: age-related cataracts, age-related macular degeneration, glaucoma, and diabetic retinopathy. Of all persons aged 75 years and over, 52% have advanced cataracts, 25% have nonexudative ARMD, 5% have exudative ARMD, and 2% to 10% have glaucoma [26].

Visual loss is often associated with morbidity in older adults: increase physical dependence, increased risk for falls, depression, and anxiety. Visual impairment may also worsen dementia and has been noted as a predisposing risk for delirium. Visual loss can significantly impact a patient's ability to drive. This fact highlights the importance of appropriate screening and eye evaluation of older adults. Approximately 40% of blindness among elderly persons is either treatable or preventable [26]. A vision assessment is a component of the "Welcome to Medicare examination." Further screening is covered for those at high risk of glaucoma. A full eye exam annually is recommended for people with diabetes mellitus and retinopathy.

It is extremely important for older adults with visual impairment to restore function and maintain independence. Early intervention and visual rehabilitation give this vulnerable population the skills and resources to minimize the effect of this disability. The older surgical patient with serious vision impairment should be seen by an occupational therapist to assure that the patient has a care plan which takes into account her/his needs.

Urinary Incontinence

Urinary incontinence is a common disorder among older adults. The prevalence of urinary incontinence increases with age in both men and woman. UI is defined as the involuntary leakage of urine and like other geriatric syndromes it is multifactorial. Acute UI is may be caused by a number of factors: neurologic conditions, fecal impaction, delirium, or polypharmacy [27].

Chronic urinary incontinence includes stress incontinence, urge incontinence, overflow incontinence, functional incontinence, and mixed patterns. Stress incontinence is caused by a decrease in outlet resistance (urethral hypermobility, intrinsic sphincter dysfunction). Episodes of incontinence may occur with increased intra-abdominal pressure (such as coughing, sneezing, and laughing). Urge incontinence is often associated with neurological disorders and is caused by overactivity of the detrusor muscles in the bladder wall, giving the sensation of urgency and urinary leakage. Overflow incontinence is the inability to completely empty the bladder caused by poor detrusor contractility. This type of incontinence may be associated to diabetes mellitus and some other neurological disorders. A common form of incontinence in frail older adults is the combination of urge and overflow incontinence. Functional incontinence refers to the loss of independent urinary control caused by diminished mobility or cognition. A careful detailed history and evaluation is key to evaluate patients with urinary incontinence.

The following are approaches that have been developed to address urinary incontinence. Behavioral therapies such us scheduled voiding and urge suppression approach are usually the first line of treatment for older adults. Pharmacotherapy has shown efficacy in treating urinary incontinence and they are widely used to treat urge incontinence or mixed incontinence (oxybutynin, tolterodine, mirabegron). These medications are associated with important side effects in older adults; hence, the clinician is encouraged to start a care plan with nonpharmacological strategies. Surgical therapy could be considered for those patients with stress UI that do not respond to other therapies. However, in those frail older adults with multiple comorbidities, surgery may impose a significant risk. Management of UI should focus on conservative therapy with a combination of behavioral therapies, pharmacotherapy, and supportive care (pads and protective garments) [22, 27]. Urine incontinence in the setting of surgical care requires a thoughtful evaluation in the context of the injury and surgical procedures.

Sleep Disorders

Sleep disorders are common in older adults. Sleep disturbances in older adults are the result of the interaction of multiple factors such as psychological and medical comorbidities. Patients with sleep disorders are more likely to develop hypertension, depression, and cardiovascular and cerebrovascular disease. It is important that clinicians routinely ask about sleep and perform initial screenings that may prompt further history and blood work.

Sleep disorders in older adults can be categorized as insomnia, hypersomnia, and movement disorder. Insomnia is defined as difficulty falling asleep or staying asleep. Insomnia is prevalent in older adults and in a study, 42% of participants reported difficulty falling asleep and staying asleep. Insomnia in older adults is often associated with significant morbidity and mortality.

Medical conditions (including chronic pain, chronic obstructive pulmonary disease, congestive heart failure, enlarged prostate, and cerebrovascular disease) have been associated with sleep complaints and insomnia [29]. Medications such as serotonin reuptake inhibitors (SSRIs), beta-blockers, bronchodilators, or diuretics may exacerbate insomnia. Behavioral treatment should be the initial treatment in older adults. Behavioral treatment has shown to be effective in all age groups. Providing nonpharmacologic strategies, sleep education, and encouraging good sleep hygiene are interventions that are frequently included when managing insomnia in older adults. Combining behavioral and pharmacologic therapy may provide better outcomes. For the pharmacologic management of insomnia, non-benzodiazepines (eszopiclone and melatonin receptor agonist) are the safest and most efficacious drugs currently available [28].

Sleep apnea is a condition in which people stop breathing while asleep. There are two types of sleep: obstructive sleep apnea (OSA) and central sleep apnea. Obstructive sleep apnea in older adults occurs in up to 70% of men and 56% of woman. This condition is associated with heart failure, atrial fibrillation, and stroke. Often it is associated with history of hypothyroidism and may be more common in women. Obtaining a detailed history and performing a physical examination that focuses on upper airway, dental structure, and face skeletal structure is important when assessing patients with OSA. Polysomnography will confirm and will determine the severity of the apnea. A CPAP is the best approach and first line of treatment for most patients. General measures such as avoidance of alcohol, hypnotics, opiates, weight loss, and optimizing treatment of chronic diseases like heart failure should be part of the management of OSA.

Sleep-related movement disorder, also known as restless leg syndrome (RLS), is characterized by an unpleasant leg sensation that disrupts sleep. Patients usually report them as creepy-crawly, burning, itching, or painful sensation that will cause insomnia and daytime sleepiness. Certain medications, including tricyclic antidepressant, SSRIs, lithium, and dopamine antagonists, have been reported to exacerbate RLS. A physical examination is usually unremarkable and no specific laboratory tests are required to establish the diagnosis. Serum ferritin is recommended as a part of the assessment because iron deficiency is often associated with RLS. The first line of treatment for RLS is dopaminergic agents (such as ropinirole or pramipexole) are both FDA approved for RLS. Nonpharmacologic approaches are also described for the management of RLS. These approaches include stopping caffeine, stopping offending medications, education, smoking cessation, and exercise.

Conclusion

The biological changes and progression of common chronic illnesses in older adults create a diminished physiological reserve. This in turn results in a weak compensatory mechanism during stress, injury, and acute illness. The interaction of this vulnerability with multiple risk factors associated with age and the insults to multiple organ systems cause the geriatric syndromes.

creening and assessment of geriatric syndromes in older adults may lower perioperative complications and decrease adverse outcomes. Nursing screening tools can be integrated into the electronic health record to systematically detect older adults with geriatric syndromes. Geriatric syndromes are common in older surgical patients. Prevention is important. Early identification and management will improve the care of older adults and provide specific strategies to successfully reduce complications in the acute care setting and subsequently in postacute care setting.

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Part II

Preoperative Assessment

6 Patient-Centered Surgical Decision Making

Tyler R. Chesney and Margaret L. Schwarze

Contents

Abstract

Populations are aging, and older adults have an increasing need for high-quality surgical care. There are inherent complexities in caring for this group with altered risk and benefit profiles as well as different patient values and goals. Given higher rates of multimorbidity, frailty, and poorer overall prognosis, older patients are at greater risk of nonbeneficial or unwanted care. Surgical interventions can have unintended consequences and unwanted burdens including loss of function, reduced quality of life, multiple transitions of care, and postoperative suffering.

In this setting, standard informed consent is not enough. Decisions need to be made in the face of uncertainty with preference-sensitive choices and a need to avoid making assumptions about patients' goals. A patient-centered

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approach using shared decision making integrates patient preferences, values, and goals with their underlying health status to allow patients and their surgeon to make decisions together about treatment strategies. Many barriers exist to patient-centered decision making including system factors, patient and family factors, and standard communication practices including a focus on risk disclosure.

In this chapter, we provide an approach to patient-centered decision making in geriatric surgery. This includes setting the stage to contextualize the surgical diagnosis within the patient's overall prognosis. This requires acknowledging and addressing the uncertainty inherent in prognostic information and in the decisions that need to be made. Surgeons then identify at least two treatment alternatives and emphasize that a choice must be made together. These options may include surgery and no surgery options, medical options, or potentially time-limited trials. A multidisciplinary approach to developing and carrying out treatment options is certainly of great benefit. Information about the different treatment options and potential outcome states should be conveyed narratively to allow visualization of what the experience of various outcomes would be and what the trade-offs are rather than focusing on isolated risk disclosure. Patient's values and preferences must be elicited with care to focus on what is possible and acceptable rather than what is wished for in unrealistic terms. Finally, a surgeon must integrate all of this information to make a treatment recommendation and should demonstrate why the recommendation is being made and that this supports the patient's goals. Indeed, a patient-centered approach to decision making in geriatric surgery is paramount to high-quality care in this complex patient population.

Keywords

Patient centered · Decision making · Communication · Goal-concordance · Nonbeneficial care · Informed consent · Geriatric surgery · Older adult · Elderly

Introduction

With the aging of populations worldwide, the need for older adults to receive high-quality surgical care is increasing, and patient centeredness is a core aim for high-quality care [1]. Older adults have a high burden of surgical disease, and nearly 500,000 older Americans undergo high-risk surgery yearly [2–6]. While many patients experience symptom and survival benefit from surgical intervention, the potential for nonbeneficial care rises in the older population. Older patients can be at higher risk due to poorer underlying prognosis and higher rates of multimorbidity and frailty [7–10].

Indeed, surgical interventions can have unintended consequences and unwanted burdens. Older adults can be at increased risk of serious postoperative complications, reductions in quality of life, and loss of functional status and can experience multiple transitions of care, increased hospital admissions, unwanted interventions, and postoperative suffering [6, 11–15]. Furthermore, the outcomes of importance for older adults may be uniquely different than younger patients with more focus on maintenance of function, time with loved ones, and quality of life and less focus on life extension [16–19].

These factors highlight the added complexity inherent in surgical care and decision making for older adults who face surgical illness. For older adults facing a choice about treatments for a surgical disease, the decision-making paradigm is shifted based on alterations to anticipated benefits and risks as well as patients' preferences and values. While there are many pitfalls that can lead to nonbeneficial care, high-quality surgical care for older adults must incorporate a patient-centered approach to decision making [20]. In this chapter, we will describe how patient-centered decision making in surgery differs from the traditional informed consent process and why this approach is important in geriatric surgery, we will outline barriers to patient-centered decision making, and we will provide a framework for patient-centered decision making in geriatric surgery.

Clinical Vignette

A frail 79-year-old woman with severe emphysema, renal dysfunction, and coronary disease presented to the hospital with a tender aneurysm in her chest and abdomen that could potentially be treated with surgery. Because of her overall fragile health, the operation was very high risk. At best, it would also require prolonged treatment in the ICU and then ongoing care in a nursing home. The patient and surgeon discussed the serious risks of surgery: a 50% chance of kidney failure, a 75% chance of pulmonary failure, and a 50% chance of death. The patient chose to undergo the 10-h invasive procedure, which repaired her aneurysm. However, the patient's family asked her doctors to withdraw all life-supporting treatments just 1 day after her operation, as they recognized that she would not have wanted subsequent burdensome treatments in the ICU or spend the rest of her days in a nursing home.

For this patient, the surgeon complied with current practice standards by obtaining informed consent by accurately disclosing potential surgical risks and benefits plus an alternative nonoperative palliative strategy. Although the patient had an undeniable need for prolonged postoperative ICU care and long-term nursing home care, she was unaware of this information and unable to use it in her decision making. Tragically, the decision started her down a care trajectory she would have avoided had she been better informed. This situation may have been avoided with a patient-centered approach, rather than the traditional informed consent process.

What is Patient-Centered Decision Making?

Patient-centered care focuses on congruence with and responsiveness to patients wants, needs, values, and preferences and has been an aspirational driver of care since the 1960s, though it has more recently been characterized as a quality standard by the Institute of Medicine [1, 21–23]. A patient-centered approach has prompted evolutions in education, research, laws, patient-physician relationships, disclosure, and decision making [21]. For surgical decision making, a patient-centered approach places focus on a broader shared decision-making process than that encompassed in the traditional informed consent process alone. Figure 1 outlines the main components of informed consent and shared decision making along with potential outcomes of each approach.

Most patient-doctor decision making employed by surgeons is grounded by the informed consent process, which is an ethical and legal requirement for surgical treatment and is designed to support self-determination [23]. The informed consent process requires discussion of the nature, purpose, risks, and benefits of a proposed intervention as well as alternatives including consequences of no surgical treatment and must be followed by explicit agreement or refusal by the patient or patient's designated decision-maker [22].

Sadly, informed consent, at least in practice and to some degree in theory, falls short of the goals of patient-centered decision making. Informed consent can assume patients have bought into aggressive postoperative care for potential complications and create the appearance that alternatives to surgery are secondary rather than real options. Informed consent may be perfectly adequate when the patient's best interests and goals are obvious, for example, a young person with colon cancer. Yet, explanation of benefits, disclosure of risk, and noting alternatives (including no surgery) do little to engage the patient in a conversation about preferences, clarify goals, or deliberate about options. For a young person who is likely to do well with surgery and likely values life-prolonging interventions, risk disclosure and presumptions about goals are sufficient. But given the nature and complexity of surgical decision making for older patients, the informed consent approach is not enough. For decision making to be truly patient centered, surgeons need to move beyond the framework of informed consent and embrace shared decision making.

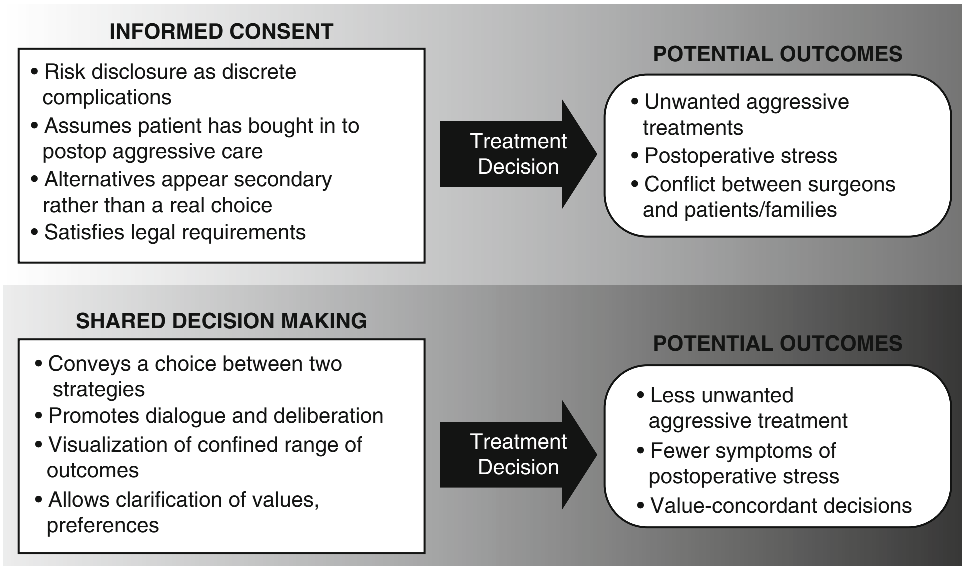

Fig. 1 The main components of informed consent and shared decision making with potential outcomes of each approach

At its heart, shared decision making posits that both surgeon and patient have important information to contribute to the decision-making process [22, 24]. The surgeon has information about outcomes and options, while the patient has knowledge about his/her personal values and goals [25]. For a decision to truly reflect a patient's autonomous wishes, an exchange of knowledge from both sides needs to occur. Thus, shared decision making is a process of information exchange between patient and doctor that leads to a decision, typically a treatment recommendation, which is well aligned with the patient's goals.

As a whole, shared decision making encompasses several components. A choice between at least two treatment strategies is conveyed. A range of outcomes are discussed narratively to allow a visualization of various potential outcome states. Dialogue and deliberation as well as clarification of values and preferences are promoted. Finally, a recommendation for treatment that matches these goals and preferences is made. For many surgical decisions, and certainly for decisions with most geriatric surgical patients, shared decision making is required if the surgeon aims to provide goal-concordant care and support patient autonomy.

Shared decision making is ideal in the setting of high uncertainty or when the outcomes are preference sensitive [22]. Some prototypical examples where shared decision making is required include decision making about prostate cancer (e.g., deciding between surgery, radiotherapy, or active surveillance) or breast cancer treatment (e.g., breast-conserving surgery with radiotherapy or mastectomy). Similarly, decisions about major operations for older patients require a clear evaluation and discussion of the outcomes of both operative and nonoperative treatment options as such interventions may not confer a survival advantage or could significantly change the patient's overall quality of life. Indeed, for older patients, understanding the trade-offs in decision making is essential [26]. Understanding how patients might value these important trade-offs is essential to providing goal-concordant care.

In geriatric surgery, shared decision making may also be important even when there is less uncertainty and more clarity about what surgeons would typically consider to be the "right" treatment in younger patients [16]. Returning to our example of colon cancer for which there are strong notions that cure-driven treatment (surgery) should be employed, this assumption may not hold for a frail older person with dementia and very poor quality of life. Consideration of a comfort-focused strategy in contrast to a survival-focused strategy using the process of shared decision making will help to identify patients for whom an operative intervention will not achieve their goals. Surgical treatment for colon cancer may not actually prolong life in this setting or even ameliorate symptoms. Consideration of the outcomes of treatment and how these outcomes are valued by the patient and family is required to determine the "right" treatment course.

Some patients or their decision-makers may report they want their surgeon to simply do what is best. Many surgeons will find this distressing particularly when the decision is highly preference sensitive or there is "no good option." This is challenging because many surgeons will want to be sure to respect patient autonomy and also have confidence that the patient and family are on board with the treatment plan. Yet the surgeon can assist such patients without fearing paternalism or making the wrong choice for the patient. Shared decision making does not require the patient to decide what to do or even express preferences for a particular treatment. Shared decision making requires that the surgeon learns about what is important to the patient – what the patient hopes for and fears – enough to recommend and support a treatment option that most reflects the patient's goals. Shared decision making helps surgeons figure out "what is best" without abandoning patients to their own autonomy.

Barriers to Patient-Centered Decision Making

Decision making about high-risk surgery is inadequately supported by current communication practices, and there are many barriers to using a patient-centered approach to decision making [27]. A recent Institute of Medicine report noted that although most patients prefer to share in decision making, "they are often not afforded the chance to participate" [28]. Other studies reveal that surgeons rarely employ a cooperative decision-making process, and systematic reviews evaluating informed consent demonstrate a need for improvement in this process which does not meet patients' informational and decisional needs [29–33]. Significant geographic variation in the volume of high-risk surgical treatments suggests clinical uncertainty among surgeons about optimal treatment strategies, further necessitating patient engagement in these high-stakes decisions [6, 34]. These conversations are challenging as surgeons work hard to inform patients about the intricacies of a highly technical procedure, worry about burdening patients with fear of possible complications, and are bound by the structure and language of informed consent.

In observational studies of preoperative decision making, surgeons routinely satisfy the legal requirements of informed consent, yet they do not provide patients the opportunity or the type of information they need to meaningfully participate in decision making [30, 35, 36]. These preoperative conversations follow a robust and consistent pattern which presents opportunities to improve and provide more patient-centered decision making (Fig. 2).

First, there is an explanatory phase that surgeons use to describe the patient's disease and treatment. They describe the patient's disease as an acute abnormality (a valve that is loose, an artery that is blocked, a tumor that is abnormal) and tell how surgery can "fix it" (tighten the valve,

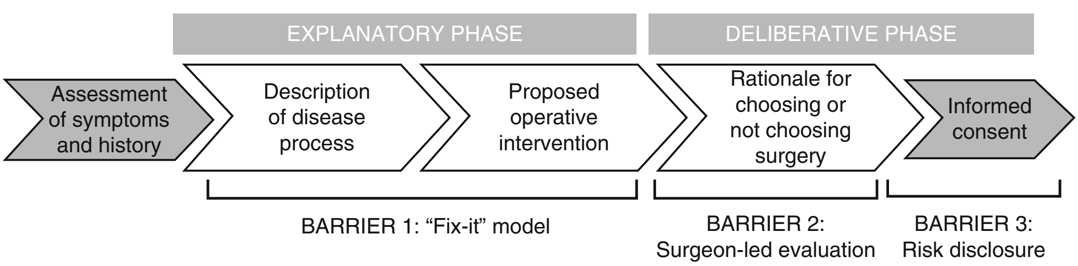

Fig. 2 The structure of usual preoperative conversations and the barriers to patient-centered decision making within them

go around the blockage, remove the tumor) [30]. This model supports an implicit message about the "benefits" of surgery: the reason to operate is to fix what has been identified as broken, and after the problem is "fixed," the patient will return to "normal." The "fix-it" model lacks an explicit description about what surgery might mean more broadly for the patient, for example, whether he or she will feel better or live longer, how surgery will affect other health problems, or what daily life might look like after surgery. Although many surgeons stress that "fix-it" is an overly simplified rationale for surgery, the surgeon's explanation about how disease is "fixed" with surgery makes it hard for patients to understand the need to deliberate about whether surgery is right for them.

Next, surgeons present their own evaluation of the trade-offs and goals of the proposed intervention during the deliberative phase. Although this deliberation occurs in front of patients and families, assumptions about the value of specific outcomes are surgeon-generated and not specifically connected to patient preferences. Typically, surgeons name risks and describe trade-offs, but they struggle to elicit patient preferences. Although surgeons encourage patients to ask questions, the invitation is ineffective as patients regularly respond with logistical or technical concerns. For example [30]:

> Surgeon: *This is an area for vision, smell, for function of legs and bladder. You could even have a stroke...or damage to the vision. You could have an infection or trouble with the healing. . .What questions do you have for me?*
>
> Patient: *Washing my hair was one.*
>
> Surgeon: *I want you to wash your hair with baby shampoo on the third day...Don't scrub the stitches.*
>
> Family: *Stitches or staples?*

Other logistic concerns that patients pose during presentation of surgical risk include the length of the operation, the date or the time of day of surgery, where to go for testing, the need to travel to and from the hospital, the ability to wear pajamas, and rules about visiting hours. While technical and logistic concerns are important to patients, this process does little to inform or engage patients in a discussion about what surgery might mean for them or set expectations for what life might be like after surgery.

Finally, informed consent requires surgeons to disclose risk, but this does not adequately inform patients about possible outcomes. Much attention is paid in the surgical literature to precise risk prediction, which characterizes the overall hazards of surgery as discrete complications for isolated physiologic systems (e.g., a 50% chance of kidney failure) [37–39]. Surgeons use this information to help patients make decisions about whether to have surgery, but they focus on objective quantification and physiologic risk disclosure without describing outcomes in a way that is relevant to patients and families [40]. Although surgeons make significant effort to describe the gravity of surgery, they are often surprised when patients have unrealistic postoperative expectations or have not bought in to the use of prolonged life support [41].

In addition to these communication practices and patterns, there are myriad systems and patient/family factors that add to the challenges of patient-centered decision making (Fig. 3) [20]. The patient-surgeon relationship is often encumbered by the acute nature of surgical illness or lack of a preexisting relationship. While surgeons are typically quite adept at overcoming these challenges, generating trust and attending to the emotional nature of serious illness can be undermined by this lack of preexisting relationship. Furthermore, while many patients live with chronic life-limiting illnesses, their understanding of the impact of these illnesses on their overall health trajectory is often limited. An acute event such as a traumatic injury, abdominal sepsis, or new cancer diagnosis may be very difficult for patients and families to contextualize within the patient's beliefs about their longer-term survival. Finally, while there are many efforts to improve advance care planning, the uptake of such interventions is low [42–44]. Few patients and family members have had conversations among themselves or with their primary care provider to clarify and document goals and values. While surgeons are increasingly asked to navigate this difficult territory with patients, there are few, if any, adjuncts to assist in bridging the gap between unarticulated goals and acute treatment decision making.

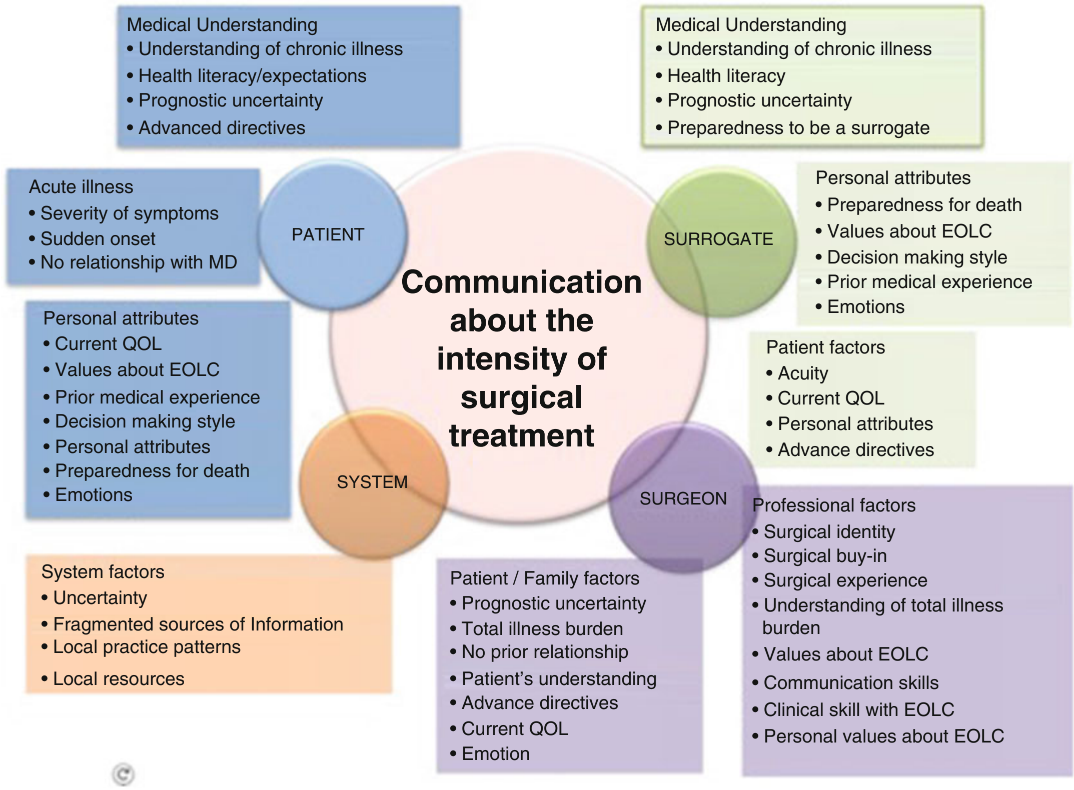

Fig. 3 Factor that may act as barriers to patient-centered communication and lead to nonbeneficial or unwanted care (From Cooper et al. [20])

Indeed, there are implicit advantages to a patient-centered approach to decision making in geriatric surgery given the complexities, uncertainties, and high risk in this population. Nevertheless, there are many barriers to the use of a patient-centered approach including traditional communication practices and training as well as system and patient factors.

Approach to Patient-Centered Decision Making in Geriatric Surgery

To assist in overcoming some of these barriers and promote a patient-centered approach, we propose the following framework for patient-centered decision making in geriatric surgery. This approach combines best practice recommendations as described by Cooper et al. and the domains of shared decision making as codified by Elwyn et al. [45, 46].

Approach to Patient-Centered Decision Making in Geriatric Surgery

1. Set the stage by contextualizing the decision with respect to the patient's overall prognosis, and address the problem of uncertainty.
2. Identify more than one treatment option and the need to make a decision together.
3. Describe the treatment options (at least two treatment strategies with the advantages and disadvantages of each).
4. Elicit patient values and goals.
5. Make a recommendation corresponding to patient values and goals

Setting the Stage: Conveying Overall Prognosis and the Problem of Uncertainty

Many acute surgical decisions are linked to life-changing illnesses. This is particularly true for older patients. Surgeons routinely describe the gravity of the patient's illness, noting treatment might require "big surgery," but often fail to clarify the patient's overall prognosis or how the patient's other illnesses, frailty, or functional status impact the overall outcome of treatment [35]. Without this type of information, patients and families will find it difficult to contextualize treatment options and the relevance of various outcomes and to consider nonsurgical options when this might truly be aligned with their goals [47, 48]. For example, a frail elderly woman might consider undergoing a colectomy if she believes her long-term prognosis is more than 2 years, but she might prefer comfort-focused care if she understood her survival is closer to 6 months due to a constellation of illnesses.

Despite the importance of an understanding of overall prognosis, surgeons may find it difficult to discuss or even raise the topic of overall prognosis because it seems alarming to patients or families [47]. Furthermore, surgeons may feel ill-equipped to estimate overall prognosis or worry about getting it wrong. There are a range of non-disease-specific prognostic indices specifically designed for older adults with multimorbidity [7]. These may be added to clinician judgement and offer a reasonable method to calibrate prognostic estimations. Nevertheless, prognostic estimation is rife with uncertainty [49]. This uncertainty can be uncomfortable and emotionally difficult for surgeons and patients alike. This uncertainty should be acknowledged directly, first by normalizing the uncertainty of prognosis and then attending to the emotional impact of experiencing an uncertain future [49]. Normalizing statements such as "while I wish I could be more certain, like predicting the weather, despite all of our tools, we can never be absolutely certain about the future" can help patients understand that precise prognostication is allusive [49]. We then must acknowledge the emotional experience of uncertainty and help patients focus on making the most of the time they have now with statements like "it is tough not knowing what the future will bring" and "what can we do to help you now, given that we are unsure of exactly what the future will bring" [49].

Most older patients do wish to communicate about prognosis [50]. Evaluating how much explicit information a patient or family wishes to hear can be done by asking a question like "how much do you want to know about the likely course of this illness?" [48]. Even for patients who initially do not want explicit information, there is much that can be done to explore the informational and emotional aspects of this wish [51]. Surgeons often embed prognostic information within their discussion of surgical outcomes: "she may not make it through the operation." Yet, this fails to signal that with or without surgery, this frail 92-year-old woman with colon cancer has life-limiting problems. One strategy to ensure patients and family members have received a signal that the patient's illness is grave is what palliative care physicians often describe as "the shot across the bow." Using phrases, such as "I'm afraid this problem is bad news," at the start of the decision-making conversation can help orient patients and families to trouble ahead and allow them to consider alternative, potentially less invasive strategies, as they understand the implications of their illness.

Identify More than One Treatment Option and the Need to Work Together to Make a Decision

In order to make a preference-sensitive, goal-concordant decision, there must be a choice between at least two options. While many patients struggle to choose between more than two options, at a minimum there must be two different treatment strategies. In surgery, these options are not particularly difficult to generate as there is nearly always a choice between having an operation and not having an operation. Yet sometimes there is a middle ground between surgery and no surgery allowing the patient and family to consider a medical-based intervention.

Another treatment strategy to propose is that of a time-limited trial. Due to the uncertainty outlined above, patients may not want to prematurely forgo treatments that might help, but they do not want to embark on a prolonged trajectory of suffering if things do not go as hoped [52]. A time-limited trial is an agreement between clinicians and a patient or family to use certain interventions, such as surgery followed by ICU care, over a defined period to see if a patient improves or deteriorates [52]. If the patient improves, this treatment strategy is continued; if the patient deteriorates, then the time-trialed treatments are ended and usually a more comfort-based approach is pursued. In this agreement, it is imperative that the time frame, markers for improvement or deterioration, and acceptable actions are agreed upon upfront, and these can be revisited and renegotiated as time passes [53].

By starting a conversation with a statement like "today we have a choice to make...," surgeons can avoid the typical pattern that starts with the surgical problem and the operation to "fix it." Furthermore, noting a patient-doctor partnership by highlighting that the decision needs to be made together can foreshadow the shared aspect of this decision and encourage patient and family participation. Given the complexity of these care needs and this decision making, a multidisciplinary approach to developing and carrying out treatment options is certainly of great benefit [18]. This may include surgical, anesthesia, and geriatric specialists, as well as nursing, physical and occupational therapy, social work, and other disciplines as appropriate.

Describe the Treatment Options

Each treatment option needs to be identified and described noting how the patient might experience each treatment including time in the hospital and recovery. Patients should have some notion about what to expect postoperatively. In addition, the pros and cons of each treatment should be described. Some might conceive of these aspects as risks and benefits, while others might support a discussion of possible outcomes and the trade-offs faced along the way. Ultimately, the patient needs to understand the consequences of each treatment and the degree of uncertainty related to both harms and benefits. When conveying information about various treatment options, as opposed to simply disclosing organ-based and isolated risk estimates, the use of narrative can facilitate conveying the experience of the various potential outcome states following different treatment choices [54].

This contextualizing information allows patients to visualize what it may be like to experience different outcomes and should incorporate the patient's underlying health as described in step 1. This step should aim to acknowledge that unwanted postoperative outcomes typically do not occur in isolation, particularly in older and more vulnerable patients, but instead often cluster together [55]. An initial postoperative complication can lead to a trajectory of further invasive investigations and treatments, prolonged hospitalization, disrupted or prolonged functional recovery, transitions in care, and poorer quality of life and survival [55–58]. Further, there can be a misunderstanding that with a surgical option, the worst outcome is intraoperative death which can be perceived as painless, but this fails to illustrate the more common situation leading to mortality that includes prolonged and aggressive ICU care, further invasive treatments, ongoing complications and declines, and a prolongation of suffering ultimately leading to death without the benefit of engaging with loved ones [59]. Additionally, instead of presenting two treatment options as recommended here, presenting surgery as the primary treatment option and other nonsurgical options as secondary limits discussion of the benefits of comfort-focused options such as time with loved ones, engagement with one's spiritual traditions is applicable, and reductions of suffering [40, 54].

Elicit Patient Values and Goals

This step seems easy, but it is actually the most difficult. Many surgeons will present a range of options and subsequently ask the patient, "what do you want?". In turn, the patient will often respond with a specific treatment preference [60]. Sadly, such information fails to illuminate what is important to the patient about the chosen treatment or reassure the surgeon that the patient's goal for surgery is a possible outcome of surgical intervention. Some patients will respond by saying, "I just want to survive." In turn the surgeon will assume the patient wants to proceed with surgical intervention. While such a decision may or may not be goal concordant, without a follow-up question about what it means to survive (e.g., go home, prolong life for as long as possible even on life-supporting interventions), the surgeon has learned very little about what is important to the patient.

Instead of questions like "what do you want?" or "do you want everything done?" to elicit values and goals, surgeons might consider "how are you thinking about this?", "what are you hoping for?", and "what do you fear?" [60–63]. Indeed, patients want to be well and at home living comfortably, but this does not help to elucidate which treatment option would most align with their goals [60]. Likewise, doing everything has many meanings; assumptions about what this means can lead to nonbeneficial and goal-discordant treatment efforts when these efforts should focus instead on what is possible and how can a patient's goals be achieved within the limits of what is possible [62]. Access to this type of information about how patients appraise specific outcomes or view the burdensome treatments required to get there is critical to ensure the chosen treatment strategy reflects the patient's values and goals.

Make a Recommendation

While eliciting values and goals takes real skill, surgeons may stumble on the step of making a recommendation for fear of being paternalistic. Some surgeons say, "my job is to tell them the options, their job is to choose" [59]. Yet this notion does not support the ideals of relational autonomy inherent in shared decision making. Patients seek out physicians' expert opinion in the same way customers seek advice from car mechanics or financial planners. Part of the presumption of these professional relationships is that the professional will guide the patient or client to an appropriate choice. Failure to make a recommendation and show how such a recommendation supports the patient's goals is abandonment of a professional duty to assist the patient.

Some patients will ask, "what would you do if I were your father?". These patients are asking for a recommendation. An appropriate response to this is not "I don't know, you aren't my father," but rather "it sounds like you are asking for a recommendation." Once the patient or family confirms this is the case, the surgeon should either make a recommendation if confident that the patient's goals and values are understood or say, "I would like to make a recommendation, but first I need to know a bit more about what is important to you." After using the techniques described in step 4, the surgeon can, with confidence, recommend a treatment strategy while revealing to the patient that this strategy supports the patient's goals. By "showing your work," the surgeon avoids a paternalistic stance and confirms that the treatment plan is goal concordant.

Conclusion

There is a growing number of older adults with a need for high-quality surgical care, and the inherent complexities in caring for this group require a patient-centered approach to decision making as there are altered risks and benefits as well as different patient values and goals in this population. Older patients are at greater risk of nonbeneficial or unwanted care given higher rates of multimorbidity, frailty, and poor overall prognosis. Standard informed consent is not enough in this setting given uncertainty, preference-sensitive choices, and the need to avoid making assumptions about patients' goals. A patient-centered approach using shared decision making integrates patient preferences, values, and goals with their underlying health status to allow patients and their surgeon to make decisions together about treatment strategies. Many barriers exist to patient-centered decision making including system factors, patient and family factors, and standard communication practices including a “fix-it” model, surgeon-led deliberation, and a focus on risk disclosure.

There is a better way to approach to patient-centered decision making in geriatric surgery. This includes setting the stage to contextualize the surgical diagnosis with an understanding of the patient’s overall prognosis, while acknowledging and addressing the uncertainty inherent in this type of information and the decisions that need to be made. Surgeons must then identify at least two treatment alternatives and emphasize that a choice must be made together. These options may include surgery and no surgery options, medical options, or potentially time-limited trials. Information about the different treatment options and potential outcome states should be conveyed narratively to allow visualization of what the experience of various outcomes would be and what the trade-offs are. Patient’s values and preferences must be carefully elicited with caution about what is possible and acceptable rather than what is wished for in unrealistic terms. Finally, a surgeon must integrate all of this information to make a treatment recommendation and should “show their work” to demonstrate why the recommendation is being made and that this supports the patient’s goals. Indeed, a patient-centered approach to decision making in geriatric surgery is paramount to high-quality care in this complex patient population.

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Frailty

7

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Contents

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Abstract

The US older population has been rapidly growing and will constitute a fifth of the total population by 2030. It is the fastest growing subset of the population. This rapid increase in the elderly population has a significant impact on the US healthcare system and, as a result, surgeons will frequently encounter senior patients who often present with unique diagnostic and therapeutic challenges. Aging patients have an increased risk of postoperative complications that result in disability, loss of functional independence, diminished quality of life, and death. Accordingly, the postoperative course of such a patient is of cardinal importance because it plays a critical role in determining recovery to complete functional independence. Increasing age and comorbidities also contribute to frailty, which is defined as a decreased physiological reserve and a decline in the resistance to stressors, which is independently associated with poor short- and long-term outcomes after surgery. Early identification of frail geriatric patients will help to identify those who require a more comprehensive and multidisciplinary approach, necessary to adequately address the significant differences in physiology and outcomes presented by this challenging group. The optimal goal for geriatric patients is not only to reduce mortality rates and complications after surgery, but to maintain and preserve a good quality of life after they are discharged, including increasing their ability to return to their preillness level of function and independence.

Keywords

Geriatric Surgery · Frailty · Sarcopenia · Frailty score · Frailty index · Aging

Introduction

In the USA, the geriatric population has significantly increased by 21% since 1980 [1]. This is due to aging Baby Boomers as well as increased life expectancy rooted in advances in the standard of living and medical health services. In the USA, those over the age of 65 now account for 14.5% (46.2 million) of the total population – by 2030, this percentage is expected to increase to approximately 20% (72.1 million) [2]. Indeed, geriatric people are the fastest growing subset of the total population. While the total US population has grown by 39% over the past 30 years, for instance, those segments older than 65 and 85 years have grown by almost 89% and 232%, respectively [1, 2].

Aging is a universal biologic process characterized by progressive physiologic and behavioral changes. Inevitably, the gradual accumulation of such transformations over time results in the decrement in performance and impairment of physiologic functions. This, in turn, leads to a diminished capacity to adapt as well as an increased vulnerability to disease and pathologic processes [3]. The rapid increase in the geriatric population has a significant impact on our health care system. It is imperative, therefore, that health care professionals integrate a solid understanding of the physiology of aging in their clinical practice. This is underscored by the increase in the number of older patients presenting to hospitals who require operative intervention. The aging population is, in fact, responsible for more than half of the total number of surgeries performed in the USA [3]. When surgeons operate on older, sicker patients, they are confronted with complex healthcare needs due to, for instance, one or more chronic conditions, polypharmacy, and, oftentimes, functional impairments.

In these typical circumstances, clues about a patient's physiologic reserve, his/her vulnerability to intraoperative or postoperative complications, and his/her short- and long-term prognoses are invaluable. This task is, however, complicated because the rate and the extent of decline in physiologic function among the aged is not uniform [3]. Consequently, regarding older surgical patients, it is challenging to predict who will have an optimal recovery and who will develop a complication that can trigger a cascade of events that may lead to unexpected mortality or permanent disability. The great heterogeneity among such patients is based on each individual's physiologic reserve, that is, the amalgamation of intrinsic host factors (such as age, sex, nutritional status, functional capacity, hormonal balance, and any preexisting medical conditions) that might increase one's morbidity and mortality after stressful events. This insight has given rise to the concept of "frailty," and its operational counterparts: "the frailty index" (FI) and "frailty scores" (FS).

In this chapter, we review the relevance of the concept of frailty in surgery, especially its role in identifying vulnerable surgical patients, improving patient care, and decreasing hospital costs. In addition, we simplify the concept of frailty and FI in order to expand its application.

What Is Frailty?

There is no consensus on a single, precise, and complete definition of frailty. Numerous authors and investigators offer multiple definitions based on their understanding and interpretation of the concept. From a clinical perspective, it can be defined as a syndrome of a decreased physiological reserve (physical and cognitive) and a decline in the resistance to stressors, which, ultimately, result in increased vulnerability to poor health outcomes, worsening mobility and disability, hospitalization, and death (Fig. 1) [4]. Alternatively, it is defined as a geriatric syndrome of increased vulnerability to environmental stressors with underlying inherent pathophysiological mechanisms related to hormonal changes as well as sarcopenia and nutritional deficiencies [5]. Multiple attempts have also been made to identify the different components and criteria for the diagnosis of frailty. Fried et al. defined frailty as the presence of three or more of the following: unintentional weight loss (10 lbs. in the past year), self-reported exhaustion, weakness (assessed by grip strength), slow walking speed, and low physical activity [5].

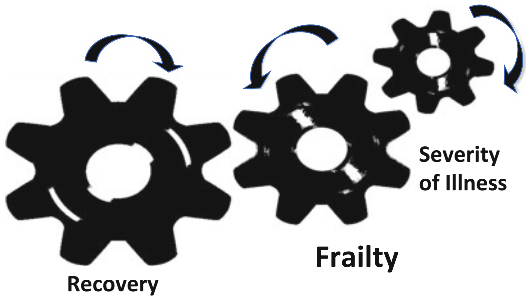

Fig. 1 Frailty "the Lethal Gear"

Somewhat differently, Rockwood and Mitnitski describe it as an accumulation of deficits (assessed via the Rockwood frailty index) that include weight loss; exhaustion or a low level of physical activity, weakness, a low energy and endurance level, and slowness [6, 7]. Clearly, these distinctive definitions of frailty (i.e., as a clinical syndrome, a phenotype, a biologic syndrome, or the accumulation of particular deficits) are the biggest barriers to a standardized application of the concept for surgical practice [8].

Limitations of Age (Superiority of Frailty Measurements)

It is also critical to distinguish between "age" and "frailty." The term "old" does not reflect a clear image of a patient's condition. It only refers to chronological age. Moreover, commonly used tools for the prediction of complications and risk adjustment cannot measure the physiologic reserve of elderly patients – they are mostly subjective and often limited to a single organ system [9]. Furthermore, these tools are rarely feasible in emergency situations because they require trained personnel and a patient's cooperation [10].

Clinically recognizable, frailty syndrome is an increased vulnerability resulting from the age-associated accumulation of deficits in multiple physiological systems, and it is worth highlighting that emerging literature suggests the superiority of frailty measurements over those based on chronological age in order to more accurately predict outcomes. The FI is well established within various disciplines of medicine as an effective assessment tool that is quickly evolving into an important component of the management of elderly surgical patients as well. It easily takes a patient's physiologic, cognitive, social, and psychological deficits into account and then translates them into a quantifiable variable. The FI is clearly superior to assessment techniques that can be cumbersome for emergency surgical patients, such as those based on physical movement and gait speed [11–13].

Pathophysiology

Frailty is also described as a phenotype of a complex proinflammatory condition or as a biologic syndrome occurring during the aging process that causes vulnerability to adverse outcomes [14]. Major factors, including genetic heritability, nutritional status, physical activity, atherosclerosis, hormones, insulin resistance, and pro-inflammatory cytokines, can lead to body compositional changes due to the loss of muscle mass and muscle strength as well as sarcopenia [15]. Likewise, a great deal of literature demonstrates the major impact of body fat on functional capacity in the elderly [16]. An increasing prevalence of high amounts of body fat, coupled with low skeletal muscle mass, is defined as sarcopenic obesity or obesity paradox, and it corresponds with a very high risk of decreased mobility in the elderly [17]. In addition, low-grade inflammation is strongly correlated with both sarcopenia and frailty. Studies on markers related to the inflammaging theory indicate that frail individuals have elevated levels of high sensitivity C-reactive protein (a soluble biomarker of inflammation) and other pro-coagulant factors. Patients with diabetes also have elevated levels of cytokines, such as tumor necrosis factor alpha and interleukin-6, which stimulate proteolysis and apoptosis in muscle cells. Furthermore, different studies show that an imbalance in hormones and nutrients is strongly related to a reduction in physiologic capacity and an increased susceptibility to disability [18, 19]. This includes an imbalance in the levels of anabolic hormones in men (testosterone, adrenal androgen, and growth hormone), an age-related decrease in sex hormones in women (including dehydroepiandrosterone sulfate, growth hormones, and IGF-1), and a loss of nutrients (such as vitamin D).

Sarcopenia: Two Sides of the Same Coin

Entailing a progressive decline in skeletal muscle mass and power, sarcopenia is one of the most serious consequences of the aging process. It accelerates after the age of 60 and, in most cases, leads to functional impairment. Sarcopenia is highly predictive of incident disability, poor quality of life, and all-cause mortality in older adults [14, 20]. Although it is a geriatric syndrome in its own right, it is the key feature of frailty (Fig. 2). As noted earlier, different operational definitions of frailty status exist side-by-side. Each one focuses on specific aspects of the syndrome and detects slightly different risk profiles. Nevertheless, there is an overall agreement about the key role that physical function plays in the determination of the status of extreme vulnerability. Following the Fried et al.'s widely used definition of frailty, a patient is assessed for unintended weight loss, exhaustion, weakness, slow gait speed, and low physical activity [21]. A diagnosis of frailty is supported when three of these features are present. Likewise, because weakness and a slow gait speed are a part of the operational definition of sarcopenia, one can safely posit that a frail individual is more likely to be sarcopenic and vice versa.

Sarcopenia, like many other age-related problems, is a multifactorial condition. Contributing factors include motor units, protein metabolism, hormones, and lifestyle. Properly understanding the impact of aging on the skeletal muscle requires attention to changes in both muscle size and muscle quality. This is particularly important when considering the potential effects of treatments, including improvements not only in muscle mass but also in function and physical performance. Sarcopenia is caused by the simultaneous

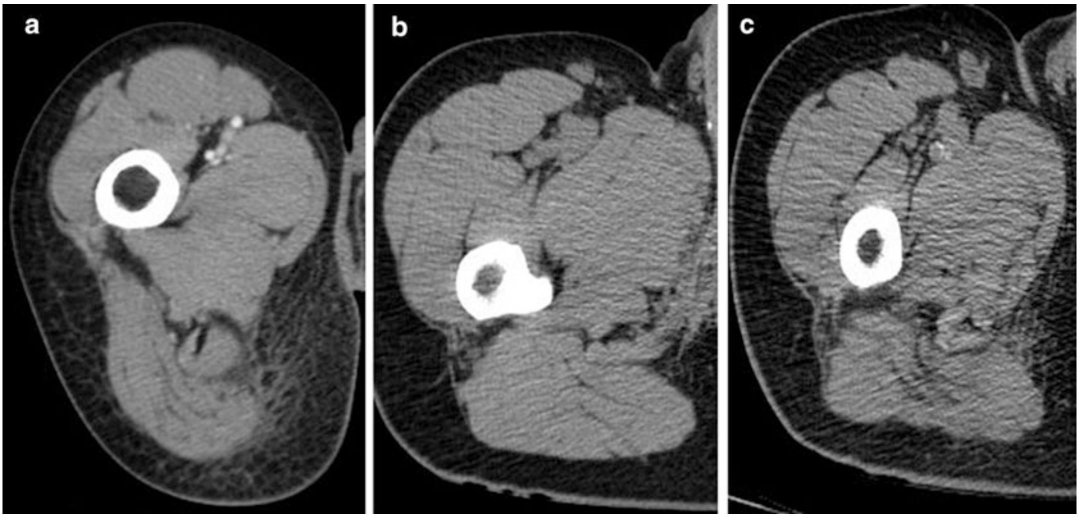

Fig. 2 CT thigh of 15 years' male (**a**) 30 years old male (**b**) and 65 years old (**c**) showing 40% lost in muscle mass in between ages 15 and 65

reduction in the number of muscle fibers and atrophy of remaining myocytes, likely due to a lower rate of myofibrillar protein synthesis and enhanced myonuclear elimination via an apoptosis-like mechanism. These findings reflect a progressive withdrawal of anabolism and an increased catabolism, along with reduced muscle regeneration capacity [22, 23]. Histological sections of aging muscle also show increased infiltration of noncontractile tissue (i.e., collagen and fat). Many factors are responsible for skeletal muscle decline: the aging process itself, genetic susceptibility, behavioral factors (e.g., less-than-optimal diet, prolonged bed rest, sedentary lifestyle), chronic health conditions, and certain drugs. Progressive muscle atrophy directly results in impaired mechanical muscle performance. Of particular importance, there is a nonlinear loss of maximum muscle strength, that is, the ability to produce muscular power is reduced even more than muscular strength [24].

Clinical Implementation of Frailty

Obviously, the usefulness of the concept of frailty in clinical practice necessitates the reliable identification of frailty in patients. Presently, the operational and practical application of the concept is captured via multiple scales composed of several variables. The FI and the FS are the most widely used.

Frailty Index

Identifying the number of health deficits of an individual forms the basis of an FI, which is calculated as a ratio of the total number of deficits (up to 70), as delineated by the Canadian Study of Health and Aging (CSHA), to the actual number of deficits present in an individual [25]. A few variables are dichotomized (yes/no) and the rest have multiple options. The variables include any comorbidity, a lessened ability to perform activities of daily living, a poor nutritional status, an impaired physical status, a lower level of cognition, and a more pessimistic health attitude in general. The greater the numbers of deficits equals a higher FI and, therefore, more extensive frailty. Of the 70 possible deficits delineated by the CSHA, at least 30 should be considered to correctly calculate an FI, which can then accurately predict worsening of health status, hospitalization, and death [6, 21]. Rockwood et al. [13] defined 0.12 as the median FI score for robust individuals, 0.30 for prefrail individuals, and a score greater than 0.40 for frail individuals [26]. Despite variable applications and methods for calculating an FI, it is a highly accurate and reliable way to describe the functional status of an individual.

Frailty Score

Fried et al. use the validated FS (ranging from 0 to 1). They defined an FS of greater than 0.20 as a cutoff-point between frail and robust individuals [21]. Quantification of frailty using the FS is based on five domains: weight loss (10 lbs. in the past year), reduced energy (self-reported exhaustion), reduced grip strength, slow walking speed (time per 15 ft.), and low physical activity (kcal/week). The FS is based on the ability of a patient to perform the activity in the five domains, and a score ranging from 0 to 1 (0 being least frail and 1 being frail) is given to each patient [21].

FI Versus FS

Clearly, a clinical implementation of frailty is impossible without a validated, operational definition [27]. While Fried's definition of frailty (based on the phenotype model) is widely used for research purposes, it can be impractical in clinical settings [27, 28]. In other words, a clinically usable definition of frailty that would allow physicians and surgeons to stratify their patients based on the risks for the treatment (e.g., operative intervention, angiography) is lacking. A wide variability in frailty assessment tools (i.e., FI and FS) makes a comparison of outcomes assessed by them difficult [29]. As a result, there are no studies comparing the FI and Fried's criteria of frailty. Though, a limitation of the FS is that it only focuses on five domains and fails to provide a complete assessment of the patient, which is provided by the FI. Clinical studies assessing frailty have commonly used the FI or a modified FI to predict adverse outcomes, including mortality, complications, and hospital length of stay (LOS), in geriatric patients. In contrast to Fried's phenotype assessment criteria (FS), we believe that the FI can be a reliable predictor of surgical outcomes.

Frailty and Kinesiology

Kinesiology, the scientific study of human movement, is increasingly used to assess the physiologic state of elderly individuals based on their velocity of movement. Alterations in body motion in the upper and lower extremity, for example, have been extensively studied in geriatric patients as a predictor of outcomes [30]. Similarly, assessment of impaired gait and balance by using lower-extremity motion sensors objectively define disease states and the risk of falls in such patients. However, the use of lower-extremity motion sensors is limited and cannot be used in physiologically compromised geriatric patients who are unable to perform gait and balance movements. Likewise, upper-extremity strength and range of motion decline with age, even though upper-extremity motion sensors are used to assess the speed and range of motion in older patients [31]. Studies do show an association between frailty evaluated via the FI or the FS and outcomes from motion sensors. Frailty algorithms use motion sensors to predict outcomes in geriatric patients, but the utility of these sensors in surgical patients to assess the risk of postoperative complications and discharge disposition is still unclear [31, 32].

Preoperative Assessment

A number of preoperative assessment tools, such as the American Society of Anesthesiology (ASA) score, Acute Physiology and Chronic Health Evaluation (APACHE) score, and the Physiologic and Operative Severity Score for the enumeration of Mortality and Morbidity (POSSUM) are used routinely, but each one has limitations. The ASA score is widely used because of its simplicity and suitability for the estimation of operative risk, but it considers only organ-specific diseases and is effective only in determining postoperative survival [33]. The APACHE score (based on age, physiologic variables, and chronic health problems) has limited value because of its complexity and low accuracy. In addition, it is mainly useful only in critically ill patients. While the ASA and the APACHE scores fail to estimate postoperative morbidity in patients, the POSSUM score estimates both morbidity and mortality. However, it can only be used in a limited way because it overestimates morbidity and mortality, and it has low accuracy [34]. Lee et al. and Eagle et al. developed criteria for the preoperative assessment of surgical patients, but it only focuses on a patient's cardiovascular function so it too has minimal utility [34]. Indeed, most scoring systems fail to incorporate the cumulative effect of all of the deficits in an aging individual's health and do not take into account the functional reserve of such an individual [35].

The FI, in contrast, incorporates all the facets of an individual's health that are currently recognized as contributing to postoperative morbidity and mortality. It takes into account the individual's chronologic age, nutritional status, comorbidities, activities of daily living, functional status, and physiologic health. A recent study assessing outcomes in vascular surgery patients demonstrated, for instance, that the FI was superior to the ASA score for predicting outcomes [36]. In another study by Tan et al., the FI was also shown to be superior to the POSSUM score for assessing outcomes in surgical patients [37]. We believe, therefore, that the FI, as a composite score, is superior to the other preoperative assessment tools and that it can be used in the preoperative assessment of patients to dependably evaluate physiologic reserve and risk stratification.

Postoperative Outcomes

Aging patients have an increased risk of postoperative complications that result in disability, loss of functional independence, diminished quality of life, and death. Accordingly, the postoperative course of such a patient is of cardinal importance because it plays a critical role in determining recovery to complete functional independence [38, 39]. Any postoperative complication is not only detrimental to a patient's recovery, it also raises costs by increasing the hospital LOS [40].

Complications

Studies show that patients with one or more postoperative complications have a higher median preoperative FI than those without postoperative complications [41]. Additionally, the median FI progressively increased with an increase in the number of postoperative complications. A median FI less than 0.12 significantly predicted postoperative complications, whereas age, sex, and the number of comorbidities taken individually were not significant predictors of postoperative complications [42]. A prospective analysis of 260 emergency general surgery patients demonstrated that frail patients had higher postoperative complications, including major complications [43]. Kristjansson et al., in a study of patients who underwent colorectal surgery, found that frail patients had a fourfold higher risk of developing postoperative complications [44]. They also found frailty to be a significant predictor of surgical complications (anastomotic leaks, surgical site bleeding, intraabdominal fluid collection) as well as of medical complications (pneumonia, arrhythmia, acute coronary syndrome) after surgery.

In another study by Garonzik-Wang et al. of patients who underwent a kidney transplant, frail patients had a twofold higher risk of developing delayed graft function in comparison with nonfrail patients [45]. Delayed graft function was independent of the chronologic age, but was significantly related to the biologic age and to preexisting deficits. Several studies correlate frailty with the development of postoperative delirium. Pol et al. demonstrated, for example, that frailty was a significant risk factor for the development of delirium after vascular surgery. Likewise, Kristjansson et al. found that the incidence of postoperative delirium was higher among frail patients compared with nonfrail patients after elective colorectal surgery [44, 46]. Assessment of long-term outcomes in elderly patients is of even more importance. The ability to identify elderly patients, who are at an increased risk of hospital readmission, recurrent falls, and mortality, can provide a potential avenue for timely intervention in this group of patients. A study by Joseph et al. that assessed six-months outcomes postdischarge in trauma patients demonstrated that in-hospital frail status as determined by the Trauma Specific Frailty Index (TSFI) was a significant predictor of trauma-related hospital readmission, recurrent falls, and six-month mortality in geriatric trauma patients.

Length of Stay

The FI reliably predicts hospital LOS in patients undergoing surgery. In several studies, for instance, frail patients required significantly longer hospital stays (65% to 89% longer) after minor and major surgical procedures compared to non-frail patients. Kasotakis et al. also found that frail patients required additional postoperative care and support, with a noticeable increase in the intensive care unit LOS, including cardiovascular pressure support, respiratory support, and monitoring. Furthermore, the number of ventilation days was higher for frail patients than non-frail patients [42, 45].

Discharge Disposition

Frailty has a proven efficacy in predicting postoperative morbidity in aging patients as well as in assessing their risk of death [47]. A steady reduction in longevity is noted with increasing FI scores. In contrast with nonfrail patients, Lee et al. demonstrate that frailty correlates with increased mortality among in-hospital frail patients [47]. Of course, the most favorable outcome for patients after surgery is being discharged to home in a state of complete functional independence. And the use of FI scores in predicting a patient's postoperative disposition has yielded positive results. In fact, frailty independently predicts the odds of an unfavorable discharge to a skilled or assisted facility after surgery. Lee et al., for example, showed that frailty was an independent, significant factor in predicting discharge to a rehabilitation institution postoperatively. Joseph et al. also showed that frailty reliably predicts the risk of unfavorable discharge disposition in geriatric trauma patients [39]. Likewise, Rockwood et al. found a significant association between frailty and discharge [26]. Similarly, Robinson et al. confirmed that a low preoperative hematocrit level and the diminished functional ability to walk on stairs were significant factors for discharge to an acute care facility [48].

Hospital Resources

Frailty has also been used as a reliable tool in predicting the costs of operative intervention among aging patients. Increased hospital and intensive care unit LOS among frail patients correspond to higher hospital costs. Robinson et al. demonstrate that the costs of hospitalization and the costs of health care 6 months after surgery were significantly higher for frail patients than for nonfrail patients. In addition, frail patients had increased rates of readmission within 30 days after their initial discharge from the hospital, further adding to costs [49].

Failure to Rescue

Failure to rescue (FTR), death after a major complication, is an important benchmark of patient safety and health care quality. It is a common index of the quality of healthcare delivery and shows how well hospitals perform once a complication arises. Several prior studies found that the in-hospital mortality rate is significantly affected by the variation in the management of complications [11]. Complications following an injury are relatively common among trauma patients, and emerging literature indicates that the majority of these complications may be independent of a hospital's quality of care. Recent evidence suggests that reducing FTR events might be the most appropriate target for quality improvement in geriatric population. A study of trauma patients showed that frail patients have 2.67 higher odds of FTR as compared to nonfrail patients [50]. Although FTR has been considered as an indicator of health care quality, recent literature strongly suggests that frailty status independently contributes to FTR. This needs to be considered in the future development of quality metrics, particularly in the case of geriatric trauma patients.

Successful rescue of patients with complications requires both timely identification of patients experiencing physical decline and the appropriate clinical interventions. Currently, very little surgical literature has reported the usefulness of the frailty index in predicting FTR in geriatric patients. However, there is growing evidence for the correlation between frailty and FTR in geriatric trauma patients. Though, more work can be done to convincingly assess the impact of frailty status on FTR in such patients [50].

Conclusion

An aging individual's frailty, as capsulized in the FI, can have a decisive impact across the spectrum of patient care, including more accurate surgical risk-benefit analysis, preoperative assessment, postoperative outcomes, disposition of discharge from the hospital, and informed clinical decision-making. With the increasing numbers of aging individuals requiring surgery, it has become imperative for the operating surgeon to take frailty into account and to calculate the FI in such patients in order to efficaciously plan patient management.

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Function and Prehabilitation

8

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Abstract

The number of surgical procedures performed in older persons is increasing exponentially. Morbidity and mortality increase with age, rising sharply after the age of 75. After major abdominal surgery, up to 20% of older patients have persistent disabilities in functional status, and a sizable minority never fully recover. Traditionally, efforts to support recovery begin in the postoperative period ("rehabilitation"), but deconditioning related to the metabolic stress of surgery and hospitalization may have already initiated a downward spiral during which the patient may become increasingly inactive, further contributing to complications

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and disability. Preoperative physical fitness, physical activity, and nutritional status are predictors of surgical complications and prolonged disability, but may be modifiable. As such, the preoperative period may represent an opportunity to intervene to optimize physiological age (functional capacity) in anticipation of the upcoming stress of surgery, potentially reducing complications and improving recovery. This strategy has been termed "prehabilitation." This chapter will focus on the potential role of prehabilitation to improve functional status in older patients preoperatively, thereby contributing to improved outcomes postoperatively. It will begin with a review of preoperative functional assessment, then summarize the current literature on prehabilitation, focused on the frail and older patient, including recommendations about the duration and intensity of prehabilitation programs in this population.

With the aging of the North American population it is estimated that the annual number of non-cardiac surgical procedures performed in older adults will increase from the present level of six million to approximately 12 million over the next 30 years [1]. As people are living well into their late 70s and early 90s, the prevalence of many conditions requiring surgery is increasing and, as a result of improved perioperative care, a higher number of older patients undergo major surgery [2]. During the last three decades the annual rate of surgical interventions has increased exponentially for men and women 75–84 years of age [3]. This demographic reality creates the need to provide special preoperative and postoperative surgical care to an increasing number of older persons. Over 30% of surgical procedures in North America are performed on persons aged 65 years or older and as a result of advances in surgical and anesthetic techniques, the overall operative mortality has declined significantly during the last 20 years [4]. Nonetheless, morbidity and mortality associated with surgery increase with advancing age and rise sharply after the age of 75 [5, 6]. Furthermore, the prevalence of comorbid diseases rises with increasing age. Over 80% of North Americans aged 65 have at least one chronic condition and 50% have at least two [7]. As the number of associated illnesses increases, so does the rate of perioperative complications. This effect is seen in all age groups but is most pronounced at the extremes of age [8].

While chronological age should not be completely ignored, physiological age (functional status and/or comorbidities) is a better predictor of operative outcome [9–11]. Major abdominal surgery reduces physiological and functional capacity by 40% to 60% [12]. The elderly, persons with cancer, and those with limited protein reserve are the most susceptible to the negative effects of surgery. Risk factors for postoperative complications include history of dementia, low preoperative serum albumin, poor exercise tolerance, and frailty [13–15]. Up to 20% of older patients have persistent disabilities in Instrumental Activities of Daily Living (IADLs) 6 months after major surgery; predictors of prolonged recovery include serious complications, poor physical status at baseline, cognitive impairment, depression and renal impairment [16].

Traditionally, efforts to support recovery begin in the postoperative period ("rehabilitation"), but patients may not be able to fully participate in a structured program because of fatigue and concerns about their prognosis. In addition, deconditioning related to the metabolic stress of surgery and hospitalization may have already initiated a downward spiral during which the patient may become increasingly inactive, further contributing to complications and disability. Preoperative physical fitness, physical activity, and nutritional status are predictors of surgical complications and prolonged disability [17–20], but may be modifiable [21]. As such, the preoperative period may represent an opportunity to intervene to optimize physiological age (functional capacity) in anticipation of the upcoming stress of surgery, potentially reducing complications and improving recovery [22]. This strategy has been termed "prehabilitation" (Fig. 1).

This chapter will focus on the potential role of prehabilitation to improve functional status in older patients preoperatively, thereby contributing to improved outcomes postoperatively. It will begin with a review of preoperative functional

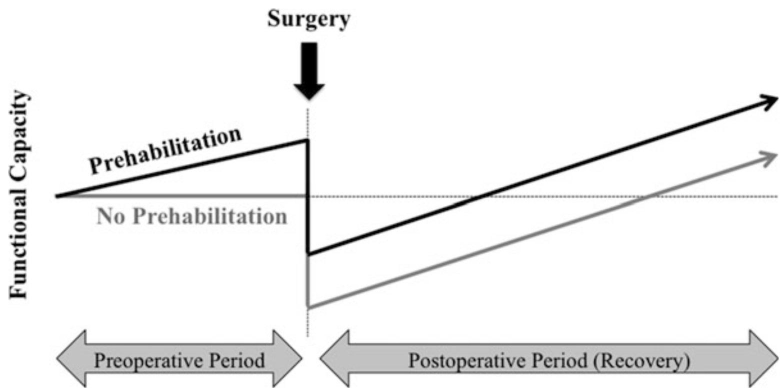

Fig. 1 Trajectory of perioperative functional capacity with and without prehabilitation. (Adapted from Carli et al. [22])

assessment, then summarize the current literature on prehabilitation, focused on the frail and older patient, including recommendations about the duration and intensity of prehabilitation programs in this population.

Preoperative Assessment for Prehabilitation

Functional impairments increase the risk of postoperative immobility, with associated complications such as atelectasis, pneumonia, multisystem deconditioning, increased length of stay, and increased mortality and morbidity [9–11]. Individuals with poor preoperative functional status have longer hospitalizations, more surgical complications, and are more likely to die within 30 days of surgery when compared to individuals with good preoperative functional fitness [22]. Poor baseline physical functioning is also a risk factor for prolonged recovery of IADLs [16]. The general approach to preoperative assessment is directed toward identification of factors that place the patient at increased risk for postoperative complications or functional decline. Although some of these factors are related to the surgical disease itself and to the type of operation required, the most important factors in the determination of risk are related to the overall health, functional status, cognitive abilities and nutritional status of the patient. Preoperative evaluation informed by the concept of prehabilitation suggests that the focus be extended from risk assessment to risk optimization, beginning with evaluation of functional reserve.

Functional reserve is the safety margin required to tolerate the metabolic consequences of major surgery, which include higher cardiac output, oxygen consumption, carbon dioxide excretion and protein synthesis, and the systemic immune response [23]. Functional reserve decreases with age and any organ system dysfunction places the elderly person at additional risk. Before planning any prehabilitation program to improve functional capacity, patients should undergo evaluations of exercise capacity, nutritional and cognitive status performed by a multidisciplinary team that includes a kinesiologist, a nutritionist and a psychologist. Here we focus on the specific assessments performed to design and monitor a prehabilitation program; a review of general and organ-specific preoperative evaluation and optimization for the older patient is outside the scope of this chapter.

Exercise Tolerance

Exercise tolerance, as an indication of functional reserve, is the single most important predictor of cardiac and pulmonary complications following non cardiac surgery [24, 25]. Evaluation begins with patient history, asking for the ability to perform routine physical activities including the maximal level of exercise a patient can achieve, to estimate peak oxygen consumption. One metabolic equivalent (MET) represents the basal oxygen consumption of a 70-kg, 40-year-old man at rest (~ 3.5 ml/kg/min). Estimated energy requirements are available for a wide variety of activities [1]. Patients considering major surgery should be able to achieve >4 METS, representing the ability to climb one flight of stairs. The inability to perform >4 METs is a predictor of increased perioperative cardiac events and long-term risk. The Duke's Activity Status Index is an example of a standardized self-assessment tool that quantifies METs using questions assessing the ability to perform a variety of increasingly strenuous physical activities [26]. However, relying on history is subjective and may overestimate exercise capacity [23].

The gold standard to assess exercise capacity is with cardiopulmonary exercise testing (CPET), which involves measurement of oxygen uptake (VO_{2max}), carbon dioxide production (VCO_2) and ventilatory measures while exercising on a cycle or treadmill to volitional exhaustion. Peak oxygen consumption and anaerobic threshold, defined as the level of oxygen consumption above which circulatory supply does not meet metabolic demand, both correlate with morbidity and mortality. Peak oxygen consumption less than 15 and anaerobic threshold less than 11 ml/min/kg are associated with increased risk of complications after major abdominal, vascular and thoracic surgery. In a classic study, Older demonstrated that in patients over 60 years old, the risk of cardiovascular mortality was less than 1% for those with an anaerobic threshold above 11 ml/min/kg, versus 18% for those with anaerobic threshold below this level [27]. This relationship has since been confirmed in multiple cohort studies [28].

However, while formal exercise testing is the gold standard, it requires additional equipment, involves an exercise effort, and is contraindicated in several cardiac, pulmonary and orthopaedic conditions. Walk tests, such as the 6-minute walk test [6MWT], which measures the distance walked in a 6-minute period in a flat corridor, are simple, objective measures of functional exercise capacity [29] . Predicted values for healthy persons are available, adjusted for age and sex [30]. Mean baseline 6MWT distances in patients undergoing colorectal and other general surgery abdominal procedures is 400–500 m, about 65–75% of predicted values [21, 31, 32]. The 6MWT distance shows moderate correlation with VO2peak in patients undergoing colorectal surgery ($r2 = 0.52$). The risk of postoperative complications is increased in patients with shorter 6MWT distances [33]. As prehabilitation programs are resource-intensive, the focus should be on selection of patients most likely to benefit from prehabilitation. Participants with lower baseline fitness (6MWT distance <400 m) have greater improvements with prehabilitation compared to those with higher fitness [34]. Furthermore, the 6MWT can be monitored throughout the perioperative period to provide a measure of the response to prehabilitation and an assessment of postoperative recovery [31, 35]. Both measurement error [36] and minimal clinically important difference [32] (MCID) for 6MWT distance for patients having colorectal surgery are estimated at around 20 m.

Sarcopenia and Frailty

Baumgartner described the term sarcopenia for age-related loss of muscle mass in elderly men. His index describes relative muscle mass calculated as appendicular skeletal muscle mass measured by dual-energy X-ray absorptiometry (DEXA), divided by the square of stature [37]. According to this index sarcopenia is defined as state of muscle mass two standard deviations below the mean muscle mass of normal for healthy individuals younger than age 30 years. Based on this calculation the prevalence of sarcopenia in people >60 years of age is 7–10%. Etiology of sarcopenia is multifactorial and includes genetic factors [38], physical activity [39], hormonal changes (including insulin resistance, elevated parathyroid hormone, and declines in serum testosterone and growth hormone) [40, 41], nutritional status (protein intake and low vitamin D levels) [42, 43], atherosclerosis, and changes in circulating pro-inflammatory cytokines [44, 45]. Newer definitions of sarcopenia include functional testing since muscle strength does not correlate with volume alone [45, 46]. The European Working Group on Sarcopenia in Older People (EWGSOP) defines sarcopenia as a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life, and death [46]. Total psoas mass (TPM) has been proposed as an objective measure of muscle loss and predictor of postoperative outcomes of major abdominal surgery

[47–49]. Psoas muscle measurements are performed at the level of L4 on CT scan. As many patients will have a CT scan prior to undergoing major abdominal surgery, TPM may provide an objective measure of sarcopenia. Lower TPM correlates with longer duration of hospital stay [50], increased cost of major surgery [51], greater complication rates, discharge disposition, and in-hospital mortality in patients with emergency surgery [52].

Sarcopenia is one aspect of frailty, a geriatric syndrome resulting from age-related cumulative declines in multiple systems resulting in impaired capacity to withstand stress and increased vulnerability to adverse health outcomes including falls, hospitalization, and mortality [53]. Phenotypic aspects of frailty and sarcopenia may overlap, including weight loss, exhaustion, weakness, slow gait speed, and low physical activity. However, frailty includes more than physical factors, encompassing psychological and social variables including cognitive status and social support [54]. Patients identified as intermediately frail or frail are at increased risk for postoperative complications [15]. Timed-up-and-go, the time required for a subject to stand from a chair without the aid of their arms, walk 10 feet, return to the chair and sit back down, is a useful screening test for frailty. Slower timed-up-and-go ($\geq$15 sec) is associated with increased complications and one-year mortality after colorectal and cardiac operations [55]. Best practice guidelines recommend evaluation of frailty and documentation of a frailty score (based on unintentional weight loss, decreased hand grip strength, self-reported low energy and slow walking) for all older patients [56]. Patients identified as frail represent an important potential target for tailored prehabilitation.

Cognitive Assessment

Cognitive impairments, either as a presurgical condition or postoperative complication, can interfere with surgical treatment and postsurgical recovery [57, 58]. Patients with dementia and/or delirium have worse perioperative outcomes. Dementia is a major risk factor for delirium, an acute reversible state of confusion, during hospitalization. Therefore, patients are evaluated for cognitive impairment in the preoperative period. The Mini-Cog test is a quick and practical screening tool for cognitive impairment that can be completed in 2–4 min. The Mini-Cog has sensitivity and specificity rates similar to the Folstein Mini Mental Status Examination (MMSE) and a standardized neuropsychological battery [59] . Participants are asked to recall three words and to draw a clock indicating an abstract time such as one forty five (1:45) or ten after 11 (11:10). The three-item word recall assesses short-term memory, while the clock drawing task assesses key features of executive function such as initiation, planning and multistep processing. Evidence of impairments should lead to referral for more in-depth evaluation.

Not all patients who perform poorly on screening examinations will have cognitive impairments. Patients with depressive symptoms may be erroneously perceived to have cognitive impairments as result of lack of effort during testing. Persons who reported more depressive symptoms preoperatively had higher incidence rates and more days of delirium postoperatively [60]. In addition, patients with depressed mood may exhibit less desire to participate in pre- and rehabilitation activities. Patients can be screened for depression using tools such as the Geriatric Depression Scale (GDS), a 15-item questionnaire that can be administered in person or over the telephone [61]. Respondents provide a yes or no response to the questions posed. A score of five indicates depression is a possibility. We have used the Hospital Anxiety and Depression Scale to screen patients for depression and anxiety prior to beginning prehabilitation. While prehabilitation may not improve these symptoms, patients with higher depression and anxiety may be more likely to benefit from the program [9].

Nutritional Assessment

Poor nutritional status is a risk factor for pneumonia, poor wound healing, and other postoperative complications. Malnutrition, defined as a decrease in nutrient reserves, occurs in 35–65% of older patients in acute care hospitals and 25–60% of institutionalized elderly [62]. Physiological changes that occur with aging, such as increased total body fat, loss of lean body mass, decreased bone density, and decreased total body water may all affect nutritional requirements [63]. The assessment of nutritional status begins by understanding the risk factors for nutritional deficiency in older adults. Factors that may lead to inadequate intake and utilization of nutrients include inability to access food (e.g., financial constraints, availability of food, limited mobility), lack of the desire to eat food (e.g., living alone, impaired mental status, chronic illness), inability to eat and/or absorb food (e.g., poor dentition, chronic gastrointestinal problems such as gastroesophageal reflux disease or diarrhea), and medications that interfere with appetite or nutrient metabolism. Nutritional risk can be assessed using the cancer-validated patient-generated subjective global assessment (PG-SGA) tool [64]. The SGA is an easily reproducible tool for assessing nutritional status from the history and physical exam [65]. SGA ratings are most strongly influenced by loss of subcutaneous tissue, muscle wasting, and weight loss. In a study of patients undergoing elective gastrointestinal surgery, both SGA and serum albumin were predictive of postoperative nutrition-related complications [66]. Nutritional assessment can identify chronic and severe protein-energy malnutrition and can also be measured using a standard 24 h dietary recall. The Mini Nutritional Assessment (MNA) is another score that was created to identify older adults at risk for malnutrition [67]. A short form of the MNA has been developed and used preoperatively [68]. Low serum albumin, a strong predictor of outcome in both non-surgical and surgical patients, correlates with increased length of stay, increased rates of readmission, decreased rates of discharge to home, and increased all-cause mortality in elderly patients [69]. In surgical patients, low preoperative serum albumin is correlated with postoperative morbidity and mortality [70, 71].

Summary

The main goal of the preoperative general and organ related assessment is to identify any coexisting disease, or decline in physiologic reserve that can be improved with a structured prehabilitation program. With this information, an accurate risk/benefit determination can be made and a personalized prehabilitation program can be tailored for each patient.

Prehabilitation to Enhance Postoperative Outcome

Prehabilitation to Attenuate Deconditioning

Strategies to minimize postoperative deconditioning in the elderly such as minimally invasive surgery together with enhanced recovery programs have been introduced to facilitate early mobilization and reduce postoperative morbidity [72]. These perioperative care programs focus mainly on the postoperative period (rehabilitation period) as the time for intervention to facilitate the return to the presurgical baseline state (recovery). Exercise, aerobic and resistance, implemented during the rehabilitation period, can improve physical status in the elderly [73]. Nevertheless, there is some realization that the preoperative period may be a very effective time for intervention as patients may be more available and amenable to interventions designed to optimize their physiological conditions in anticipation of the upcoming stress of surgery. This preconditioning period is defined as “surgical prehabilitation,” meaning a process of care that enables patients to better withstand the stress of surgery through the augmentation of functional capacity. Surgical prehabilitation then represents an opportune time for clinical and pharmacological preparation (for example smoking and alcohol cessation, better control of hypertension and of diabetes, treatment of anemia), and holistic interventions (e.g., relaxation, yoga, dietary modification). The role of procedure-specific, evidence based, personalized, structured programs, including physical exercise, nutritional counselling and supplements, and anti-anxiety strategies, together with elements of medical optimization, need to be addressed in the context of a multidisciplinary approach whereby all the stakeholders involved in surgical and medical geriatric care come forward. This concept of prehabilitation is founded on the principle of "marginal gains aggregation" whereby multiple small interventions collectively achieve a far superior effect [74]. Topp and Ditmyer have proposed that, by applying a presurgical exercise program in patients to improve functional ability before a stressor such as surgery, postoperative recovery and achievement of a minimal level of functional ability would occur more rapidly compared to patients who remain inactive throughout the surgical admission (Fig. 1) [75].

Literature on Surgical Prehabilitation

While most of the published literature on surgical prehabilitation incudes patients >60 years of age, few have specifically addressed issues unique to the elderly and frail. Particular attention has been paid to prehabilitation for orthopedic surgery (hip and knee arthroplasty, and spine), however other surgeries studied include cardiac, vascular and abdominal. The primary role of exercise in disease prevention is well recognized, and the benefits of physical activity have been shown in many medical conditions, such as hypertension, stroke, coronary artery disease, diabetes and chronic obstructive pulmonary disease (COPD). Regular exercise has been shown to improve aerobic capacity, to decrease sympathetic over reactivity and insulin resistance, and promote lean body mass. There is an emerging interest in understanding how structured physical exercise can influence postoperative recovery and disease progression. It is thought that by increasing patient's aerobic capacity and muscle strength through increased physical activity before surgery, physiologic reserve would be enhanced, the body would be in better condition to attenuate the negative aspects of surgery, and postoperative recuperation would be facilitated. Three systematic reviews including approximately 400 patients have been published [11, 20, 76]. In the first review, four to eight weeks of preoperative exercise was shown to reduce postoperative complication rates and accelerate hospital discharge in patients undergoing cardiac and abdominal surgery. Conversely, the outcome after joint arthroplasty, and in particularly knee arthroplasty, was not significantly different whether preoperative exercise was used or not [76]. A second systematic review examined 15 studies and concluded that total-body prehabilitation improved postoperative pain, length of stay, and physical function, but was not consistently effective in improving health-related quality of life or aerobic fitness in the few studies that examined these outcomes [20]. Another systematic review of eight studies reported some physiologic improvement with preoperative exercise, but with limited clinical benefit. Overall, there were several limitations with some of the studies, and the exercise regimens were not always structured and were also of different intensity. Finally, adherence to the exercises were not systematically reported. Although some physiologic improvement during the prehabilitation period was achieved in most studies, this change did not consistently translate into improved clinical outcomes [11].

In view of the paucity of studies in abdominal surgery, we performed a randomized trial comparing the impact of a 4-week, home-based, cycle exercise program, based on 75% of VO_2 peak, to a sham intervention to increase walking and breathing exercises on functional walking capacity (6MWT) [77]. While there was no difference in 6 MWT at the end of the prehabilitation period or in the postoperative period, the proportion showing an improvement in walking capacity was unexpectedly greater in the control group than the intense exercise group (47% vs 22%). Full compliance to the intense program was recorded by only 16% of participants, indicating that the prescribed exercise regimen could not be maintained. Predictors of poor surgical outcome included deterioration in functional exercise capacity while waiting for surgery, age greater than 75 years, and high levels of anxiety. These results suggested that an intervention based on intense exercise alone may not have been sufficient to enhance functional capacity in elderly patients, and attention must also be turned to improve nutrition, anxiety and perioperative care processes which might impact exercise performance. Extreme care has to be taken when prescribing physical activity as a single modality to some patients who lack physiological reserve, like frail elderly patients known to have decreased muscle mass and low protein reserve, who may thereby not be able to tolerate an increase in exercise prior to surgery without sufficient protein and energy supplementation. In view of these findings, further studies were conducted using a multidisciplinary approach incorporating nutritional counseling and nutritional supplements and deep-breathing exercises together with a moderate exercise program including aerobic and resistance exercises [19, 78]. In addition, perioperative surgical care was standardized following the Enhanced Recovery After Surgery (ERAS) perioperative care guidelines, which included smoking and alcohol cessation, glycemic control, anemia correction, pharmacological optimization of medical conditions (hypertension, arthritis, coronary heart disease, metabolic disorders), intraoperative control of intravenous fluid administration, normothermia, opioid sparing analgesia, early nutrition and early mobilization [79]. Adherence to this multidisciplinary prehabilitation protocol was 70%, resulting in significant improvements in preoperative functional walking capacity in over 50% of participants and better maintenance of physical activity postoperatively. Over 80% of patients receiving prehabilitation were recovered to their baseline functional capacity by 8 weeks after surgery, compared to 60% of patients who did not receive the prehabilitation plan [21, 78]. There was no difference in clinical outcomes. However, in a recent randomized study of patients scheduled for elective abdominal aortic aneurysm (AAA) repair (mean age 73), a six-week period of preoperative supervised exercise program resulted in reduced complications (42% vs 23%) and shorter duration of hospital stay [80].

A recent consensus opinion by colorectal surgeons addressed exercise prehabilitation in patients undergoing colorectal surgery [81]. It was agreed that physical activity before surgery was to be encouraged in patients with colorectal cancer, however the duration of prehabilitation would have to take into account the type and urgency of surgery. In most studies, the time interval for prehabilitation has been proposed to be between 4 and 8 weeks, with shorter time periods for patients with lung or abdominal cancer, and longer periods for more chronic conditions, such as spine surgery.

Prehabilitation for the Frail Elderly Patient

Many older patients in treatment for cancer are not apparently frail or functionally impaired. Screening to provide timely intervention for the more vulnerable ones who require extra treatment to prevent disability is imperative, in order to preserve function, prevent complications, and generate heath care saving. There is a strong evidence that older adults who are physically inactive, in poor nutritional state and with impaired mental function have low levels of functional health and higher rate of postoperative complications [16]. Patients with low baseline functional capacity have the most to gain from prehabilitation. A recent study [34] reported that elderly patients with low baseline walking capacity (6MWT distance<400 m) improved by 10–15% with a structured multimodal prehabilitation during the preoperative period, and maintained these gains after surgery [34]. It remains to be seen however whether the positive changes in functional status achieved with prehabilitation will result in better postoperative clinical outcomes such as reduced complications and hospital stays after colorectal surgery.

Duration of Prehabilitation

One common question asked by surgeons is about the duration of the preconditioning intervention, in fact some concern has been expressed that enrolling a cancer patient in such a program might put him/her at risk as the disease continues to advance. There is limited published work on preoperative exercise in elderly cancer patients, especially in a time frame dictated by national cancer waiting time limits [81]. The duration of prehabilitation can vary according to the type of surgery, for example chronic conditions such as arthroplasty might require 6–10 week to increase muscle strength and balance. The limitation to exercise and training as a result of pain can reduce the duration of time available to increase the physical reserve. Provision of adequate analgesia in these patients can expedite the physical pre-conditioning and increase muscle strength as illustrated by a recent case report of pre-habilitation of an elderly patient scheduled for total knee arthroplasty who underwent a radio-frequency block 6 weeks before surgery to relieve pain, and who was able to complete the pre-habilitation program with earlier recuperation of her functional capacity in the first 2 months after surgery [82]. For patients with cancer the time is more limited, and 4–6 weeks of prehabilitation is an acceptable duration to increase physiological reserve [83, 84]. The question remains whether those patients with poor physical condition and functional status who need surgery should wait to be optimized before surgery. There is strong evidence that surgery in these patients represents a serious risk leading to postoperative complications and prolonged recovery [85]. The high rate of postoperative complications and the prolonged length of hospital stay make these high risk patients more vulnerable and prone to readmission and higher mortality. The ideal time to design a prehabilitation plan would be at the preoperative clinic, where medical and surgical risk stratification is undertaken and an appropriate window of time is identified to implement the preconditioning.

Preoperative Exercise Activity to Enhance Functional Capacity

A traditional approach to the pre-operative time frame is to encourage rest in order to best prepare the patient for their upcoming surgery, but bed rest has deleterious effects on lean muscle mass, homeostatic mechanism, physical function, lower extremity strength/power, aerobic capacity and insulin sensitivity [86–88] . One of the core features of prehabilitation – besides medical optimization, nutrition counseling and anxiety reduction – is exercise, which not only involves prescribing an effective "dose" to improve physical function but also maximizes patient adherence to the program prescribed. Exercise includes regular physical activity that is incorporated into a planned and structured program for the specific goal of improving fitness. This program results in a certain "dose" of exercise that must be tailored to fit the desired outcomes for the patient. Prescribing exercise requires consideration of intensity, duration, frequency and modality. Adhering to a lower "dose" of physical activity (i.e.,: accumulating 30 min of physical activity over a day) has clear health benefits in the elderly [89]. In addition to cardiovascular exercise, it is equally important to consider resistance and flexibility training as important components of exercise. The exercise program should be safe and of an appropriate intensity to stimulate positive physiological adaptations. As the patient becomes accustomed to the intensity and adapts to the demands of the exercise performed, the intensity must be increased accordingly, although there must be a balance between the "ideal" intensity/amount of exercise, as proposed by existing guidelines/exercise principles, and what is feasible for the patient to perform [90]. This highlights a need for qualified personnel to both prescribe the exercise and supervise the program during the training period in order to achieve maximal benefits and maintain safety. These factors are of particular importance given the proximity of the program to the time of surgery and the physical conditions of many older patients.

Although prehabilitation includes a structured exercise program, the patient should also be encouraged to partake in daily movement and avoid prolonged sitting time. The use of technologies such as pedometers and accelerometers (i.e.,: Fitbit), along with encouraging a certain number of steps per day (i.e.,: 10,000 steps/day), may be an approach that is meaningful and provides immediate feedback to the individual. Replacing sedentary time with standing or light physical activity has positive effects on health related quality of life in the colorectal cancer population. Recent data from our laboratory indicates a wide range of program delivery preferences, ranging between patients who enjoy exercising alone to those who require more social support and group class environment (Ferreira et al., unpublished observations).

The beneficial effects of exercise training, if the stimulus is of sufficient intensity, can occur as rapidly as bed rest negatively impacts physical function. A moderate intensity trimodal prehabilitation program that improved functional walking capacity in the preoperative period was delivered in a median of 24.5 days. Patients undergoing prehabilitation improved by an average of 25 m (SD 50) while the control patients *declined* by an average of 16 m (SD 46) [21]. Patients who deteriorate during prehabilitation may be at increased risk for serious postoperative complications [9]. Not only are ameliorations in preoperative walking capacity achievable in the 4 week time frame, but it is also possible to significantly modulate the intensity and quantity of exercise performed. By participating in prehabilitation, it is possible for patients to increase their physical activity levels to meet current guideline recommendations [91].

Optimizing Prehabilitation with Nutrition

Protein requirements are elevated in stressed states to account for added demands of hepatic acute phase proteins synthesis, and the synthesis of proteins involved in immune function and wound healing. Dietary protein intake should thus be a central focus of nutrition-related anabolic strategies in anticipation of surgery, and should range between 1.2 and 2 g/kg/day. This range permits flexibility to adjust intake based on current nutritional status, physical activity level, presence of comorbid conditions and inflammatory state. Patients are counselled to achieve a total daily protein intake within this range, and the diet has to be adjusted accordingly. Interestingly, available evidence suggests that community-dwelling elderly do not meet current protein recommendations, which is estimated at a minimum of 1 g/kg/day in healthy older adults to promote optimal muscle aging [92]. In fact, the Quebec Longitudinal Study on Nutrition as a Determinant of Successful Aging [93], estimated that half of the cohort of 1793 community-dwelling seniors consumed less than 1 g/kg/day.

Several studies have identified that consuming 25–35 g of protein in a single meal maximally stimulates muscle protein synthesis (MPS). Based on the evidence of this ceiling effect, an equal distribution of daily dietary protein across meals has been proposed [94, 95]. The idea being that the anabolic response to a single dose of amino acids can be compounded when repeated multiple times per day. Given the emerging findings to support an even distribution of daily protein intake in healthy populations, and the evidence that substantive high quality amino acids are required to stimulate a typical anabolic response in elderly patients, it seems reasonable to suggest that daily protein requirements for older surgical patients be met through moderate protein (~25–35 g) consumption at every meal.

The stimulatory effect that amino acids after exercise have on MPS appears to be enhanced. In fact, protein ingestion post-resistance exercise (performed until failure) has been found to stimulate rates of myofibrillar protein synthesis above fasting rates for 24 h [96, 97]. This 24 h period post-resistance exercise has been dubbed the "anabolic window" to reflect what appears to be a period of increased sensitivity of MPS to aminoacidemia, also known as the "muscle full effect." Commercially available post-exercise supplements are usually composed of whey, casein, or soy. According to a recent report from the Food and Agriculture Organization of the United Nations (FAO), protein quality should be assessed using the Digestible Indispensable Amino Acid Score. Using this method to assess protein quality, milk proteins (including casein, milk protein concentrate, whole milk powder, and whey protein isolates) are among the greatest sources of high quality protein [98].

Monitoring Prehabilitation

To monitor the improvement of physiologic reserve and gains in muscular strength with the prehabilitation program, assessments of grip-strength, 6MWT and lean body mass are performed [99]. Ageing is associated with a progressive reduction of muscle tissue volume [100, 101] and a concomitant reduction in strength [102], but it is unclear whether this diminution causes the corresponding age-related decreases in bone mineral density [103]. The reduction in muscle tissue, and thus strength, worsens daily functional ability of elderly persons. However, it has been shown that resistance training can counteract the atrophy and loss of strength in this age group [104–106], potentially improving coordination, balance and perhaps bone mineral density. Relative muscle strength can be increased by 20–200% by weight training [107–113], even after the age of 80 years [103]. This is larger than the corresponding increase in muscle mass. Tracy and colleagues demonstrated that elderly individuals can improve quadriceps muscle strength by 27%, corresponding to a 12% increase in muscle mass, after 9 weeks of weight training [114]. A large part of the improvement in strength is not only from increases in cross-sectional area of muscle, but also due to a neural component. In addition, a recent review has suggested that the magnitude of the exercise-induced muscle response is far greater than the corresponding response in bone mineral density [111]. For example, high-impact weight training only results in about a 1% increase in bone mineral density of femoral neck and spine in postmenopausal women [115].

Exercise capacity can also be measured using maximal oxygen uptake (VO_2). The cardiovascular and musculoskeletal systems are central to achieving and maintaining functional independence, which is a prerequisite for discharge from a health-care facility, as is independent functioning of the individual in the community setting [75]. It has been shown that maximal oxygen uptake (VO2max) can improve by 20–30% in response to 6–12 months' training in previously sedentary older women and men [75, 116–118]. However, there is a heterogeneity of the training response as gains in VO2max can range anywhere from 0 to 1 l/min with a coefficient of variation of about 8% (202 ml/min) [116]. The increase in VO2max correlated with a lower maximal heart rate of 3–7% due to the larger stroke volume at least in part [117, 118]. This is actually independent of age [118].

In elderly males, two-thirds of the increase in VO2max after training is due to a higher maximal cardiac output, while only one-third is due to the wider arteriovenous oxygen difference at maximal exercise [119]. In contrast, in elderly women this improvement has been shown to only result from enhanced arteriovenous oxygen difference at maximal exercise. This suggests that there are no real central adaptations to exercise training in elderly women [119]. It has also been shown that there is moderate increase in aerobic capacity with short-term training. Govindasamy et al. showed that training at 70% of VO2max for 1 h per day, four times per week for 4 weeks improves maximal oxygen uptake by 6.6% and reduce submaximal heart rate by 10 beats per minute [120].

These results could indicate a rapid cardiovascular improvement in elderly people over a short period [121]. Since endurance-trained adults appear to undergo greater rates of decline in VO2max with advancing age compared with sedentary adults [122], one may presume that endurance training throughout the lifespan may not be beneficial. However, endurance-trained older individuals are able to perform physical tasks that cannot be performed by their sedentary peers, at least with the same degree of exertion or effort [122]. This is possible because endurance-trained older individuals possess higher levels of aerobic capacity compared to their sedentary peers of the same age. Since VO2max is a more powerful predictor of mortality than other established risk factors for cardiovascular disease [123], and because age and bed rest contribute to a decrease in VO2max, it is intuitive to have elderly patients perform aerobic exercise training during prehabilitation. Furthermore it has been shown that 1 MET (Metabolic equivalent = 3.5 ml/kg/min) increase in VO2max confers a 12% increase in long-term survival [123]. This further underlines the importance of aerobic exercise training during prehabilitation to improve outcome.

Conclusions

Prehabilitation for older surgical patients is feasible and can improve or maintain preoperative and postoperative functional capacity (see Box 1 for example of a program). It follows that prehabilitation, based on structured, personalized exercise and nutritional supplementation, should be considered an integral part of optimal perioperative care, where appropriate risk stratification, medical optimization, patient education and evidence-based perioperative (e.g., ERAS) care pathways are essential elements. The emerging interest in prehabilitation for the surgical patient is evident from the increasing number of registered clinical trials. Further research on prehabilitation for the elderly surgical patients is needed, specifically addressing the effectiveness and safety of different types of exercise, and the minimum requirement of proteins and other nutrients to complement the exercise in order to enhance muscle strength and increase physiological reserve in the frail older population. Furthermore, there is a need to determine what is the cost-effectiveness of single and multiple modalities, the short and long term impact on clinical outcomes such as length of stay, hospital readmissions, emergency department visits, perioperative complications and time to rehabilitate. Given the aging of population, the number of elderly patients requiring surgery will increase. It is our responsibility to ensure these patients receive the greatest opportunity to return to their preoperative functional status and good quality of life.

Box 1 4-Week Prehabilitation Program for an Elderly Frail Patient Scheduled for Major Abdominal Surgery [22, 124, 125, 126]

1a. Baseline assessment of strength, flexibility, and endurance

• strength: timed up and go (TUG), 2-min step test

• flexibility: chair sit-and-reach test, back scratch test

• endurance: 2-min walk test, 6 min walk test.

Box 1 4-Week Prehabilitation Program for an Elderly Frail Patient Scheduled for Major Abdominal Surgery [22, 124, 125, 126] (continued)

1b. Baseline nutritional assessment to meet protein and energy needs

• 3-day calorie count, PG-SGA, NRS 2000

2. Prehabilitation exercise regime carried out three times per week (home based or supervised by physical therapist or certified trainer; check how safe the exercise is when performed alone; eventually involve caregivers)

Types of exercises; 1–2 sets of each exercise consisting of 10–15 repetitions, 2–3 times per week, alternate with aerobic exercise

Strength (Upper)

- shoulder flexion horizontal abduction
- shoulder blades squeezing
- seated row biceps and triceps curls

Strength (Lower)

- hamstring curls
- ankle pronation
- static quads
- bridging
- hip abduction exercises

Breathing exercise: abdominal breathing, 10–12 deep breaths, three times/day

Cardiovascular ambulation(fast pace for 15–20 min to increase pulse by 10–15%) (3 times per week on alternate days, after 60 min of rest)

2. Evaluation of progression:

(a) Timed up and go (TUG)
(b) 2 min walk test, 6 min walk test
(c) Sit to stand test

Borg scale (The Borg scale assesses the level of perceived exertion in response to

(continued)

Box 1 4-Week Prehabilitation Program for an Elderly Frail Patient Scheduled for Major Abdominal Surgery [22, 124, 125, 126] (continued)

exercise. The scale can be used to monitor improvement of fitness during anexercise program).

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9 Preoperative Cognitive Assessment in Older Adults

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Contents

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Abstract

Cognitive impairment and dementia are common with advancing age. As our population ages a larger number of older adults will undergo surgical procedures requiring anesthesia. While patients with a diagnosis of dementia are less likely to undergo elective surgery and anesthesia, a growing body evidence demonstrates that surgery and anesthesia are more common in older adults when compared to younger adults and children. Interestingly, 20–44% of older patients presenting for elective surgery have undiagnosed probable cognitive impairment that may put them at risk for adverse perioperative outcomes. Accordingly, the detection of probable cognitive impairment is important as it allows for time in the

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preoperative period for patient and family counseling, identification of surrogate decision-makers, and potential modification to intraoperative and postoperative care to enhance patient-centered outcomes. There are several tools available to detect probable cognitive impairment in the preoperative period. This chapter describes the prevalence of preoperative cognitive impairment, its relationship to postoperative outcomes, and reviews some of the screening tools that can be used to detect cognitive impairment in older patients.

Keywords
Cognitive impairment · Dementia · Delirium · Informed consent · Shared-decision making · Surgery · Preoperative evaluation

Introduction

Worldwide the population is aging due to improving social conditions and medical advances leading to an increased average life expectancy. The 2010 Census Bureau reported that almost 13% of the US population was 65 years old or older. By 2050, this age group is expected to comprise 20% of the total population with 19 million of people over the age of 85 [1]. In 1996 more than half of the procedures in cardiothoracic, general surgery, ophthalmology, orthopedics, and urology were performed in patients aged 65 or older [2]. By 2007, nearly 36% of all surgical inpatient procedures in the USA were performed in older adults, and this number is expected to double by 2020 [3]. Therefore, with the aging of the population there are going be an increase in the number of older patients undergoing surgery and anesthesia.

Advances in surgical and anesthetic techniques have reduced perioperative morbidity and mortality in the elderly [4]. Although surgery has potential benefits in older patients, the rate of perioperative morbidity and mortality continues to increase with age [5, 6]. Postoperative delirium and postoperative cognitive dysfunction (currently a research classification rather than a formal diagnosis) are two of the most common perioperative complications in the elderly surgical population and are associated with a higher risk of morbidity and long-term mortality following surgery and anesthesia [7, 8].

The changes that occur in the older brain may be partially responsible for this increased risk of perioperative cognitive morbidity. However, unlike other major organ systems it is rarely evaluated in the preoperative period despite evidence that it should be. In this chapter, we will discuss changes in the aging brain and how baseline cognitive impairment may be a predictor of adverse outcomes.

The Aging Brain

In a recent review, Brown and Purdon [9] dissertate on the neurophysiology and neuroanatomical changes of normal aging. They found evidence for loss of volume and thickness of the prefrontal cortex that play an important role in attention and executive function. Moreover, normal aging is associated with changes in neuronal morphology, synapse number, and a decreased production of the major neurotransmitters. The older brain also has a diminished maintenance capacity making it more vulnerable to oxidative stress and inflammation that may facilitate neural injury. When taken together, these factors may contribute to a decrease in brain plasticity and hinder the old brain's ability to fully recover from the stimulus of surgery, anesthesia, and hospitalization. In patients with baseline preoperative cognitive impairment, this cognitive and neuronal plasticity may be further reduced, which puts these patients at risk for adverse postoperative outcomes including delirium and cognitive dysfunction that may persist for several months following a surgical procedure [10–14].

Cognitive Impairment and Dementia

Cognitive impairment and dementia are common in older adults and there is an increasing incidence with advancing age. Worldwide, approximately 35.6 million people were demented in 2010 and there are expectations that by 2050 there will be 115.4 million people worldwide with dementia [15]. Mild cognitive impairment (MCI) is also common among older adults. The estimated prevalence of mild cognitive impairment in population-based studies ranges from 10% to 20% in persons older than 65 years of age. MCI is defined by the presence of subjective memory complaints in the setting of objective memory impairment in patients with preserved ability to function in daily life. Patients with MCI are at increased risk of dementia but not all go on to develop it. Dementia is diagnosed when there is significant cognitive impairment in at least one cognitive domain (learning and memory, language, executive function, complex attention, perceptual-motor function, and social cognition) that is acquired and represents a significant decline from a previous level of functioning. In dementia, these cognitive deficits interfere with independence in everyday activities, must not occur exclusively during a period of delirium and are not better accounted for by another mental disorder (such as major depressive disorder or schizophrenia) [16, 17].

Undiagnosed preoperative cognitive impairment is common in the geriatric surgical patient. The prevalence of preoperative cognitive impairment in the setting of elective surgical procedures range between 20% and 44% and may be higher in emergency procedures [12, 14, 18, 19]. Without formal screening, cognitive impairment is difficult to detect even in the primary care setting where primary care physicians failed to identify cognitive impairment 20–76% of the time during a routine visit [20, 21]. Not surprisingly, one study demonstrated a prevalence of baseline cognitive impairment or dementia of 68% in patients 60 years of age or older undergoing elective or emergent vascular surgery and the impairment was unrecognized in 88.3% of these patients suggesting that health care providers failed to identify cognitive impairment without formal screening [12].

This is important because individuals with cognitive impairment, advanced age, and functional impairment are at risk for the development of postoperative delirium [7, 22]. In particular, impaired executive function is a predictor of postoperative delirium in patients without impairments in activities of daily living [23]. Delirium is associated with increased medical costs, longer hospital length of stay, higher 30-day readmissions and rates of institutionalization at hospital discharge along with functional and cognitive decline [7, 24]. Traditionally it has been suggested that delirium is associated with an increased mortality rate, but a recent meta-analysis examined the impact of incident postoperative delirium on mortality and concluded that there is insufficient evidence to support an independent association between delirium and mortality after noncardiac surgery [6]. In addition, preoperative cognitive impairment has been associated with increased postoperative complications, including postoperative delirium, longer hospital length of stay, discharge to a higher level of care, persistent postoperative cognitive dysfunction, and mortality after surgery [10, 11, 13, 14, 22].

Preoperative Cognitive Screening

As described above, preoperative cognitive impairment is frequently unrecognized without formal screening yet is associated with significant morbidity and mortality [21, 22].

The American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) and the American Geriatrics Society (AGS) collaborated to create best practices guidelines around optimal perioperative care of the geriatric surgical patients [25]. These guidelines recommend performing a preoperative cognitive screen and if positive to consider referring the patient to a specialist for subsequent evaluation. Similarly, the AGS Expert Panel on Postoperative Delirium in Older Adults elaborated evidence-based recommendations regarding the optimal care of older adults at risk for delirium and recommend screening for cognitive decline prior to a surgical procedure [26]. Additionally, the European Society of Anesthesiologists issued evidence and consensus-based guidelines for the prevention and treatment of postoperative delirium and strongly recommended preoperative cognitive screening [27].

When patients were surveyed in a preoperative anesthesia clinic, one study noted that the majority of individuals believed that a short memory test should be performed prior to having a surgical procedure and that if a memory test could help predict surgical outcomes they would want the test performed on them [19]. Moreover, identifying cognitive impairment preoperatively can help clinicians identify patients who are at risk for adverse postoperative outcomes allowing for a cost-effective way to direct precious health care resources toward their care.

The ideal cognitive screening tool during the preoperative evaluation should be brief, easily administered and scored, with high sensitivity and specificity for cognitive impairment, high inter-rater reliability, and should be validated across multiple languages, cultures, and education levels in older adults [19, 28]. The goal should not be to diagnose dementia or cognitive impairment, but rather to identify those individuals who performed poorly on a preoperative cognitive screening test to direct vigilance, more focused care, and further evaluation.

The Mini Mental State Examination (MMSE) is the most widely studied screening test to measure cognitive impairment [29], but other instruments are as effective, easier to perform, and are freely available [30]. Practical screening tests that can be quickly performed in a preoperative evaluation are shown in Table 1. Here we will discuss those cognitive screening tools that are available for clinical and research purposes that can be completed in 10 min or less that might be suitable in the elective or urgent preoperative setting.

Mini Mental State Examination (MMSE)

The MMSE is a widely used, 30-point cognitive screening tool that is well validated to screen for dementia with high sensitivity and specificity [29, 30]. It consists of 20 questions that cover multiple cognitive domains and has been translated into many languages worldwide. It takes on average 10 min to complete, but it may take longer in demented patients. Each point is given for a correct answer and, traditionally, the cut-off for dementia is <24/30. The MMSE has substantial age, education, and cultural bias and appropriate cut-off scores have been studied to improve its performance [31]. One of the main limitations of this tool is that is copyrighted and not freely available [30]. Moreover, it has a low ceiling effect and MCI patients may score in the normal range. MMSE has been widely used to detect cognitive impairment in the perioperative setting and a poor performance is associated with worse perioperative outcomes [13, 32]. Studies demonstrate that patients with undiagnosed baseline cognitive impairment were at higher risk for developing postoperative delirium and being discharged to a higher level of care [13, 32].

Montreal Cognitive Assessment (MoCA)

The Montreal Cognitive Assessment (MoCA) is a 30-point screening test that takes approximately 10 min to administer. This tool assesses numerous cognitive domains (Table 1) and, when compared to other screening tests, shows a better ability to detect MCI [30]. In a validation study, using a cutoff score of 26, the MoCA detected 90% of mild cognitive impairment and 100% of mild Alzheimer's disease with a specificity of 87% [33]. Time constraints and the complex scoring system are some of the test limitations but when the clinicians have more time and there are pointed concerns from the patient and family member, the MoCA test can be useful as an instrument given that it is more comprehensive and tests a variety of domains. The tool is freely available at the website www.mocatest.org.

One study enrolled patients older than 60 years of age admitted for elective or emergent vascular procedures and used the MoCA to evaluate the prevalence of cognitive impairment (defined as MoCA < 24). In this cohort, the MoCA detected cognitive impairment or dementia in 68% of the patients and this was unrecognized in 88.3% [12]. Preoperative cognitive impairment using the MoCA has demonstrated ability to predict postoperative complications, including postoperative delirium [12, 34].

Mini-Cog

The Mini-Cog is a quick, easily administered, and validated cognitive assessment tool that measures memory with a three-object recall after a distraction test of executive function which utilizes a

Table 1 Cognitive Screening Tools

	Time to administer	Description/ Cutoff	Cognitive domains	Diagnostic accuracy pooled (95% confidence interval) (30)		Advantages	Limitations	Availability	Studied in perioperative setting	Perioperative outcomes
				Sensitivity	Specificity					
Brief < 10 min										
MMSE	8–10 min (up to 15 min if demented patient)	20 questions; 30 points/ Dementia <24/30; age and education norms (different cutoff levels)	Orientation, memory, language, attention, visuospatial	Dementia 0.81 (0.78–0.84); MCI 0.62 (0.52–0.71)	Dementia 0.89 (0.87–0.91); MCI 0.87 (0.80–0.92)	Extensively studied; translated and validated in various languages; often used as a reference for comparative evaluation of other assessment tools; best performance for at least moderate cognitive impairment	Low ceiling (MCI may score 25–30); low sensitivity for MCI; affected by vision, physical and coordination impairment; copyrights; education, cultural language and age bias (not gender)	www4.parinc.com/ Copyright	Yes (13, 32)	POD and discharge to a higher level of care
MoCA	10 min	30 points; designed for those who score <24 on the MMSE/ Dementia <24/30; MCI <26/30	Orientation, memory, language, attention, visuospatial, and executive function, (abstraction, naming)	Dementia 0.91 (0.84–0.95); MCI 0.89 (0.84–0.92)	Dementia 0.81 (0.71–0.88); MCI 0.75 (0.62–0.85)	Validated in many conditions including MCI, AD, and PD dementia; more sensible for MCI than MMSE	Education bias; complex scoring; affected by vision, physical and coordination impairment	www.mocatest.org/Free	Yes (12, 34)	POD and HLOS

(continued)

Table 1 (continued)

	Time to administer	Description/ Cutoff	Cognitive domains	Diagnostic accuracy pooled (95% confidence interval) (30)		Advantages	Limitations	Availability	Studied in perioperative setting	Perioperative outcomes
				Sensitivity	Specificity					
Very brief < 5 min										
Mini-Cog	2–4 min (less if no CI)	3 item recall (3 points for each word) and CDT (0 or 2), maximum 5 points, algorithm for scoring/ CI ≤ 2	Memory, visuospatial, and executive function	Dementia 0.91 (0.8–0.96)	Dementia 0.86 (0.74–0.93)	Validated in multiple languages and cultures; little or no education, language or race bias; tested and feasible in preoperative setting; high inter-rater variability	Use of different word list may affect failure rates; CDT may be challenging if lack of contact with analog clocks, low experience with writing and drawing, and very low levels of educational attainment	www.mini-cog.com/ Free	Yes (11,14,19)	Complications, POD, HLOS, discharge to other place than home, mortality
GPCOG	5 min (4 min cognitive testing and <2 min for the	15 points; 2 steps: step 1 – CDT + questions; if $\leq$4 CI, if 5–8 indeterminate and triggers step 2-	Orientation, memory, language, visuospatial/ executive function, and other living functions	Dementia 0.92 (0.81–0.97)	Dementia 0.87 (0.83–0.90)	Available as a web-tool; translated in various languages; not affected by cultural or linguistic	Studied in primary care setting; necessary informant present	www.gpcog.com.au/ Free	Not extensively	–

	informant section)	informant-based assessment with 6 questions/ CI ≤ 4 or 3 negative answers on step 2				background (not affected by depression, age, gender, years of education, and physical and mental status); combines patient and informant data; quick; easily accepted by clinicians and patients				
Verbal Fluency Test	1 min	List of words (category or letter) in 60 s; 1 point for each word/ CI < 15	Executive function, semantic memory and language	Dementia 0.80 (0.73–0.86)	Dementia 0.82 (0.73–0.88)	Limited training to administer correctly; administer in person or over the phone; no pen or pencil	Education and cultural bias; anxiety	Free	Yes (45, 46)	POD

MMSE Mini Mental State Examination, *MCI* mild cognitive impairment, *POD* postoperative delirium, *MoCA* Montreal Cognitive Assessment, *AD* Alzheimer Disease, *PD* Parkinson disease, *HLOS* hospital length of stay, *CI* cognitive impairment, *CDT* clock drawing test, *GPCOG* General Practitioner Assessment of Cognition clock-drawing task [35]. Although memory loss is a common symptom of dementia, executive function impairment may precede memory decline [36]. One point is award for each correctly recalled word. The clock drawing is scored as normal if the clock has the correct time and is grossly normal. Dementia has been correlated with a score of ≤ 2 [35]. The time for completion of the test averages between 2.5 min and 3.7 min in demented patients in a medical setting [35]. The Mini-Cog can be administered reliably with little practice and the instrument and instructions for its administration can be found at the website www.mini-cog.com. This tool has been translated in various languages and has little or no language and education bias [37]. Nonetheless, the clock drawing may be challenging in those individuals who have very low levels of educational attainment, lack of experience in writing or drawing, or lack regular exposure to analog clocks. The Mini-Cog was first developed for primary care but has been studied in other settings [35, 38]. In a recent systematic review and meta-analysis on cognitive testing, the Mini-Cog was found to have a better diagnostic performance for dementia and to be simpler and shorter than the MMSE [30]. In a review aimed at identifying brief cognitive tools that could be used to detect preoperative cognitive impairment in a clinical setting, the Mini-Cog was considered one of the best screening tools with a 99% sensitivity and 93% specificity for dementia [28].

The Mini-Cog has been endorsed by ACS/AGS guidelines [25] and was found to be a feasible cognitive screening tool with a high inter-rater reliability in the geriatric elective surgical population [19]. The overall incidence of impaired cognition at baseline using the Mini-Cog ranges from 23% to 44% in surgical patients [11, 14, 19]. Poor performance on Mini-Cog has been associated with increased incidence of adverse outcomes including in-hospital complications, postoperative delirium, longer hospital length of stay, higher rate of discharge to an intuitional care facility, and higher 30-day readmission rate and mortality [11, 14]. Interestingly, patients unable to complete the Mini-Cog showed a higher risk of mortality at 1 year [11].

General Practitioner Assessment of Cognition (GPCOG)

The General Practitioner Assessment of Cognition (GPCOG) was developed and validated for primary care and includes both cognitive testing items and informant data [39]. This instrument comprises two sections with the first step including nine items of orientation, memory, and a clock drawing test (4 min) and a second step with six items (2 min) where the informant is asked if the patient is having more trouble with memory and performing other daily tasks including, for example, taking care of his or her medication, A score of 4 or less on the first step defines cognitive impairment. A score of 5 through 8 prompts an informant-based assessment, and a negative response to three of the six items indicates cognitive impairment with a sensitivity of 85% and specificity of 86% [39]. Results suggest that this test might have some utility in detecting patients with MCI as two-fifths of non-demented patients who scored low had sub-threshold cognitive impairment [39]. The GPCOG was found to be reliable and to perform as well as MMSE in detecting dementia [39, 40]. The GPCOG, available as a web-based tool (www.gpcog.com.au), is translated to various languages and, although it has not been extensively studied in the perioperative setting, it is a practical test with a high level of acceptance amongst patients and general practitioners [31]. One of the main limitations of this tool is that requires an informant to be present at the moment of the preoperative evaluation that is willing to participate.

Verbal Fluency Test

Verbal fluency is defined as the capacity to produce a logical and satisfying sequence of spoken words during a given time interval, normally 60 s [41]. The verbal fluency tests assess the ability to produce a list of words that start with a specific letter (phonemic verbal fluency) or within a category (semantic verbal fluency) and relies on the preservation of language, semantic memory, and executive function domains [41]. Impaired verbal fluency is well documented in patients with Alzheimer Disease, and the verbal fluency test (VFT) has been shown to have a high sensitivity in discriminating dementia from normal older controls [42]. In scoring the verbal fluency test, one would count up the total number of animals or words that the individual is able to produce. A score of under 17 indicates concern, although some practitioners use <15 as a cutoff. Semantic fluency has also been shown to be reduced in patients with mild cognitive impairment [43]. Nonetheless, as most rapid cognitive screening tools, education bias and the ceiling and floor effects are some of its limitations. A systematic review concluded that the verbal fluency tests have less predictive power than other more comprehensive instruments [30].

The Animal Fluency Test (AFT) is a simple and very brief cognitive screening tool that assesses semantic fluency by asking patients to name as many animals as they can in 60 s [44]. In this test, each point is given for each animal named and scores under 15 have demonstrated 88% of sensitivity and 96% of specificity in detecting Alzheimer dementia [42]. Besides being very quick and easy, it requires minimal training to administer, does not require pen or paper, and can be performed in patients with motor disability. When the cognitive assessment was performed in patients without recognized dementia or cognitive impairment, the AFT identified cognitive impairment in 52% of patients compared to the 56% identified with the MoCA [44].

One study that evaluated preoperative cognitive function with the AFT tool determined that this is a feasible test in clinical practice and found the prevalence of cognitive impairment to be 29% [45]. Naming fewer animals on this semantic fluency test is associated with a higher risk of developing postoperative delirium [45, 46].

Optimizing Patients with Cognitive Impairment

After identifying cognitive impairment, it is important to ensure patients, and their caregivers are aware of the potential postoperative complications associated with preexisting cognitive impairment to inform clinical decision-making, review postoperative care/instructions, and set expectations. The 2012 ACS/AGS guidelines recommend that if probable cognitive impairment is identified by a cognitive screening test preoperatively, the patient should be referred to a primary care physician, geriatrician, or mental health specialist [25]. While it is helpful to seek care of a professional for medication review and formalized recommendations by a geriatrician, given the prevalence of cognitive impairment this is often not feasible for every patient to see such a specialized provider. However, there are simple nonpharmacological and behavior modifying actions which can be undertaken to decrease the risk of postoperative delirium and other complications such as advising patients to bring sensory assistive devices such as hearing aids and glasses so that they are immediately available in the postoperative period. Additionally, it is helpful to engage families and caregivers in the perioperative setting, have them bring in pictures, familiar items and, if possible, encourage them to stay overnight in the hospital for reorientation [47]. Further interventions include sleep enhancements, i.e., minimizing interruptions overnight once the patient is clinically stable, daily orientation with day/night cycle, and use of large-print clocks. Lastly, prescribing health care providers should modify traditional postoperative prescribing and limit use of benzodiapezines, and anticholinergic medications such as diphenhydramine and scopolamine as these can increase risk of delirium in cognitive impaired patients who are already predisposed.

Formal programs such as the orthopedic co-management [48], Hospital Elder Life Program (HELP) [49], and modified Hospital Elder Life Program (mHELP) [50] have been shown to be beneficial to improve outcomes in individuals with cognitive impairment. In orthopedic co-management programs, individuals are cared for by both geriatricians and orthopedic surgeons that utilize key geriatric friendly principles such as early mobility, minimizing teethers such as Foley catheters and telemetry, standardized protocols to decrease unwarranted variability, and early discharge planning. HELP is an interdisciplinary program mostly run by volunteers which has six interventions targeting cognitive impairment, sleep deprivation, immobility, visual impairment, hearing impairment, and dehydration. Similarly, mHELP has daily programs such as orienting communication, oral and nutritional assistance, and early mobilization have been shown to decrease rates of delirium after abdominal surgery [50]. All of these programs have been shown to decrease the risk of adverse outcomes in elderly patients.

Conclusion

Cognitive impairment is prevalent in older adults. Preoperative cognitive screening is both easily performed and may identify those patients at highest risk so that they may receive more personalized care to enhance postoperative outcomes.

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Nutrition in the Geriatric Surgical Patient

10

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Abstract

The elderly population is particularly vulnerable to malnutrition due to a number of physiologic, psychologic, and socioeconomic changes associated with aging. Diagnosis is challenging and a number of screening modalities have been described. Reliance upon biochemical testing (albumin and prealbumin) alone is not recommended. Multiple screening tools such as Mini Nutritional Assessment (MNA), Nutrition Risk Index (NRI), Malnutrition Universal Screening Tool (MUST), and Nutritional Risk Screening-2002 (NRS-2002) have varying degrees of accuracy. Because malnutrition and "at risk for malnutrition" are strongly predictive of poor clinical outcomes, intervention is recommended, though reversal of malnutrition in the elderly is particularly difficult after significant lean body mass has been lost. Prehabilitation with nutrition and exercise begins in the preoperative stage, continuing through the perioperative period, and continues beyond the immediate postoperative period.

Keywords

Malnutrition · Nutritional risk · Mini Nutritional Assessment · Anorexia of aging · Enteral nutrition · Parenteral nutrition · Prehabilitation

Clinical Vignette

A 72-year-old woman presents to your clinic for evaluation after a routine screening colonoscopy identified a cancerous polyp in the cecum. She lives alone after her husband died 6 months ago. She has had a poor appetite since his death and although she denies significant weight loss, she admits that she hasn't weighed herself recently. Her only medical comorbidities are hypertension (for which she takes atenolol) and hypothyroidism (for which she takes levothyroxine). She weighs 132 lbs (59.9 kg), is 5 ft 7 in, and has a BMI of 20.7.

What tools would you use to screen this patient for malnutrition?
What interventions can you implement to optimize this patient for surgery?

Introduction

By the year 2030, one in five people in the United States will be over the age of 65. The elderly population will continue to increase to 88.5 million by 2050 – more than double what it was at the time of the 2010 census [1]. This change translates into an increase in surgical volume in the elderly as well. In 2007, one-third of all inpatient surgical procedures were performed on elderly patients, and in the next few years, that number is projected to double [2, 3].

The elderly population is particularly vulnerable to malnutrition. The prevalence of malnutrition in the elderly reported in the literature is variable, with rates as high as 60% [4, 5]. This inconsistency can be attributed to a range of geographic locations and varying methods of assessment [6]. Using a pooled analysis of 4,000 elderly patients from 12 countries on five continents treated in multiple settings evaluated with only one assessment tool, the overall prevalence of malnutrition was 23%. When further categorized by treatment setting, the prevalence was highest in rehabilitation centers and hospitals (51% and 39% respectively), and was lower in nursing homes and in the community (14% and 6%) [7]. The prevalence of patients "at risk of malnutrition" was even higher at 46% – meaning two-thirds of the entire study population was either at risk of malnutrition or already identified as malnourished [7].

Malnutrition has serious consequences in the elderly. Malnourished elderly patients (as defined by a body-mass index (BMI) of <20 kg/m^2) have a 1-year mortality rate approaching 50% [8]. In order to improve care, including surgical care of the elderly, it is imperative that malnutrition be recognized and addressed appropriately.

Factors Contributing to Geriatric Malnutrition

Between the ages of 20 and 70, mean energy (calorie) intake decreases by 1,062 kcal/day in men and 481 kcal/day in women [10]. On average, men over age 65 in the USA were shown to lose 0.5% of their body weight each year [11]. There are a number of changes associated with aging – physiologic, psychologic, and socioeconomic – that predispose this population to under-nutrition.

Physiologic

Changes to appetite, taste, olfactory, and visual acuity, chronic disease, physical disability, and dentition can impact food choice and dietary intake. Appetite declines with age, with elderly persons eating smaller meals, eating fewer snacks between meals, and feeling full more rapidly. This trend is referred to as the "anorexia of aging" [4]. The processes present in younger people that impact appetite and correct for over- or undernutrition are not as effective in older people. One study underfed healthy community-dwelling young (mean age 24) and old men (mean age 70) and then documented the responses when they were allowed to eat freely again. The young men over-ate above their baseline consumption to compensate and quickly regained weight, while the older men only returned to their baseline dietary intake and did not regain lost weight [12]. This study suggests an inability among the elderly to quickly rebound from acute undernutrition, similar to the type of acute insult that occurs with a major operation. These patients take longer to regain lost weight and remain malnourished for a prolonged period.

Also contributing to a decline in appetite with aging is deterioration of the senses of taste and smell. The threshold to detect tastes increases with age, with salt being the most difficult to taste; however these changes are variable and the extent of the impact on energy consumption is unproven [13]. The sense of smell is particularly important to stimulate interest in food. This sense, however, deteriorates after age 50 [14], and the consumption of a nutritionally balanced diet is often negatively impacted by removing this stimulus. Additionally, the process of obtaining nutrients from food – from chewing, to slowed absorption – is greatly impaired in the elderly. Dentition alone can change diet and limit the variety and amount of food able to be consumed, particularly protein intake [4].

Even the GI tract itself affects the process of obtaining nutrition. For instance, aging results in impaired gastric emptying and early satiety due to an increase of nitrous oxide in the fundus that occurs with aging [15]. Other comorbidities and chronic medical conditions that occur with aging can also contribute to malnutrition. For instance, diseases that limit mobility either by deformity (such as rheumatoid arthritis), or by limited functional capacity (such as respiratory diseases) can cause malnutrition by impairing feeding, shopping, and food preparation. Chronic medical conditions also require the use of prescription medications, many of which have adverse effects that can limit nutrition. These medications can have a myriad of side effects, including anorexia, nausea, diarrhea, and early satiety among other gastrointestinal symptoms ([16, 17]. Often, with a large number of medications prescribed, it is difficult to parse out symptoms caused by drug interactions.

Body composition changes with age, resulting in an increase in fat and decrease in lean body mass such as skeletal muscle [13]. Up to 3 kg of fat-free muscle mass is lost each decade after 50 years of age [4]. The change in body composition is attributed to several factors, including decreased physical activity, reduced growth hormone and sex hormone levels, and changes in metabolic rate. Testosterone and other androgens decrease with age, contributing to sarcopenia [4]. Additionally, decreases in growth hormone and insulin-like growth factor 1 (IGF-1) affect age-related changes in appetite and food intake [13].

Psychologic

Psychological variables that impact food choice and nutrition include loneliness, bereavement, food likes/dislikes, and mental awareness [5]. Depression occurs in 2–10% of elderly people in the community [18]. In the elderly population, this condition tends to be associated with decreased appetite, loss of body weight, and subsequent malnutrition. While only seen in about 60% of younger adults with depression, weight-loss is noted to be a symptom of depression in nearly all elderly patients [13]. Treating depression has been reported as an effective way of promoting weight gain [4]. Additionally, the elderly tend to live alone and there is an association between loneliness and decreased appetite in the elderly. When not eating alone, older people will eat significantly more [19]. Finally, the prevalence of dementia increases with age, often affecting feeding behaviors and leading to weight loss [16].

Socioeconomic

Socioeconomic factors also impact nutrition in the elderly, as this patient population is often in retirement with a lower or fixed income. Expenses for treatment of the chronic medical conditions associated with aging, such as prescription medication costs, can further limit income available for purchasing nutritious food [20]. Low income can cause "food insecurity," a state where people cannot afford nutritious food, leading to malnutrition [6]. Social factors such as convenience of cooking facilities, distance to food stores, availability of transportation, and access to preferred foods also impact nutrition. When examining activities of daily living, 12% of older persons required help with managing finances, 29% needed help with shopping, and 16% could not prepare food independently [13]. All of these factors contribute to the overall anorexia of aging that makes the elderly population especially vulnerable to malnutrition and its consequences.

Nutritional Assessment of Geriatric Patients

History and Physical Exam

In order to intervene appropriately to optimize nutrition in elderly patients, malnutrition must first be identified. There is a vast array of nutritional assessment strategies that have been employed clinically for this patient population, beginning simply with history and physical exam. These traditional means rely on the patient or caregiver reporting symptoms such as a history of weight loss or changes in diet and detecting physical findings associated with malnutrition such as muscle wasting or edema. The clinician should always begin with history and physical before proceeding to more sophisticated screening tools.

Subjective Global Assessment

One assessment method that formalizes and incorporates the history and physical exam is the subjective global assessment (SGA), introduced by Detsky in 1987 [21]. The SGA includes functional capacity and the clinican's overall impression of the patient's status which they designate as "normal," "mildly malnourished," or "significantly malnourished" [21]. To make that subjective judgment, clinicians assess for a history of weight loss and poor dietary intake and loss of subcutaneous tissue and muscle wasting on physical exam. The

SGA does not include laboratory testing. In validation studies, Detsky et al. demonstrated a sensitivity of 82% and specificity of 72% when using the SGA to predict infection secondary to poor nutritional status – better than six other methods including several laboratory tests and other nutritional indexes [21].

Despite the high level of sensitivity and specificity shown by Detsky, the successful use of the SGA to predict malnutrion is limited by several factors. First, it is most effective when performed by clinicans experienced with the assessment. In additional validity testing in other clinicians, the same level of sensitivity was difficult to replicate. For instance, one study compared the SGA form completed by two independent clinicians to a combination of anthropometry and measurement of serum protein. The two observers had an agreement level of 77.8% and there was significant variability between the two observers in predicting malnutrition (82% vs. 66%) [22]. These studies suggest that SGA is a reliable assessment tool in the hands of experienced clinicians. Similarly, a review of the literature reveals that the SGA performs similarly to traditional methods of determining nutritional status, such as laboratory testing and anthropometry, but concludes that alternative nutritional assessment tools, which will be discussed later in this chapter, are more reliable in detecting malnutrition than the SGA [23]. Another limitation of this method is that the physical signs of muscle wasting and subcutaneous fat loss emphasized by the SGA are often late signs of malnutrition, making the SGA less useful in detecting early malnutrition and also less helpful in re-evaluating progress after interventions for malnutrition [22]. While the SGA does provide a way to translate the history and physical exam into assigning a degree of malnutrition in the hands of an experienced clinician, it is not the ideal assessment tool.

Biochemical Markers

Albumin

In the past, the serum albumin level has been used to define malnutrition under the assumption that albumin level is proportional to the severity of malnutrition. Hypoalbuminemia was presumed to represent a deficit that can be corrected by increasing dietary protein intake. Although this association may be true in a purely protein deficient state, such as Kwashiorkor, in general, the relationship between albumin and malnutrition is far more complex [24]. Albumin levels are affected by many additional factors unrelated to nutrition status. Clinical factors that alter protein anabolism or catabolism including liver cirrhosis and certain drugs (such as steroids) likewise impact albumin levels [25].

Albumin production is limited in the setting of inflammation as protein synthesis shifts toward the production of cytokines and the protein is lost from the intravascular space to the interstitium [22, 27]. In this regard, it behaves as a negative acute phase reactant [26]. Thus, in the inflamed state, the serum albumin level may be low even in well-nourished patients. The half-life of albumin is 18 days, yet the albumin level has been observed to decrease rapidly after hospital admission – too immediate a response to be explained by malnutrition alone.

In addition to the effects of various disease and inflammatory processes, aging itself is associated with a modest decline in serum albumin levels, with a decrease of 0.8 g/L per decade after age 60 [22, 28, 29]. Even recumbent posture has been reported to a decrease in albumin levels [30]. With a multitude of influences, serum albumin lacks the sensitivity and specificity to be an accurate indicator of nutrition. However, albumin has been reported as an accurate predictor of mortality and overall health status [22, 24, 31]. A study of patients in a geriatric rehabilitation unit at a Veterans' Affairs hospital reported that 3 months after discharge, albumin was the strongest predictor of long-term mortality. Patients with albumin less than 35 g/L had 2.6 times greater mortality than those with serum albumin levels above 40 g/L [32]. Subsequent studies from the same group indicate that inflammation at the subclinical level may contribute to the lower albumin levels [26]. At the present time, the body of knowledge suggests that albumin is a valuable biomarker of severity of illness and predictive of perioperative complications, including mortality, prior to elective major surgery [33]. This predictive ability is diminished in the setting of critical illness [34–36]. However, the connection between albumin and nutrition is tenuous at best and likely confounded by comorbid illness [24, 26, 37]. There has been no convincing evidence that aggressive nutritional therapy (independent of treating the comorbid illness) directly increases serum albumin, and that improved serum albumin resulting from nutritional optimization leads to improved outcomes.

Transthyretin (Prealbumin) and C-Reactive Protein

Like albumin, *prealbumin* (also known as transthyretin (TTR)) has been used as a metric of protein malnutrition since the 1970s [38]. Despite its misleading name, prealbumin is not a precursor to albumin. Originally named in reference to its relationship to albumin on a protein electrophoresis plate, prealbumin plays a variety of roles including thyroxin transport and vitamin A transport through formation of a complex with retinol-binding protein [39, 40]. The normal range of prealbumin is reported as 150–350 mg/L and the half-life of prealbumin is 2 days. A consensus statement regarding the use of prealbumin in nutrition evaluation was issued in 1995. Per this statement, a level between 50 and 109 mg/L indicated significant risk of malnutrition and a level of less than 50 mg/L was an indicator of poor prognosis [41]. Furthermore, an increase of less than 40 mg/L within 8 days despite providing 100% of protein need is indicative of need for further intervention and also of poor outcomes [41]. However, factors other than nutrition status alone can also impact prealbumin levels.

Like albumin, the use of serum prealbumin is complicated by the fact that levels also change rapidly when protein synthesis shifts toward acute-phase proteins in the setting of systemic inflammation [42–46]. Because prealbumin also acts as a negative acute phase reactant, there has been a movement toward including *C-reactive protein* (CRP) in acute metabolic panels to assess whether changes in prealbumin are due to an inflammatory process secondary to acute illness or by malnutrition [45, 47].

CRP levels respond quickly to tissue injury – 4–6 h faster than other acute phase reactants, though aging has not been shown to affect measured values [40]. CRP will decrease within 3–5 days after trauma or the resolution of sepsis as other proteins like albumin and prealbumin begin to increase. Based on this relationship, a *Prognostic Inflammatory and Nutritional Index* (PINI) has been created to assess the severity of disease processes and predict survival. In a study of patients in an acute geriatric unit, a PINI score of greater than or equal to 25 was predictive of in-hospital mortality. Hypoalbuminemia, on the other hand (less than or equal to 30 g/L), was associated with disability but did not predict mortality [48].

Additional studies provide similar evidence to support the use of prealbumin combined with CRP to assess for protein-calorie malnutrition. In a study of Belgian geriatric units, prealbumin was measured at the third day of admission and at discharge. A prealbumin level of 170 mg/L was considered to represent increased risk of malnutrition, and patients with a prealbumin concentration of less than 200 mg/L were provided with caloric supplementation. The patients receiving supplementation were admitted with lower prealbumin and higher CRP levels than patients not receiving supplementation. Those patients were then discharged with higher prealbumin and lower CRP levels than the group without supplementation. Although prealbumin levels do appear to reflect dietary repletion, the levels are not specific, as severity of illness and inflammation influence the same markers [49]. Similarly, Mears has reported on the outcomes of a malnutrition screening program that used prealbumin levels for patient assessment at the time of hospital admission and monitoring throughout patients' hospitalization [50]. In that study, patient care improved with early and accurate identification of patients with protein-calorie malnutrition. Less invasive and less expensive methods of nutritional supplementation were required due to the early diagnosis and length of hospital stay and readmission rates were decreased. Not only was patient care improved, but these effects, along with the ability to add the diagnosis as a comorbid condition for Medicare reimbursement, also led to a significant financial benefit to the hospital [50].

Prealbumin-based malnutrition screening has been shown to identify more patients as being malnourished than albumin screening and is able to provide early and correct identification of patients at risk of malnutrition [47, 49, 50]. Another positive aspect of prealbumin-based screening is that it does not change drastically with increasing age in healthy individuals, unlike albumin levels, which change significantly [51]. Although imperfect, the sensitivity of prealbumin in identifying malnutrition and the minimal change with age make it a useful marker in nutritional assessment in the elderly in the uninflamed state. It is important to emphasize, however, that the use of serum protein markers, including albumin and prealbumin, is *not* validated in critical illness and their use in this setting is discouraged by the Society of Critical Care Medicine (SCCM) and the American Society of Parenteral and Enteral Nutrition (A.S.P.E.N.) [52].

Other Biochemical Markers

While not commonly used in clinical practice, there are additional biochemical markers that have been described as indicators of malnutrion. As part of the vitamin A transport complex formed with prealbumin, *retinol-binding protein* (RBP) is also a marker of nutrition [40]. Levels of prealbumin and RBP are comparable except in vitamin A deficiency. RBP remains stored within the liver until vitamin A levels normalize. Like prealbumin, it has a short half-life (12 h) and decreases with liver disease, stress, and inflammation. RBP levels are increased in the setting of renal failure [53]. Also, levels do change with age, and the mean and median levels for healthy nonagenarians and centenarians are overall lower in men and higher in women [54].

Insulin Growth Factor-I (IGF-I), like prealbumin and RBP, is a protein with a short half-life (2–4 h) and was found to fall during periods of protein malnutrition and rise with refeeding [55]. Baseline levels begin to decrease when patients are in their fifth decade and are reduced by 35–60% by their tenth decade. Levels are affected by renal and hepatic failure, autoimmune disease, inflammation, and stress [40]. IGF-I predicts "life-threatening" and "life-threatening infectious" complications in patients over the age of 76 and correlate with other measurements of nutrition [56].

Fibronectin is a glycoprotein produced by endothelial cells, fibroblasts, macrophages, and the liver. It has been explored as a nutritional marker because of its short half-life (4 h). Levels were noted to fall in the setting of starvation within 2 days and return to normal within 5 days of refeeding, prompting the possibility of use as a marker of protein malnutrition [57]. Because it is not produced solely in the liver, fibronectin is less influenced by liver disease. However, fibronectin levels are impacted by burns, infections, and shock as well as the lipid content in some enteral feeding formulas [40]. While plasma fibronectin concentration does increase within a week of nutritional therapy initiation, it does not seem to change significantly thereafter. It also does not correlate with other measures of nutrition and is not predictive of patient outcomes [58].

Total lymphocyte count (TLC) has also been suggested as a marker of malnutriton. Malnutrition was observed to be associated with a decrease in TLC and a TLC of less than 1,500/mm^3 was associated with a four-fold increase in mortality [59]. One study compared TLC to anthropometry measurements, serum albumin, total cholesterol levels, and total score on the mininutritional assessment (MNA) in patients age 65–95. The authors found that there was no difference among the patient groups (grouped as "severely low," "low," or "normal" TLC) in relation to the other measurements of nutrition. TLC did decrease with increased age, but did not change with other nutritional markers [60]. TLC does not appear to be an appropriate or accurate marker of nutrition in the elderly population.

Body Composition and Anthropometric Measures

The 2012 consensus statement on malnutrition from A.S.P.E.N. has included the loss of muscle mass as part of its definition of malnutrition, bringing focus to the assessment of muscle loss

[61]. Physical exam alone to subjectively assess muscle mass and muscle loss is an unreliable method. Methods of body composition and anthropometric measures have therefore been developed to better estimate lean muscle mass and assess nutritional status.

The simplest model to estimate body composition is one that divides the body as a sum of two components: fat mass and fat-free mass (FFM). FFM includes multiple tissues including skeletal and nonskeletal muscle, organs, total body water (TBW), bone, and connective tissue. TBW can be used to estimate FFM by using the following equation that includes a hydration constant:

$$\mathrm{TBW}\ (\mathrm{kg})/0.73 = \mathrm{FFM}\ (\mathrm{kg})$$

The hydration constant is less reliable in the settings where hydration is variable and in obesity. An alternative calculation to TBW involves lean body mass (LBM) or lean soft tissue (LST) which represents all of FFM except bone and is measured by dual-energy X-ray absorptiometry (DXA) [62]. DXA analyzes soft tissue overlying bone in vivo and works best in areas with well-defined bone such as the arms and legs where a sum of the lean soft-tissue mass of the arms and legs is used to define appendicular skeletal muscle [63].

Body cell mass (BCM) is another method of assessing body composition. BCM represents the total mass of oxygen-consuming and work-producing cells in the body, which is assumed to be the non-fat cellular portion of tissues like skeletal muscle, organ tissue, etc. Although BCM cannot be directly measured, there are several methods to estimate this compartment including neutron activation analysis to determine total body nitrogen, total body potassium counting, and intracellular water measured by multiple dilution. All these calculations can be used to assess nutrition and nutrition interventions, though the varying levels of difficulty and expense lead to more common usage in research than clinical practice [62].

While body composition can be estimated mathematically, there are two bedside methods that can also be used estimate lean muscle mass. Bioimpedance and ultrasound assessment have been recommended by A.S.P.E.N. as direct methods of assessing body composition. Bioimpedance is measured by devices that produce an electric current at varying frequencies between electrodes placed in specified locations on the body [64]. The flow of the current through the body is affected by body composition – electrolyte-rich blood and muscle conduct the current while fat and bone do not. The change in voltage as the current passes through the body's tissue – the impedance – is detected by electrodes. This raw data is used to calculate body composition and estimate FFM based on the assumption that the body is comprised of five cylinders with constant cross-sectional area with patient's height representing the length of the conductor [62]. Devices to measure bioimpedance are not interchangeable – the equations used for the body composition calculations are specific to each device. The accuracy of bioimpedance measurements is dependent upon consistency in terms of set up such as electrode placement and body positioning as well as environmental factors such as temperature. Even biological changes in the patient can impact measurements; for instance electrolyte abnormalities or edema can alter resistance values [64].

Ultrasonography

An readily available option to estimate lean tissue at the bedside is ultrasonography. Ultrasound has recently been shown to predict FFM by taking the sum of measurements from several anatomic sites. Muscle thickness is measured and used to estimate total body FFM [65]. This method is limited by operator experience and the subjective nature of interpreting the image and identifying muscle boundaries during measurement of muscle thickness. Also, muscle thickness changes depending on whether or not the muscle is contracted or relaxed. Ideally, measurements should be taken consistently with the patient in the supine position where muscles are more likely to be relaxed and compressible. The amount of pressure to apply while taking muscle thickness measurements has not yet been standardized; some studies advocating for maximal compression and others for no compression [62]. One study reported that ultrasound measurements of the biceps, forearm, and midthigh muscle thickness FFM in patients with multiorgan failure correlated with DXA-determined estimates of FFM [66]. Muscle thickness can also be used to predict outcomes as shown by a study from the University of Vienna in which quadriceps muscle thickness was shown to inversely correlate with length of stay in ICU patients [67]. Despite the potential limitations, ultrasound-measured muscle thickness has been shown to be a low cost, noninvasive, and reliable method of estimating FFM.

Anthropometry

In addition to the multiple direct bedside methods and calculations that exist to estimate body composition, an indirect means is also available in the form of anthropometry. One component of anthropometry is body mass index (BMI), which is calculated by dividing weight (kg) by height squared (m^2). BMI alone, though, is imprecise in estimating lean body mass. Other anthropometric measurements include body circumference, which can be measured in multiple locations including midbrachial, calf, waist (measured midway between the most inferior rib and the iliac crest), and hip circumference (measured at the widest point of the buttock). Using the waist and hip measurements, a waist-to-hip ratio (WHR) can be calculated and used to determine visceral obesity and identify patients with increased mortality risk [68]. However, increased relative risk of mortality is less pronounced in elderly patients over the age of 65 [69]. The *knee-heel length* is also particularly relevant in the elderly population, where patients are often unable to stand upright for traditional height measurements. Stature height can then be predicted using equations developed from the third National Health and Nutrition Examination Survey (NHANES III) from the National Center for Health Statistics [70]. Other measurements include subscapular, triceps, suprailiac, and thigh skinfold thickness measurements; however these require the use of calibrated calipers [68]. Cross-sectional studies in various countries have provided normative reference data for age-, gender-, and disease-specific anthrompometric measurements [68, 71]. Anthropometric measurements can be applied to predict overall level of independence and function, as illustrated by a cross-sectional study of elderly patients receiving home care in Germany showing that patients requiring a higher level of care for their needs had lower anthropometric values [72].

Sarcopenia and Frailty

In 2006, a special interest group on nutrition in geriatrics was created within the European Society for Clinical Nutrition and Metabolism (ESPEN). One of the concepts further defined by this special interest group was age-related sarcopenia – “the loss of muscle mass and muscle strength associated with aging” [73]. Age-related sarcopenia is the result of intrinsic and extrinsic factors. Intrinsic changes with age include a decrease in anabolic hormones, increased muscle cell death, decreased number of alpha-motoneurons innervating skeletal muscle, and increased proinflammatory cytokines. External factors include decreased intake of protein and vitamin D [73].

In its most extreme form, sarcopenia can progress to frailty syndrome. Frailty is a lack of physiological reserve in multiple organ systems leading to increased vulnerability [74]. Frailty is an independent predictor of 30-day morbidity and mortality and institutionalization after surgery and trauma [74, 76–78]. While there are multiple screening tools for frailty, the American Geriatrics Society/National Institute on Aging has adopted the frailty phenotype introduced by Fried et al [75]. Screening for the frailty phenotype is based on five criteria: weight, grip strength, subjective fatigue, physical activity, and walking speed measurements [75].

Functional Assessment

In measures of anthropometrics and body composition, adequate protein nutrition is represented by fat-free mass (muscle). Since muscle mass is associated with muscle function, function is now being examined as an indicator of nutrition. Functional status can be measured in terms of voluntary and involuntary muscle function. The theory behind the use of function as a surrogate for nutrition status is that muscle structure changes with protein undernutrition leading to loss of contractile elements, increased muscle fatigue, and altered contraction patterns [79]. Function measured with hand grip strength and quadriceps strength is also related to mortality, while muscle mass was not [80]. Electrical stimulation testing can test involuntary muscle contraction and provide an objective measure of function, but more practical testing is available to assess voluntary function. Some commonly used measures are hand grip, knee extension, or hip flexion strength. Past studies have shown that handgrip dynamometry can accurately assess muscle function, which can then be correlated with nutritional status [81]. Diminished handgrip strength is included in the A.S.P.E.N. consensus statement as a characteristic of malnutrition [61]. The use of handgrip strength as a surrogate of nutrition is limited by a lack of consensus on measurement. Additionally, small changes in posture or hand position can change measured grip strength [79].

Nutritional Assessment Scoring Systems

The unidimensionality of most of the exams and laboratory values discussed up to this point limits their efficacy in identifying malnutrition in the complex geriatric population. For this reason, multifaceted assessment tools have been introduced into clinical practice.

Mini Nutritional Assessment

The Mini Nutritional Assessment (MNA) was designed specifically as an assessment tool for the elderly, and as such takes into account many age-related risk factors of malnutrition. In particular, it includes an evaluation of both the physical and mental limitations that impact nutrition in geriatric patients [82]. The original version of the MNA, now called the "full MNA," uses a set of 18 questions, with the first six questions serving as a trigger for further assessment. The questions fall within four categories (anthropometric measures, a general assessment, dietary assessment, and subjective/self-assessment) and can be completed in under five minutes. The six screening questions (originally called the Mini Nutritional Assessment Short Form, or MNA-SF) were found to have the same accuracy as the full version, and are thus now used in clinical practice as the MNA [83]. Using this tool, patients are classified as well-nourished, at-risk for malnutrition, or malnourished based on their overall score on the multiple components [84]. The MNA-SF screening questions are included in Fig. 1.

Of note, the MNA does *not* include biochemical markers as part of the assessment. During the development process, the sensitivity and specificity of the MNA without serum testing remained 96% and 98% [85]. Exclusion of blood samples allows minimization of cost and disruption to the patient. Early detection by the MNA of elderly patients at risk of malnutrition allows for interventions prior to clinical deterioration [84]. Risk for malnutrition or malnutrition identified by the MNA is also predictive of adverse outcomes and mortality [82].

GNRI

The *Nutrition Risk Index (NRI)* is an assessment tool that has been used to identify patients at risk of developing postoperative complications [9]. This score, which in theory shows protein nutrition intake and the stress associated with underlying disease, includes albumin concentration and weight loss. However, the NRI is limited by the same factors that limit albumin as a marker of malnutrition – factors other than protein intake affect serum albumin levels [9]. The *Geriatric Nutritional Risk Index (GNRI)* is a similar tool used for elderly patients in the acute care setting

Mini Nutritional Assessment MNA®

Nestlé NutritionInstitute

Last name:			First name:	
Sex:	Age:	Weight, kg:	Height, cm:	Date:

Complete the screen by filling in the boxes with the appropriate numbers. Total the numbers for the final screening score.

Screening

A Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?
0 = severe decrease in food intake
1 = moderate decrease in food intake
2 = no decrease in food intake ☐

B Weight loss during the last 3 months
0 = weight loss greater than 3 kg (6.6 lbs)
1 = does not know
2 = weight loss between 1 and 3 kg (2.2 and 6.6 lbs)
3 = no weight loss ☐

C Mobility
0 = bed or chair bound
1 = able to get out of bed / chair but does not go out
2 = goes out ☐

D Has suffered psychological stress or acute disease in the past 3 months?
0 = yes 2 = no ☐

E Neuropsychological problems
0 = severe dementia or depression
1 = mild dementia
2 = no psychological problems ☐

F1 Body Mass Index (BMI) (weight in kg) / (height in m)^2
0 = BMI less than 19
1 = BMI 19 to less than 21
2 = BMI 21 to less than 23
3 = BMI 23 or greater ☐

IF BMI IS NOT AVAILABLE, REPLACE QUESTION F1 WITH QUESTION F2.
DO NOT ANSWER QUESTION F2 IF QUESTION F1 IS ALREADY COMPLETED.

F2 Calf circumference (CC) in cm
0 = CC less than 31
3 = CC 31 or greater ☐

Screening score (max. 14 points)

12 - 14 points: Normal nutritional status
8 - 11 points: At risk of malnutrition
0 - 7 points: Malnourished ☐☐

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For more information: www.mna-elderly.com

Fig. 1 The Mini Nutritional Assessment (MNA) (®Société des Produits Nestlé S.A., Vevey, Switzerland, Trademark Owners. © Nestlé, 1994, Revision 2009. N67200 12/99 10M)

[86] and is calculated using height, weight, BMI, and serum albumin. With those parameters, albumin and actual weight are compared to ideal body weight in the following equation initially described by Bouillanne et al. [86]:

$$\mathrm{GNRI} = [1.489 \times \text{albumin (g/L)}] + [41.7 \times (\text{weight}/\text{ideal body weight})]$$

The calculated GNRI is grouped into four grades, with a score of >98 as no risk and a score of <92 as high risk. Patients with nutritional risk at the time of admission when evaluated with the GNRI are more likely to develop complications and have longer lengths of stay [87].

MUST

The malnutrition universal screening tool (MUST), though not developed specifically for geriatric patients, is another assessment tool available for adult patients of any age group and in any care setting [88]. The premise of the tool was to utilize the association between poor nutrition and impaired function to identify risk factors for which to screen. Subsequent validation studies confirmed the resultant loss of function accompanying varying degrees of weight loss across the spectrum of nutrition status (as represented by BMI) [82]. The MUST consists of three components – BMI score, weight loss score, and acute illness score – which are each given a numerical value ranging from 0 to 2. The weight loss score is determined by evaluating the percentage unintentional weight loss in the preceding 3–6 months and the acute disease effect score is based on poor oral intake for at least the preceding 5 days (or predicted poor intake over the subsequent 5 days). The scores are then combined to determine an overall risk score, which is categorized as low, medium, or high risk of malnutrition. The MUST can be completed within 3–5 minutes [88] and has shown to be a reliable identifier of nutritional risk in both the community and healthcare settings [82]. The components of MUST are shown in Fig. 2.

The tool is easy enough for patients to screen themselves. One study showed that 96% of patients found the MUST assessment easy to understand and there was 90% agreement between the self-screening results and the results obtained by a trained health care professional [89].

NRS 2002

The Nutritional Risk Screening-2002 (NRS-2002) scoring system builds from the MUST assessment. This tool utilizes the same markers of nutrition as MUST to identify patients at risk of malnutrition, but takes into account the fact that disease severity changes nutrition needs by including a fourth component that reflects stress metabolism. ESPEN, therefore, recommends the use of this screening tool in hospitalized patients [82]. Extent of undernutrition is given a score from 0 to 3, while disease severity is given a score on the same scale. These are then added together. The goal is to initiate nutritional support in patients above a certain risk score [90] (Fig. 3).

Like the MNA and GNRI, higher scores on the NRS-2002 assessment correspond with worse clinical outcomes. For instance, patients with moderate or high nutritional risk on this screening were found to have a longer average length of stay than those without nutritional risk [9].

Impact of Nutrition on Outcomes

Once malnutrition is diagnosed in the elderly population, it is important to understand the effects of this state on outcomes, particularly surgical outcomes. In elderly people, malnutrition is an independent predictor of mortality in all settings – the community, nursing home, hospital, or recently discharged from the hospital [4]. A study of malnutrition and risk of complications was performed in patients presenting to University Hospital Zurich's Department of Surgery for elective GI surgery. This group of 200 patients was screened for malnutrition preoperatively within 24 h of admission with three assessment tools (including NRS), then followed longitudinally, monitoring for complications. Complications were graded from 1 to 5, with grade 1 complications as the

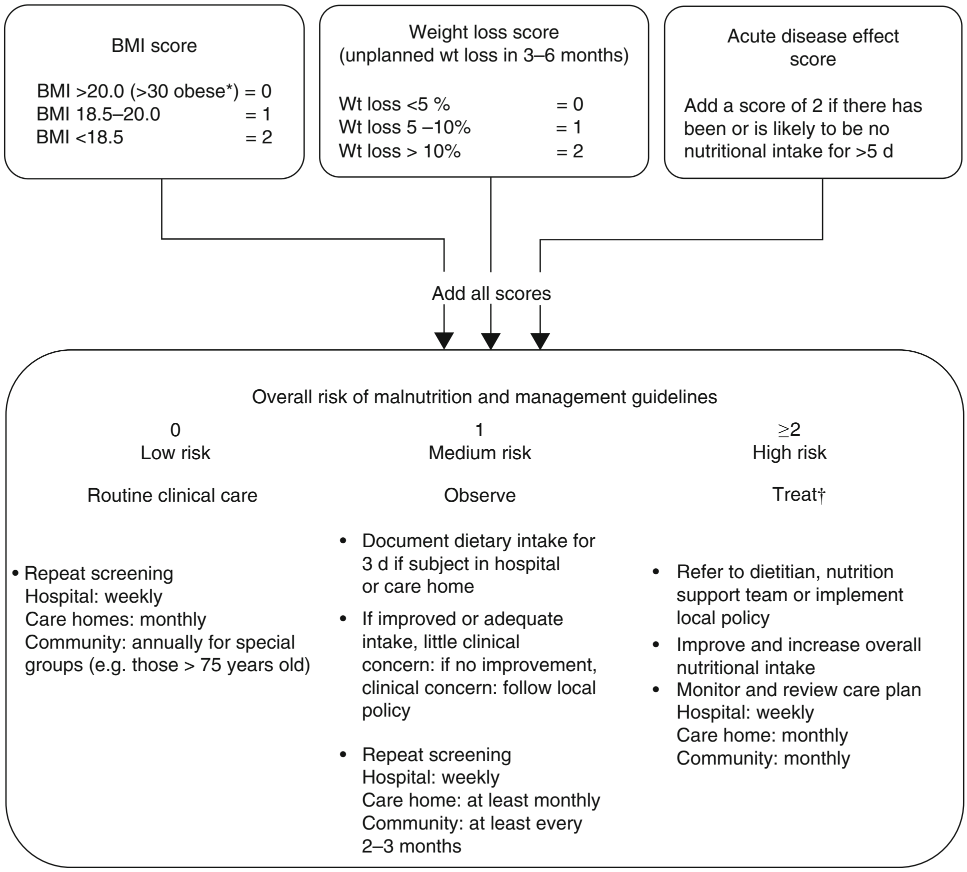

Fig. 2 Malnutrition universal screening tool [88] (Reprinted from British Journal of Nutrition, Volume 92 (5), Stratton RJ, et al. *Malnutrition in hospital outpatients and inpatients: prevalence, concurrent validity and ease of use of the 'malnutrition universal screening tool' (MUST) for adults,* Page 800, Copyright 2004, with permission from Cambridge University Press. The 'Malnutrition Universal Screening Tool' is reproduced here with the kind permission of BAPEN (British Association for Parenteral and Enteral Nutrition). For further information on MUST, see www.bapen.org.uk)

most minor and grade 5 resulting in death of the patient. This study found a correlation between nutritional risk and postoperative complications. In fact, every patient found to be at high risk of malnutrition as defined by the NRS developed a postoperative complication. The complication rate was 64% in patients at nutritional risk, while it was only 20% in patients without nutritional risk. Those patients at risk of malnutrition also had more severe complications, with 45% of patients at nutritional risk developing grade 3–5 complications compared to 7% of patients not at nutritional risk developing the same severity complications [9]. Similarly, a prospective cohort study conducted in 26 hospital departments (including geriatrics) in 12 countries used the NRS-2002 to assess the relationship between nutritional risk and outcomes. In over 5,000 patients studied, patients determined to be at risk of malnutrition had more complications, higher mortality, and increased length of stay compared to patients identified as not at risk [6, 91].

These outcomes were similarly reported in geriatric patients at risk of malnutrition. Data from the University of Alabama at Birmingham's Study of Aging were also used to assess the association between malnutrition and mortality. In this study, 978 elderly patients over age 65 were followed longitudinally over 8.5 years. Patients found to be at high nutritional risk were more

Table 1 Initial screening

		Yes	No
1	Is BMI <20.5?		
2	Has the patient lost weight within the last 3 months?		
3	Has the patient had a reduced dietary intake in the last week?		
4	Is the patient severely ill? (e.g. in intensive therapy)		

Yes: If the answer is 'Yes' to any question, the screening in Table 2 is performed.
No: If the answer is 'No' to all questions, the patient is re-screened at weekly intervals. If the patient e.g. is scheduled for a major operation, a preventive nutritional care plan is considered to avoid the associated risk status.

Table 2 Final screening

Impaired nutritional status		Severity of disease (≈ increase in requirements)	
Absent Score 0	Normal nutritional status	Absent Score 0	Normal nutritional requirements
Mild Score 1	Wt loss > 5% in 3 months or Food intake below 50–75% of normal requirement in preceding week	Mild Score 1	Hip fracture* Chronic patients, in particular with acute complications: cirrhosis*, **COPD***. *Chronic hemodialysis, diabetes, oncology*
Moderate Score 2	Wt loss > 5% in 2 mths or BMI 18.5-20.5 + impaired general condition or Food intake 25–60% of normal requirement in preceding week	Moderate Score 2	Major abdominal surgery* Stroke* *Severe pneumonia, hematologic malignancy*
Severe Score 3	Wt loss > 5% in 1 mth (>15% in 3 mths) or BMI <18.5 + impaired general condition or Food intake 0-25% of normal requirement in preceding week in preceding week.	Severe Score 3	Head injury* Bone marrow transplantation* *Intensive care patients (APACHE>10).*
Score:	+	**Score:**	**= Total score**
Age	if ≥ 70 years: add 1 to total score above	**= age-adjusted total score**	

Score ≥3: the patient is nutritionally at-risk and a nutritional care plan is initiated
Score <3: weekly rescreening of the patient. If the patient e.g. is scheduled for a major operation, a preventive nutritional care plan is considered to avoid the associated risk status.

NRS-2002 is based on an interpre-tation of available randomized clinical trials. *indicates that a trial directly supports the categorization of patients with that diagnosis. Diagnoses shown in *italics* are based on the prototypes given below.
Nutritional risk is defined by the present **nutritional status** and risk of impairment of present status, due to **increased requirements** caused by stress metabolism of the clinical condition.

A nutritional care plan is indicated in all patients who are

(1) severely undernourished (score = 3), or (2) severely ill (score = 3), or (3) moderately undernourished + mildly ill (score 2 + 1), or (4) mildly undernourished + moderately ill (score 1 + 2).

Prototypes for severity of disease
Score = 1: a patient with chronic disease, admitted to hospital due to complications. The patient is weak but out of bed regularly. Protein requirement is increased, but can be covered by oral diet or supplements in most cases.
Score = 2: a patient confined to bed due to illness, e.g. following major abdominal surgery. Protein requirement is substantially increased, but can be covered, although artificial feeding is required in many cases.
Score = 3: a patient in intensive care with assisted ventilation etc. Protein requirement is increased and cannot be covered even by artificial feeding. Protein breakdown and nitrogen loss can be significantly attenuated.

Fig. 3 NRS-2002 score table [90] (Reprinted from Clinical Nutrition Volume 22(4), Kondrop J, et al., *ESPEN Guidelines for Nutrition Screening 2002*, Page 420, Copyright 2003, with permission from Elsevier http://www.sciencedirect.com/science/journal/02615614)

likely to have been hospitalized at each 6 month interval [92]. Another study reviewed geriatric admissions retrospectively over the course of 18 months in Australia. Using the MNA within 72 h of admission, 53.1% of the study population was identified as at risk of malnutrition and 17.3% was malnourished. These patients were less likely to be discharged home and 46% of malnourished patients had a poor outcome, such as admission to a higher level of care or death. They also had a longer length of stay and comparatively higher risk of mortality within the next 18 months. It is estimated that the cost of treating these malnourished or at risk patients is 20% higher than patients with a similar diagnosis but without nutritional risk [93]. Likewise, in another study, 150 elderly patients were recruited and screened with the MUST assessment. Of that group, 58% were identified as at risk for malnutrition and had higher rates of in-hospital and post-discharge mortality and longer hospital stays than low risk patients [94]. The association between clinical outcomes and risk of malnutrition is depicted in Fig. 4.

Considering surgical patients, those with malnutrition have a higher likelihood of developing complications after major surgery [95, 96]. In particular, wound complications such as dehiscence and anastomotic leak, and infectious complications such as surgical site infections, are associated with poor nutrition [97]. Malnutrition also influences overall functional status throughout the perioperative period. To demonstrate the impact of malnutrition on long-term functional status postoperatively, a German group followed 97 elderly patients at a large urban hospital with hip fractures. Patients had been evaluated with the MNA prior to hip fracture and were observed during their hospitalization and for 6 months after discharge. In the patients identified as malnourished or at risk for malnutrition, functional status was worse at all stages of care – prefracture, while inpatient, and at 6 months after discharge [98].

The American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) prioritizes appropriate preoperative assessment of the geriatric surgical patient. In their guidelines released in conjunction with the American Geriatrics Society, the group recommends using a screening tool preoperatively to identify patients at *severe nutritional risk (SNR)* [97]. This tool is comprised of three criteria: BMI <18.5 kg/m^2, serum albumin <3.0 g/dL without renal or hepatic dysfunction, and unintentional weight loss >10–15% in the preceding year and is adapted from criteria set forth by ESPEN. Patients are considered at severe nutritional risk if any of the three criteria are met, and further nutritional assessment is recommended [97]. When utilizing this tool preoperatively in geriatric patients, SNR is associated with poor postoperative outcomes. A study of elderly patients undergoing pancreaticoduodenectomy for benign disease at one institution were screened

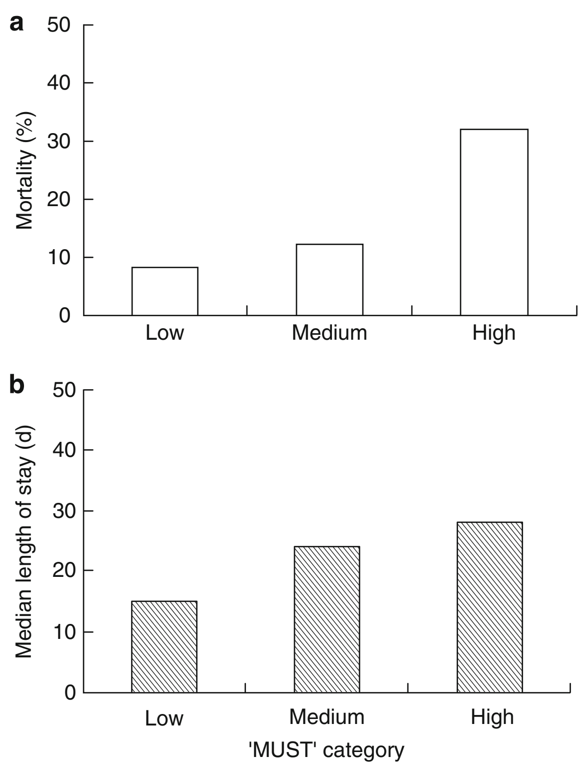

Fig. 4 Outcomes depicted by malnutrition risk, as identified with MUST: (**a**) in-hospital mortality, (**b**) length of hospital stay [94] (Reprinted from British Journal of Nutrition, Volume 95(2), Stratton RJ, et al. *'Malnutrition Universal Screening Tool' predicts mortality and length of hospital stay in acutely ill elderly*, Page 328, Copyright 2006, with permission from Cambridge University Press)

preoperatively for SNR. Those patients identified had a 5-year survival rate of 64.8% compared to 92.5% in patients of the age without SNR [99].

Nutrition Optimization

Energy Requirements in the Elderly

After the diagnosis of malnutrition or nutritional risk has been made in an elderly patient, the next concern that arises is how to address this state. Individualized nutrient balance can be estimated by directly determining nutrient intake compared to calculated energy expenditure/nutrient losses [100]. Alternatively, protein and energy requirements can be estimated for this patient group. At baseline, the recommended energy intake for healthy adults is 25 kcal/kg/day and the recommended intake of protein in adults is 0.8 g/kg/day [17]. This recommendation for protein nutrition was determined by the New Mexico Aging Process Study, a longitudinal study of nutrition in healthy elderly patients that was performed from 1979 to 2003 [101]. Data from 1980 to 1990 of this study shows that women with protein intake greater than 0.8–1.2 g/kg of body weight had fewer health problems over the 10-year study period than women consuming <0.8 g/kg. Similarly, those patients who died or dropped out of the study due to illness had decreased energy intake [102]. This information suggests that protein supplementation can improve outcomes.

Both energy and protein requirements are increased during periods of stress, such as hospitalization or surgical intervention. In order to prevent loss of lean muscle mass, protein intake must account for the increased breakdown in periods of stress and also in the setting of chronic medical conditions that result in protein loss, such as end-stage renal disease. Patients undergoing continuous renal replacement therapy (CCRT) are recommended 2.5 times the typical amount of protein [17]. Similarly, in the severely ill elderly patient, the recommended requirement of protein is at least 1.0–1.2 g protein/kg/day and 20–30 kcal/kg/day of non-protein energy [103]. During acute hospitalization, though, it is difficult to balance energy intake with basal energy expenditure (BEE). In acutely hospitalized elderly men and women (over age 80), the estimated energy expenditure in most patients is higher than energy intake. The resulting negative energy balance leads to a measurable decline in mid-arm muscle circumference during the hospital course [104]. With elderly patients shown to be at risk of undernutrition during hospitalization, some studies even suggest a protein intake of 1.5 g/kg/day in elderly malnourished patients in an attempt to overcome protein losses and to replenish lean body mass [103, 105]. However, in a prospective cohort study, 21% of the included elderly patients were shown to have an average intake of less than 50% of their estimated maintenance energy requirements while hospitalized. These patients were found to have a higher rate of both in-hospital and 90-day mortality [106].

Perioperative Nutrition Management

Early initiation of nutritional intervention is extremely important in elderly patients because it is much more difficult to restore lost muscle mass. Body cell mass is restored at a much slower rate in the elderly as compared to younger patients [107]. When determining etiology for this undernutrition, one common factor was frequent *nil per os* (NPO, nothing by mouth) orders and lack of utilization of oral supplementation, enteral, and parenteral nutrition [106]. Surgery itself is a traumatic event with a significant risk of complications. Even without adverse outcomes, deconditioning and altered muscle mass related to immobility during hopsitalization lead to reduced functional capacity extending for weeks beyond actual discharge. Elderly patients, with their reduced lean muscle mass, are particularly at risk of these consequences [105].

Sometimes, even when patients are identified as being malnourished or at risk of malnourishment, appropriate nutritional therapy is not initiated preoperatively. This phenomena is illustrated by a multicenter Belgian study in which 66% of the patients over 70 years were found to be malnourished but none of those patients had been referred to a dietician or started on supplementation [6]. With evidence of missed opportunities for nutritional intervention, a new focus has been placed on improving nutrition in the perioperative period.

Oral supplementation

As illustrated in the study by Sullivan [106], hospitalization itself increases the risk of malnutrition, as patients are often placed on restrictive diets based on their chronic diseases (such as excluding sweets for diabetics or limiting calories for “heart healthy” diets), or made NPO for tests and interventions [17]. One way to improve perioperative nutrition is to avoid prolonged preoperative fasting. Other than in the setting of emergency surgery or delayed gastric emptying, patients receiving clear liquids within 2–3 h of surgery are at no greater risk of aspiration than those who have been fasting for 12 h. In fact, patients who are loaded with carbohydrate supplementation the night before and 2 h before surgery had lower risk of postoperative insulin resistance and improved muscle mass [108]. Similarly, there is no benefit to routine nasogastric tube decompression or delayed postoperative oral intake. Early oral and enteral nutrition does decrease infectious complications, hospital length of stay, and ICU length of stay [108].

Another simple intervention to encourage oral intake is to allow patients more freedom in their diet to choose foods that appeal to them (like salty foods and sweets) and opt for monitoring chronic conditions closely as opposed to strictly restricting intake of certain foods [17].

In addition to encouragement of ad lib oral intake, oral nutritional supplements (ONS) can also be utilized preoperatively. The question of the value of oral supplementation in improving nutrition and functional status has been evaluated with mixed results. One study showed that, while elderly patients in the community did have increased weight and decreased falls, functional status remained unaffected [109]. In orthopedics in particular, interventions to optimize oral nutrition have been shown in multiple studies to result in improved outcomes. In a study of elderly patients with femoral neck fractures, once daily oral supplementation (250 ml, 20 g protein, 254 kcal) given for 30 days in the intervention group led to decreased mortality and complication rates both in-hospital and at 6 months after the fracture [110].

The results of the study of orthopedic patients contrast with the outcome of another study in which elderly patients with malnutrition were randomized and the intervention group given 8 weeks of supplementation starting at hospital discharge. For the follow-up period of 24 weeks, weight, BMI, anthropometrics, handgrip strength, quality of life, and need for health care professional or social services were documented. The patients receiving supplementation were shown to have a significant improvement nutrition status at 24 weeks compared to their baseline that was not seen in the control group; however the two groups were similar thereafter. Functional capacity as measured by handgrip strength improved in the supplemented group and was significantly improved over the control group until week 8, but then declined again [111]. In this study, there was no clear-cut benefit seen for oral supplemental nutrition after discharge. This study leads to the question of whether or not discharge is too late to initiate nutritional interventions in a population and whether resources should be focused on preventative interventions [111].

To better demonstrate the effects, Milne and colleagues performed a meta-analysis that included 62 trials and 10,187 randomized patients. They found that supplementation does result in small weight gain consistently in most studies. While there was no evidence to support that supplementation improved functional status or decreased mortality in all patients, it did show a beneficial effect on mortality for patients identified as undernourished. Additionally, this review found more evidence to support that supplementation reduces complications, though further investigation is needed in the future, as the studies were deemed to be poor quality [112]. Despite the reported success of some individual studies, based on meta-analysis, outpatient counseling and oral nutritional supplementation of elderly malnourished patients in the community did not show consistent results [113].

In addition to oral supplementation of protein and energy, vitamin supplementation is also necessary in elderly patients. Vitamin D is commonly deficient in this age group and can lead to depression, cognitive changes, and increased fracture risk. Patients over 70 years should receive at least 800–1,000 IU of vitamin D daily. Hospitalized or institutionalized patients have an increased risk of developing vitamin D deficiency due to the lack of sun exposure. Vitamin B12 deficiency is also common and can be seen in patients with prior gastric surgeries or pernicious anemia as well as other neurologic or psychologic conditions. Normally, vitamin B12 and folate are obtained adequately by diet alone, but in some patients oral supplementation may be required. B12 can be supplemented orally at a dose of 1,000 mg/day, but deficiency does not tend to become apparent until after several years of decreased absorption [17, 100]. Calcium can also be depleted in geriatric patients. The recommended dietary intake in this patient population is 1,200 or 1,500 mg/dL to reduce the risk of osteoporosis and impaired functional capacity [108]. Doubling of the daily multivitamin dose can be safely done while nutritional support is ongoing and until normal nutritional status is achieved [100].

Enteral Nutrition

Enteral nutrition (EN) is indicated regardless of risk of malnutrition, and is recommended to start immediately if the patient is not expected to eat for more than 7 days after surgery or if they cannot maintain more than 60% of the recommended oral intake for 10 days or more [108, 114, 115].

Preoperative (EN) has been shown to reduce postoperative complications in cancer patients receiving 3,500–4,000 cal/day (or 150% of calculated basal energy expenditure) when compared to oral diet alone [108]. Both ESPEN and ASPEN guidelines emphasize the importance of preoperative nutritional optimization by recommending that operative interventions be postponed for enteral nutrition in patients with elevated nutritional risk [108]. ESPEN defines severe nutritional risk as weight loss of 10–15% within 6 months, BMI of less than 18.5 kg/m^2, SGA grade C or albumin less than 3.0 g/L in the absense of renal or hepatic dysfunction [115].

Supplementary EN in addition to oral nutrition has not been shown to be particularly beneficial outside of hip fracture patients and are poorly tolerated in the elderly [114]. Patients receiving supplemental nocturnal tube feeds with hip fractures did show improved outcomes. Patients were divided into three groups based on anthropometric measurements. Patients from the “thin” and “very thin” groups were divided into a control and intervention group. Overnight supplementary enteral feeds were given via nasogastric tube (28 g protein,1,000 kcal) to the intervention group in addition to ad lib oral diet during the day. The group receiving supplmental feeds had improved anthropometric measurements and plasma protein levels as well as shortened hospital length of stay and rehabilitation time [116].

There is also less evidence for the benefit of post-operative EN. Gastrointestinal cancer patients receiving preoperative and perioperative enteral feeds only had the same outcomes as patients whose feeds were continued through the postoperative period (though there was an improvement in both groups when compared to patients receiving no enteral nutrition). Oral supplementation has not been shown to improve clinical outcomes or functional capacity [108].

When comparing enteral and parenteral nutrition, EN is preferred unless contraindicated, as in intestinal obstruction, ileus, severe shock, or intestinal ischemia [115]. In a review of 35 clinical trials performed by ESPEN, there is a significant benefit in EN when compared to PN in terms of length of hospital stay, infectious complications, and cost [108]. Tube feeds should not, however, be initiated without careful consideration. For instance, tube feeds should not be given over oral nutrition for ease of care, as elderly patients can typically maintain their nutritional needs with oral nutrition and assisted feeding or oral supplements. Additionally, the decision to start tube feeding in elderly patients requires reflection of the ethics surrounding this intervention, such as considering whether enteral will change outcomes or aid recovery or if the intervention is appropriate in maintaining the patient's expressed wishes and goals of care [114].

In the elderly, enteral feedings via percutaneous endoscopic gastrostomy (PEG) are tolerated much better than feeds via nasogastric (NG) tube. Patients with neurological dysphagia were able to tolerate 93–100% of PEG feeds as opposed to only 55–70% of NG tube feeds [114]. ESPEN does recommend placement of a jejunostomy feeding tube if the patient is already undergoing major abdominal surgery [115]. Regardless of access type, longer-term supplementation beyond 4 weeks is recommended through definitive non-oral access. In terms of tube feed formula, feeds with immune-modulating substrates like argine are recommended for patients undergoing elective surgery for head and neck cancer and major abdominal surgery for cancer. Multiple meta-analyses have shown decreased postoperative complications rates and hospital length of stay in trauma and general surgical patients receiving immune-modulating tube feed formulas [114].

Parenteral Nutrition

Age alone is not a contraindication to parenteral nutrition (PN). In the elderly population, routine postoperative PN is generally not recommended in general surgical patients as they had a 10% greater incidence of complications [108]. A potential complicating factor of using PN in elderly patients is higher rates of insulin resistance leading to hyperglycemia and cardiac and renal dysfunction and may require that lipid content be increased. PN formulas should be adjusted to use higher lipid content [103]. Although there is a higher risk of vascular erosion from central catheters in the elderly age group, parenteral nutrition is still recommended when oral or enteral nutrition is impossible or without sufficient nutrition for >7–10 days [103, 115]. In a review of 13 prospective randomized control trials, moderate to severely malnourished gastrointestinal cancer patients fed for 7–10 days with PN had a pooled reduction in postoperative complications compared to oral nutrition by 10%; however, only one of these studies of preoperative PN showed a statistically significant decrease in mortality [108].

In the geriatric population in particular, it is important to consider the ethical aspects of PN, treating it as an intervention and not routine care. Probability of recovery and goals of care should be weighted in the decision to initiate PN [103].

Refeeding Syndrome

During the initiation of any nutrition regimen in an undernourished elderly patient, attention should be paid to the risk of refeeding syndrome. In this syndrome, phosphate can drop precipitously with introducing glucose rapidly electrolyte shifts also result in lower serum levels of potassium and magnesium. Thiamine levels can similarly drop. All of these changes occurring with rapid refeeding can invoke neurologic symptoms [103]. In patients with delirium at baseline, these symptoms can be significant. It is important to note, however, that most cases of full-blown refeeding syndrome have been reported decades ago and occurred in the setting of *severely* malnourished patients receiving very high caloric loads (up to 75 kcal/kg/day). In modern practice, it is extremely rare to encounter the refeeding syndrome. Isolated refeeding hypophosphatemia is very common, but the clinical significance of this laboratory finding remains to be determined [117]. Electrolyte levels, particularly potassium, magnesium, and phosphate, should be closely monitored (daily or more frequently as necessary) in the first few days of starting nutrition therapy and low levels should be aggressively treated with intravenous replacement. Withholding nutrition in the setting of mild hypokalemia, hypomagnesemia, and hypophosphatemia in the absence of clinical symptoms is not recommended.

"Prehabilitation"

Widening the scope of intervention beyond the immediate preoperative period, the concept of "prehabilitation" emerged from the desire to preemptively counteract the acute stress and negative effects of surgery by improving functional capacity preoperatively. Effective prehabilitation includes both nutrition and exercise interventions and begins preoperatively, continuing through the perioperative period, and continues beyond the immediate postoperative period. One proposed prehabilitation process was tested in colorectal cancer patients prior to colon resection. Patients participating in moderate-intensity exercise and anxiety reduction strategies in addition to the "enhanced recovery after surgery" (ERAS) protocol were more likely to return to their preoperative baseline by 8 weeks after surgery ([105]. Using this same model, the goal of nutritional interventions should be to optimize patients for the stress of surgery as opposed to reacting to and replacing protein loss. Patients at risk of malnutrition can be identified preoperatively using the various assessment tools previously described and interventions initiated [115]. Tools like the MNA not only identify patients with malnutrition but also help target preoperative interventions by reviewing where points are lost in the assessment – simple interventions like supervision during eating for institutionalized patients with functional impairments can improve oral nutrition intake [84]. Similarly, interventions that allow patients to make their own food choices can improve oral nutritional intake. One study changed the food service in a long-term care facility from preplated to cafeteria-like arrangement where patients were able to choose the type of food and amount they'd prefer to eat. This intervention resulted in increased energy intake among residents of the facility at risk of malnutrition [118].

Another example of prehabilitation is found in a multidisciplinary program utilized for elderly orthopedic patients with hip fractures. Patients received either standard nutrition or care from an integrated team that initiated nutritional support during the initial hospitalization and coordinated the transition of care to the outpatient setting for further maintenance. Using multiple measures of nutrition, there was a significant difference in energy intake between the two groups in the first week, with the intervention group taking in more daily energy and more mean protein. When nutrition was reassessed at 3 months, fewer patients in the intervention group were identified as malnourished or at risk of malnutrition [119].

Comprehensive Geriatric Assessment

The Comprehensive Geriatric Assessment (CGA) falls under the umbrella of prehabilitation. Identifying factors that contribute to poor outcomes in the elderly patient population can allow for preoperative interventions to be made. In the traditional model of preoperative assessment, focus is placed on individual systems or subjective assessments. Alternatively, the CGA provides a multidisciplinary approach that offers a complete evaluation of the elderly patient and cohesive plan of care for preoperative optimization that focuses on deficient areas [84]. The original concept of the CGA comprised four major domains – physical health, functional status, psychological health, and socioenvironmental factors [120]. These domains have been further expanded to include a number additional areas that include activities of daily living (ADL), instrumental activities of daily living (IADL), cognition, depression, fall risk, nutrition, polypharmacy, and social support. For purposes of the CGA, the MNA is typically used to evaluate nutrition [84]. CGA has been utilized with success across a variety of clinical services. One study chose to focus specifically on elderly preoperative patients and the usefulness of CGA in predicting outcomes. Patients with impairments in more than five of eight areas were found to be more likely to have an adverse outcome with an event rate of 37.8%. They were also more likely to die while in-hospital, have prolonged lengths of stay, or need to be institutionalized upon discharge [120].

Conclusion

The elderly population in the USA is expected to grow significantly over the next several decades. This group is especially at risk for malnutrition. The anorexia of aging and the physiological, psychological, and socioeconomic factors that contribute to a loss of lean muscle mass have already made undernutrition a prevalent condition in both the community and across all healthcare settings. Malnutrition is a predictor of poor clinical outcomes and contributes significantly to morbidity and mortality. Prompt recognition is therefore required in order to initiate timely interventions. Traditional serum testing, though straight forward, is not accurate in identifying malnourished patients or in monitoring the efficacy of interventions. Multimodal assessments that account for changes in functional capacity and severity of illness are more appropriate. It is now evident that reversal of malnutrition in the elderly is particularly difficult after significant lean body mass has been lost. Current treatment goals have shifted to emphasize the prevention of malnutrition as opposed to reaction to the state, promoting preoperative optimization and prompting initiation of enteral nutrition postoperatively. Looking forward, the future of managing geriatric patients in the surgical setting will continue to build on this foundation of prevention and include a multidisciplinary team and a holistic approach to overall care, including nutrition.

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Medication-Related Problems in Surgical Patients

11

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Abstract

Older adults take more medications than any other age group. Evidence suggests polypharmacy increases throughout the last year of life of older adults, fueled not only by symptomatic medications but also by long-term preventive treatments of questionable benefit ([1] too many drugs 2017). The greater the number of medications a patient receives, the greater the likelihood of experiencing a medication-related problem. In the elderly, this can have disastrous repercussions. Surgeons are trained to individually evaluate the risks versus benefits of any given procedure. Equally important, surgeons should evaluate the risks versus benefits of medications they will commonly utilize. As healthcare moves rapidly toward a value-based model of care, understanding medication risks in the elderly becomes every team members' responsibility. Central to a patient's care coordination is the safe transition of their medications between care settings. Disparate data systems, lack of accountability, and interoperable electronic medical records contribute to medication *wreckonciliation*. While the correct term is medication reconciliation, the use of "wreckonciliation" is meant to underscore the difficulties in adequately determining a patient's true medication list. This chapter will focus on common medication-related problems (MRPs) that can result in postoperative complications.

Examples of age-related physiologic changes affecting drug pharmacokinetics

Physiologic change	Direction of change	Drugs affected by this change	Result of change
Serum albumin	↓	Phenytoin, naproxen, valproate, and warfarin	Increased free (active) fraction of drug; increased effects
α_1-Acid glycoprotein	↑	Propranolol, antidepressants, lidocaine, methadone, and quinidine	Decreased free (active) fraction of drug; decreased effects
Body fat	↑	Fat-soluble drugs (e.g., benzodiazepines)	Increased volume of distribution; increased half-life and potential for accumulation
Lean muscle mass	↓	Digoxin	Decreased volume of distribution; increased concentration; lower loading dose is needed
Body water	↓	Water-soluble drugs (e.g., lithium)	Decreased volume of distribution; increased concentration and effects
Hepatic blood flow	↓	High-hepatic extraction ratio drugs (e.g., morphine, meperidine, lidocaine, and isosorbide)	Decreased first-pass metabolism; increased effects
Hepatic metabolism (phase 1: reduction, oxidation, hydroxylation, and demethylation)	↓	Diazepam, alprazolam, triazolam, theophylline, quinidine, propranolol, phenytoin, and imipramine	Decreased metabolism; increased half-life and concentration
Renal function	↓	Aminoglycosides, digoxin, ciprofloxacin, and allopurinol	Decreased clearance; increased effects, toxicity, or both

(continued)

Biology of Aging

With advancing age, organ systems decline at varying rates and independent of each other. An individual's organ reserve capacity helps conceptualize the ability to rebound from illness, injury, or insults. In the absence of disease, an elderly patient's organ system declines may not impair daily function [2, 3]. However, in the setting of illness or advance disease, what might otherwise be considered insignificant in a younger patient becomes a major threat to organ function in the elderly. The ability to withstand even a minor insult can be decreased, and recovery may be delayed. Appreciating medication-related factors that affect an organ system's reserve capacity is an imperfect science. The principles of pharmacokinetics help frame an understanding of how physiologic changes with aging affect medications [4]. Understanding pharmacokinetic changes associated with aging can help surgeons better anticipate MRPs. Pharmacokinetics is defined as the delivery of a drug to its site of action. This includes drug absorption, distribution, metabolism, and excretion. These changes are reviewed here in general terms to provide a background for the discussion of specific drug classes [5] (Table 1).

Table 1 Pharmacokinetic changes with aging

Absorption	Extent not affected
	Rate is reduced or unaltered
	Increased gastric pH
	Unchanged passive diffusion
	Decreased active transport
	Decreased first-pass effect
	Decreased GI blood flow with certain diseases (e.g., HF)
Distribution	Decreased total body water
	Decreased lean body mass
	Decreased serum albumin
	Increased body fat
	Increased or decreased free fraction of highly plasma protein-bound drugs
	Higher concentration of water-soluble drugs
Metabolism	Decreased liver blood flow
	Decreased liver size
	Decreased enzymatic activity
	Variable decreased and increased $t_{1/2}$ for phase 1 oxidation drugs
	Decreased clearance and increased $t_{1/2}$ of drugs with high extraction ratio
Excretion	Decreased GFR
	Decreased renal blood flow
	Decreased tubular function
	Decreased clearance and increased $t_{1/2}$ for drugs eliminated primarily by the kidneys

GI Gastrointestinal, *GFR* Glomerular filtration rate, *HF* Heart failure

Drug Absorption

The amount of oral drug absorption (bioavailability) is dependent on many factors not related to age, including the presence of food, drug ionization, and dosage formulation [6]. Absorption can occur anywhere along the gastrointestinal tract. Oral drug absorption can also include buccal absorption of medications specially designed to disintegrate in patients unable to swallow. Some formulations are designed to release medication in response to changes in intestinal pH or osmolality. In general, older adults tend to have a slight increase in gastric pH. This increase is unlikely to result in altered drug absorption [6, 7].

When the stomach pH is significantly altered, it is possible to impact drug absorption. For example, proton pump inhibitors (PPIs) can reduce the antifungal activity of ketoconazole and itraconazole. It is now recognized that PPIs can reduce the activity of mycophenolate mofetil [117]. Proton pump inhibitors can also affect drug absorption by interacting with adenosine triphosphate-dependent P-glycoprotein (e.g., inhibiting digoxin efflux).

Older adults tend to experience two alterations that can lead to clinically significant changes in the rate of oral drug absorption. First, changes in gastrointestinal blood flow may reduce portal circulation and delay gastric absorption. For example, these changes can be seen in some heart failure or cirrhosis patients with substantial hepatic congestion. And second, decreased gastric emptying, resulting from conditions such as Parkinson's disease or diabetes, may also delay the rate of absorption, but not the extent of drug absorbed [7, 8]. Unless therapeutic failure is observed, no changes in dosing are required to overcome delays in gastric absorption.

Oral bioavailability can be substantially altered in the presence of food, resulting in drug-food interactions. For example, patients who receive calcium supplementation while taking quinolones have a 50% reduction in the absorption of the quinolone due to chelation with calcium. The authors recommend discontinuing most oral calcium supplementation during the postoperative period to prevent potential chelation interactions with antibiotics. Bisphosphonate bioavailability is exceedingly low when taken with anything other than water.

Levodopa absorption is substantially decreased when consumed with a high-protein meal [9]. In addition, certain foods can significantly alter drug levels and actions. Patients on warfarin who alter their intake of vitamin K-containing foods risk changes in their international normalized ratio (INR). Consumption of grapefruit irreversibly inhibits intestinal CYP450 3A4 isoenzyme activity. This results in presystemic decreases in metabolism leading to increases in therapeutic concentrations that can last for up to 72 h. In summary, the rate of absorption may be delayed with aging, but the overall extent of absorption is unlikely to be altered.

Limited information is available about topical drug absorption changes as a result of aging. Topical administration is a way to minimize first-pass metabolism, provide more continuous therapeutic drug concentrations, and potentially improve medication adherence. For example, postoperative pain control may include the use of fentanyl or lidocaine patches. In general, decreases in skin thickness and integrity may alter drug absorption and subsequently peak concentrations. When comparing healthy young volunteers with healthy elderly volunteers receiving transdermal fentanyl patches, the older patients demonstrated higher systemic concentrations of fentanyl and correspondingly greater adverse effects resulting in drug discontinuation [10]. An additional concern when administering medications in patch form is the ability to safely remove the patch without damaging the underlying skin. Finally, all patches utilize adhesives that can cause localized skin irritation. The use of presurgical skin disinfectants and body preparations may contribute to heightened skin sensitivity to patch adhesives.

Distribution

The distribution of drugs is altered by the aging process. Total body and intracellular water decrease, as does muscle mass, whereas body fat increases [2, 3]. These changes have important implications for drug distribution that can affect both the half-life of a compound and the concentration of the drug in various tissues (e.g., lipophilic versus hydrophilic saturation). The volume of distribution of water-soluble drugs is likely decreased because of the decreased total body and intracellular water described above. This results in higher concentrations of hydrophilic substances as they have a smaller volume in which to distribute. Similarly, the volume of distribution for lipid-soluble drugs tends to be higher because of increased fat stores, resulting in prolonged and less predictable half-lives. Changes in protein binding can also alter receptor site activity. When medications exhibit substantial protein binding (generally >90%), the potential for protein-binding interactions due to changes in serum albumin becomes more pronounced. For example, in the case of low albumin levels, the relative proportion of free or unbound drug may be increased, enhancing the pharmacologic and toxic properties of the drug. To further illustrate this point, consider the highly protein-bound drug phenytoin. By convention, when ordering phenytoin levels what is typically reported is the total drug level [11]. In the setting of low albumin, however, the free drug concentration may be high, resulting in toxicity despite a total level in the therapeutic range. In contrast, the carrier protein α-acid glycoprotein may increase with age, as it does with illness, so drugs that bind to this protein may have a lower proportion unbound; an example is propranolol [12]. Another caveat with drug levels is that normal ranges are often established on young persons; therefore targeting lower therapeutic drug levels in older adults may minimize the risk of toxicity. The important exception to this approach is for antibiotic therapy where specific minimum inhibitory concentrations (MIC) are specified. Finally, some evidence suggests that conformational changes in the ability of albumin to bind drugs increase as one ages [11]. Therefore, despite a normal albumin level, the affinity of albumin to bind to medications may be reduced.

Metabolism

First-pass metabolism, liver size, and blood flow tend to decrease with age by 20–30%. Drugs that depend on extensive first-pass metabolism, such as agents with a high-hepatic extraction ratio, may have higher therapeutic levels resulting from decreased hepatic metabolism [9, 13, 14]. Pertinent to a surgeon, it is estimated that morphine exhibits a 33% reduction in clearance in the elderly as a result of decreased first-pass metabolism [14]. Therefore, the effects of morphine may last longer in the elderly. However, this does not constitute a reason to avoid morphine in older patients. Drugs that have high-hepatic extraction ratios also exhibit decreased metabolism and potentially increased therapeutic concentrations. Atorvastatin is a high-hepatic extraction ratio drug with increased serum concentration (40%) and area under the concentration curve (30%) [14]. Therefore, closer attention to liver function tests and potential dose reduction may be warranted. Similar findings occur with simvastatin and lovastatin.

Pharmacogenomics and the Cytochrome P450 Enzymes

The field of pharmacogenomics continues to develop rapidly. It is postulated that much of the variability in drug response can be explained through pharmacogenomic changes in drug metabolism. However, drug metabolism can also be affected by diet, smoking, alcohol intake, and medication adherence [4, 14, 15]. Polymorphisms in the drug-metabolizing enzymes influence drug safety and efficacy. Patients may have genetic polymorphisms that result in extensive or poor metabolism. Pharmacogenomics refers to the influence of genes in determining drug metabolism, safety, and efficacy. As most drugs are metabolized by the liver and involve one or more enzymatic pathways, the ability to prescreen a patient for potential genetic variants that affect drug response has clinical utility. Individualizing medication therapy based on a patient's specific metabolic genotype is available for selected medications. The ability for surgeons to easily interpret these results, the clinical utility of genomic findings, and the application to clinical practice all warrant careful consideration before ordering any pharmacogenomic study. The single greatest variable to drug response remains patient adherence.

Appreciating potential changes in drug metabolism with aging and the influence of genetic factors that alter metabolic functions is central to the field of pharmacogenomics. For example, genetic polymorphism and changes in hepatic blood flow can explain interpatient variability to medications commonly used in the surgical intensive care unit [15]. The use of codeine in patients deficient in cytochrome (CYP) 2D6 results in poor conversion of codeine to morphine (the active metabolite) [14, 15]. Therefore, switching to an equianalgesic dose of morphine based on the failed codeine regimen can result in drug toxicity. Patients who are extensive metabolizers may experience poor pain control from oxycodone. Additionally, the use of clopidogrel in CYP2C19 poor metabolizers results in decreased antiplatelet activity.

The influence of age on the CYP450 system is variable. While some drugs metabolized via pathways involving microsomal oxidation are slowed with aging and may have active metabolites, broader probes for hepatic microsomal activity have shown inconsistent results [14–17]. For example, early studies of diazepam and chlordiazepoxide in the elderly demonstrated longer and less predictable half-lives. However, both these drugs are highly lipophilic and therefore have a larger volume of distribution given the increase in adipose tissue common in aging. Changes in drug distribution are now thought to account more for the prolonged and erratic half-life than decreases in metabolism [18, 19]. Regardless, neither agent is recommended for elderly patients.

Metabolism via glucuronide conjugation is minimally changed with advancing age, and metabolites tend to be inactive [14, 15]. Thus, drugs metabolized through these pathways, including benzodiazepines such as lorazepam, oxazepam, and temazepam, have shorter, more predictable half-lives. Therefore if a benzodiazepine is needed, these will be shorter acting in elderly patients (Table 2) [8, 18, 19]. Drug inhibition of enzymatic pathways typically occurs at a faster rate than induction of the same pathways. The ability to induce hepatic enzymes to the same extent as in younger individuals is unclear. Some agents commonly associated with enzyme induction include phenytoin, carbamazepine, phenobarbital, and chronic alcohol use. An example of a potent inhibitor is valproic acid.

Table 2 Half-life of common benzodiazepines

Drug	Half-life in adults <65 years (h)	Half-life in adults ≥65 years (h)
Lorazepam	12.7	14.4
Alprazolam	11.7	15
Diazepam	M[a] 35.0–44.5	M 61.7–71.5
	F[b] 44.0–45.5	F 79.4–101
Chlordiazepoxide	10.1	18.2

Source: Data from [8, 18, 19]
[a]Male patients
[b]Female patients

Renal Elimination

The kidney is the main route of elimination for most drugs. On average, there are declines in glomerular filtration rate and renal blood flow with advancing age, although up to one-third of elderly persons have no substantial changes in renal function [20, 21]. Because of decreases in muscle mass and therefore creatinine production, serum creatinine levels may not accurately reflect renal function. Therefore, it is strongly recommended that creatinine clearance be calculated for every elderly patient. Even patients with seemingly normal serum creatinine levels may have a decreased creatinine clearance [22, 23]. Renal function can be represented in a variety of formats and is often calculated for clinicians in the EMR (e.g., eGFR, MDRD, Cockcroft and Gault) [24–26]. It is important to recognize that all the available methods have limitations [27, 28]. The most widely used method is the Cockcroft and Gault equation:

The Cockcroft and Gault formula (1973)

$CCr=\{((140-\text{age}) \times \text{weight})/(72\times SCr)\}\times 0.85$ (if female)

Abbreviations/ Units

CCr (creatinine clearance) = mL/minute

Age = years

Weight = kg

SCr (serum creatinine) = mg/dL

This equation is valid when serum creatinine is at steady state. It is the authors' approach to use the resulting creatinine clearance to determine a range of possible renal function by adding and subtracting five points to the calculation. Many medications have specific dosing guidance based on creatinine clearance. Therefore, knowing the range of a patient's creatinine clearance allows for more conservative dosing if necessary and compensates for patient variability in serum creatinine. When renal dose adjustments are necessary, surgeons should reduce the dosage or extend the dosing interval of primarily renally excreted drugs. This also applies to drugs with active metabolites that may have prolonged durations of action during renal insufficiency. For example, glyburide should not be used in patients with a creatinine clearance <50 mL/min because of reduced elimination of a renally active metabolite leading to greater hypoglycemia. The Veterans Health Administration (VHA) Pharmacy Benefits Management (PBM) Services, Medical Advisory Panel (MAP), and VA Center for Medication Safety (VA MedSAFE) issued a national bulletin advising providers to switch all patients with a calculated creatinine clearance of <50 mL/min to glipizide [29]. Glyburide is also included on the Beers Criteria for this very reason.

Medication-Related Problems in the Elderly

Polypharmacy, Potentially Inappropriate Medications, and the Surgeon

Surgeons are often in the difficult position of operating on an older patient with complex comorbidities and equally complex medication regimens. While in the surgeon's care, decisions must be made about discontinuing certain medications, placing others on hold, and when/who should restart any medications that were changed. While surgeons don't typically start chronic maintenance medications, they must coordinate and reconcile existing mediation regimens as patients transition their care to/from the surgeon to post-operative services. This is a critical period that results in significant medication errors.

Polypharmacy is more than the absolute number of medications a patient receives; importantly it includes any medication that is inappropriate. Polypharmacy is a significant problem for many older adults. Medications that are medically not necessary, including those not indicated, not effective, or constituting a therapeutic duplication, would be considered polypharmacy. Polypharmacy is common across care settings and increases in prevalence as patients transition from community settings to skilled nursing homes.

In a nationally representative probability sample of community-dwelling adults aged 57–84 years old, Qato et al. found that more than half of older adults used five or more prescription medications, over-the-counter medications, or dietary supplements [35]. Almost one-third of this study population used five or more prescription medications, and the prevalence of the use of five or more prescription medications increased steadily with age. Data from the Centers for Medicare and Medicaid Services (CMS) estimate that 58% of community-dwelling elderly are taking three or more different acute and chronic medications in a year. Additionally, polypharmacy has been shown to increase within the last year of life [1].

Medication reconciliation is foundational to ensuring safe and appropriate medication use and is the responsibility of every team member. A 2014 Medicare Payment Advisory Commission report to congress noted that Medicare Part D enrollees' medical problems may be "caused or exacerbated by their heavy use of medications (polypharmacy), and they are at increased risk of adverse drug events, drug-drug interactions, and use of inappropriate medications."

Potentially inappropriate medications (PIM) in the elderly are associated with poor quality of life, falls, physical disability, high healthcare use increased costs, increased risk for adverse drug events, delirium and mortality [30–32]. PIMs in the elderly can lead to increased hospitalization [152]. For example, older veterans taking more than five medications were almost four times as likely to be hospitalized from an ADE [15]. Common drug classes associated with ADEs include anticoagulants, NSAIDs, cardiovascular medications, diuretics, antibiotics, anticonvulsants, benzodiazepines, and hypoglycemic medications [13, 15, 16]. Use of specific PIMs such as sedative hypnotics and anticholinergics can result in falls, fracture, delirium, and hallucinations [153].

In a study of health outcomes, 40% of individuals 65 and older filled at least one PIM prescription and 13% filled two or more [154]. Drug-related problems occurred in 14.3% of this population who had at least one PIM, whereas only 4.7% of those with no PIMs had a drug-related problem.

Preoperative Medication Therapy Management

The increased emphasis on guideline-based medicine often results in patients receiving multiple agents for a condition in order to conform to "best practices." Patients with heart failure, hypertension, and diabetes can easily exceed six or more medications based on current clinical practice guidelines [36]. In this example, all six medications may be appropriate while still increasing the risk for potential ADEs.

Medication management in elderly patients is more complex than in younger patients, and each added medication increases the potential for interactions, adverse events, and therapeutic competition (i.e., when treatment for one condition may adversely affect a coexisting condition). For example, clinically significant drug interactions are more likely to occur when a patient takes five or more medications, and the likelihood for falls increases when an older adult takes four or more medications. Additionally, 75% of older adults have multiple chronic conditions, and within this population, one-fifth of older adults receive medications that may adversely affect coexisting conditions [37].

Lack of coordinated prescribing between primary care providers and specialists remains a critical issue, despite advances in interoperability of health information systems. Furthermore, patients may fill prescriptions from multiple pharmacies thereby circumventing the pharmacist's ability to screen for drug-drug interactions. Collectively, there is a loss of control over ensuring medication safety and appropriateness.

As healthcare payment reform models evolve from "volume to value," more episodes of care are bundled (i.e., comprehensive care for joint replacement and cardiac care), more risk is assumed by providers, and greater accountability is required in coordinating medications across care settings.

Medication Selection in Older Adults

The general approach to prescribing in older adults must also take into account the selection of medications. Beginning in 1991, geriatric experts have developed recommendations for potentially inappropriate medication use in older adults (defined as age 65 years and over) [118]. Originally published by Mark Beers, MD, MPH, the recommendations became known as the "Beers Criteria of Potentially Inappropriate Medication" and have been updated every 6–7 years, with the most recent update slated for 2019 [119]. These recommendations have been developed and adopted by the American Geriatrics Society and are intended to identify medications that should not be used or used with caution in older adults due to higher rates of adverse events than in younger populations, which compromises the risk-benefit ratio for these medications. The recommendations are intended for use by clinicians, however, and have also been widely adopted in research and as a quality measure for monitoring and comparing quality of prescribing.

The Beers Criteria are constructed in five different domains: the first identifies medications that should generally be avoided for all older adults; the second identifies medications that should be avoided in older adults with specific diseases; the third identifies medications that may be used, but with caution; the fourth identifies clinically relevant (non-antibiotic) drug interactions in older adults, and the fifth identifies medications (non-antibiotic) that should be avoided or reduced in those with renal insufficiency. The authors suggest clinicians become familiar with these recommendations and incorporate them into clinical practice, perhaps through electronic reminders or decision aids, to optimize patient care patterns and quality metrics.

The majority of research identifying potentially inappropriate prescribing utilizes the Beers Criteria as a gold standard for identifying inappropriate medications. However, a European tool has also been developed to aid in optimizing medication use in older adults [120]. Named the STOPP/START criteria (Screening Tool of Older Person's Prescriptions and Screening Tool to Alert doctors to Right Treatment), these tools share a number of similarities. The STOPP/START criteria offer recommendations not only for medications to avoid but also indications for certain medications in older adults (i.e., annual influenza vaccination or ACE inhibitors in systolic heart failure). Of note that the Beers Criteria have also published a list of alternatives to potentially inappropriate medications with the 2015 update [121].

The preoperative evaluation is an opportunity for surgeons to significantly improve medication use by identifying and de-prescribing potentially inappropriate medications. When evaluating medications, surgeons should utilize the Beers Criteria as a resource in avoiding potentially inappropriate or high-risk medications in the elderly. Explicit lists of high-risk medications are also incorporated into HEDIS quality measures established by the National Committee for Quality Assurance (NCQA). These quality measures are important factors in determining an organizations overall quality scores and influence reimbursement rates.

An often repeated saying in geriatrics is that any new symptom in an elderly patient should be considered a drug side effect until proven otherwise. During the course of treatment, the patient should be monitored closely and regularly for adverse effects. Regardless of age, 95% of all adverse drug reactions (ADRs) are predictable extensions of the pharmacology of the drug. Proper dosage adjustment based on renal and hepatic function can reduce the likelihood of experiencing an ADR. Once the desired effect is achieved and maintained, or the inciting event has passed, taper and discontinue the medication.

Medication Review and Reconciliation

The maxim of geriatric prescribing is to "start low, go slow, and sometimes say no." While perhaps overly simplistic and not applicable to all medications (i.e., antibiotics), the message is clear – medications are potentially dangerous in the elderly and should be used with caution [38–40]. Furthering the maxim, if starting low, it follows that you should also discontinue slowly (if possible). While many drugs can be discontinued quickly, others (e.g., benzodiazepines, beta-blockers, and clonidine) should be tapered to avoid adverse drug withdrawal effects. With this background in mind, several underlying principles can help minimize the occurrence of MRPs and maximize adherence to prescribed drug regimens. Although they may seem rudimentary, they are nonetheless helpful to review (Table 4).

The Joint Commission requires medication reconciliation upon each transition into, within, or out of a healthcare organization as a part of its National Patient Safety Goals. The standards apply to both inpatient and ambulatory care settings. The medication reconciliation process requires that organizations interview the patient (or an appropriate representative) to document a complete list of the patient's current medications upon admission to the organization and communicate a complete list of medications to the next provider of service when a patient is referred or transferred to another setting, service, practitioner, or level of care within or outside the organization. This step is extremely important in both reducing potential harms from medication errors and identifying potential adverse effects from a current (prescribed, over-the-counter, or even illicit) medication.

Discrepancies between what patients think they should be taking, what they are actually taking, and what is recorded in the medical record are common [122]. Medication reconciliation can prevent medication-related problems resulting from forced adherence, a common occurrence resulting from a medication being restarted in a patient who stopped or changed their medication without notifying their primary provider. Elderly patients are often reluctant to admit they have stopped a medication or altered the dose.

Many institutions incorporate pharmacist and/or pharmacy technicians to conduct the medication reconciliation process. In most instances, pharmacists or technicians will interview patients to generate a medication list and then confirm the list from pharmacy dispensing records or review of prescription bottles, allowing for a measure of adherence. This list generated from patient report (subjective measure) and confirmed with dispensing information or review of prescription bottles (objective measure) is then compared with the medication list within the institution. Discrepancies are then corrected or justified (reconciliation) and repeated prior to discharge or transfer of care to the next institution. The intent of this safety goal is to improve the safety of medication use within all healthcare institutions.

When obtaining a full medication history, it is ideal to have the patient or a family member bring all medications with them. The authors recommend instructing patients to bring all prescription and active nonprescription bottles to their presurgical screening visit. Examining the pill bottles can provide valuable information about the individual's medication management abilities. For example, you might be able to determine the number of providers following the patient, if they use only one pharmacy (important for drug interaction screening) and if there is duplication of medications from multiple providers, and the physical appearance of the bottles (recently filled prescription bottles that are filthy may be indicative of the individual's home environment), if the refills are on time, the pills are in the right bottles, the pills are mixed together, and the pill counts are accurate. Given that many drugs with potential toxicity and interactions are available without a prescription, every patient should also be asked about the use of OTC, herbal, or alternative medications.

Pharmacist interventions with inpatients may decrease subsequent hospital and emergency visits and medication-related readmissions [43, 44]. Inclusion of pharmacists on daily rounds in the intensive care units is encouraged to help improve overall prescribing [45]. Utilization of computerized provider order entry can further reduce medication errors [46]. When preparing discharge prescriptions, keep medication regimens simple. Once-daily dosing substantially improves adherence. If a complicated regimen is necessary, the hospital pharmacist may be able to arrange for the patient's community pharmacy to dispense the medication in a pill box or have them blister packed. These approaches may enhance adherence to the regimen. Providing the patients with a *legible* list of their medications with directions written in lay terms is perhaps the single most important strategy to prevent medication-related problems. Many hospitals have pharmacists available for comprehensive medication counseling and to assist in streamlining regimens.

De-prescribing

As noted at the beginning of the chapter, the problem of polypharmacy increases with age and the presence of comorbid disease. In the current healthcare environment, new complaints presented by patients are quickly addressed by adding new medications, perpetuating the polypharmacy problem in older adults. De-prescribing is the practice of reducing potentially inappropriate or ineffective medications and has achieved important successes through improved perception of well-being and reduced medication costs.

De-prescribing can be defined as: “the systematic process of identifying and discontinuing drugs in which existing or potential harms outweigh existing or potential benefits within the context of an individual patient’s care goals, current level of functioning, life expectancy, values, and preferences. . . . De-prescribing is not about denying effective treatment. It is a positive, patient-centered intervention. . .and requires the same good prescribing principles that apply when drug therapy is initiated” [123].

A number of barriers exist to de-prescribing: clinical complexity among those with polypharmacy paired with limited time in patient-provider interactions, fragmented care among multiple providers, incomplete information on indications and prior experience with alternative modes of therapy, ambiguity in and changing care goals, uncertainty in risks and benefits of continuing vs. discontinuing a medication, and the social/community expectations of more rather than fewer medications to manage symptoms [124, 125].

Table 3 Drugs/combinations to watch carefully in the elderly

Warfarin-NSAIDs[a]
Warfarin-quinolones[b]
ACE inhibitors-potassium supplements
ACE inhibitors-spironolactone
Anticholinergics (such as oxybutynin, amitriptyline, and meclizine)
Anticoagulants
Digoxin-amiodarone
Insulin

[a]NSAID class does not include COX-2 inhibitors
[b]Quinolones that interact include ciprofloxacin, enoxacin, norfloxacin, and ofloxacin

Despite such barriers, a number of successful de-prescribing trials have shown improvements in meaningful patient outcomes as reductions in emergency room visits [126], unplanned hospitalizations in heart failure patients [127], as well as patient-reported outcomes such as quality of life [128]. A study targeting chronic users of benzodiazepines, traditionally difficult to discontinue because of physical and psychological dependence, found a nearly fivefold increase in rates of discontinuation or dose reduction among those receiving a simple de-prescribing intervention [129]. This study found no safety concerns (seizures or withdrawal effects) as a result of the intervention; however other studies have shown adverse drug withdrawal events may occur in up to 30% when consistent taper schedules are absent [130] (Tables 3, 4, and 5).

Specific Prescribing Issues

Delirium

Delirium is a significant concern in older surgical patients because of its prevalence and relationship with detrimental acute and chronic outcomes. Delirium occurs in up to 70% of postoperative older adults and can increase morbidity and mortality and among survivors has been associated with postoperative cognitive dysfunction and dementia [132–134]. Our emphasis in this chapter is limited to a discussion of the pharmacologic management in older adults, whereas a more

Table 4 Principles of safe geriatric prescribing

Take a detailed medication history (including over-the-counter and herbal/alternative preparations)
Establish clear, feasible therapeutic endpoints
Know the clinical pharmacology of drugs prescribed; use a few drugs well; balance safety with efficacy
Begin with a low dose of a drug and titrate up to achieve the desired response
Keep the regimen as simple as possible
Review medications regularly and discontinue those no longer needed
Remember that new symptoms (and illness) can be caused by a drug as well as by a new illness
Select the least costly alternative whenever possible
Encourage compliance. Utilize available pharmacy resources for counseling, written information, special packaging, and other reminder devices

Source: Steinman and Hanlon [131]

thorough discussion of predisposing and precipitating risk factors and diagnosis is discussed elsewhere in the book.

Risk factors can be thought of as "predisposing factors," making one vulnerable to developing delirium and "precipitating factors," which directly or indirectly lead to it. Among the predisposing factors are cognitive impairment, visual impairment, severe illness, and renal insufficiency [48]. Precipitating factors include the use of physical restraints, malnutrition, bladder catheterization, iatrogenic events, and the number and type of medications [49]. Certain medications have been linked to a particular risk of postoperative delirium (e.g., meperidine and benzodiazepines) [50, 135]. Anticholinergic medications may also increase the risk of delirium and include diphenhydramine which is commonly used in hospital settings for sleep and prophylaxis of allergic reactions during transfusions [136, 137]. One study noted that the simultaneous addition of three or more medications to a drug regimen in the hospital was a significant contributing factor to delirium, suggesting that the sheer volume of new medications in certain hospitalized patients may be sufficient to overwhelm their reserve capacity (it should be noted that as the number of prescribed medications increased, there was a greater likelihood of at least one of the medications being psychoactive) [49].

A number of strategies may be employed to decrease the risk of delirium; however these efforts should be focused on identifying and managing the underlying illness and normalizing sleep and activity patterns. The hospital setting is notorious for scheduling medications or monitoring around the clock that interrupts normal sleep-wake cycles. Although it may be necessary for acutely or severely ill patients or during the immediate postoperative period, these interventions should be minimized as soon as possible. These nonpharmacologic interventions may reduce delirium incidence by 35–40% [51, 52]. Holding, reducing, or discontinuing medications thought to increase the risk of delirium is warranted, though this should be done with attention to the indication, duration of use, and with respect to the potential for adverse drug withdrawal effects.

Pharmacologic prevention and treatment is not recommended in routine clinical care [138–140]. Two systematic reviews of pharmacologic management of delirium in surgical populations failed to recommend any medication, found mixed results for medications in the prevention of delirium (antipsychotics, ketamine, dexmedetomidine, and morphine), and insufficient data to make a recommendation for pharmacologic treatment of delirium in postoperative populations [139]. The authors did, however, identify that reducing perioperative sedation levels through targeted bispectral index monitoring reduced delirium incidence and duration. However, the preferred choice of agent used for anesthesia and optimal sedation target have yet to be determined.

Because of potential serious side effects (all antipsychotics hold a black box warning for increased risk of stroke and death in older adults with dementia) [56–58], they should not be used to treat insomnia or other minor complaints. It is important to look for delirium as the potential cause of a new-onset behavioral disturbance or thought disorder, so the underlying etiology can be determined and treatment of the primary process initiated.

As noted above, use of antipsychotics in postoperative delirium is not routinely recommended due to insufficient evidence at this time. However, studies have been conducted that suggest antipsychotics may have a future role in preventing postoperative delirium; the dose, frequency, and duration have yet to be determined before this practice is adopted. Antipsychotics may be employed if delirious patients experience agitation that interrupts care or has the potential to cause harm to the patient or staff. No agent has proven superior efficacy or tolerability in short-term delirium trials. The older, "typical" agents, such as haloperidol (starting dose 0.25–0.5 mg, maximum daily dose 2.0 mg), are inexpensive and are available in oral, intramuscular, and intravenous preparations. Parenteral preparations (intravenous and intramuscular) of antipsychotics may be particularly helpful in the setting of acute agitation or if the patient is unable to take oral medications. Haloperidol is more likely to produce extrapyramidal side effects with prolonged use, but less likely to cause sedation, orthostasis, and anticholinergic effects than lower-potency agents. Among the extrapyramidal effects are parkinsonian.

Antipsychotics

Antipsychotics are used to treat hallucinations, delusions, paranoia, and extreme agitation or physical violence [53]. They tend to not be useful for pacing or wandering, behaviors sometimes seen in older adults with dementia.

Tardive dyskinesia is a potential serious side effect of neuroleptic use and one of the reasons their use should be limited to severe agitation and restricted to short periods of time. Tardive

Table 5 Strategies for Improving Medication Adherence and Reconciliation

Barrier	Talking points
Cost	*Diagnose barrier: copay requirements too high, overall medication spend too high, income insufficient to meet medication costs* • Switch to 90-day Rx for maintenance meds • Maximize generic medication prescribing • Switching to mail order often results in lower copay • Review insurance formulary to ensure med is lowest tiered, clinically appropriate agent in that class • Look for extraneous med spending – e.g., herbals/vitamins/minerals • Check for low-income subsidy for Medicaid recipients • Consider patient assistance programs (*not manufacturer coupons*): typically for specialty agents only and provided by a foundation (The Assistance Fund)
Difficulty refilling meds	*Diagnose barrier: transportation issue, cost issue, confusion/complexity of refill process?* • Have pharmacist attempt Rx synchronization so that all meds filled simultaneously • Switch to local pharmacy with delivery service and/or pillbox-prefill option • Enlist surrogate to oversee refills • See if pharmacy has a refill app • Consider auto-refill programs
Forgetfulness/confusion	*Diagnose barrier: underlying cognitive disorder, overly complicated regimen, lack of medication education, level of education, health literacy, conflicting information from providers, psychosocial environment overwhelming, no med management system, hoarding?* • Screen for memory disorder – TICS/MiniCog/MMSE/MOCA/SLUMS • Medicare eligible can receive annual comprehensive medication review (CMR) – contact your local pharmacist • Direct pt back to local pharmacist for a scheduled medication therapy management session (some pharmacists will schedule these visits) • Ensure medication list identifies indications/goals of care • Identify pt's source(s) of medication information – may listen to neighbors, believe what is on TV or internet. Stress that what is advertised can be misleading. Talk to pharmacist or provider • Empower patients to review medications with providers at each office visit

(continued)

Table 5 (continued)

Barrier	Talking points
	• Encourage the use of a pill box or reminder system: ○ Set an alarm on phone ○ Link taking medication to a daily routine like brushing teeth/eating meals ○ Free phone apps to remind and track meds such as Mango Health and Round Health by Circadian Design • Refer to behavioral health for hoarding/psychosocial stressors
Overly complex med regimen	*Diagnose barrier: functional limitation in dexterity, vision, hearing, swallowing, cognition or challenge to lifestyle, polypharmacy* • Consolidate to less frequent dosing • Identify opportunities for deprescribing • Consider alternative dosage formulations if swallowing barrier exists • Review if pill splitting is a barrier • Look for complex med directions (e.g., every other day, restrictions on food/meals) • Use pillbox/auto prefill systems • If discontinuing med, alert pharmacy to deactivate the discontinued prescription to prevent an accidental refilling of discontinued medication
Tablet splitting	*Diagnose barrier: functional limitation in dexterity, vision, cognition or challenge to lifestyle, polypharmacy, time consuming* • Advise against as this increases the likelihood of med errors during hospital admissions • Advise against as this makes pts appear suboptimally adherent even if taking as instructed by provider • Contact provider for new Rx reflecting the correct dose
Side effects	*Diagnose barrier: new onset of signs or symptoms temporally related to medication administration, fear of side effects, used as an excuse to stop medications* • Obtain side-effect history – is this an actual SE or perceived SE? • Notify provider of side effects and reconnect with the patient with instructions. In many cases, the provider may decide that the benefit outweighs the risk • Is the side-effect in response to what was seen on TV/internet? Talk to MD or PharmD • Is there an FDA-issued recall/alert for this issue? Follow FDA advice • Has this person experienced prior side effects/appears "hypersensitive" to medications? If so, is this affecting pt's ability to take current medications?
Goals of care not aligned with medication use	*Diagnose barrier: no immediate result from new Rx, lack of perceived benefit from chronic Rx, patient beliefs, condition resolved* • Review pts beliefs to identify cultural, religious, moral, ethical reasons for not taking Rx • Many patients being treated for chronic conditions fail to see immediate results and prematurely discontinue therapy. Talk about expectations of taking the medication and the prevention of a worse outcome and preservation of quality of life • When a new therapy is started, check-in on the patient to ensure that they are taking the medication as directed and do not have any barriers with taking the medication (rather than waiting for the next visit for the pt to talk about the issue) • Did pt appropriately discontinue med? Did condition resolve? Was provider alerted?

Medication Review Checklist

Step One: Chart Review

Prepare care medication list for review with patient. Consider new starts, changes in therapy, discontinuations from hospital discharge instructions or provider office visits. Use the following sources:

- Discharge Summary
- Provider notes
- Claims data

Step Two: Patient Interview

With medication list prepared from sourced documents above, interview patient and obtain best-possible medication history. Goals of interview are to determine overall medication management strategy, potential non-adherence, and accuracy of medication list. Use the following questions to guide your interview:

Confirm Medication Changes

1. **Did any doctor start a new medication recently?**
2. **Did any doctor stop a medication recently?**
3. **Did any doctor change the dose of your medications recently?**

Identify Patient Discrepancies

4. **Have *YOU* recently started any new medications?**
5. **Have *YOU* changed the dose or stopped any of your medications recently?**
6. **Do you take any over-the-counter meds, vitamins, minerals, herbals?**

Identify Barriers to Adherence

(Refer to Adherence Strategies Document)

7. **Have any of your medications been causing side effects?**
8. **Do you ever forget to take your medicine?**
9. ***If applicable*: Your profile indicates that you may have run out of some medications. Is that correct?**

Medication Management Issues

10. **Please describe how you manage your medications? Can prompt with the following:**
    a. **Do they use a pillbox?**
    b. **Do they receive help in taking medications?**
    c. **Do they order their own refills?**
    d. **Do they have difficulty obtaining their refills?**
    e. **Do they combine it with any previously dispensed medication?**
    f. **Do they require reminders to take medications?**
    g. **Do they feel confident in your ability to manage your medications?**
    h. **Can they read the label on a medication bottle?**
    i. **Do they have a medication list? Is it up to date?**

Step Three: Documentation

Created by Christina Polomoff, PharmD & Sean Jeffery, PharmD

Having completed steps 1 – 3 now you can document the medication review. Based on your patient interview, update any changes to the medication regimen. Note any discrepancies between the medication list and the patient interview.

1. Medication Changes

- Medication(s) Started:
- Medication(s) Changed:
- Medication(s) Discontinued:

2. Medication Discrepancies identified from patient interview

3. Adherence and Medication Management Issues – list barriers and recommendations

dyskinesia starts as fine movement of the tongue, a facial tic, or lip smacking but may progress in the extreme to affect speech, eating, and breathing. Additional features include tremor, bradykinesia, and masked facies. Akathisia may also be manifested as motor restlessness, pacing, or disturbed sleep and may be reported as discomfort or anxiety. A danger is that these features may be misinterpreted as increasing psychosis, with the neuroleptic dose then being increased, resulting in worsened symptoms. As a result, it is often better to decrease the dose as an initial response to such symptoms to see if they are alleviated.

Furthermore, it may be irreversible. Older adults and women are most likely to develop tardive dyskinesia, and it is more likely to be severe and less likely to be reversible in the older adults. It is less clear that treatment duration and type of agent are important contributors to risk [54, 55]. The primary treatment is to taper and discontinue the drug.

"Atypical" agents, such as risperidone (starting dose 0.25–0.5 mg, maximum daily dose 2.5 mg) and olanzapine (starting dose 2.5–5 mg, maximum daily dose 20 mg), have been touted as having fewer extrapyramidal side effects, although the risk does increase with increasing dosage. These agents have not been proven more effective or safe in short-term trials in critical care or postoperative settings [139, 140]. Olanzapine or quetiapine (starting dose 25 mg, maximum daily dose 200 mg) may be helpful in individuals who have insomnia in addition to psychosis, although these effects may be problematic with longer-term use and are off-label.

Many of the problems with neuroleptic use result from patients being left on the drug long after the inciting event has resolved and after discharge from the hospital. Three studies have shown that approximately 30% of patients receiving a new antipsychotic during a critical illness continue to receive the antipsychotic at discharge [141–143]. If agents are prescribed on an as-needed, or pro re nata (PRN), basis, the indication for use and maximum daily dose should be clearly stated in the orders. The maximum daily doses provided for agents outlined above are guidelines; while they may be exceeded, this should be done cautiously and under close supervision because of the increased risk of side effects.

Of note, antipsychotics are included in the Beers Criteria as potentially inappropriate medications for older adults due to the lack of proven evidence in efficacy and their severe adverse event profile. These effects add to the importance of judiciously using these medications only for the appropriate indications (psychosis and agitation where the health and safety of the patient or caregivers is threatened) and at as low a dose and for as short a duration as is clinically necessary.

Antidepressants

The cardinal features of depression are the "vegetative" or depressive signs and symptoms, including increased or decreased sleep, decreased activity level, fatigue, decreased concentration, increased or decreased appetite or weight, motor slowing or agitation, guilt, suicidality, chronic somatic complaints, and pain [59]. Although standardized instruments, such as the Geriatric Depression Scale, can be useful adjuncts, diagnosis still relies on the recognition of depressive signs and symptoms [60]. As described above in the description of delirium, onset of depressive symptoms in the acute/post-procedural period should be carefully weighed against a diagnosis of delirium. It is important to rule out underlying medical illnesses contributing to depression, such as stroke, myocardial infarction, congestive heart failure, thyroid disorders, uremia, and certain cancers. Medications may contribute as well, including central-acting antihypertensives and b-blockers, narcotics, antipsychotics, benzodiazepines, antihistamines, and sedative/hypnotics [61].

Once these contributing factors have been ruled out and target signs or symptoms identified, the choice of agent again depends in part on the characteristics or features of the patient and the desired side effect profile [59, 62, 63]. Pharmacologic treatment of depression should be offered in conjunction with nonpharmacologic behavioral and support strategies (such as problem solving therapies, social support, etc.), since pharmacologic strategies alone are often not sufficient to result in remission. Treatment success is similar across the wide range of therapeutic options to treat depression; however adverse event profiles prioritize certain classes in older adults.

Both the Beer's and the STOPP/START criteria offer strong recommendations to avoid tricyclic antidepressants (e.g., amitriptyline, nortriptyline, imipramine, and doxepin) due to poorly tolerated adverse events in older adults (Beer's ref). These adverse events include sedation, orthostasis, and a host of anticholinergic-related adverse events including dry mouth, urinary retention, and constipation. Several studies have also shown a relationship between chronic use of these medications and irreversible cognitive impairment (Fox SER, Gray JAMA Int Med, Campbell Pharmacotherapy). Monoamine oxidase (MAO) inhibitors are another class identified by Beer's as potentially inappropriate in older adults because of their potential serious interactions with certain medications and tyramine-containing foods. Therefore preferred antidepressants in older adults begin with selective serotonin reuptake inhibitors (SSRI) or serotonin norepinephrine reuptake inhibitors (SNRI) for those with certain indications.

Because of their enhanced safety and tolerability profiles, selective serotonin and norepinephrine reuptake inhibitors are the current preferred agents for treating depression in older patients [63, 65]. In general, citalopram/escitalopram and sertraline are safe, effective, low cost, and well-tolerated by older patients and are reasonable initial choices. Second-line therapy can include venlafaxine or duloxetine as monotherapy or combination therapy with SSRI and a medication with complementary mechanisms, such as mirtazapine or bupropion. For patients with poor sleep, poor intake, and anxiety as features of their depression, mirtazapine would be an option. For patients with neuropathic pain and depression, duloxetine is an alternative. The latter options may minimize the number of medications by treating multiple symptoms with a single agent. Most agents take several weeks to have an effect on mood, but beneficial effects on sleep or appetite may be seen sooner. Remission is achieved in approximately one-third of new antidepressant users; therefore it is important to monitor for improvement in symptoms and adjust or discontinue therapy to optimize efficacy and minimize polypharmacy. Treatment with an antidepressant should not be considered a failure until 4–6 weeks of use are confirmed (through some measure of adherence) with a therapeutic dose.

Class-wide side effects of SSRI/SNRI include gastrointestinal upset, headaches, dizziness, and sexual dysfunction. Because serotonin receptors are present in platelets, this class may also increase bleeding risk, though bleeding events are only increased when an SSRI/SNRI is used in conjunction with other antiplatelets or antithrombotics (such as aspirin, clopidogrel, warfarin) (add ref). Antidepressants have also been correlated with an increased risk of falls, due to their central site of activity, and represent a significant concern in both community-dwelling older adults and those residing in assisted living or advanced care facilities.

In addition to adverse events related to medication use, potential adverse withdrawal events may also arise from intentionally or unintentionally stopping antidepressants (along with all other centrally acting medications) too quickly. Included in this risk are narcotics or other habit-forming scheduled medications. Adverse withdrawal events for antidepressants may include neurological, psychological, cardiovascular, gastrointestinal, and flu-like symptoms and usually occur within 3 days of abrupt discontinuation [144]. The medication reconciliation process should be sensitive to all sources of medications and prescription and recreational drugs, throughout each transition to avoid untoward effects of adverse drug withdrawal of centrally acting medications.

Anxiolytics

Pharmacologic intervention for anxiety is warranted if symptoms are sufficiently severe to interfere with daily coping or enjoyment of life. In general, treatment should be short term: for a grief reaction or as an adjunct to supportive therapy to develop coping strategies. It is again important to rule out contributing disorders such as congestive heart failure and chronic obstructive pulmonary disease.

Historically, anxiolytic therapy relied heavily on the use of benzodiazepines [53, 67]. However, given the metabolic changes that occur with aging, potential for dependency, cognitive impairment in older adults, and increased risk for falls, benzodiazepines have fallen out of favor as preferred agents for anxiety. Those that are still used are most often short-acting agents such as lorazepam (starting dose 0.5 mg/day) and oxazepam (starting dose 7.5 mg/day). These are preferred because of their more predictable half-lives and duration of action. All benzodiazepines share potential side effects, including sedation, dizziness, depression, confusion, agitation, and disinhibition. Dependence can develop, and tolerance to their effects often occurs after 2–4 weeks of continuous use. Consequently, it is best to use these agents short term. Many anxiolytics are not recommended for use longer than 4 weeks.

Because a withdrawal reaction or "rebound" characterized by tremor and agitation can occur after abrupt withdrawal, benzodiazepines should be tapered prior to discontinuing. Tannenbaum and colleagues have shown that benzodiazepines can be successfully withdrawn, even in patients with decades of use. While this approach requires preplanning a taper regimen, it is an option for some elective surgery patients and may help reduce postoperative delirium by removing offending agents. Excellent patient and provider resources on how to successfully taper and discontinue benzodiazepines are available at www.deprescribing.org.

As treatment of anxiety has gravitated away from benzodiazepines, other agents like SSRIs, SNRIs, and buspirone (starting dose 5 mg twice a day) have increased in use. Buspirone is a non-benzodiazepine anxiolytic that is less likely to cause dependence, sedation, or psychomotor retardation. However, it has a delayed onset of action (several weeks) and lacks the soporific and muscle relaxant effects of benzodiazepines. Its primary side effects are dizziness and nausea. Barbiturates should be avoided because they are less effective and have greater addictive potential than other available agents [67, 68].

Sedative/Hypnotics

Disturbed sleep is a common complaint among older persons, particularly in the hospital [53, 69]. Part of this is due to changes that occur in sleep patterns with aging, including a phase shift (falling asleep and waking up earlier than in prior years) and more disruptions to sleep. Poor sleep is often a proxy marker to other underlying medical factors that contribute to sleep difficulties, including anxiety, depression, pain, itching, nocturia, and congestive heart failure. Disturbed sleep may manifest as difficulty falling asleep, difficulty staying asleep, or early morning awakening. Medications that may contribute include amphetamines, steroids, selegiline, decongestants, caffeine, and alcohol. A number of other factors may play a role among hospitalized patients, including daytime naps, intravenous lines, catheters, traction, and frequent wakings for medications or treatments. After establishing by history if sleep is disturbed, the mainstay of treatment should be nonpharmacologic interventions directed at potential contributing factors. For example, cognitive behavioral therapy has been proven effective as a long-term strategy improving sleep.

Any decision to use sedative/hypnotics must carefully balance the risks and benefits of this class of medications. There are no safe sleeping pills as they are all variously associated with increased risk of falls, confusion, and daytime sleepiness. Overall evidence of efficacy is limited with this class of medications; in general they increase sleep time in aggregate by approximately 20 min. If drug treatment is indicated, short-term use (suggested maximum duration of use is 7–10 days) is advised. Among the benzodiazepines, short-acting agents are preferred because they are less likely to cause carryover sedation the following day. Temazepam (starting dose 7.5 mg) has a reasonable duration of action but a delayed onset of action and so must be given approximately 1–2 h before bedtime. Nonbenzodiazepine hypnotics, such as zolpidem, zaleplon, and eszopiclone, are alternatives that, while commonly used, are still identified as high-risk medications in the elderly and appear on the Beers Criteria [70]. If the primary problem is difficulty falling asleep, ramelteon is another option. If persons are depressed and have sleep difficulties, treatment with a sedating antidepressant is preferable to separate treatment with two different medications.

Trazodone (25–100 mg p.o. within 1 h of desired sleep time) is commonly used for its sedating properties; however there is limited evidence of long-term benefits, and given its long half-life, some patients report excessive daytime sleepiness.

Many patients will obtain over-the-counter (OTC) sleep aids such as diphenhydramine or melatonin. It is therefore important to screen for OTC sleep aids. Melatonin has a cult-like following in the community where it is widely touted as a natural sleep aid. However, overall evidence of efficacy is very limited and generally related to circadian disorders. As the pineal gland secretes melatonin in response to exposure to AM bright light, a nonpharmacologic recommendation to improve circadian rhythm sleep is to encourage patients to be exposed to sunshine between 9 and 11 am for at least 30 min.

Comorbid behavioral health problems can significantly impact sleep. If someone has a thought disorder and disturbed sleep, a sedating neuroleptic is preferred, but neuroleptics should not be used for sleep alone as these carry black box warnings.

Pain Management

Pain is a common complaint among elderly persons and can have a substantial impact on quality of life and physical functioning. It is beyond the scope of this chapter to review in detail the pharmacologic management of pain in surgical patients. Instead, this section will highlight common concerns regarding frequently used pain medication. Pain management guidelines are undergoing significant scrutiny for safety, efficacy, and contributions to the broader public health crisis of opioid abuse. Overuse of opioid prescriptions has contributed to an epidemic of abuse and significantly increased the number of overdose deaths annually. The elderly are especially at risk as pain management guidelines have advocated opioids as first-line agents. A generation of seniors have significant amounts of unused opioids in their possession, potentially serving as a point source for addicts. Moreover, use of opioids in the elderly can contribute to cognitive impairment, falls, and other troublesome side effects. Adequate treatment is thus important, but caution must be exercised because of the strong potential for adverse effects with many of these agents. As such, it is helpful to follow the stepwise approach for assessing the nature and extent of pain, determining its etiology, and starting with lower doses of less-potent agents. A variety of instruments are available to help gage the current severity of pain and the effectiveness of treatment [71, 72].

The first line of therapy often consists of acetaminophen, tramadol, or topical nonsteroidal anti-inflammatory agents (NSAIDs) [74]. Most guidelines now recommend acetaminophen rather than nonsteroidals for the first-line treatment of pain because of their side effect profiles in older adults [NEW]. Acetaminophen lacks the anti-inflammatory properties of NSAIDs; however acetaminophen is safe, effective, inexpensive, and well tolerated by older persons with mild to moderate pain. Caution should be exercised in the setting of liver disease or alcohol use. Given acetaminophens' ubiquity in over 600 commercially available products, unintentional acetaminophen overdose is the main contributor to acetaminophen-induced hepatotoxicity [75]. Caution must be taken to ensure that patients avoid compound medications that include acetaminophen, which may contribute to their unknowingly exceeding recommended daily limits (3 g/day).

Aspirin and the nonsteroidals can cause gastrointestinal bleeding and renal insufficiency, worsen hypertension, and can interfere with platelet function. A variety of central nervous system (CNS) side effects may also be seen with nonsteroidals, and therefore they are no longer recommended for long-term pain management in older adults. Topical NSAIDs are generally well tolerated given the lower systemic absorption from these agents. Because these are applied topically, they are of most benefit to localized pain. Additionally, brand-name topical agents are often very high cost and restricted. Generically available topical NSAIDs exist and are equally analgesic.

If pain is not controlled with these agents, a trial of topical lidocaine may also be reasonable if the pain is localized and neuropathic in nature. Topical lidocaine (ointment, cream, or patch) is generally well tolerated with the most common adverse effect being headache [73, 74]. However, lidocaine patches are very expensive and typically require prior authorization approval.

Tramadol (50 mg every night, then 25–50 mg immediate release every 6 h; maximum daily dose 400 mg) is modestly effective for mild to moderate pain. Common side effects include constipation, nausea/vomiting, dizziness, headache, and somnolence. Tramadol can also increase the risk of seizures or serotonin syndrome when used with antidepressants or monoamine oxidase inhibitors (MAO), serotonin reuptake inhibitors, and tricyclic antidepressants [74].

Opioid analgesics are the next line of treatment [72–74]. Use of the lowest effective dose for the shortest period of time can help prevent abuse and misuse of opioids. Common opioids, such as codeine, oxycodone, and hydrocodone, may provide relief alone or are available in conjunction with nonopioid analgesics like acetaminophen. All opioids have similar potential side effects, among which are respiratory depression, constipation, urinary retention, nausea and vomiting, delirium, and myoclonus. The patient should be monitored closely and appropriate dose adjustments made when these side effects appear. Prophylactic bowel regimens are often necessary and should be initiated when the narcotic is started. Stool softeners will result in all "mush and no push," and therefore stimulant laxatives are necessary. Tolerance to some of the effects may appear and may require continuous, rather than as-needed, administration schedules. For respiratory depression, the opiate antagonist naloxone may be helpful. Meperidine should be avoided in the elderly, as it must be used with caution in patients with renal insufficiency and its metabolite, normeperidine, may cause seizures.

Topical analgesics such as capsaicin may be helpful for conditions such as herpes zoster. Nonpharmacologic modalities such as heat, cold, massage, biofeedback, and transcutaneous electrical nerve stimulation (TENS) help in certain situations. Nerve blocks are another potential option for certain types of refractory pain. A recent trial of an interdisciplinary analgesic program in orthopedic patients found that intervention participants had less pain postoperatively at 6 months and better physical performance [76].

Antihistamines

Histamine H_1 receptor blockers are commonly used for the treatment of allergies and allergic reactions; occasionally they are used as sedative/hypnotics. Antihistamines such as diphenhydramine should not be used as sleep medications as they can cause confusion and acute urinary retention. First-generation antihistamines have prominent anticholinergic properties and should be used cautiously in the elderly. Newer agents with relatively low anticholinergic properties, such as loratadine, are preferred to treat allergy symptoms.

Histamine H_2 receptor blockers, used to inhibit gastric acid secretion, can be safely used in elderly persons. Histamine H_2 receptor blockers, used to inhibit gastric acid secretion, can be used safely in the elderly provided the dose and duration of therapy are kept to a minimum and adjusted for renal function. If used prophylactically during the perioperative period, the dose should be decreased and ultimately discontinued as soon as possible. All of these agents can cause alterations in mental status if not carefully dosed.

Antibiotics

There are two major clinical categories of antibiotic usage among surgical inpatients:

perioperative prophylaxis and the treatment of postoperative infections. Aging-related changes in pharmacokinetics of antibiotics will have limited impact on prophylactic use of antibiotics and a more significant impact on dose and scheduling of treatment regimens. Although this chapter does not focus on specific antibiotic recommendations for procedures or site infections, it addresses the general principles of antibiotic choice, dosing, and specific side effects in the geriatric patient.

Given changes expected in payment systems (see earlier comments), surgeons will become increasingly responsible for prevention and treatment of infections both in the acute care setting and possibly extended care and rehabilitation settings. Growth of clinical pharmacy services, along with partnership of infectious disease physicians and antimicrobial stewardship programs, is available to surgeons in both inpatient and extended care or rehabilitation facilities. These local programs are specifically charged with optimizing use of antibiotics with attention to treatment success, resistance, and cost and are supported by a number of organizations, including the Centers for Disease Control and Prevention and Infectious Diseases Society of America. Important to the long-term care setting, in 2016 the Centers for Medicare and Medicaid Services' "Mega-Rule" is requiring facilities to develop an Infection Prevention and Control Program (IPCP) that includes an Antibiotic Stewardship Program and designate at least one infection preventionist on-site.

It is important to consider technologic devices (grafts, stents, pacemakers, transplanted organs, and dialysis catheters) as important factors in the selection of antibiotics in the elderly surgical patient. Both the devices themselves and the medications (immunosuppressive drugs and anticoagulants) that patients may be on as a result need to be taken into consideration when choosing an antibiotic regimen. With increasing antibiotic resistance constricting options for care, and new antibiotic development lagging, it is imperative that the proper choice of antibiotic be made by taking into account possible drug interactions (Table 6), the side effect profile of a particular drug, the appropriate dose in a given patient, the antibiogram, and whether this is empiric or targeted treatment based on cultures and sensitivities [78].

Selection of an antibiotic for surgical prophylaxis should be (1) active against the pathogens most likely to contaminate the surgical site, (2) given in an appropriate dose and time that ensures adequate serum and tissue concentrations during the period of potential contamination, (3) safe, and (4) administered for the shortest effective period to minimize adverse effects, the development of resistance, and costs. Prophylactic antibiotic regimens in acute care settings often include first- or second-generation cephalosporins, such as cefazolin or cefuroxime rather than broad-spectrum antibiotics [145]. A single dose of cefazolin 2 g or cefuroxime 1.5 g is recommended for most patients and may be readministered depending on details of the procedure. Depending on the specific type of surgical procedure, vancomycin has been recommended as either a primary or as an adjuvant agent for patients who are presumed or known to have *S. aureus* colonization, in institutions where a "high" prevalence of MRSA exists and when a surgical procedure involves a prosthetic joint insertion, sternotomy, or vascular graft insertion. The recommended dose of vancomycin for prophylaxis is a fixed dose of 1000–1500 mg or a weight-adjusted dose of 10–15 mg/kg.

While the maxim of geriatric prescribing, "start low, go slow," is true for most classes of drugs, this practice is not advisable with antibiotic use. This is especially true in the critically ill surgical patient and may in fact contribute to the problem of antimicrobial resistance. Understanding when pharmacokinetic changes in the elderly are important and call for dose adjustments is imperative [80]. Proper dosing of antibiotics and other drugs in older adults reduces the incidence of ADRs. This point is especially important in light of the fact that the incidence of ADRs increases with advancing age and the effects are more serious in frail elderly patients than in their younger counterparts [81]. In general, improper dosing is a more frequent cause of error in therapy than is the use of an inappropriate drug [82].

Judicious clinical practice requires the prescribing physician to be aware of age-related

Table 6 Selected antibiotics and their drug interactions

Antibiotic	Other drugs	Effect
Ampicillin	Anticoagulants	Anticoagulation
Aminoglycosides	Amphotericin B	Nephrotoxicity
	Cyclosporine	Nephrotoxicity
	Loop diuretics	Ototoxicity
	Neuromuscular blockers	Respiratory paralysis
	NSAIDs	Nephrotoxicity
	Vancomycin	Nephrotoxicity
Cefoperazone, cefotetan	Anticoagulants	Anticoagulation
Clindamycin	Muscle relaxants	Frequency of respiratory paralysis
Ciprofloxacin	Antacids/sucralfate/cations (vitamins and calcium supplements)	Absorption of ciprofloxacin if taken within 2 h
	NSAIDs	CNS stimulation/seizures
	Anticoagulants	Anticoagulation
Fluconazole	Tacrolimus	Tacrolimus level with toxicity
	Cyclosporine	Cyclosporine level, nephrotoxicity
	Ca channel blockers	Ca channel blocker level
	Anticoagulants	Anticoagulation
	Theophylline	Theophylline level
Metronidazole	Alcohol	Disulfiram-like reaction
	Oral anticoagulants	Anticoagulation
Imipenem-cilastatin	Cyclosporine	Cyclosporine level
Trimethoprim-sulfamethoxazole	Anticoagulants	Anticoagulation

Source: Data from [78]

changes in drug absorption, distribution, metabolism, and elimination. These have been described earlier in this chapter. Of these factors, the one with the most direct clinical relevance to antibiotic dosing is the decline in renal function. Most clinicians are aware of the need to decrease the dose of certain nephrotoxic antibiotics, such as aminoglycosides, in the setting of acute renal insufficiency or decreased creatinine clearance. However, other commonly used drugs such as quinolones and most cephalosporins need to be dose-adjusted for a creatinine clearance of less than 30 ml/min [83]. Table 7 lists selected antibiotics whose dosages need to be adjusted [84, 85].

Although aminoglycosides remain important drugs for treating serious infections, alone or in combination with other drugs, the availability of quinolones, monobactams, and carbapenems, agents with broad-spectrum coverage and less nephrotoxicity, makes the use of aminoglycosides less common in elderly persons. Risk factors for the development of aminoglycoside-induced nephrotoxicity include diabetes mellitus, dehydration, advanced age, and duration of treatment [86]. In addition to nephrotoxicity, aminoglycosides may also cause ototoxicity. This is more likely to occur in elderly patients especially if given in high dose or for prolonged periods because ototoxicity is cumulative. Furthermore, the risk of ototoxicity is greater in patients concomitantly taking a loop diuretic [87–89]. Appropriate monitoring of trough aminoglycoside levels can minimize potential adverse events. Several analyses of pooled data from randomized controlled studies in adults found that once-daily aminoglycoside dosing may be associated with less nephrotoxicity and no greater ototoxicity than with multiple daily doses [90–93]. Keep in mind, however, that once-daily aminoglycoside dosing is not appropriate for, or recommended in, any patient with a creatinine clearance <30 ml/min.

Table 7 Selected antibiotics requiring dose adjustment when used for treatment in those with renal insufficiency

Antibiotic	Usual dose	Dose for CrCl 10–50 ml/min	Dose for CrCl <10 ml/min
Cefazolin	1–2 g q8 h	1–2 g q12 h	1–2 g q24–48 h
Cefuroxime	0.75–1.50 g q8 h	0.75–1.50 g q12 h	0.75–1.50 g q24 h
Ceftazidime	2 g q8 h	2 g q12–24 h	2 g q24–48 h
Cefotaxime	2 g q8 h	2 g q12–24 h	2 g q24 h
Penicillin G	0.5–4.0 million units q4 h	75% of dose	20–50% of dose
Ampicillin	1–2 g q6 h	1–2 g q6–12 h	1–2 g q12–24 h
Piperacillin-tazobactam	3.375–4.5 g q6–8 h	2.25 g q6 h	2.25 g q8 h
Piperacillin	3–4 g q4–6 h	3–4 g q6–8 h	3–4 g q 8 h
Ticarcillin-clavulanate	3.1 g q4 h	3.1 g q8–12 h	2 g q12 h
Aztreonam	2 g q8 h	50–75% of dose	25% of dose
Ertapenem	1 g q24 h	0.5 g q24 h	0.5 g q24 h
Imipenem-cilastatin	0.5 g q6 h	0.25 g q6–12 h	0.125–0.25 g q12 h
Metronidazole	7.5 mg/kg q6 h	7.5 mg/kg q6 h	50% of dose
Vancomycin	1 g q12 h	1 g q 24–96 h	1 g q4–7 days
Gentamicin	1.7 mg/kg q8 h	1.7 mg/kg q12–24 h	1.7 mg/kg q48 h
Amikacin	7.5 mg/kg q12 h	7.5 mg/kg q24 h	7.5 mg/kg q48 h
Amphotericin B	0.4–1 mg/kg q24 h	0.4–1 mg/kg q24 h	0.4–1 mg/kg q24 h
Fluconazole	100–400 mg q24 h	50% of dose	50% of dose
Ciprofloxacin (IV)	400 mg q12 h	400 mg q12–24 h	400 mg q18–24 h

Source: Data from [85]
CrCl creatinine clearance

Regarding hepatic metabolism of antibiotics, although liver size and blood flow tend to decrease with age, in the absence of serious liver disease and subsequent hepatic dysfunction, antibiotic dosages do not need to be adjusted. Drug-induced hepatitis in patients treated with antituberculous agents, especially isoniazid, increases in incidence from 2.8/1000 in patients <35 years old to 7.7/1000 in patients 55 years old [87, 94]. Therefore, liver function tests must be performed frequently prior to and during the course of antituberculous therapy. Antibiotics that require dose adjustments in patients with hepatic dysfunction include cefoperazone, clindamycin, erythromycin, isoniazid, ketoconazole, nafcillin, and rifampin (Table 8). Beta-Lactam antibiotics (penicillins, cephalosporins, cephamycins, carbapenems, and monobactams) have varying characteristics of absorption, peak concentration, bioavailability, and metabolism. These topics are described in detail in standard texts and are not covered here. In general, bioavailability is relatively poor after oral administration, which has implications for the switch from intravenous to oral preparations, and pharmacokinetics are similar after intramuscular or intravenous administration [84].

Table 8 Selected antibiotics requiring dose adjustment in the presence of severe hepatic dysfunction

Nafcillin
Cefoperazone
Clindamycin
Erythromycin
Ketoconazole
Isoniazid
Rifampin

Cephalosporins are relatively safe drugs to use in older persons. Dosages for certain cephalosporins need adjustment for renal insufficiency (Table 7). The broad spectrum of activity of ceftriaxone together with its convenient once-daily dosing makes it an ideal drug for empiric use in a variety of clinical infections in the older adults [95, 96]. In addition, it has both renal and biliary excretion and as a result needs little adjustment for renal insufficiency. A lesser known side effect of ceftriaxone is the formation of biliary sludge with prolonged use [97].

Carbapenems (imipenem-cilastatin, meropenem, and ertapenem) are occasionally used in the postoperative patient because of their broad spectrum of activity. Their pharmacokinetics are similar to that of cephalosporins, and they require dose adjustment for renal insufficiency because they are excreted renally. The cilastatin component of imipenem-cilastatin has no antibacterial activity, but is used to inhibit renal tubular metabolism of imipenem, thereby increasing the urinary concentration of the active drug. Major adverse effects of the carbapenems, especially imipenem-cilastatin, are related to the CNS, including seizures, somnolence, and confusion and are dose-related [103]. This is more likely to occur in the elderly with a history of a CNS lesion, prior seizure disorder, or renal insufficiency.

Aztreonam is a monobactam that has only aerobic gram-negative bacterial coverage. Its pharmacokinetics are similar to that of the cephalosporins. It is frequently used in patients with renal insufficiency as a substitute for aminoglycosides, although it too needs dose adjustment in such patients. It lacks cross-reactivity with other b-lactam antibiotics and can be used safely in patients with severe allergy to penicillin or cephalosporins [104, 105].

The fluorinated quinolones are widely used. Compared with the first-generation fluoroquinolones (norfloxacin and ciprofloxacin), subsequent fluoroquinolones (ofloxacin, levofloxacin, and moxifloxacin) have a broad spectrum of aerobic gram-positive and gram-negative bacterial activity along with the same excellent pharmacokinetic profile. The gram-positive coverage, especially in vitro activity against *Streptococcus pneumoniae*, of the earlier quinolones (ciprofloxacin) is not as good as that of the new generation of quinolones. In addition, they are active against intracellular organisms such as *Legionella*, *Mycoplasma*, *Chlamydia*, and *Mycobacterium*. They are well absorbed orally, with a high degree of bioavailability that makes them especially useful drugs in the transition from intravenous to oral dosing. They also have excellent tissue penetration. Care should be taken with the oral administration of these drugs to ensure that they are administered 2 h before or after antacids, sucralfate, or other multivalent metallic cations as their absorption can be severely impaired, leading to therapeutic failure [106, 107]. Renally eliminated fluoroquinolones (ofloxacin and levofloxacin) need to be dose-adjusted when the creatinine clearance is $<$50 ml/min.

Along with the increased usage of this class of antibiotics, there have been reports of specific side effects when prescribing these drugs in older adults. Certain quinolones can cause QT interval prolongation. They should be avoided in patients with known prolongation of the QT interval, patients with uncorrected hypokalemia or hypomagnesemia, and patients receiving class I or class II antiarrhythmic drugs [108]. Elderly patients on corticosteroids, especially in the setting of chronic renal insufficiency, are also at risk for Achilles tendon rupture [109].

An important and well-documented drug interaction of quinolones with warfarin is particularly noteworthy in the postsurgical patient. The prothrombin time (PT) and INR need to be closely monitored to prevent bleeding complications [110, 111]. Lastly, fluoroquinolones have been associated with CNS toxicity in older adults. These reactions take the form of confusion, psychosis, or seizures and may be dose-dependent, with higher likelihood in those with existing neurologic disease or a compromised blood-brain barrier [2, 146, 147].

With the increase in the number of infections due to methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci, alternatives to vancomycin are needed. Linezolid, a fluorinated oxazolidinone active against gram-positive organisms and most commonly used vancomycin alternative, is a nonselective inhibitor of monoamine oxidase (MAOI). In the elderly patient with the potential for polypharmacy as discussed above, drug interactions need to be kept in mind when using this antibiotic. Linezolid is on the list of drugs with serotonergic activity that may cause serotonin syndrome. The most common drug combinations associated with serotonin syndrome are MAOIs with selective serotonin reuptake inhibitors (SSRIs). Since SSRIs are frequently used for the treatment of depression, this is an important drug interaction to keep in mind [112–114].

No discussion of antibiotic use is complete without mention of *Clostridium difficile*-associated diarrhea (CDAD) – a challenge in the care of all hospitalized patients, particularly older ones. Surgical patients comprise 55–75% of all patients with CDAD [115]. Initial treatment regimens remain the same in this population and include oral metronidazole (cheap and generally effective) for mild-moderate infections or oral vancomycin (expensive and concern for antibiotic resistance) for severe infections; however, there is an increased frequency of treatment failure and CDAD recurrence among elderly persons. Prolonged tapering course of antibiotic treatment with anion-exchange resins, oral lactobacillus, or nonpathogenic yeast such as *Saccharomyces boulardii* and fecal transplants (enema with feces from healthy donors) or combinations of the above may need to be considered [148]. Risk factors for CDAD include prolonged use of proton pump inhibitors, highlighting yet another reason to deprescribe this class of medications if not clearly indicated.

Summary

A number of factors can potentially influence the risk-benefit equation for drug use in an older population, including age-related physiologic changes in organ system function, increased likelihood of comorbid diseases affecting organ systems that are the intended site of drug action or are responsible for the metabolism or clearance of a drug, and increased likelihood of multiple chronic medications, which may increase the possibility of drug interactions. It is prudent for surgeons to be mindful of medication-related problems in older adults and be an active medication management steward when selecting, dosing, administering, and monitoring drug effects and side effects.

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Cancer in Older Adults

12

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Abstract

The management of cancer, often considered a disease of the elderly, is becoming an increasingly common challenge for surgeons and oncologists caring for older adults. As the geriatric population has grown, so too have opinions and standards as to what constitutes an appropriate treatment approach in the elderly cancer patient. Not surprisingly, oncology treatment regimens in elderly populations have become increasingly individualized. When applying these tailored treatment paradigms to elderly cancer patients, a crucial consideration is whether the benefits of a proposed cancer treatment outweigh their perceived risks within the context of patients' residual life expectancy. In some circumstances, optimal implementation of these tailored approaches may require deviation from treatments that would otherwise constitute standard of care in younger patients of similar cancer and stage. As such, a strong working knowledge of the nuances involved in the preoperative assessment of the elderly cancer patient, as well as alternative treatment strategies, is crucial for surgeons caring for these patients to ensure optimal perioperative and postoperative decision-making, care, and outcomes.

Keywords

Elderly · Cancer · Life expectancy · Decision-making capacity · Goals of care · Comprehensive geriatric assessment · Surgery · Radiation · Chemotherapy

Introduction

Americans aged 65 years and older now comprise approximately 13% of the total population [1]. As the population of the United States (USA) continues to age and Americans live longer, the US Census Bureau estimates that this figure will eclipse 20% by 2030. As such, it is not surprising that the management of cancer, often considered a disease of the elderly, is becoming an increasingly common challenge for surgeons and oncologists caring for older adults [2]. As of 2016, cancer and its complications were the most common cause of death in persons aged 60–79 years [3].

Just as the geriatric population has grown, so too have opinions and standards as to what constitutes an appropriate treatment approach in the elderly cancer patient. In decades past, it was routinely accepted that reasonable postoperative outcomes could be expected in the hands of technically seasoned surgeons adopting strict selection criteria. Given the continued shift in the US healthcare system away from surgical paternalism and toward patient-centered, value-based care, the traditional assumptions and approaches toward operative geriatric oncology may also no longer be valid [4, 5].

Numerous clinical studies have stressed the importance of focusing on patients' physiologic age, rather than simply their chronological age; in turn, oncology treatment regimens in elderly populations have become increasingly individualized. When applying these tailored, treatment paradigms to elderly cancer patients, perhaps the most important consideration is whether the benefits of a proposed cancer treatment outweigh their perceived risks within the context of patients' residual life expectancy. In some circumstances, optimal implementation of these tailored approaches may require deviation from treatments that would otherwise constitute standard of care in younger patients of similar cancer and stage (e.g., substitution of chemoradiation with or without local excision for neoadjuvant chemoradiation and abdominoperineal resection in an elderly patient with a low, locally invasive rectal adenocarcinoma). As such, a strong working knowledge of the nuances involved in the preoperative assessment of the elderly cancer, as well as alternative treatment strategies, is crucial for surgeons caring for these patients to ensure optimal perioperative and postoperative decision-making, care, and outcomes [3].

Preoperative Considerations

Life Expectancy

Typical considerations when developing a treatment plan for an oncologic condition involve the natural history of that condition, the patient's tumor stage and its perceived "biologic aggressiveness," the efficacy and risks of the proposed treatments, and the risks of cancer recurrence and death. As noted above, responsible oncologic planning in older cancer patients must also acknowledge residual life expectancy as a fundamental component of the decision-making process. Although life expectancy in the USA continues to increase (Fig. 1), likely as a consequence of advances in diagnostic capabilities and increasingly efficacious interventions and pharmaceutical agents, it is important to remember that most life expectancy calculators do not incorporate a patient's specific cancer diagnosis into their algorithms. These estimations must instead be completed within the clinical arena and require a realistic appraisal of the patient's cancer prognosis, as well as their current and future quality of life (both without cancer treatment and after treatment) [3, 6]. A growing body of literature suggests that a significant gap exists between oncologists' assessments of future life expectancy and patients' comprehension of the quantity and quality of that life. To truly honor the informed consent process, the treating surgeon/oncologist must consider the patient's cancer within the context of their projected life expectancy to optimize communication and patient-centered decision-making [7].

Decision-Making Capacity

Also inherent in the proper implementation of the informed consent (and subsequent discussion of proposed treatments) is a patient's ability to process information and make decisions independently. A patient's decision-making capacity should ideally be determined shortly after cancer diagnosis but before initiation of cancer treatment [3]. In accordance with accepted legal criteria for demonstrating decision-making capacity, a patient must understand the relevant information communicated by the physician; acknowledge his or her

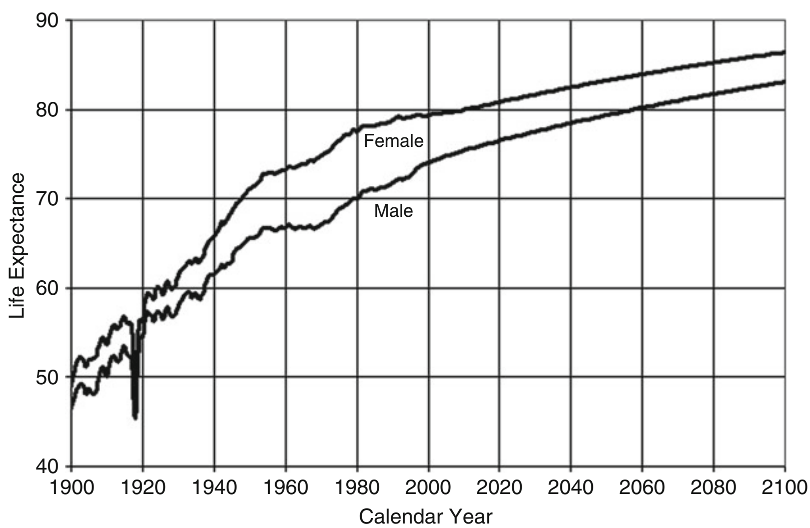

Fig. 1 Life expectancy at birth by sex and calendar year (1900–2100). Line graph illustrating average life expectancy by the year of birth (Adapted from the US Social Security Administration, Actuarial Study 120, August 2005 https://www.ssa.gov/OACT/NOTES/actstud.html)

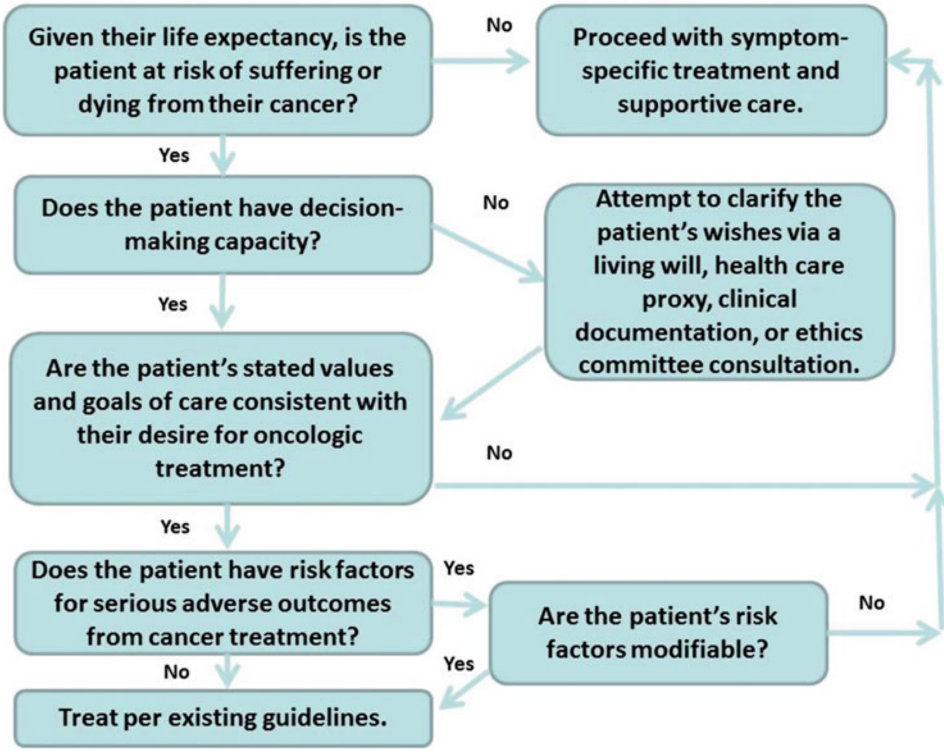

Fig. 2 Decision-making algorithm in the elderly cancer patient. Proposed algorithm to assist in the evaluation and treatment planning of the elderly cancer patient (Adapted from NCCN. Older Adult Oncology (Version 2.2016) http://www.nccn.org/professionals/physician_gls/pdf/senior.pdf)

medical condition, treatment options, and likely outcomes; engage in a rational discussion regarding treatment options; and be able to indicate his or her treatment choice [2]. Although the specifics of how best to assess decision-making capacity fall within the purview of the surgeon/oncologist's usual practice, a proposed algorithm is shown in Fig. 2 [3].

Goals of Care

Another crucial step when crafting a treatment plan in elderly cancer patients is an explicit discussion of the physician and patient's goals of care. Surgery, radiation therapy, and systemic therapy can be deployed for attempted cure or simply to palliate a patient's cancer and ideally improve quality of remaining life [6]. Previous studies suggest that despite extensive and repeated counseling by oncologists regarding the rationale and intent of a specific treatment, a significant proportion of patients remain unaware that their treatment is not curative [7]. As such, it is imperative to discuss the patient's prognosis and chances for "cure" at the time of the initial oncologic evaluation before eliciting the patient's goals of care. Furthermore, this discussion may need to be repeated at various intervals during the patient's care, particularly in the setting of serious toxicity/complications, changes in treatment plan, or disease progression. Although of particular importance to the older cancer patient, adherence to this approach is widely considered best practice irrespective of a cancer patient's age.

Comprehensive Geriatric Assessment

Another tool that should be utilized to better estimate an elderly patient's fitness for oncologic intervention is comprehensive geriatric assessment

(CGA). CGA is a validated, detail-oriented method by which a patient's overall physical, mental, and emotional suitability for surgery can be evaluated through a multidisciplinary assessment of comorbidity, "geriatric syndromes," and existing support systems [3, 6, 8]. A full CGA is outlined in the first column of Table 1.

Comorbidities requiring careful preoperative assessment include cardiopulmonary disease, liver disease, and renal insufficiency. In accordance with current American College of Cardiology and American Heart Association recommendations, all patients undergoing major non-cardiac surgery should be evaluated for perioperative cardiac risk [9]. Postoperative myocardial infarction (MI) is associated with hospital mortality rates of 15–25%, and patients experiencing nonfatal perioperative MI are at significantly increased risk for cardiovascular death and additional nonfatal MIs during the 6 months after surgery [10]. Identification of elderly patients with higher cardiac risk profiles is critical since these patients are more vulnerable to perioperative cardiac adverse events during the perioperative period, as well as during neoadjuvant/adjuvant therapy [2].

Similarly, postoperative pulmonary complications are common and contribute considerably to overall morbidity and mortality. Some degree of pulmonary compromise is often associated with postsurgical recovery, regardless of age. Elderly oncology patients, many of whom may require large thoracic/abdominal incisions for tumor extirpation, are no exception. As such, older patients should be carefully evaluated to assess their risk of developing postoperative pulmonary complications. Patient-related factors, such as history of chronic obstructive pulmonary disease, cigarette use, and functional status, must be considered. In patients deemed to be at increased risk, the implementation of preoperative prevention strategies (e.g., smoking cessation, pulmonary

Table 1 Comparison of a CGA, G-8 screening tool, and CARG

Comprehensive geriatric assessment	G-8 screening tool	CARG chemotherapy toxicity prediction tool
1. *Functional status* ADL – activity of daily living IADL – instrumental activity of daily living performance status (ECOG) 2. *Comorbid medical conditions* Charlson comorbidity index, polypharmacy 3. *Cognitive function* Mini-Mental State Examination 4. *Psychological state* Geriatric Depression Scale 5. *Social support* Living conditions, caregivers, access to care 6. *Nutritional status* Mini Nutritional Assessment 7. *Geriatric syndrome* Dementia, depression, delirium, falls, osteoporosis, neglect or abuse, failure to thrive, nutritional deficiency	1. Has food intake declined over the past 3 months due to loss of appetite, digestive problems, and chewing or swallowing difficulties? 2. Weight loss during the last 3 months 3. Mobility (bed bound, does not go out, goes out) 4. Neuropsychological problems (none, mild–severe dementia) 5. Body mass index 6. Takes more than three medications per day 7. In comparison with other people of the same age, how does the patient consider his/her health status? 8. Age: < 80, 80–85, > 85	1. Age ≥ 72 2. Type of cancer (GI/GU) 3. Number of chemotherapy drugs (one vs. multiple) 4. Chemotherapy dosing (standard vs. reduced) 5. Hemoglobin <11 g/dL in male and <10 g/dL in female 6. Creatinine clearance <34 mL/min 7. Hearing fair or worse 8. Number of falls in the last 6 months ≥ 1 9. IADL: taking medication with some help/unable 10. Limitation in walking one block 11. Decreased social activity at least sometimes

CARG Cancer and Aging Research Group, *ECOG* Eastern Cooperative Oncology Group, *GI/GU* gastrointestinal/genitourinary function testing, perioperative intensive inspiratory muscle training, etc.) may be appropriate and beneficial [2].

Many elderly oncologic patients are afflicted with varying degrees of hepatic dysfunction and renal insufficiency. For those with known disease, preoperative coordination with the patient's primary care physician, gastroenterologist/hepatologist, and/or nephrologist is strongly recommended. A serum comprehensive metabolic panel should be obtained prior to surgery, and liver function tests, glomerular filtration rate, and albumin/creatinine values should be reviewed to identify patients with subclinical hepatic dysfunction/renal insufficiency who may require additional medical evaluation and/or intervention prior to surgery. All medications should be reviewed, and appropriate agents should be dosed in accordance with patient's creatinine clearance (instead of serum creatinine alone) [2].

In addition to the aforementioned comorbidities, various geriatric syndromes proven to increase perioperative morbidity and mortality can also afflict elderly surgical patients. The incidence of dementia, among the most prevalent of age-related disorders within this population, rises exponentially with increasing age over 65 years [11]. In elderly patients without a known history of cognitive impairment, a detailed history and cognitive assessment (e.g., Mini-Cog) are indicated [2, 12]. Depending on the results, additional specialty referral may be needed. Careful documentation of preoperative, baseline cognitive status is required, and surveying knowledgeable family members about recent functional decline is highly recommended. Ideally, these cognitive assessments should be completed during the preoperative evaluation, since presence of dementia may adversely affect the accuracy/validity of subsequent preoperative assessments [2].

Similarly, clinical depression is not uncommon among elderly surgical patients and among patients older than 71 years and has an estimated prevalence of 11% [13]. Established risk factors include female sex, disability, bereavement, sleep disturbance, and prior history of depression. A new diagnosis of cancer can often exacerbate subclinical depression, if already present. Clinical depression can adversely impact the evaluation, treatment, and recovery processes; as such, preoperative depression screening is advised. Available, validated screening tools, such as the Patient Health Questionnaire-2, can prompt additional referral for specialty consultation, if necessary [2, 14].

Alcohol and substance abuse can dramatically increase the risk of postoperative morbidity and mortality and adversely impact the ability to successfully administer neoadjuvant/adjuvant chemotherapy in elderly surgical patients. Routine screening via the CAGE or another similar questionnaire is recommended [2, 15, 16]. Patients identified to be at high risk for alcohol/substance abuse should ideally be referred to a substance abuse specialist for preoperative abstinence or medical detoxification; at a minimum, perioperative withdrawal prophylaxis should be utilized [2].

Postoperative delirium is a common complication in elderly surgical patients, with an estimated incidence ranging from 5.1% to 52.2% [17]. It is associated with higher hospital utilization/costs, perioperative morbidity mortality and complications, longer lengths of stay, higher rates of post-discharge institutionalization, and slower functional recovery [18–20]. Proper screening and documentation (in the outpatient setting) can in turn optimize perioperative management, including avoidance of use of antihistamines, benzodiazepines, drugs with strong anticholinergic side effects, and meperidine for analgesia during the inpatient, postoperative period [2].

Frailty, a syndrome of decreased physiologic reserve and resistance to stressors clinically distinct from comorbidity or disability, increases elderly patient vulnerabilities to various poor health outcomes, including worsening mobility, falls, hospitalization, and death [21, 22]. Frailty has also been shown to be a powerful independent predictor of postoperative adverse events, including increased lengths of stay, morbidity/mortality, and post-discharge institutionalization [23]. Several, "user-friendly" frailty measures exist which can be implemented in the clinical setting to optimize and streamline care during the perioperative period. One example, developed by Robinson

Table 2 Geriatric assessment markers for frailty, disability, and comorbidity

Criteria	Definition	Points
Cognition	Mini-Cog ≤ 3	1
Nutrition	Albumin ≤ 3.3 g/dL	1
Physical Stability	Falls ≥ 1 in past 6 months	1
Anemia	Hematocrit $< 35\%$	1
Disability	Dependence ≥ 1 ADLs[a]	1
Comorbidity	Charlson index ≥ 3	1

[a]Activities of daily living
Adapted from Robinson TN, et al. *Ann Surg*. 2009 Sep;250 (3):449–55

et al., is shown in Table 2; a total patient score greater than or equal to 4 is predictive of 6-month mortality with sensitivity of 81% and specificity of 86% [2, 24, 25].

An important related factor, functional dependence, was the strongest predictor of postoperative 6-month mortality in a recent prospective study of elderly patients undergoing major operations with subsequent intensive care unit admission [24]. In the setting of likely postoperative stomas and/or drains, patient independence and agility may be crucial. Outpatient screening should measure the patient's ability to independently perform daily activities (i.e., functional status) and should inquire about any history of falls. Deficits in hearing, vision, and swallowing should be documented, and limitations of gait and ambulatory mobility should be objectively quantified using the Timed Up and Go test or another similarly validated technique [25]. Based on these assessments, preoperative occupational/physical therapy can be considered, and proactive discharge planning can be implemented [2].

Another common geriatric syndrome, malnutrition, is also associated with increased risk of adverse postoperative events and, in particular, infectious and wound complications [26]. Previous studies have documented significant rates of malnutrition among elderly patients, with prevalence estimates ranging from 5.8% in the community to 13.8% in nursing homes, 38.7% in hospitals, and 50.5% in rehabilitation settings [27]. Attention paid to preoperative nutritional status is especially important in patients scheduled for procedures that may put them at risk for postoperative malnutrition (e.g., esophagectomy, total gastrectomy, pancreaticoduodenectomy, etc.). As such, nutritional status should be routinely assessed in the preoperative setting and should include calculation of body mass index (BMI), measurement of serum albumin and prealbumin, and documentation of unintentional weight loss within the previous 6 months. Patients with a BMI less than or equal to 18.5 kg/m2, serum albumin less than or equal to 3.0 g/dL, or reported unintentional weight loss of more than 10% within the previous 6 months are considered to be at high risk for malnutrition; these patients should undergo a full, preoperative nutritional assessment by a dietician and have a formal perioperative nutritional plan developed to address any anticipated deficits [2].

Polypharmacy, a common problem in elderly patients that has been associated with increased risk of cognitive impairment, morbidity, and mortality, should be routinely assessed in this population. As such, surgeons caring for elderly cancer patients should carefully review and document each patient's complete medication list, including the use of non-prescription agents and herbal supplements – particularly if neoadjuvant therapy is planned to minimize the risk of adverse drug reactions. In accordance with existing national guidelines, medications proven to reduce perioperative risks of adverse events (e.g., cardiac, etc.) should be started or continued. The addition of new medications should be minimized, and potentially inappropriate agents that may increase the risk of adverse drug reactions should be discontinued preoperatively [2].

Assessment of the patient's socioeconomic status (SES) and degree of social support is an important but often overlooked element of the CGA. Low SES and lack of social support can severely limit the elderly patient's ability to adhere with planned neoadjuvant and/or adjuvant therapy and comply with preoperative instructions (e.g., pre-habilitation, bowel preparation, etc.). Furthermore, lack of social support has been shown to be associated with increased treatment-related mortality [3, 28]. When developing a complex, multidisciplinary treatment plan for an elderly cancer patient, the oncology care provider must ascertain the patient's ability to comply with the logistics and cover the costs of the various required therapeutic elements. Otherwise, financial limitations, travel restrictions, and care obligations to an infirm spouse/partner may jeopardize care that could have been potentially mitigated via upfront referral to the treating institution's social worker and/or financial counselors [3].

Treatment Approaches

Planning and Sequencing of Care

Regardless of patient age, optimal oncologic care requires careful planning, collaborative multidisciplinary care, and adherence (whenever possible) to the most up-to-date clinical guidelines. Among elderly populations, consideration of the patient's expectations and goals of care are an integral part of this process, as modifications or omissions of specific treatment paradigms may be appropriate or required. For example, in an octogenarian woman with significant comorbidities and marginal functional outcome, it may be appropriate to treat her newly diagnosed breast carcinoma via surgical extirpation without adjuvant therapy. Proper planning should also consider the patient's ability to comply with scheduled treatments and tolerate potential toxicities/complications that may ensue [3, 6]. Elderly patients with cognitive deficiency, polypharmacy, and limited social support are more likely to become non-compliant over the duration of their cancer care [3]. Potential non-compliance can range from failure to complete a bowel preparation prior to colorectal surgery to outright refusal to take oral chemotherapeutic agents.

Surgical Therapy

Given the scope and complexity of many oncologic surgical procedures, postoperative morbidity and mortality are not uncommon, particularly in elderly patients. In an effort to preemptively mitigate these risks, the role of nutritional and/or physical pre-habilitation is increasingly being explored. A growing body of evidence supports the use of pre-habilitation programs focusing on increased pulmonary fitness and physical activity levels, particularly prior to cardiopulmonary surgery [6, 29]. In a 2016 systematic review by Moran et al., a pre-habilitation regimen encompassing aerobic activity, resistance training, and inspiratory spirometry was associated with reduced postoperative morbidity following abdominal surgery [29]. Given that many elderly cancer patients present with frailty and/or impaired functional status, further work to define the benefits of pre-habilitation in these populations is especially important [3, 29].

Among elderly cancer patients, particularly those with advanced age, advanced comorbidity, and/or marginal functional status, perhaps the most critical decision facing the surgical oncologist is whether to proceed with a curative surgical resection or a palliative procedure. Irrespective of patient age, a definitive curative procedure should be strongly considered in fit elderly patients with good performance status if a negative margin (i.e., R0) resection is technically feasible. In more frail patients with significant comorbidities and/or limited life expectancy (e.g., an 88 year old man with a metastatic, near-obstructive right colon cancer), modified extirpative procedures or palliative procedures may be more appropriate. Whenever possible, the least invasive and morbid palliative option that will reduce symptoms and optimize patient quality of life should always be implemented first. Palliative surgical interventions, however, play an important role in the treatment of the elderly cancer patients and should be included in the surgical oncologist's armamentarium [30, 31].

Although its benefit has been well established, postoperative rehabilitation is often underutilized, even among elderly cancer patients [32]. Clear advantages of rehabilitation after cancer surgery include improved physical fitness (and associated activity levels), increased quality of life, decreased costs of care, and decreased missed work days and rates of early retirement [33]. Given the physical and functional challenges often faced by geriatric surgical cancer patients, surgical oncologists should assign the same degree of importance to referral to and compliance with rehabilitation as they do to the other aspect of the patient's multidisciplinary care [32].

Radiation Therapy

While radiation may be applied in curative, adjuvant, or palliative settings in the elderly, there are more opportunities to consider radiotherapy as a curative mode of therapy in elderly cancer patients who are not deemed to be candidates for attempted curative resection. As such, a broad familiarity with radiation fractionation schedules (with or without radiosensitizing chemotherapy) is useful in presenting elderly patient with viable treatment options that may be better tolerated. As frequent travel to and from radiation therapy facilities is often challenging in elderly patients, shorter hypofractionated schedules are frequently advantageous from a logistical perspective [34]. Setup for radiation for elderly patients may sometimes require deviation from the most optimal position due to decreased mobility. The incorporation of advanced technologies, with more focused dose delivery and image guidance to decrease setup error, has made these "nonstandard" treatments more feasible [35].

While data exist describing increasing cellular radiosensitivity with age, the clinical response to radiotherapy is not always so clear [36]. In practice, while some elderly patients are quite sensitive to radiation, there are others who tolerate treatment better than their younger counterparts. Most retrospective series analyzing this topic have reported that age alone is not a good predictor of toxicity and that elderly patients often tolerate treatment quite well [37–40]. However, a more holistic approach to radiation toxicity allows one to make pretreatment predictions that can be valuable in treating elderly patients.

Smith et al. have proposed a framework for conceptualizing radiotherapy in the elderly [41]. This structure incorporates four factors to be considered when determining the risk/benefit ratio of radiotherapy in the elderly: locoregional tumor behavior, competing cancer and non-cancer morbidity and mortality risks, functional reserve, and palliative requirements. Of note, while it is important to avoid overtreatment of elderly patients, the authors also warn against undertreatment that may stem from underestimating the patient's true life expectancy or the aggressiveness of the cancer. Consideration of these factors in the context of a multidisciplinary evaluation is thus crucial to the optimal care of elderly cancer patients.

Systemic Therapy

While the surgical and radiation oncology care may be limited to a defined time, the medical oncologist often follows patients through the disease continuum from diagnosis through the late stages of palliative care. Supporting an older patient through this journey is often a very challenging and involved task that requires attention to multiple factors that affect the patient's care. These challenges are encountered daily by medical oncologists around the world and will become more prevalent in the future [42]. Medical oncologists are becoming more comfortable in caring for these older patients and prescribing anticancer therapy. This was well demonstrated by Vijayvergia et al. who reported an increase in the number of older patients and patients with multiple comorbidities that received multi-agent therapy for metastatic colon cancer over the last two decades [43]. Despite this trend older patients continue to be underrepresented in clinical trials, and high evidence data to guide treatment approach is lacking in many circumstances [44–46]. In recent years a few studies have been published demonstrating the feasibility of conducting elderly specific clinical trials and the utility of these data in guiding the management of older patients. One such example is the AVEX study which set the stage for front-line therapy with 5-fluorouracil and bevacizumab in older metastatic cancer patients who are not candidate for standard multidrug regimens [47].

As with cancer surgery, chronological age alone should not be used as a sole factor to determine the patient's ability to undergo anticancer systemic therapy. This is especially important when considering chemotherapy treatments that are often prolonged and carry significant toxicity risks. The medical oncologist is tasked with the difficult duty of differentiating between those older adults who are fit and would benefit from chemotherapy and those who are frail and would derive little benefit from this approach. Furthermore, many older adults may appear somewhat fit prior to starting treatment but are at high risk of development of side effects that will affect their function, quality of life, and longevity. These treatment decisions must be made through a shared discussion with the patient and caregivers since patient's goals and values would weigh highly on the final treatment plan. Studies have shown that older patients would value quality of life over length of life in the setting of cancer therapy [48].

Specific Chemotherapy-Related Challenges

Older patients have an altered response to chemotherapy as compared to their younger counterparts, mainly due to physiologic changes related to the aging process. These changes in organ function are often underestimated and remain undetected without a thorough evaluation. Decrements in renal and hepatic function, altered GI motility, loss of cardiac and marrow reserves, changes in cognition, and decrements in bone and muscle mass may increase the risk for treatment-related toxicity. Furthermore, the high incidence of comorbidities adds additional challenges to the planned therapy. The Centers for Disease Control and Prevention estimates that 80% of older adults have at least one chronic condition and 50% have two or more conditions that affect their care [49]. The presence of multiple comorbidities results in patients receiving additional medications and often dealing with the challenges of polypharmacy. The reported rate of polypharmacy among older cancer patients varies in the literature [50]. One study reported up to 63% of these patients have the potential for adverse drug interaction, with majority of these patients receiving an average of eight medications [51]. The definition of polypharmacy among cancer patients continues to be debated. A recent study of 385 patients over the age of 70 with cancer reported that an average of 6.5 medications predicted for frailty and an average of 5.5 medications predicted for falls. In this single institution study, the proposed cutoff was five medications or more that would define polypharmacy in an older cancer patient [52]. Delivering chemotherapy along with multiple other medications can clearly alter the activity of the anticancer therapy and result in drug-drug interactions that can affect toxicity rates and efficacy. Careful review of the medication list and elimination of unnecessary agents are necessary to decrease these interactions and maximize the efficacy and tolerance.

As noted above, changes in normal organ function are prevalent among older patients and heavily affect treatment tolerance and efficacy (Table 3). Effects of these changes in the gastrointestinal tract especially affect the older patient's ability to tolerate chemotherapy. Nausea, vomiting, and diarrhea that are commonly induced by chemotherapy can be very debilitating and result in dehydration and significant morbidity in an older patient with limited reserve. Multiple medications are available today for management of chemotherapy-induced nausea and vomiting. Serotonin (5-HT3) receptor antagonists, neurokinin-1 receptor antagonist, and corticosteroids are most commonly used and are quite effective in controlling these symptoms. These drugs, however, carry additional toxicities such as QTc prolongation, constipation, fatigue, and confusions. Thus careful selection of these agents based on the emetogenic potential of the regimen must be undertaken [62].

Glomerular filtration rate (GFR) also decreases with age and results in delayed renal excretion of many agents and increase in rate of toxicities as a result. As serum creatinine measurement may not be a good indicator of GFR in older patients, calculation of the creatinine clearance to assess the true renal function is required for all patients prior to chemotherapy initiation. A study by Peterson et al. reported an increase of about 12% in the odds for chemotherapy-related toxicity with every decrease of 10 mL/min in creatinine clearance. The study also confirmed the lack of predictive value of serum creatinine alone as a predictor of chemotherapy toxicity [53].

Table 3 Physiologic changes of aging and their effect on chemotherapy tolerance

System	Changes	Impact on chemotherapy tolerance	Recommended intervention
Cardiovascular	Decreased ventricular compliance Valvular thickening Increased vessel wall thickness Diastolic dysfunction Decreased cardiac reserve	Increased risk for heart failure Increased risk for arrhythmias Increased risk for blood pressure changes – which may lead to falls	Monitor use of cardiotoxic drugs Monitor polypharmacy EKG/ECHO monitoring based on recommended guidelines when using cardiotoxic drugs
Gastrointestinal	Decreased acid production Decrease in protective mechanisms Decreased motility and absorption Decreased hepatic drug clearance	Increased risk for mucositis and diarrhea which can lead to dehydration Decreased medication absorption Increased risk for drug overdose due to slow hepatic metabolism	Close monitor for GI-related adverse events Support with anti-nausea and antidiarrheal agents Monitor for drug interaction Consider dose reduction
Pulmonary	Decreased lung compliance Decreased FEV1 and vital capacity Increased residual volume Decreased respiratory center sensitivity Decreased mucociliary function	Increased work of breathing Decreased pulmonary capacity/ reserve Increased risk for pulmonary infections	Pulmonary evaluation prior to surgery or radiation Influenza/pneumonia vaccination Smoking cessation
Renal	Decreased GFR Tubular renal function Dysregulation of renin angiotensin system Impaired vitamin D metabolism	Drug-related nephrotoxicity – need for dose reduction Increased risk for electrolyte abnormalities	GFR/CrCL calculation for each patient + appropriate dose reductions Avoid nephrotoxic drug Evaluate for polypharmacy Monitor electrolytes
Hematologic	Increased risk for myelosuppression Increased risk for anemia Increased risk for thrombocytopenia	Increased risk of febrile neutropenia and infections Increased risk for fatigue Increased risk for bleeding	Prophylactic use of G-CSF Close monitoring of blood counts Monitor for additional medications that increase risk of bleeding, i.e., anticoagulation

EKG electrocardiogram, *ECHO* echocardiogram, *GI* gastrointestinal, *FEV1* forced expiratory volume 1, *GFR* glomerular filtration rate, *CrCl* creatinine clearance, *G-CSF* granulocyte colony-stimulating factor

Myelosuppression is the most common adverse event encountered by older patients receiving chemotherapy, and its incidence increases dramatically with aging [54–56]. For example, the risk of severe neutropenia in studies of elderly patients with non-Hodgkin's lymphoma ranged between 15% and 89% depending on the regimen used and averaging at 50% [57]. Similar data was reported among breast cancer patients with increase in the rate of dose reductions due to myelosuppresion among patients over the age of 65 [58]. The prophylactic use of granulocyte colony-stimulating factors (G-CSF) is effective in reducing the risk of febrile neutropenia and documented injections that are associated with dose-intensive chemotherapy regimens [59]. Many guidelines recommend the prophylactic use of G-CSF for patients who are at high risk based on age and when the risk of febrile neutropenia is expected to exceed 20% [60, 61]. Despite these recommendations, a recent study by Choi et al. reported a low percentage of older patients that receive this therapy despite undergoing therapy with high-risk regimens.

Additional examples of physiologic changes that are encountered with aging and directly affect anticancer therapy are outlined in Table 3. These highlight the importance of through evaluation of the patient's comorbid conditions, physical health, and other medications. Furthermore, personalization of therapy based on the patient's individual assessment is necessary to ensure the desired benefit and least toxicities possible.

Targeted Therapy and Immunotherapy

In recent years multiple new agents have been added to the treatment arsenal of various cancers. These drugs include monoclonal antibodies such as bevacizumab and trastuzumab, tyrosine kinase inhibitors such as sorafenib and sunitinib, and finally immunotherapies such as ipilimumab and pembrolizumab. As with other modalities of therapy, older patients comprised a small portion of the subjects who took part in the studies leading to approval of these agents, and thus data is limited with regard to their tolerance of these drugs. Those studies that included older patients overall demonstrated a similar efficacy in older and younger patients treated with these agents [62]. Nevertheless, there are still concerns about increased toxicities with these agents among older patients. Some of these agents have now been used for a significant time to allow post-marketing information regarding the tolerance in older patients. For example, the use of bevacizumab in older patients with metastatic colon cancer has been found to be safe, without any significant increase in toxicities in comparison to younger patients [47]. Conversely, older patients were found to have similar efficacy but higher rates of grade 3 or higher toxicities with erlotinib therapies in the advanced lung cancer [63]. Similarly, the benefit associated with trastuzumab in the treatment of HER2-positive breast cancer is equivalent in older and younger patients, yet the risk of trastuzumab-induced cardiotoxicity seems to be increased in the older patient population [64]. As oncologists become more comfortable using these agents, additional research is needed to clarify the specific considerations that are required when using them in the older patient population.

The use of monoclonal antibodies targeting immune checkpoint molecules (CTLA-4, PD-1, PD-L1) has emerged as a novel treatment approach in recent years. Currently these drugs are approved for use in multiple cancers including melanoma, non-small cell lung cancer, and renal cancer. Studies are ongoing that will likely result in approval of these agents in other cancers as well. However, data regarding their use in older patients is sparse. In addition, there are concerns regarding "immune-senescence phenomenon" – age associated impairments in the immune system that could affect efficacy of these agents [65]. These drugs can lead to prolonged antitumor response yet carry the risk of immune-related adverse events and toxicities that are distinct from the typical chemotherapy-related toxicities. A recent meta-analysis of over 5,000 patients treated with these agents demonstrated similar efficacy and survival benefit among older and younger patients [66]. Most studies to date also demonstrated similar toxicity profile among older and younger patients receiving these agents [67, 68]. Nevertheless, older patients must be monitored closely while on these agents for early detection and initiation of therapy should an immune-related adverse event arise.

Many of the targeted agents are orally administered and thus are thought to be a good choice for an older adult with cancer. However, the use of oral medication raises concerns for compliance and adherence to prescribed therapy. Studies have shown that nonadherence to oral anticancer regimen is common among older patients [69]. Factors associated with nonadherence include poor communication, disease/treatment complexity, co-payment, motivation, social support, and patient's perception. These factors must be taken into consideration when determining the treatment approach for each individual patient. Furthermore, close follow-up to ensure the drug is used appropriately and reiteration of the instructions will likely improve compliance and efficacy of the therapy.

Evaluation Prior to Systemic Therapy

Comprehensive geriatric assessment is recommended as the gold standard tool for a thorough assessment of an older patient prior to chemotherapy initiation [70]. A full CGA will evaluate all important domains that could affect the patient during the therapy (Table 1). In a study by Kenis et al., 70% of 967 patients over the age of 70 years had an abnormal screening assessment at diagnosis or disease progression. A subsequent CGA unmasked geriatric issues in 51% of participants. These observations resulted in planned interventions and changes in cancer-directed therapy in 25% of these patients [71]. Similar findings were documented in a trial of 937 patients aged $\geq$70 years, the majority of whom had an Eastern Cooperative Oncology Group performance status (ECOG PS) $\leq$ 1 (72%). CGA detected 73% of patients to be "at risk" (57% with instrumental activities of daily living (IADL) and 51% with ADL deficits) [71]. Despite the extensive data supporting the incorporation of a geriatric assessment into clinical oncology practice, time and personnel constraints have resulted in limited uptake of this approach.

Multiple screening tools (i.e., VES-13, G-8 scale, etc.) have been developed that could identify patients who could benefit from a full geriatric assessment and referral to a geriatrician (Table 1) [72, 73]. A recent study identified the G-8 scale as the best screening tool for identification of patients that would benefit from a geriatric assessment and found it to be independently prognostic of 1-year overall survival [73]. Recently several elderly specific tools for predicting chemotherapy-associated toxicity, using CGA factors, have been developed [46, 74, 75]. These models aim at providing the treating physician with a quick tool that will identify patients who are at risks of chemotherapy toxicities in a busy oncology practice. The model developed and validated by Hurria et al. and the Cancer and Aging Research Group (CARG) includes an evaluation of multiple domains that have been found to directly correlate with the risks of chemotherapy-related toxicities [46, 74, 76, 77]. Completion of this questionnaire is quite simple, and feasibility studies showed the ability to incorporate these data in a clinical practice and research setting [74, 78]. This tool has been found to have significantly higher predictive ability when compared to evaluation by ECOG PS. It allows the oncologist to assess the risks of chemotherapy toxicity to the older patient and enables the physician to have an informed discussion with the patient prior to initiating therapy. Ideally these types of evaluations should be repeated multiple times throughout the disease course. This knowledge will assist the physician in monitoring the patient through therapy and management of treatment-related toxicities, identify areas of frailty that could be improved, and aid in having goals of care discussions.

The use of chemotherapy and other antineoplastic agents for the treatment of older patients with cancer carries significant challenges and high risks for toxicities. As oncologists continue to increase the number of older adults that are under their care, available tools must be incorporated into routine practice to ensure proper evaluation and personalization of therapy. The old "eye ball" test that many physicians use is likely to lack the ability to detect all the active issues and result in less optimal care. Additional research to further define the best treatment approach, recommended dosing, and supportive care measures for older patients in different types of cancer will further enhance our care of this growing patient population.

Disease-Specific Treatment Recommendations in Elderly Cancer Patients

As emphasized throughout this review, cancer care in elderly patients should be tailored to carefully account for both patient and cancer characteristics. Whenever possible, basic cancer treatment paradigms should be adhered to. As outlined below, however, adjustments to various components of care (made within a multidisciplinary context) should also be considered and, often, may be more appropriate.

Breast Cancer

Unlike their younger counterparts, elderly women with invasive breast cancer have a distinctly improved, stage-adjusted prognosis. Invasive breast cancers in older women are more likely to be estrogen and progesterone receptor-positive receptors and less likely to harbor HER2 mutations [79]. Surgical treatment of elderly patients mirrors that of younger individuals and may include mastectomy or breast conservation therapy in combination with sentinel lymph node biopsy. In accordance with the results of the ACOSOG Z0011 trial, women of all ages may not require completion axillary lymphadenectomy if they have early-stage breast cancer (T1-T2), undergo breast conservation therapy with subsequent chemotherapy, and have limited nodal involvement [80]. In geriatric patients who do not meet these criteria, it may still be reasonable to omit axillary lymphadenectomy in patients with significant comorbidity, less biologically aggressive tumors, or if it will not influence the choice of adjuvant systemic therapy [3].

The extent of radiation therapy can also be tailored to the individual elderly breast cancer patient. As suggested by the results of the PRIME II study, it may be reasonable to omit the radiation component of breast conservation therapy for early-stage tumors (T1-T2) with benign histopathologic features (i.e., estrogen receptor-positive, node-negative) in women aged 65 years or older [81]. Furthermore, expert opinion also endorses the exclusion of radiation therapy in women aged 70 years or older who undergo margin-negative breast conservation therapy, have stage I receptor-positive disease, and who will complete 5 years of endocrine treatment [3, 81]. For the aforementioned reasons, the recommendation regarding use of adjuvant endocrine therapy in geriatric women is unchanged [3].

Unfortunately, the significance of adjuvant chemotherapy in this population is less clear. Although some studies suggest a decreased benefit among patients of advancing age treated with systemic therapy, others studies have demonstrated that geriatric patients with aggressive or metastatic carcinomas do obtain the same benefits from first-line systemic therapy as younger patients [82, 83]. As noted above, however, older women are more susceptible to toxicity from chemotherapeutic agents and should be closely monitored for required dose reductions or treatment changes [3].

Lung Cancer

Surgical therapy in geriatric patients with non-small cell lung cancer (NSCLC) largely mirrors recommendations in younger patients. Fit patients with early-stage disease should undergo operative extirpation and mediastinal lymphadenectomy, regardless of age [84]. Among elderly patients with early-stage NSCLC and significant comorbidities (including limited pulmonary reserve), stereotactic body radiation therapy (SBRT) represents a reasonable treatment alternative with similar overall and recurrence-free survival [85]. In patients with larger tumors requiring more extensive resections, pneumonectomy is associated with a significantly higher risk of mortality risk among elderly patients and should only be performed following serious consideration [3, 86].

Recommendations for adjuvant systemic therapy are similar in younger and older patients with early-stage NSCLC. In geriatric patients with unresectable locally advanced disease, definitive chemoradiation also confers similar overall survival, regardless of patient age [87]. However, associated toxicities were more severe in elderly patients and should be anticipated in patients with impaired fitness. In elderly patients with advanced/metastatic NSCLC, multiple phase III studies have confirmed that single- or double-agent chemotherapy is superior to supportive care alone in terms of overall survival and quality of life [88–90]. Again, however, toxicity remains a concern and should be closely monitored for, especially in elderly patients with decreased performance status [3].

Geriatric patients with early-stage small cell lung cancer should undergo concomitant multimodality therapy, including surgical resection if complete extirpation is possible [91, 92]. In the setting of extensive disease, elderly patients, like their younger counterparts, should receive systemic chemotherapy alone [93]. Both cisplatin- and carboplatin-based regimens have been shown to be equivalent with regard to overall survival [3, 94].

Colorectal Cancer

As with other malignancies, the surgical treatment of colorectal cancer should be guided by location and stage, not patient age. Even in patients with isolated hepatic metastases, studies demonstrate similar survival outcomes following liver resection in elderly patients compared to their younger counterparts [95]. In patients with rectal cancer, it is well established that elderly patients have a higher frequency of treatment complications, both during the neoadjuvant and postoperative settings [96]. This observation highlights the importance of optimal patient selection and an individualized approach to cancer care but should not discourage use of stage-based neoadjuvant treatment protocols or extirpation procedures, as deemed appropriate [3]. In patients with significant comorbidity and/or impaired functional status, less morbid surgical procedures (i.e., local excision combined with neoadjuvant radiotherapy with or without adjuvant systemic therapy) or a "watch and wait" strategy (following complete clinical response after neoadjuvant therapy) can be considered [97, 98]. In patients who refuse surgical resection (and/or are not surgical candidates), definitive chemoradiation alone (with or without adjuvant systemic therapy) is a viable treatment option [99].

5-Fluorouracil-based chemotherapy remains the standard of care for adjuvant therapy (or palliative care in the metastatic setting), irrespective of age [100]. Although the majority of studies of systemic therapy for colorectal cancer have not identified an increased incidence of chemotherapy-related toxicities among elderly patients, treating oncologists should practice close surveillance during therapy [3]. Limited data are available regarding the use of newer systemic agents and combinations among elderly patients. In addition to traditional chemotherapy, bevacizumab and anti-epidermal growth factor receptor (EGFR) antibodies (e.g., cetuximab, panitumumab, etc.) have shown much promise in the metastatic setting among geriatric patients and should be considered [3, 101–103].

Liver Cancer

Surgical treatment options for elderly patients diagnosed with hepatocellular carcinoma (HCC) include both liver resection and transplantation (although patients with more advanced age are often no longer considered for transplantation by many programs). Although surgical approaches to resection (e.g., non-anatomic versus anatomic resection) are consistent among age groups, special attention to underlying liver function at presentation and planned future liver remnant (which predicts risk of postoperative liver dysfunction/failure) is of particular importance in elderly patients. Although prospective data are limited, retrospective studies have confirmed that, when properly selected, outcomes of surgery for liver cancer in older patients are similar to those in younger patients [104]. In elderly patients with significant comorbidity and/or impaired functional status, liver-directed therapy, such as percutaneous radiofrequency or microwave ablation, trans-arterial chemoembolization, and SBRT, should be strongly considered [3].

Among elderly patients with advanced/metastatic HCC, standard systemic therapy largely consists of therapy with sorafenib. Although overall survival among HCC patients treated with sorafenib has been shown to be equivalent among both older and younger cohorts, agent-induced toxicities are more common in patients aged 70 years and older [105]. If prescribed within this age group, caution should be observed and close surveillance maintained [3].

Prostate Cancer

Regardless of age, the treatment of prostate cancer should be based on the patient's life expectancy, their tumor's stage and biologic aggressiveness, and the presence or absence of symptoms. While watchful waiting is a viable option in elderly men with low-risk prostate cancer, the combination of radiation therapy and androgen deprivation therapy (ADT) of variable duration has also been proven to be an effective treatment strategy in men with localized high-risk prostate cancer who do not wish to pursue surgical resection and/or are not viable surgical candidates [3, 106]. Side effects associated with long-term use of ADT (28–36 months) are commonly reported among elderly men (e.g., osteoporosis, thromboembolism, sarcopenia, etc.), and thus, close monitoring is warranted [107]. Short course ADT (4–6 months) has also been shown to be efficacious in patients with locally advanced prostatic cancer and is associated with less treatment-related toxicity [3, 108].

Bladder Cancer

Standard care for patients with locally advanced bladder cancer, irrespective of age, includes radical cystectomy and pelvic lymphadenectomy [3]. Population-based data have demonstrated that definitive surgical therapy is equally effective in both elderly and younger patients with bladder cancer [109]. Improved survival was similarly observed across age groups with administration of neoadjuvant chemotherapy in patients with muscle-invasive disease [110]. In contrast, multiple studies have demonstrated that intravesical administration of Bacillus Calmette-Guerin immunotherapy is less effective in elderly patients with bladder cancer [3, 111].

Ovarian Cancer

Although the use intraoperative staging, surgical cytoreduction, and adjuvant systemic therapy remains the standard of care in women with ovarian carcinoma, population-based studies have unfortunately demonstrated underutilization in elderly patients [112, 113]. Reasons for underuse include lack of access to optimal surgical care, distance to treatment facility, and existing comorbidities. Lower enrollment rates of elderly women in prospective clinical trials for ovarian cancer have resulted in the paucity of level I data in this population. Although individualized care should be emphasized, special attention should be paid to the primary roles of surgery and chemotherapy in this patient cohort. Regarding selection of systemic agents, retrospective studies demonstrate that platinum-based doublet chemotherapy is reasonable for patients 70 years or older, as is intraperitoneal chemotherapy [114, 115]. Not surprisingly, however, agent-specific dose modifications and associated toxicities are more common among older women [3].

Melanoma

Despite recent advances in the care of melanoma, surgical excision remains the keystone of curative therapy. As in younger patients, elderly patients with melanoma should undergo wide local excision of the primary site with nodal evaluation/excision performed as per current guidelines [116]. Should significant comorbidity and/or poor functional status make surgery under general anesthesia prohibitive, a reasonable alternative is wide local excision under local anesthesia and omission of nodal evaluation/excision. For primary lesions which cannot be completely resected, adjuvant radiation therapy should be considered [3].

As with younger patients, elderly patients with locally advanced or metastatic melanoma have enjoyed treatment success with newer immunotherapy agents. Ipilimumab, perhaps the most well-known monoclonal antibody used in the treatment of melanoma, has been shown to increase overall survival in previously treated patients afflicted with metastatic melanoma. Multiple studies have confirmed that this survival benefit is consistent in patients above the age of 65 [117, 118]. Similarly, increased overall survival among elderly metastatic melanoma patients has also been confirmed with the use of the BRAF kinase inhibitor vemurafenib and the selective MEK1/MEK2 inhibitor trametinib [119, 120]. Systemic therapy with immunotherapy agents represents the standard of care for all patients with unresectable disease, regardless of age [3].

Conclusion

Optimal care of the elderly cancer patient requires careful consideration of patient- and tumor-related factors and thoughtful deployment of curative surgery or palliative procedures within a multidisciplinary context. A patient-centered CGA is absolutely essential and must consider patients' life expectancy, goals of care, comorbidities, functional status, and socioeconomic/social context, rather than simply patients' chronological age. Whenever possible, preoperative interventions to address various geriatric syndromes and optimize emotional/physical fitness for surgery – as well as neoadjuvant and/or adjuvant multimodal therapy – should be considered and utilized. Although advanced age can be associated with increased rates of treatment-related toxicity, an individualized, methodical, coordinated approach to surgical care in elderly cancer patients can result in excellent short- and long-term perioperative, functional, and oncologic outcomes.

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13 Diabetes in Older Adults

Margo S. Hudson and Nadine E. Palermo

Contents

Abstract

Diabetes mellitus is a complex and chronic illness which affects patients of all ages. Recent estimates predict increased prevalence in the aging population as well as worldwide. Older adults are at increased risk of both acute and chronic diabetes-related complications with adverse consequences on overall health and mortality. Several important factors distinguish inpatient and outpatient management in this patient population.

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Keywords

Diabetes mellitus type 1 · Diabetes mellitus type 2 · Older adult · DKA · Hypoglycemia · Insulin · Cardiovascular disease · Microvascular complications

Introduction

According to the latest estimates from the International Diabetes Federation (IDF), the number of individuals with diabetes worldwide now exceeds 415 million [1]. The Center for Disease Control (CDC) predicts continued rise in diabetes prevalence in the United States with estimated projections affecting one in three adults by 2050 [2]. More than 25% of patients age 65 and older have diabetes which is among the highest

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proportion of any age group [3]. The cost of diabetes care shows a similar increase with a 40% rise seen in the last decade, now over $176 billion dollars, with approximately 59% spent on patients over age 64 [4]. In recent years, there has been a tremendous focus on individualizing treatment and ongoing interest for a consensus to address recommendations for older adults with diabetes. In this chapter, we will review the pathophysiology of diabetes and special considerations and challenges in the management of diabetes in older adults.

Epidemiology, Pathophysiology, and Diagnosis of Diabetes

Diabetes mellitus is a common metabolic disorder which results from complete or partial deficiency in insulin. The most prevalent forms of diabetes are type 1 and type 2, which account for approximately 5–10% and 90–95%, respectively. While in the past it has been suggested that the age at diagnosis determines the subtype, the landscape of diabetes is more complicated, and these traditional paradigms have changed. This is particularly important to consider in older adults. While type 2 diabetes is the predominant subtype, patients may be diagnosed with type 1 diabetes at any age. Patients with type 1 diabetes are also living longer [5]; therefore, this phenotype will be seen in older adults. This distinction in identifying the subtype is essential to understand as the underlying etiology governs the most appropriate and effective treatment strategy.

Classical type 1 diabetes is due to autoimmune-mediated destruction of pancreatic beta cells, which over time results in complete insulin deficiency. In this subtype of diabetes, there are often positive autoimmune antibodies or "biochemical markers" present. The most commonly detected antibodies include islet cell antibodies, glutamic acid decarboxylase 65 (GAD 65), anti-insulin, anti-IA-2, and zinc transporter 8 (ZNT8). Classical type 1a diabetes is defined as the presence of one or more of the aforementioned antibodies. However, some patients with type 1 diabetes do not display the common "biochemical markers" which reflect beta cell immunity, yet these patients have insulin deficiency. Regardless of the etiology, patients with type 1 diabetes must be considered insulin deficient and should not be without exogenous insulin.

Type 2 diabetes results from impaired insulin secretion often in the setting of insulin resistance rendering the patient relatively insulin deficient. Some of the key functions of insulin occur in the muscle (increasing glucose transport into the cells), liver (inhibiting glucose release and promoting glycogen storage), and adipose tissue (forming triglycerides and inhibiting lipolysis). In insulin resistance, insulin is less effective at producing these results, and more insulin must be produced to maintain normal glucose levels. Insulin resistance is increased in states of inflammation, in excess nutrition, and from glucocorticoids to name a few causes [6]. When insulin secretion cannot keep up with insulin needs, type 2 diabetes will result. A myriad of factors including age-related beta cell decline [7], decreased insulin secretion [8], increased adiposity, and changes in physical activity [9] contribute to the pathogenesis of type 2 diabetes. For most patients with type 2 diabetes, in contrast to type 1 diabetes, non-insulin agents may be used initially, and over time insulin replacement may or may not be required. It should be noted that there are many other atypical forms of diabetes such as monogenic diabetes syndromes, maturity-onset diabetes of the young (MODY), cystic fibrosis-related diabetes (CFRD), pancreatic diabetes due to pancreatitis or surgery, and new-onset diabetes after organ transplant (NODAT) [10]. Treatment strategies should be matched to the underlying etiology.

Older adults are at increased risk for both diabetes and prediabetes, and the American Diabetes Association (ADA) recommends all adults age 45 years or older be screened every 1–3 years and at younger ages with other risk factors for dysglycemia [10]. Diabetes mellitus may be diagnosed based on plasma glucose levels (fasting, 2-h postprandial following 75 g oral glucose tolerance test (OGTT)) or hemoglobin A1c (A1c). In the setting of symptomatic hyperglycemia or

Table 1 Diagnostic categories for hyperglycemic disorders

Diagnostic criteria for diabetes mellitus
FPG≥126 mg/dL (7.0 mmol/L)
2 h post prandial glucose ≥ 200 mg/dL dining OGTT
A1c ≥ 6.5% (48 mmol/mol)
Random PG ≥ 200 mg/dL, symptoms of hyperglycemia or hyperglycemic crisis
Diagnostic criteria for pre-diabetes
FPG 100–125 mg/dL "impaired fasting glucose" (IFG)
2 h post prandial glucose 140–199 mg/dL during OGTT "impaired glucose tolerance" (IGT)
A1c 5.7–6.4%

Modified from American Diabetes Association [10]
A1c hemoglobin A1c, *FPG* fasting plasma glucose as defined as no caloric intake for minimum 8 h, *PG* plasma glucose, *OGTT* oral glucose tolerance test (following 75 g anhydrous glucose dissolved in water)

hyperglycemic crisis, the diagnosis of diabetes mellitus is clear. In all other cases, a confirmatory test should be done to formally establish a diagnosis of diabetes (see Table 1).

The same biochemical testing used to screen for diabetes may be used to detect prediabetes, impaired fasting glucose (IFG), or impaired glucose tolerance (IGT). See Table 1 for criteria for these categories [10–12]. Identifying patients with prediabetes is important because progression to diabetes can be prevented [13], and when these patients have other acute illnesses, glucose tolerance can quickly deteriorate leading to hyperglycemia.

It is important to note that A1c results should be interpreted in the setting of other factors that may affect the glycation of hemoglobin such as hemoglobinopathies, anemia, hemodialysis, recent transfusions, medications (erythropoietin), and splenectomy. One may consider using fructosamine and 1,5-anhydroglucitol (1,5-AG) to assess glycemic control.

Acute and Chronic Complications

Type 1 and type 2 diabetes are associated with higher mortality at all ages, and deaths are largely due to cardiovascular disease complications. In a large Canadian study, mortality was 70% higher in patients with diabetes age 65–74 compared to nondiabetic peers [14]. It has been estimated that men with type 2 diabetes will lose nearly 12 years of life and women lose 14 years [15] from complications of diabetes. Importantly, recent efforts at better control of glucose, blood pressure, and lipids have led to a decrease in complication rates and improved mortality [16, 17] giving cause for optimism.

Acute Complications

Acute complications of diabetes include hypoglycemic and hyperglycemic emergencies. Hypoglycemia occurs when glucose levels are below 70 mg/dL and severe hypoglycemia when glucose is below 40 mg/dL [18]. Severe hypoglycemia can lead to arrhythmias, seizures, coma, and death. In the hospital, any hypoglycemia is associated with higher mortality [19]. For patients on insulin with hypoglycemia in the hospital, mortality was four times greater than patients on insulin who did not have hypoglycemia. Lower BMI, renal dysfunction, hepatic dysfunction, and cognitive decline put patients at higher risk for hypoglycemia. Patients at particular risk are those with unpredictable eating patterns especially in the hospital or skilled nursing facility. Patients with recurrent episodes of hypoglycemia will often lose symptoms of hypoglycemia, a phenomenon called hypoglycemia unawareness [20]. This can only be treated with vigorous avoidance of hypoglycemia. Many of the newer medications for type 2 diabetes do not lead to hypoglycemia which can have significant benefit for older patients.

Hyperglycemic crises include diabetic ketoacidosis (DKA), hyperglycemic hyperosmolar syndrome (HHS), and the overlap syndrome that has been called hyperosmolar ketoacidosis (HK). These syndromes are characterized by hyperglycemia, dehydration, and severe electrolyte depletion. Their natural histories and associated mortality risk vary. DKA has the lowest mortality, reported now to be <5% across institutions in the United States and <1% in several reported institutions. HHS, however, is associated with mortality over 15% in several studies, and the concomitant presence of

Table 2 Classification of hyperglycemic crisis

	Mild DKA	Moderate DKA	Severe DKA	HHS
Blood glucose (mg/dL)	>250	>250	>250	>600
PH	<7.30	7.12–7.24	<7.15	>7.30
HCO3	15–18	10 to<15	<10	>18
Urine/serum ketones	+	+	+	+/−
Serum Osm (Osm_{eff})				> 320
AG	>10	>12	>12	Variable
Mental status	Alert	Alert/Drowsy	Stupor/Coma	Stupor/Coma

Serum effective osm (Osm_{eff})=2[Na] + Glucose/18
AG anion gap, *Osm* osmolality

ketoacidosis yields mortality rates as high as 30% for HK. Precipitants for hyperglycemic crises include noncompliance with medication, introduction of a new medication such as glucocorticoids, or development of an intercurrent illness such as infection or myocardial infarction. Diagnostic criteria for hyperglycemic crises [21] are listed below (see Table 2).

Prompt recognition and aggressive treatment are necessary for good outcomes in the older population. Primary treatment requires insulin, fluids, and electrolyte replacement and should be done in the hospital in a setting based on severity and usual hospital practice. Algorithms for management of hyperglycemic crisis are available [21], and a simplified outline is shown here (Fig. 1).

Chronic Complications

Landmark studies such as the United Kingdom Prospective Diabetes Study (UKPDS) looking at type 2 diabetes [22] and the Diabetes Control and Complications Trial (DCCT) looking at type 1 diabetes [23] demonstrated the direct relationship of hyperglycemia to microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular (cardiovascular, cerebrovascular, and peripheral vascular disease) diabetes complications. We are now starting to understand the pathophysiology of complications. One recently recognized pathway is the irreversible glycation of proteins which then form cross-linked macroprotein derivatives known as AGEs (advanced glycation end products). AGEs bind to their receptor RAGE (receptor for AGE) and damage endothelium, nerve tissue, glomerular podocytes, and many of the other tissues we commonly consider to be impacted by diabetes [24]. Our understanding of the mechanisms of glucose-induced tissue damage may lead to targeted treatments in the future. However, we also know the central importance of hypertension and hyperlipidemia to development of complications.

Diabetes is the leading cause of blindness and end-stage renal disease (ESRD) in the United States and a major contributor to amputation. The main risk factors for the development of microvascular complications include duration of diabetes as well as glucose control. The figure below shows the direct impact of A1c on complication rates in type 1 diabetes [25, 25] (see Fig. 2). For each 1% drop in A1c that a patient can achieve, risk for retinopathy decreases by 45%! In type 2 diabetes, each 1% drop in A1c reduces risk of microvascular complications by 37% [26]. Newly recognized diabetic complications include soft tissue damage (diabetic cheiropathy, tendon contractures, and adhesive capsulitis) [27] and diabetic bone disease which can lead to increased fractures and Charcot foot deformity.

Patients with diabetes also have two to four times the rate of macrovascular complications compared to controls [28, 29]. Long-term follow-up studies of UKPDS and DCCT have shown that improved glucose control improves cardiovascular outcomes [30, 31]. Every 1% drop in A1c results in a 14% risk reduction for myocardial infarction. In both the DCCT and the UKPDS trials, intensive treatment was only maintained for 6–10 years during the active trial, and then A1c levels converged to remain at

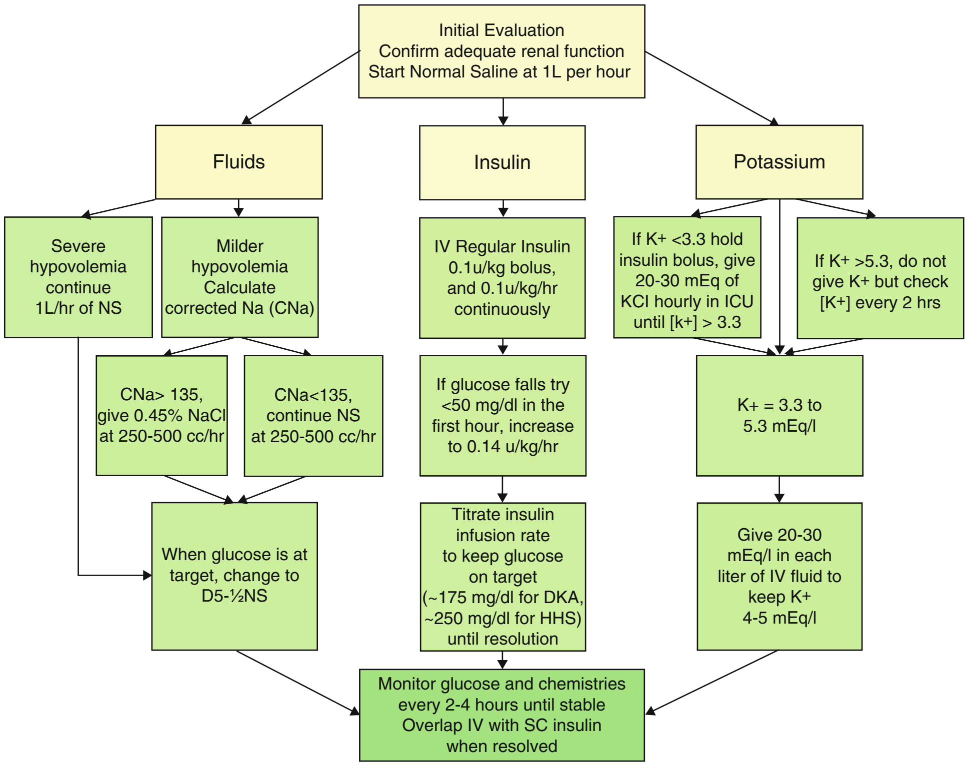
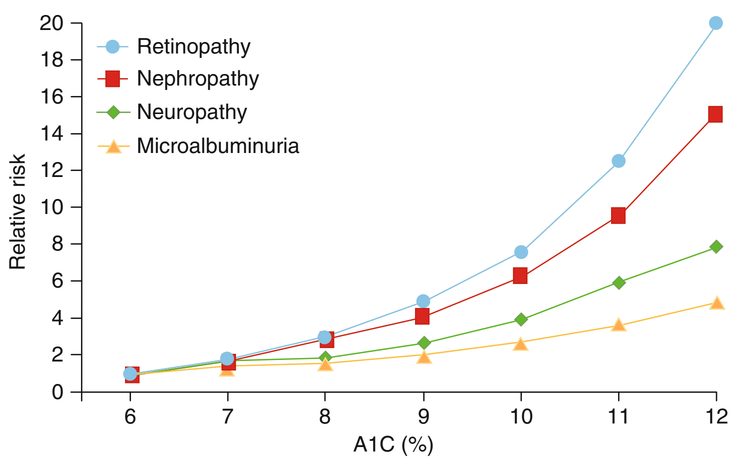


Fig. 1 Schemata for the management of diabetic ketoacidosis (Used with permission [21])

Fig. 2 DCCT A1C levels and the risk of complications in type 1 diabetes [23]



approximately 7.5–8% for up to an additional 20 years. Yet risk reduction for microvascular and macrovascular disease has remained at 25–50% and 13–40% [30, 31]. This phenomenon of lifelong benefit from good glucose control early on in diabetes is now termed "metabolic memory" and has helped change practice.

Some of the newer agents for diabetes such as the SGLT-2 inhibitor empagliflozin and the GLP-1 receptor agonist liraglutide may also lower cardiovascular risk through mechanisms beyond glucose control [33, 34] since benefits can be seen within months of initiating therapy. Cardiovascular event risk reduction in the range of 13–38% has been reported.

Treatment approaches beyond glucose control have also demonstrated improvement in diabetic complications. Blood pressure control can lower microvascular complication rate by up to 37% [32] and macrovascular risk by up to 50%. ACE-Is, and ARBs have had particular success in preventing progression of nephropathy [35, 36]. Lower blood pressure control is not always better as the ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial showed. This was a large randomized study looking at cardiovascular outcomes in type 2 diabetes patients at high risk for cardiovascular disease. The trial looked at achieving systolic blood pressure below 120 mmHg versus 140 mmHg and found no overall benefit though there was lower stroke rate with the more intense BP control [37]. Lowering LDL cholesterol levels with statin therapy has been very effective at primary prevention of macrovascular complications [38]. Statin therapy is now recommended for all patients with diabetes over age 40 [39] unless contraindicated. Moderate- or high-intensity statin therapy (equivalent to 40–80 mg of atorvastatin) is considered beneficial for patients with diabetes over the age of 75 with higher dose for those with known cardiovascular disease.

Diabetes doubles the risk for cognitive impairment and dementia, adversely affecting quality of life [40]. This is multifactorial and includes a 100–150% higher rate of vascular dementia and a 45–90% higher rate of Alzheimer's disease. Hypertension and hyperlipidemia as well as hyperglycemia play a role. More rapid cognitive decline is associated with higher A1c and longer duration of diabetes. There is a strong correlation between microvascular complications and cognitive impairment [41]. However, intensive control of diabetes was not shown to improve cognitive outcomes in older patients with type 2 diabetes [42]. Intensive control may even be hazardous in older patients because episodes of severe hypoglycemia may double the risk of dementia. The relationship is complex since patients with dementia also have higher rates of hypoglycemia [43, 44]. Depression is also an independent contributing factor to dementia in patients with type 2 diabetes [45].

Goals of Treatment in Older Adults

While several studies have demonstrated the importance of achieving and maintaining glycemic control, it is noteworthy to mention that many of the larger trials were not designed for patients age 75 or over and there is limited evidence in this patient population. Based on the available data, attempts to achieve near-normal glycemic control have not always been favorable in older adults. The glucose arm of the ACCORD study which looked at achieving A1c levels below 6.0% versus below 8.0% was terminated early as intensive glycemic control was associated with increase in death and higher rates of hypoglycemia in older adults [37]. It is because of this that the ADA position statement suggests patients with "longer duration of diabetes, known history of hypoglycemia, advanced atherosclerosis, and advanced age / frailty" may not benefit from intense or "tight" glycemic control [46]. As older adults with diabetes often have other medical comorbidities and substantial variability in their overall health status, goals of diabetes treatment should be individualized with emphasis on preventing significant hyperglycemia and clinically relevant hypoglycemia. There are several challenges in this patient population including irregular nutrition, decline in renal function, cognitive and functional impairment, polypharmacy, and costs of medication, all of which can contribute to barriers in care of older adults with diabetes. It is equally important to consider caregivers in treatment plans, and regimens are often designed with this in mind.

Blaum et al. sought to develop a framework to assist with determining appropriate diabetes treatment strategies for older adults [47]. In this study, they defined three health status groups: relatively healthy, patients who may have difficulty with diabetes self-management, and a limited benefit group due to coexisting conditions. The relatively healthy group had fewer than three chronic illnesses and no significant cognitive or visual impairment and was fairly independent with activities of daily living (ADLs). The second group was comprised of patients with one or more of the following: three or more chronic illnesses in addition to diabetes, mild cognitive impairment, severe vision impairment, and two or more dependent ADLs. The third group, limited benefit group, represented those patients with the poorest overall health status with moderate to severe cognitive impairment, two or more dependent ADLs, and/or residence in a long-term care facility. In this study, a large proportion of older adults had clinically complex comorbidities and a spectrum of health status which can make self-management of diabetes challenging. It was estimated that approximately 22% of patients over age 51 with diabetes have health challenges that could make self-care of diabetes difficult. Therefore, careful considerations in determining individualized glycemic targets are needed [47]. It is now widely accepted that less stringent A1c goals may be appropriate in some patient populations especially older adults at risk for hypoglycemia and limited life expectancy with multiple comorbidities. Below is a graphical depiction considering these factors to assist with determining glycemic targets [48] (Fig. 3).

Tools of Glucose Management

As noted above, treatment goals for diabetes should always be individualized but especially so in the older adult. For patients who are frail, have heart disease or dementia or hypoglycemia unawareness, and are at high risk of hypoglycemia and its deleterious consequences, higher glucose levels may be appropriate, and the goal of using "hypoglycemia-free" medications may be indicated.

Likewise, patients with shortened life expectancy may not benefit from risk reduction for chronic complications, and treatment goals may be limited to preventing symptoms of hyperglycemia and hypoglycemia. On the other hand, many older adults are quite vigorous, and there is no reason to modify goals from those of younger patients (Table 3).

Treatment of hyperglycemia in type 2 diabetes should start with medical nutrition therapy and lifestyle intervention. For obese or overweight patients, weight loss in the range of just 5–10% can markedly improve glucose control [49] especially when combined with increased activity. Recent data on best macronutrient mix for weight loss has not been consistent with an earlier trial showing no greater success with low-carbohydrate versus low-fat diets [50] and a more recent trial showing better outcomes with low-carbohydrate diets [51]. Even when weight loss is not a goal,

Fig. 3 Considerations for treatment in older adults with diabetes

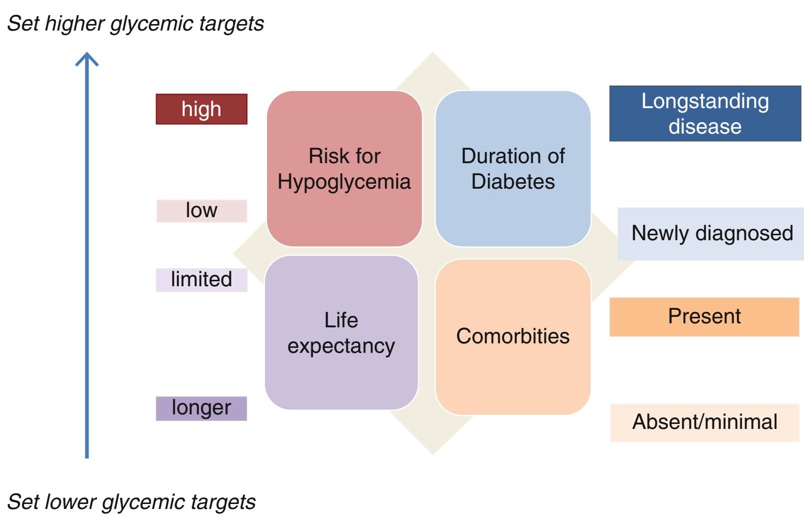


Table 3 Recommendations for glucose, blood pressure, and lipids in older adults with diabetes

Health status	A1c goal	Pre-meal glucose target (mg/dL)	Bedtime glucose (mg/dL)	BP target (mmHg)	Statin use
Healthy	< 7.5%	90–130	90–150	<140/90	Yes if tolerated
Intermediate: multiple co-existing illnesses, moderate cognitive dysfunction	< 8.0%	90–150	100–180	<140/90	Yes if tolerated
Poor: end-stage co-morbidities, severe cognitive decline	< 8.5%	100–180	110–200	<150/90	Only if benefit can be expected

Modified from Diabetes Care 2017:40(supp 1):s99–104

adherence to diet modification is important. Diet recommendations can be compatible with patient preference and culturally sensitive but should include suggestions for monounsaturated fats over saturated fats, whole grain, high-fiber foods over refined grains, and avoidance of sugar-sweetened beverages. For patients on prandial insulin, insulin doses and carbohydrate content need to be coordinated [52].

For most patients with type 2 diabetes, however, diet and exercise alone are not sufficient for glucose management. There are many classes of drugs available now for treatment, and choosing which one or which combination is appropriate for each patient can be confusing. The main considerations in choosing a drug are efficacy at lowering glucose, risk for hypoglycemia, cost, side effects, contraindications, and whether the drug is oral or injectable. The main mechanisms of action (MOA) are increasing insulin release, improving insulin action, increasing glucose excretion, blocking glucose absorption, or replacing insulin. Table 4 lists non-insulin-based medications and MOA. Many new drugs are being developed, and many existing ones are available in fixed dose combinations which are not included here.

Insulin-sensitizing agents improve insulin action but do not work in the absence of insulin. Biguanides are insulin sensitizers and have been used for many years. Currently the only available member of this class is metformin. The exact mechanism of action of metformin is not well established, but its primary effect is to lower liver production of glucose. Some newer studies implicate an effect on the intestine as well. Metformin has enjoyed a wide acceptance as first-line therapy for type 2 diabetes. It is oral, comes in once-a-day formulations, is low cost, and, because it is a sensitizer, it does not cause hypoglycemia. It has been associated with improved cardiovascular outcomes. Common side effects include nausea and diarrhea. Because a previously available drug in this class, phenformin, had been associated with lactic acidosis, the FDA has been quite cautious in the use of metformin in renal insufficiency. But there is good evidence that metformin can be safely used even with eGFR down to 30–45 ml/min/1.73m^2 with some dose modifications [53]. Age should not be a reason to avoid use of metformin.

Thiazolidinediones are another class of drugs that work by improving insulin action. The primary effect is improved postprandial glucose levels due to increased glucose uptake by muscle and adipose tissue. These drugs are PPARγ (peroxisome proliferator-activated receptor gamma) nuclear activators. They promote adipose tissue differentiation and production of the hormone adiponectin which improves insulin signaling. The two available drugs in this class include pioglitazone and rosiglitazone. Rosiglitazone has been implicated in worse cardiovascular outcomes which has decreased its use. These drugs are oral, available as generics, and do not cause hypoglycemia. They also lower hepatic fat content. But they cause weight gain, fluid retention, increase heart failure rates, and increase fracture risk. In general they are not recommended for use in most older patients.

Sulfonylurea agents have been available for longer than the other classes of non-insulin-based drugs. They work by binding to the SUR

Table 4 Treatments for diabetes

Drug class	Generic name	Mechanism of action
Insulin sensitizers:		
Biguanide	Metformin	Lowers hepatic glucose output, may also work through gut
Thiazolidenedione	Pioglitazone Rosiglitazone	Increase glucose uptake in muscle and fat cells, decreases hepatic steatosis
Insulin secretogogues:		
Sulfonylurea agent	Glimepiride Glipizide Glyburide	Increase insulin secretion independent of glucose level(high hypoglycemia risk)
Meglitinide	Repaglinide Nateglinide	Increase insulin secretion with some glucose dependence(less hypoglycemia risk)
Incretin agents: DPP4 inhibitors	Sitagliptin Linagliptin Vildagliptin Saxagliptin Alogliptin	Prolong naturally produced GLP-1 increasing insulin and decreasing glucagon in a glucose dependent manner
Incretin based agents: GLP-1RA	Liraglutide Dulaglutide Exenatide Lixisenatide Albiglutide	Long-acting agonist for GLP-1 receptor, increase insulin secretion, decrease glucagon secretion, decrease appetite, prolong gastric emptying, glucose level dependent
Glycosuric agents:		
SGLT-2 inhibitor	Empagliflozin Canagliflozain Dapagliflozin	Decrease glucose reabsorption in the kidney
Lesser used agents:		
α-glucosidase inhibitor	Acarbose Miglitol	Decrease glucose uptake in the gut
Dopamine agonist	Bromocriptine	Modulates hypothalamic control of metabolism
Bile acid sequestrant	Colesevelam	Binds bile acid
Amylin analog	Pramlintide	Approved for use in type 1 DM, decreases glucagon and gastric emptying

receptor on the ATP-dependent K channel in the beta cell which leads to insulin secretion. This effect happens regardless of glucose levels, so it is important to note the risk of hypoglycemia. Three drugs in this class ("second-generation" sulfonylureas) are primarily in use: glyburide, glimepiride, and glipizide. They are all available as generics and are oral. Glyburide has been associated with the highest rates of hypoglycemia and should not be used in older adults [54]. Mitiglinides, repaglinide, and nateglinide also bind to the ATP-dependent K channel in the beta cell. They have a short duration of action and do not contain sulfur which may be helpful in some cases of allergy. Repaglinide can cause hypoglycemia, but it is rare with nateglinide.

The incretin system has recently become a target of drug development. When food enters the gut, it triggers the release of the incretin hormones, GIP and GLP-1. These hormones "prime" the beta cells to secrete more insulin in response to rising glucose levels. They also suppress glucagon, slow gastric emptying, and decrease appetite, all designed to limit postprandial glucose rise. In type 2 diabetes, GLP-1 is deficient. Two strategies are available to increase GLP-1 effect. Degradation of GLP-1 can be limited by inhibiting DPP-4, the enzyme that breaks down GLP-1. This class of drugs is known as DPP-4 inhibitors. The other strategy is to develop agonists that bind to the GLP-1 receptor but are resistant to DPP-4, the GLP-1 RA class of drugs.

There are currently several available DPP-4 inhibitors. They are oral and with glucose-dependent reduction have less risk for hypoglycemia. They are well tolerated and can be used in renal insufficiency and even ESRD (some require dose modification). Their efficacy at lowering A1c is limited, averaging 0.5–0.8%, and they are not available as generics at this time. Most cardiovascular outcome studies of DPP-4 inhibitors have been neutral [55]. They have a favorable side-effect profile. Pancreatitis may be increased, but overall risk is quite low. A recent meta-analysis found rates of 0.28% versus 0.15% with placebo [56]. They are an excellent choice for frail elders who do not require significant lowering of A1c.

GLP-1 RA therapy is becoming widely used. A1c lowering can equal or exceed 1%. Weight loss of 4–5 kg is also a significant benefit. All drugs in this class are currently available as injectables only, but several are available as weekly preparations. There are no generics and cost can be substantial. Side effects include nausea and nodules at the site of injections. Use is contraindicated in patients with gastroparesis or in patients with high risk of medullary thyroid cancer (due to animal studies that have not been replicated in humans). Two recent cardiovascular outcome studies have shown modest benefit [34, 57]. As with the DPP-4 inhibitors, pancreatitis risk may be increased but is still at a low rate.

The newest class of drugs is the SGLT-2 inhibitor class. These drugs inhibit glucose and sodium uptake in the proximal renal tubule causing a glucose and sodium diuresis. A1c lowering is in the range of 0.7% on average. They are oral and are associated with modest weight loss. Side effects include genitourinary infections, dehydration leading to worsening renal function, increased rate of DKA (sometimes with lower glucose values or "euglycemic" DKA), and possible increase in fracture risk. In a recent large trial of empagliflozin, cardiovascular outcomes including mortality were improved by over 30%, and empagliflozin recently became the first glucose-lowering agent to receive FDA approval for lowering cardiovascular risk [33]. Interestingly, renal outcomes were also better [58].

Other available classes used less frequently because of cost, lack of efficacy, or side effects. α-Glucosidase inhibitors, acarbose and miglitol, are oral and work by inhibiting intestinal glucose absorption. Because glucose is delivered to the colon, side effects such as gas, bloating, and diarrhea are frequent, limiting patient acceptance. The dopamine agonist bromocriptine is available in a rapid release formulation for type 2 diabetes. It has a novel mechanism, working centrally to perhaps reset the sympathetic nervous system. It is expensive and lowers A1c on average less than 0.5%, but there has been one cardiovascular outcome study that showed benefit [59]. Colesevelam is a bile acid sequestrant that is generally used to lower cholesterol but in combination with metformin can lower A1c by 0.6%. Constipation and flatulence are limiting side effects. Finally pramlintide is an injectable analog of the naturally occurring peptide amylin. Amylin is co-secreted with insulin and slows gastric emptying as well as suppresses glucagon. It must be given with each meal and causes significant nausea limiting its use. It is the only non-insulin-based drug approved for use with type 1 diabetes.

Insulin use should not be avoided in older patients with diabetes. Insulin must be used for patients with absolute insulin deficiency such as type 1 diabetes and pancreatic-based diabetes from cystic fibrosis, recurrent pancreatitis, or pancreatectomy. In type 2 diabetes, insulin should be used regardless of age when combinations of non-insulin-based medications do not reach glycemic targets. Insulin dosing complexity requires that the patient and/or caretaker fully understands how to administer insulin and how to recognize when adjustments are indicated. Ability to monitor glucose values by using point-of-care glucose testing is crucial for the safe use of insulin.

There are many different types of insulin currently available, and many more are being developed [60]. Pharmacokinetics including onset of action, time-to-peak action, and duration of action are the main differences between insulins. Insulin is naturally secreted in two patterns, continuously in low doses to suppress hepatic glucose output (basal) and in short bursts to cover postprandial glucose spikes (bolus). The goal of treatment is to mimic these normal physiologic patterns. Insulin can structurally be identical to natural human insulin or can have various amino acids or other

Table 5 Summary of insulin pharmacokinetics

Category	Name	Human or analog	Onset of action	Peak action	Duration of action
Rapid acting	Lispro U-100	A	10–15 min	1 h	4 h
	Lispro U-200	A			
	Aspart U-100	A			
	Glulisine U-100	A			
Fast acting	Regular U-100	H	15–30 min	2 h	6 h
Intermediate	NPH U-100	H	1 h	5–6 h	10–12 h
	Regular U-500	H	1 h	4 h	6–8 h
Long acting	Detemir	A	90 min	Minimal peak effect	20 h
	Glargine	A	90 min	No peak	24 h
	Glargine U-300	A	90 min	No peak	30 h
	Degludec U-100	A	90 min	No peak	42 h
	Degludec U-200	A			
"Pre-mixed"	Human 70/30	H	15–30 min	2–3 h	8–10 h
	Aspart 70/30	A			
	Lispro 75/25	A			

substitutions and additions (termed analog insulin). Adding protamine to insulin was the earliest way to prolong action, and the insulin can be completely protaminated (NPH) or partially so (premixed). Insulin can also vary by concentration. Most standard concentrations are U-100 (100 units/cc), but U-200, U-300, and U-500 concentrations are available. Table 5 lists current insulins.

In type 1 diabetes, basal and bolus insulin must be combined, or the patient can use rapid-acting insulin continuously infused by a pump. In type 2 diabetes, most patients started on insulin begin with basal once a day or premixed twice a day, and bolus insulin is added as needed [61]. Insulin can be used in combination with most oral agents, but combinations must make "sense." An algorithm for combining all available agents is shown below [48] (see Fig. 4).

With appropriate use of the many available glucose-lowering agents, most older patients can reach glucose targets safely.

Management of Glucose in the Hospital

The current definition of hyperglycemia in the hospital is any glucose over 140 mg/dL [18]. Hyperglycemia is a very common problem in the hospital with 26% of patients admitted having known diabetes and another 12% with hyperglycemia from undiagnosed diabetes or acute physiologic stress [62]. In the ICU, up to 70% of all patients develop hyperglycemia. Stress hyperglycemia is a transient hyperglycemia in patients without diabetes which resolves after the illness resolves. Recent ADA recommendations for defining clinically significant hypoglycemia in the hospital is a BG <54 mg/dL and severe hypoglycemia is a glucose associated with cognitive changes [10]. However, previously, hypoglycemia had been defined as any glucose below 70 mg/dL, and severe hypoglycemia is a glucose below 40 mg/dL.

Patients with diabetes have long been recognized to have worse outcomes than nondiabetic peers. During surgery, in particular, patients with diabetes have higher rates of MI, renal failure, and postoperative infections [63]. This may be due in part to comorbidities of vascular disease and kidney disease, but hyperglycemia itself has long been felt to contribute. In patients with myocardial infarction and diabetes, sustained hyperglycemia is correlated with an increase in mortality by 25–50%. To demonstrate the importance of stress hyperglycemia on outcomes, in this same study of MI, in patients with stress hyperglycemia, mortality is increased by 200–400% [64]!

The key management question is whether controlling hyperglycemia will improve outcomes, and there have been many trials looking at

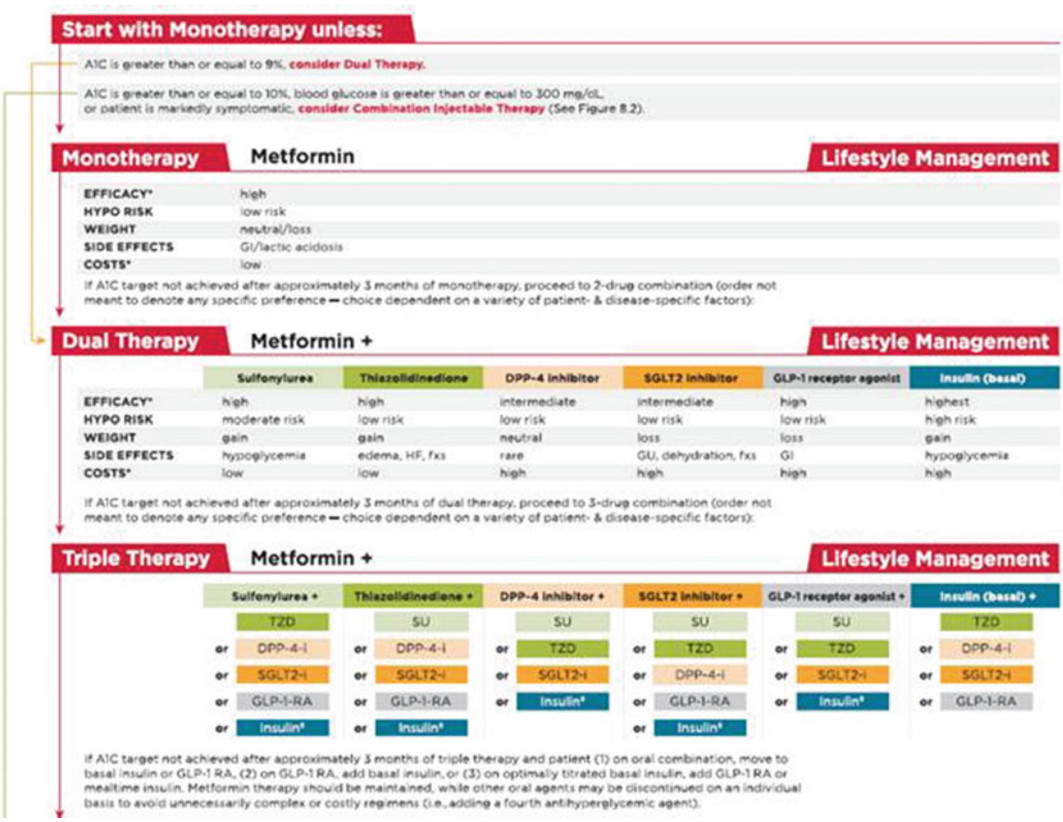


Fig. 4 Treatment algorithm [48]

inpatient outcomes and glucose control. One of the first nonrandomized demonstrations was in cardiac surgery patients. Using IV insulin infusion for 72 h postoperatively in patients with known diabetes, glucose was maintained in well-defined target ranges which were lowered over time, from below 200 mg/dL to 175 mg/dL to 150 mg/dL, and the team was able to reduce sternal wound infection rates and mortality to levels comparable to those without diabetes [65]. In a single center study, Van den Berghe then expanded the concept using IV insulin infusion in the ICU setting for all surgical patients. All patients (not just known diabetes) were randomized to a trial of maintaining glucose in the 80–110 mg/dL range with IV insulin or to conventional treatment of insulin to maintain glucose around 200 mg/dL. She demonstrated improved mortality and other outcomes with this technique [66]. However, when used in a medical ICU setting, there was no benefit for maintaining glucose in this "euglycemic" range, and rates of severe hypoglycemia were six times higher [67]. The definitive randomized, multicenter medical, and ICU trial was NICE-SUGAR (The Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation). Of note, this trial excluded cardiac surgery patients. It tested two glucose target ranges 80–110 mg/dL and 140–180 mg/dL maintained by IV insulin infusion. Surprisingly mortality was better in the group with the higher glucose goals. Severe hypoglycemia occurred less frequently in these patients, and this may have contributed to the mortality differences [68].

Outside of the ICU, there are very few randomized trials of glucose control. The RABBIT-2 surgery trial [69] looked at patients with known diabetes undergoing elective surgery and randomized them to two groups, those managed with short-acting correctional insulin only (sliding scale) and those with scheduled weight-based insulin using long-acting and short-acting insulin (basal bolus). Mean glucose levels were 145 mg/dL in the basal-bolus group and 172 mg/dL in the sliding-scale-only group. Composite outcomes of adverse events including postoperative infections and renal failure were 24% in the sliding-scale group compared to 8.6% ($p < 0.003$) in the basal-bolus group. But the basal-bolus group had higher rates of hypoglycemia with 3.8% having severe hypoglycemia in the basal-bolus group compared to none in the sliding-scale group ($p = 0.057$).

Hypoglycemia has been associated with adverse outcomes in several inpatient studies, and the elderly are especially vulnerable [70]. Hypoglycemia is the major factor limiting management of hyperglycemia in hospitalized patients. Current management recommendations for inpatients are essentially a compromise between risks of hypoglycemia and benefits of treating hyperglycemia.

Glucose goals for treatment are based on results of these and similar studies. For most patients in the ICU, if glucose is greater than 180 mg/dL, an IV insulin infusion protocol should be initiated. Glucose should be maintained in the 140–180 mg/dL range with lower goals of 110–140 mg/dL appropriate for some patients, such as cardiac surgery patients, with the caveat that it can be achieved without hypoglycemia. There are many IV insulin infusion protocols published [71]. They all involve using regular insulin mixed in a standard solution (usually 1 unit/cc) and infused at a rate that is adjusted at least hourly based on current glucose level and rate of change from prior level. There are even commercial computer programs [72] to assist with this. IV insulin drips using the ranges suggested here are quite safe and effective if the nursing staff is familiar with them, but they are quite labor-intensive.

Because the drip rate is dependent on rapid and accurate determination of glucose, providers should understand the limits of the methods used. Arterial glucose values are higher than capillary which are higher than venous values, independent of method used. Glucose testing sent to the lab has long turnaround times and is not practical for adjusting the infusion. Glucose values done with a blood gas analyzer are probably most accurate for "point-of-care" testing but may not be readily available. Glucose meter testing with meters developed for outpatient use may not be accurate in settings of extremes of hematocrit, hypothermia, acetaminophen overdose, and other conditions [73]. The Centers for Medicare and Medicaid Services (CMS) has raised the issue of accuracy of using outpatient meters for ICU patients, but at this time, using them remains the standard of care [74].

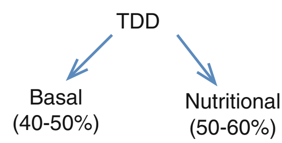
On the general medical floors, the use of oral agents to control glucose is discouraged because of the issues of potential fluctuating renal function (metformin), unpredictable eating, and risk of hypoglycemia (sulfonylureas) and fluid retention (thiazolidinediones), and the use of basal-bolus insulin regimens has become the standard practice. The three components of basal-bolus insulin therapy include the basal dose (a long-acting analog insulin daily or intermediate-acting human insulin twice daily) and the prandial dose (usually a short-acting human or analog insulin) combined with the correctional dose of a short-acting insulin. Analog insulins are preferred in most institutions because of better action profiles, but human regular and NPH can be effectively used [18]. The key to writing safe and effective insulin orders, especially for insulin-naive patients, is the use of order sets [69]. The main determinant of insulin dosing is weight, but elderly patients require lower weight-based dosing than younger ones. Renal insufficiency will also decrease insulin needs, and the use of high-dose glucocorticoids will increase insulin dose. Once initial insulin orders are written, the inpatient team should review and adjust on a daily basis. A guideline for writing insulin orders is in Fig. 5. Usually 50% of the initial calculated daily dose (total daily dose or TDD) is given as basal insulin such as glargine daily or NPH BID. The other 50% of the dose is given in equal amounts before meals usually with a rapid-acting insulin analog such as lispro or aspart. For patients on continuous enteral feedings, giving the prandial dose as regular insulin

Fig. 5 Approach to initiation and titration of insulin

Step 1

Baseline TDD estimate	0.5 unit/kg/day
Age > 70 years	-0.1 unit/kg/day
Renal insufficiency (eGFR < 45)	-0.1 unit/kg/day
Advanced Cirrhosis	-0.1 unit/kg/day
Pancreatic deficiency (chronic pancreatitis, cystic fibrosis,s/p pancreatectomy,)	-0.1 unit/kg/day
HbA1c > 10%	+0.1 unit/kg/day
Currently on glucocorticoids with equivalent of prednisone 40 mg/day or greater	+0.1 unit/kg/day
FINAL TDD estimate	=

Step 2: Components of insulin program
basal, nutritional, correctional



Example: 60 kg patient with TDD estimate 0.5 unit/kg/day
0.5 x 60=30 units TDD with 50% basal and 50% nutritional
30/2=15 units basal and 15 units prandial (5 units AC)

Step 3: Access *frequently* (at least daily) and titrate to goal by 10-20%

Increase by 10% for glucose values 140-180 mg/dL
Increase by 20% for glucose values over 180 mg/dL
Decrease by 10% for glucose values 70-99 mg/dL
Decrease by 20% for glucose values <70 mg/dL

divided into four equal doses every 6 h can be effective. Correctional scales can be ordered based on the calculated total daily dose (TDD). Generally for TDD below 40 units, the correctional scale would be 1 unit for every 50 mg/dL glucose above goal. If the calculated TDD is 40 units, higher correctional scale should be 2 units for every 50 mg/dL glucose increment above goal. Glucose target goals are "fasting" glucose levels below 140 mg/dL and "random" glucose target below 180 mg/dl, and glucose values below 70 mg/dL require adjustment of insulin dosing [75].

Managing glucose at the time of a procedure is difficult and not well studied. In this setting it is very important to identify those patients with absolute insulin deficiency (type 1 diabetes) if at all possible so that they are never without basal insulin, even when NPO. These patients are at risk for rapidly developing DKA if insulin is withheld even for as little as 4–6 h. For patients on oral agents, they are usually told to take them the day before surgery but not the day of surgery. For those on insulin, a simple approach is for patients to take their full dose of basal insulin the evening before unless they are prone to hypoglycemia in which case they can take 80% of their dose. For those patients who take basal insulin in the morning, one approach is to have them take half their dose, especially if patient is using NPH. Patients should not take rapid-acting insulin prior to their procedure. During the procedure and immediately afterward, it is important to check point-of-care glucose at least every 4 h to identify and treat significant hyperglycemia or hypoglycemia. Some patients may require IV insulin during the procedure and immediately postoperatively. After a procedure it is very important to restart basal insulin. If dose determination is unclear, use weight-based insulin order set as described above for assistance.

For patients who use insulin pumps, a discussion should be initiated prior to any elective procedure about whether the patient will continue to use the pump during and after the procedures. Well-informed patients can continue to use pumps during and after a procedure. The patient should follow the advice of their physician, but in general the pump can be used at normal rates until day of procedure. If glucose values are well controlled, pump can be continued at a "basal" rate of about 80% of usual throughout a procedure with anesthesia checking glucose frequently. For procedures lasting longer than 4 h, transitioning to IV insulin infusion can be considered. After the procedure, the patient can resume the use of the pump once recovered from anesthesia unless the patient is too sedated. In the event that a patient is unable to manage postoperatively, the pump should be removed and the patient placed on basal-bolus insulin as above.

Conclusion

Diabetes is a common chronic illness. With increased prevalence of approximately 25% in older adults, special considerations in management are needed. Focus on individualizing treatment will help match therapy to patient needs. Algorithmic approach to inpatient and outpatient dysglycemia can assist in achieving goals and preventing acute and chronic complications.

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14 Cardiac Disease in Older Adults

Wilbert S. Aronow and William H. Frishman

Contents

Abstract
Cardiovascular function in older persons is significantly affected by the aging process itself and by those acquired diseases of the cardiovascular system that are more prevalent with age. Some of the cardiovascular disorders that are more prevalent in older persons include systemic hypertension, left ventricular hypertrophy, left atrial enlargement, an abnormal left ventricular ejection fraction, atrial fibrillation, congestive heart failure (especially with a normal left ventricular

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ejection fraction), coronary artery disease, ischemic and thromboembolic stroke, peripheral arterial disease, extracranial carotid arterial disease, aortic stenosis, aortic regurgitation, mitral regurgitation, mitral annular calcium, hypertrophic cardiomyopathy, and pacemaker rhythm. These physiologic and pathologic changes of the aging cardiovascular system must be taken into consideration during the clinical assessment and management of older patients who need to undergo surgical procedures and general anesthesia.

Keywords
Aging · Cardiovascular function · Hypertension · Atrial fibrillation · Coronary artery disease · Heart failure · Stroke · Peripheral arterial disease · Aortic stenosis · Mitral annular calcium

Introduction

Age-related changes in the cardiovascular system, overt and occult cardiovascular disease, and reduced physical activity affect cardiovascular function in older persons. With aging, there is a loss of myocytes in both the left and right ventricles with a progressive increase in myocyte cell volume per nucleus in both ventricles [1] and an inability to regenerate new myocytes [2]. There is also a progressive reduction in the number of pacemaker cells in the sinus node, with only 10% of the number of cells present at age 20 remaining at age 75 [3]. Wall thickening and dilatation are structural changes that occur within large elastic arteries during aging [4].

Gonzalez et al. have demonstrated in an animal model that chronologic age also leads to telomeric shortening in cardiac progenitor cells [5]. Aging affects the growth and differential potential of cardiac stem cells, interfering not only with their ability to sustain physiologic cell turnover but also with their capacity to adapt to increases in pressure and volume loads [6, 7].

Afterload

Resistance to the ejection of blood by the left ventricle is called afterload. There are two components to afterload: peripheral vascular resistance and characteristic aortic impedance. Peripheral vascular resistance is the steady-state component and provides opposition to steady blood flow. Characteristic aortic impedance is the dynamic component and opposes pulsatile blood flow. Peripheral vascular resistance is measured by dividing the mean arterial pressure by the cardiac output; it is inversely proportional to the cross-sectional area of the peripheral vascular beds. Characteristic aortic impedance is measured as the time variation in mean arterial pressure/flow through the aorta; it is inversely proportional to the arterial compliance (the distensibility of the arterial wall). An indirect measurement of afterload is the pulse wave velocity, which measures the propagation speed of pressure waves traveling from proximal to distal arterial segments; it increases as arteries become less compliant.

With aging, the large elastic arteries become dilated with a reduction in compliance [8]. Progressive thickening of the aortic media and intima is associated with aortic enlargement [9]. There is an age-associated increase in arterial stiffness resulting from changes in the arterial media, such as thickening of the smooth muscle layers, increased fragmentation of elastin, an increase in the amount and characteristics of collagen, and increased calcification [10]. These structural changes are associated with a reduction in aortic distensibility due to increased aortic stiffness with an increase in pulse wave velocity [10]. The structural changes in the arterial wall are independent of coexisting atherosclerosis. Avolio et al. [11] showed an increase in pulse wave velocity with age in farmers from Guangzhou Province in southern China despite a low prevalence of atherosclerosis in this population. The age-associated increase in stiffness and decrease in distensibility of large elastic arteries are not found in distal arteries [12].

The increase in arterial wall thickening and decrease in endothelial function with aging are associated with an increase in arterial stiffness and a decrease in compliance [13]. Age-associated structural changes in the arterial media that increase vascular stiffness include increased collagen content, covalent cross-linking of the collagen, decreased elastin content, elastin fracture, and calcification [14, 15].

Impedance spectral patterns have shown an age-related increase in characteristic aortic impedance and peripheral vascular resistance [16]. The reduction in arterial compliance contributes more to the age-related increase in afterload than does the loss of peripheral vascular beds [16]. Peripheral vascular resistance was not age-related in healthy persons screened for occult coronary artery disease in the Baltimore Longitudinal Study of Aging [17] but increased with age in persons not screened for occult coronary artery disease [18]. Arterial stiffening appearing as an increase in pulse wave velocity is associated with degeneration of the vascular media independent of atherosclerosis. Arterial stiffening causes earlier occurrence of wave reflection from peripheral sites to the ascending aorta during left ventricular ejection. Therefore aortic and carotid phasic pressures increase to a greater magnitude at a later time during left ventricular ejection, causing an increase in systolic and pulse pressures and a delayed peak in the aortic pressure pulse contour.

Circulating levels of catecholamines increase with age, especially with stress, although beta-adrenergic vasodilation of vascular smooth muscle decreases [19]. α-Adrenergic vasoconstriction of vascular smooth muscle does not change with age [20]. The impaired vasodilator response to β-adrenergic stimulation with age is most important during exercise and contributes to the increased afterload associated with aging.

Increased afterload causes an increase in blood pressure. With aging, there is an increase in systolic blood pressure and a widened pulse pressure. A slight decrease in diastolic blood pressure occurs after the sixth decade [21, 22]. The increase in systolic blood pressure is due to interactions of aging, cardiovascular disease, and lifestyle factors, such as dietary sodium intake, body weight, and level of physical activity [22]. An age-associated increase in the index of aortic stiffening was not found in normotensive persons on a low sodium chloride diet [23]. The increase in carotid augmentation index (an index of aortic stiffening) in highly trained older men was half of that expected on the basis of age alone [24]. The prevalence of abnormal aortic stiffness increases steeply in the community with advancing age, especially in the presence of diabetes mellitus and obesity [25].

As aortic compliance decreases with aging, the transfer of kinetic energy from the blood ejected during left ventricular systole to potential energy stored in the elasticity of the aortic wall is decreased. Consequently, return of the potential energy stored in the elasticity of the aortic wall back to the kinetic energy of blood flow during diastole also is decreased. Therefore the left ventricle must eject its stroke volume into a less compliant aorta with greater pressure and force to achieve adequate cardiac output. The increased pulse wave velocity also causes the pressure in the aorta to increase and peak later during systole, contributing to the increased systolic blood pressure and widened pulse pressure.

Posterior left ventricular wall thickness increased with increasing age in normotensive men and women screened for occult coronary artery disease in the Baltimore Longitudinal Study of Aging [26]. Data from persons in this study suggested that the increase in left ventricular wall thickness associated with aging is mediated by an increase in systolic blood pressure [26]. Aging is also associated with an increase in the prevalence of hypertension and cardiovascular disease and, therefore, with the left ventricular hypertrophy seen by echocardiography.

Age-associated left ventricular hypertrophy is caused by an increase in the volume but not in the number of cardiac myocytes. Fibroblasts undergo hyperplasia, and collagen is deposited in the myocardial interstitium. Increased afterload results in an increase in left ventricular systolic stress and the addition of sarcomeres, in parallel, which causes increased left ventricular wall thickness with a normal or reduced left ventricular chamber size and an increased relative wall thickness.

In the Framingham Heart Study, echocardiographic left ventricular hypertrophy was observed in 33% of men and 49% of women older than 70 years [27]. In our older population, echocardiographic left ventricular hypertrophy was found in 226 of 554 men (41%) with a mean age of 80 years and in 539 of 1243 women (43%) with a mean age of 82 years [28].

In our older population, systolic or diastolic hypertension was present in 255 of 664 men (38%) with a mean age of 80 years and in 651 of 1488 women (44%) with a mean age of 82 years [29]. In another study of our older population, systolic or diastolic hypertension occurred in 108 of 215 Blacks (50%) with a mean age of 81 years, in 411 of 1140 Whites (36%) with a mean age of 82 years, and in 19 of 54 Hispanics (35%) with mean age 81 years [30]. Echocardiographically diagnosed left ventricular hypertrophy occurred in 66 of 92 hypertensive Blacks (72%), in 194 of 346 hypertensive Whites (56%), and in 8 of 15 hypertensive Hispanics (53%) [30]. However, it was observed in only 2 of our 88 older persons (2%) without hypertension or overt cardiac disease [31].

Regular aerobic endurance exercise attenuates age-related reductions in central arterial compliance and restores levels in previously sedentary healthy middle-aged and older men [32]. Regular aerobic endurance exercise also can prevent the age-associated loss in endothelium-dependent vasodilation and restore levels in previously sedentary middle-aged and older healthy men [33]. These are mechanisms by which regular aerobic endurance exercise contributes to a decreased risk of cardiovascular disease in older persons [32, 33].

Preload

Preload is the filling volume of the left ventricle. Preload is determined by many factors that influence blood return to the heart and by the mechanical properties of the heart during diastolic filling of the left ventricle.

Resting left ventricular end-diastolic volume, measured by radionuclide ventriculography using multiple gated pool acquisition imaging or by echocardiography, is not age-related in healthy persons, indicating that the resting preload does not change with age [8, 17, 34]. Although resting preload does not change with age, left ventricular early diastolic filling decreases with age.

Passive filling of the left ventricle occurs during the rapid filling and diastasis phases of early diastole. With age, left ventricular stiffness is increased, left ventricular compliance decreased, left ventricular wall thickness increased, left ventricular relaxation impaired, and left ventricular early diastolic filling decreased. This may result in hypotension if preload is reduced. An age-related increase in systolic blood pressure also reduces left ventricular early diastolic filling, leading to hypotension if preload is reduced. Left ventricular filling during early diastole is decreased 50% from age 20 to age 80 [8, 35, 36].

Despite the reduction in early diastolic filling of the left ventricle with age, preload is maintained because left atrial contraction becomes more vigorous to increase late diastolic filling of the left ventricle [8, 34–40]. Augmentation of late diastolic filling of the left ventricle prevents a decrease in left ventricular end-diastolic volume. The ratio of late diastolic Doppler peak transmitral velocity (peak atrial, or A wave, velocity) to early diastolic Doppler peak transmitral velocity (peak rapid filling, or E wave, velocity) increases from approximately 0.6 at 30 years of age to 1.2 at 70 years of age [41]. A reduction in the E/A wave ratio with age reflects a reduction in left ventricular compliance. An age-related increase in left atrial size resulting from increased wall stress due to increased left atrial pressure counteracts the effects of decreased left ventricular compliance with age. In our older population, 619 of 1797 older persons (34%) had echocardiographic left atrial enlargement [28].

Age was the most powerful independent variable for left ventricular filling in healthy persons in the Framingham Heart Study [42]. Age was inversely associated with the E wave (peak early diastolic filling velocity) and was directly associated with the A wave (peak late diastolic filling velocity). Other independent variables that contribute to a lesser degree to left ventricular filling were heart rate, PR interval measured from the electrocardiogram (ECG), gender, left ventricular systolic function, and systolic blood pressure. Increasing the heart rate reduces peak early diastolic filling and increases peak late diastolic filling velocity. The PR interval on the ECG is inversely associated with peak early diastolic filling velocity. Women have slightly higher peak early diastolic filling velocities than men. Left ventricular systolic function is directly associated with peak early diastolic filling velocity. Increasing the systolic blood pressure increases the peak late diastolic filling velocity [42, 43]. Age-associated abnormalities in Doppler measures of myocardial filling and relaxation are only partially minimized by lifelong endurance training [44].

A decrease in preload is not well tolerated in older persons. Reduced intravascular volume, reduced venous return to the heart, vasodilation by drugs or disease states, and the use of drugs such as nitrates or diuretics reduce preload and may cause reduced cardiac output and hypotension in older persons. Decreased compliance of the left ventricle and decreased cardiac and vascular responsiveness to β-adrenergic stimulation [45] cause older persons to be highly dependent on the Frank-Starling mechanism to increase cardiac output. Older persons are more susceptible to developing orthostatic hypotension [46–48]. Impaired baroreceptor reflex sensitivity [49], decreased cardiac responsiveness to β-adrenergic stimulation [45], loss of arterial compliance, decreased venous return due to increased venous distensibility, impaired compensatory mechanisms for maintenance of fluid volume and electrolyte balance, increased incidence of common precipitating diseases and disorders, and the use of multiple drugs contribute to orthostatic hypotension. Older persons are also more susceptible to developing postprandial hypotension [45–48].

Marked reductions in postprandial systolic blood pressure in older persons may predispose them to symptomatic hypotension and to falls, syncope, angina pectoris, and transient cerebral ischemic attacks [50–54]. At 29-month follow-up, a marked decrease in postprandial systolic blood pressure in older persons was associated with an increased incidence of falls, syncope, new coronary events, new stroke, and total mortality [54]. Whether therapeutic interventions to prevent a marked reduction in postprandial systolic blood pressure in older persons can reduce the incidence of falls, syncope, new coronary events, new stroke, and total mortality at long-term follow-up must be investigated.

Because left atrial contraction can contribute up to 50% of left ventricular filling in a poorly compliant left ventricle, the development of atrial fibrillation may result in a marked reduction in cardiac output because of loss of the left atrial contribution to left ventricular late diastolic filling. A rapid ventricular rate associated with atrial fibrillation also reduces the time for diastolic filling of the left ventricle, resulting in a marked decrease in cardiac output.

The incidence of atrial fibrillation also is increased with age [55, 56]. In 2101 older persons in a nursing home, the prevalence of chronic atrial fibrillation was 5% in persons aged 60–70 years, 13–14% in persons aged 71–90 years, and 22% in persons 91 years and older [56]. Atrial fibrillation in older persons is associated with an increased incidence of new thromboembolic stroke [55, 56] and new coronary events [57, 58].

Cardiac output increases during exercise in healthy older persons owing to an increase in venous return to the heart, increasing the diastolic filling of the left ventricle and allowing an increased stroke volume to be ejected during exercise [59]. This is the Frank-Starling mechanism. The maximal heart rate response to exercise decreased with age in healthy persons in the Baltimore Longitudinal Study of Aging [17], whereas exercise stroke volume increased with age to maintain the exercise cardiac output [17]. The increase in exercise stroke volume resulted from an increase in left ventricular end-diastolic volume (preload) via the Frank-Starling mechanism. In contrast, healthy non-older persons achieved an increase in exercise cardiac output primarily by an increase in heart rate. Exercise stroke volume increased in non-elderly healthy persons owing to a slight increase in the left ventricular end-diastolic volume and a large decrease in the left ventricular end-systolic volume. The exercise-induced increase in heart rate and reduction in left ventricular end-systolic volume in nonolder persons are probably mediated by β-adrenergic stimulation. The increase in left ventricular end-diastolic volume during exercise in healthy older persons suggests that the age-associated reduction in resting early diastolic filling of the left ventricle does not persist during exercise.

Contractility

The intrinsic ability of the heart to generate force does not change with age in healthy persons, although the duration of contraction and relaxation is prolonged in senescent animals [60, 61]. Prolongation of the left ventricular ejection time [62] and the preejection period [63] with age in healthy persons indicates that prolongation of contraction occurs with age. Prolongation of the duration of contraction in senescent animals is associated with increased muscle stiffness and prolongation of the action potential duration [64]. These age-related changes are associated with cellular changes in the excitation-contraction coupling mechanism [65] and are an adaptive response to preserve contractile function in response to an age-induced increase in afterload.

There is no reduction in resting left ventricular ejection fraction (LVEF) or circumferential fiber shortening in old persons with no evidence of heart disease [8, 17, 34, 66, 67]. However, systolic function with exercise decreases with age. In the Baltimore Longitudinal Study of Aging, old persons showed less exercise-induced increase in LVEF than did younger persons because of an age-related increase in left ventricular end-systolic volume [17]. However, the absolute values of LVEF at maximal exercise in healthy old persons rarely decrease from basal values [17]. Age-associated reductions in maximal heart rate and left ventricular contractility during maximal exercise are manifestations of decreased β-adrenergic responsiveness, with aging partially offset by exercise-induced dilation of the left ventricle [68].

Diastolic Function

Aging is associated with prolongation of the isovolumic relaxation time, reduced early diastolic filling of the left ventricle, and augmented late diastolic filling of the left ventricle [35, 38, 41]. Normal aging changes that affect the left ventricular diastolic function include increased systolic blood pressure, increased left ventricular wall thickness, decreased left ventricular early diastolic filling, prolonged left ventricular diastolic relaxation, increased left atrial size, and increased left ventricular late diastolic filling [69].

With aging occurs slowing of the rate at which calcium is sequestered by the sarcoplasmic reticulum following myocardial excitation, which causes reduced relaxation of the left ventricle [65, 70, 71]. Accumulation of calcium at the onset of diastole may reduce left ventricular diastolic relaxation and early diastolic filling [70]. Reduced oxidative phosphorylation and cumulative mitochondrial peroxidation occurring with age may also reduce the left ventricular diastolic function [72, 73].

Increased left ventricular stiffness with age due to increased interstitial fibrosis and cross-linking of collagen in the heart impairs left ventricular diastolic relaxation and filling [1, 74–76]. Myocardial ischemia in the absence of coronary artery disease caused by decreases in capillary density and coronary reserve with age may further decrease left ventricular diastolic function in older persons [1, 77].

In addition to a reduction in left ventricular diastolic relaxation and early diastolic filling caused by age, older persons are more likely to have left ventricular diastolic dysfunction because they have an increased prevalence of hypertension, myocardial ischemia due to coronary artery disease, and left ventricular hypertrophy due to hypertension, coronary artery disease, valvular aortic stenosis, hypertrophic cardiomyopathy, and other cardiac disorders. The increased stiffness of the left ventricle and prolonged left ventricular relaxation time decrease left ventricular early diastolic filling and cause higher left ventricular end-diastolic pressures at rest and during exercise in elderly persons [78, 79].

In patients with congestive heart failure (CHF) associated with left ventricular systolic dysfunction, the LVEF is less than 50%. There is a reduced amount of myocardial fiber shortening, the stroke volume is reduced, the left ventricle is dilated, and the patient is symptomatic.

With CHF due to left ventricular diastolic dysfunction with normal left ventricular systolic function, the LVEF is normal. Kitzman et al. [80] demonstrated that during exercise, persons with CHF and normal left ventricular systolic function but abnormal left ventricular diastolic function were unable to increase stroke volume normally, even in the presence of increased left ventricular filling pressure. Myocardial hypertrophy, ischemia, or fibrosis causes slow or incomplete left ventricular filling at normal left atrial pressures. The left atrial pressure increases to augment left ventricular filling, resulting in pulmonary and systemic venous congestion. The development of atrial fibrillation may also cause a reduction in cardiac output and the development of pulmonary and systemic venous congestion because of loss of the left atrial contribution to left ventricular late diastolic filling and decreased diastolic filling time due to a rapid ventricular rate.

In a prospective study of 2535 persons older than 60 years (mean 82 years), CHF developed in 677 (27%) [81]. In a prospective study of 1160 men and 2464 women older than 60 years, mean age 81 years, CHF developed in 29% of older men and in 26% of older women [82]. Older persons are more likely than nonolder persons to develop CHF because of abnormal left ventricular diastolic dysfunction with normal left ventricular systolic function. Table 1 shows that the prevalence of normal LVEF in older persons with CHF ranges from 34% to 52% [81, 83–88]. The prevalence of normal LVEF with CHF is also higher in older women than in older men [81, 83–88].

A normal LVEF was present in older persons with CHF in 44% of 55 African-American men versus 58% of 110 African-American women, in 46% of 24 Hispanic men versus 56% of 34 Hispanic women, in 35% of 148 White men versus 57% of 303 White women, and in 38% of 227 older men versus 57% of 447 older women [88]. Table 2 shows the prevalence of a normal LVEF in 572 older persons with CHF in men and in women of different age groups [81]. In the community, advancing age and female gender are associated with increases in vascular and ventricular systolic and diastolic stiffness even in the absence of cardiovascular disease [89]. This contributes to the increased prevalence of CHF with a normal LVEF in older persons, especially in older women.

LVEF should be measured in all patients with CHF in order that appropriate therapy may be given [90–94]. For example, digoxin should not be used to treat persons with CHF and normal left ventricular ejection fraction if sinus rhythm is present [69, 95–99]. By increasing contractility

Table 1 Prevalence of normal left ventricular ejection fraction in older patients with congestive heart failure

Study	Results for patients with CHF and normal LVEF
Wong [83]	41% of 54 persons, mean age 80 years
Aronow [84]	47% of 247 persons, mean age 82 years
Cardiovascular Health Study [85]	63% of 269 persons, mean age 74 years
Framingham Heart Study [86]	51% of 73 persons, mean age 73 years
Pernenkil [87]	34% of 501 persons, mean age 81 years
Aronow [81]	50% of 572 persons, mean age 82 years
Aronow [88]	51% of 674 persons, mean age 81 years

LVEF, left ventricular ejection fraction; CHF, congestive heart failure

Table 2 Association of congestive heart failure with normal left ventricular ejection fraction with gender and age in 572 older patients

Age (years)	Normal left ventricular ejection fraction
60–69	22% of 18 men and 37% of 38 women
70–79	33% of 54 men and 44% of 79 women
80–89	41% of 86 men and 59% of 219 women
≥90	47% of 19 men and 73% of 59 women
All ages	37% of 177 men and 56% of 395 women with congestive heart failure

Adapted from Aronow et al. [81]

through increasing intracellular calcium ion concentration, digoxin may increase left ventricular stiffness, increasing left ventricular filling pressure and adversely affecting CHF due to left ventricular diastolic dysfunction. Patients with CHF due to abnormal LVEF tolerate higher doses of diuretics than do patients with CHF and normal LVEF. Patients with CHF due to left ventricular diastolic dysfunction and normal LVEF need high left ventricular filling pressures to maintain an adequate stroke volume and cardiac output and cannot tolerate intravascular depletion. These patients should be treated with a low-salt diet with cautious use of diuretics rather than with large doses of diuretics. Patients with abnormal LVEF should not be treated with calcium channel blockers [100, 101].

Table 3 Cardiovascular responses to exercise in healthy older persons

Maximal heart rate is decreased with age
Exercise stroke volume is increased with age to maintain cardiac output
Increased exercise stroke volume with age results primarily from increase in left ventricular end-diastolic volume by Frank-Starling mechanism
Decrease in muscle mass with age plays a role in age-associated decreases in systemic arteriovenous oxygen difference and in VO_2max at peak exercise
Left ventricular end-diastolic and end-systolic volumes are increased during peak exercise with age
Peak exercise left ventricular ejection fraction is reduced with age
Exercise-induced decrease in the left ventricular end-systolic volume index and increases in the cardiac index, stroke volume index, and left ventricular ejection fraction from the rest are greater in older men than in older women

Cardiovascular Response to Exercise

The maximal oxygen consumption (VO_2max) is the best overall measurement of cardiovascular fitness [102]. VO_2max is the product of cardiac output and the systemic arteriovenous oxygen difference at peak exercise. Maximal cardiac output – the heart rate multiplied by the stroke volume at peak exercise – is a more direct measurement of cardiovascular reserve than is VO_2max [102]. VO_2max is decreased with age [103, 104]. The degree of decrease of VO_2max with age is affected by physical conditioning, subclinical coronary artery disease, smoking, and body weight. Table 3 lists the cardiovascular responses to exercise in healthy older persons and clinical implications.

In the Baltimore Longitudinal Study of Aging, older male athletes had a higher peak exercise VO_2max than older sedentary men [105]. The greater peak exercise VO_2max in older male athletes than in older sedentary men was achieved by a higher cardiac index and a greater systemic arteriovenous oxygen difference. The higher peak exercise cardiac index in older male athletes than in older sedentary men was due to a higher stroke volume index with similar maximal heart rates. Long-term endurance training also is associated with enhanced ventricular diastolic filling indices [106]. Older age is associated with a decreased exercise efficiency and an increase in the oxygen cost of exercise, which contributes to a decreased exercise capacity. These age-related changes are reversed with exercise training [107].

A decrease in maximal systemic arteriovenous oxygen difference occurs with age [108]. The decrease in muscle mass with age may play a major role in the reduction in systemic arteriovenous oxygen difference at peak exercise and in VO_2max [109].

Fleg et al. [110] also investigated the effect of age on peak upright cycle exercise in healthy sedentary men and women aged 22–86 years in the Baltimore Longitudinal Study of Aging. Peak cycle work rate was reduced with age in both men and women but was greater in men than in women at any age. Both men and women had peak exercise reductions in heart rate, cardiac index, and LVEF and increases in the left ventricular end-diastolic volume index and end-systolic volume index with age. Peak exercise stroke volume index did not vary with age in men or women. The exercise-induced reduction in left ventricular end-systolic volume index and the increases in cardiac index, stroke volume index, and LVEF from rest were greater in older men than in older women.

Age-Related Changes in Cardiovascular Function

Table 4 lists some age-related changes in cardiovascular function in healthy older persons and clinical implications. Contractility at rest does not change with age, but the duration of left ventricular contraction and relaxation is prolonged. Age-associated decreases in maximal heart rate and in left ventricular contractility during maximal exercise are manifestations of reduced β-adrenergic responsiveness with age partially offset by exercise-induced dilation of the left ventricle.

Decreased arterial compliance contributes more to the age-related increase in afterload than does the loss of peripheral vascular beds. The impaired vasodilator response to β-adrenergic stimulation with age is most important during exercise and contributes to the increased afterload associated with age. Resting preload does not change with age. Left ventricular early diastolic filling is decreased with age. Augmentation of late diastolic filling of the left ventricle prevents a reduction in left ventricular end-diastolic volume with age. The maximal heart rate response to exercise is decreased with age. Exercise stroke volume is increased with age to maintain the exercise cardiac output, resulting from an increase in preload by the Frank-Starling mechanism. VO_2max and the systemic arteriovenous oxygen difference at peak exercise are decreased with age. Aging also selectively impairs endothelium-dependent function [111].

In addition to age-related changes in cardiovascular function and deconditioning due to a sedentary life style, older persons also have a higher prevalence and incidence of cardiovascular disorders that impair cardiovascular performance than do nonolder persons. Older persons are more likely than nonolder persons to develop CHF secondary to abnormal left ventricular diastolic dysfunction with normal left ventricular systolic function. There is also an age-related increase in pulmonary artery systolic pressure [112].

Table 4 Some age-related changes in cardiovascular function in healthy elderly persons

Contractility at rest does not change with age
Duration of left ventricular contraction and relaxation is prolonged with age
Decrease in arterial compliance contributes more to age-related changes Increase in afterload than does loss of peripheral vascular beds
Resting preload does not change with age
Left ventricular early diastolic filling is decreased with age
Augmentation of late diastolic filling of the left ventricle prevents a reduction in left ventricular end-diastolic volume with age
Cardiovascular responses to exercise with age are noted in Table 3
Age-associated reductions in maximal heart rate and left ventricular contractility during maximal exercise are manifestations of decreased β-adrenergic responsiveness with age partially offset by exercise-induced dilation of the left ventricle
Aging selectively impairs endothelium-dependent function

Treatment of Congestive Heart Failure

The LVEF should be measured in all persons with CHF in order for appropriate therapy to be given [90–94]. For example, digoxin should not be used to treat persons with CHF and normal LVEF if a sinus rhythm is present [69, 95–99]. Large doses of diuretics and nitrates should also be used cautiously in persons with CHF and a normal LVEF [100].

Calcium channel blockers such as diltiazem, nifedipine, and verapamil exacerbate CHF in persons with CHF associated with abnormal LVEF [113]. Diltiazem increased mortality in patients with pulmonary congestion associated with abnormal LVEF after myocardial infarction [114]. The Multicenter Diltiazem Postinfarction Trial showed, in persons with a LVEF less than 40%, that late CHF at follow-up was increased in patients randomized to diltiazem (21%) versus those randomized to placebo (12%) [115]. Prospective studies have demonstrated that the vasoselective calcium channel blockers amlodipine [116] and felodipine [117] did not significantly affect survival compared with placebo in patients with CHF associated with an abnormal LVEF. There was a significantly higher incidence of pulmonary edema in the persons treated with amlodipine (15%) than in those treated with placebo (10%) [116]. The American College of Cardiology Foundation (ACCF)/American Heart Association (AHA) guidelines recommend that calcium channel blockers should not be given to persons with CHF associated with abnormal LVEF [101].

Abnormal Left Ventricular Ejection Fraction

Table 5 shows the ACCF/AHA class I recommendations for treating patients with current or prior symptoms of CHF with reduced LVEF [101]. Older persons with CHF associated with abnormal LVEF should be treated with a low-sodium diet and with diuretics plus an angiotensin-converting enzyme (ACE) inhibitor [118, 119] plus a beta-blocker such as metoprolol CR/XL [120], carvedilol [121], bisoprolol [122], or nebivolol [123]. An angiotensin receptor blocker should be used if the patient is intolerant to an ACE inhibitor because of cough or angioneurotic edema [124]. Regular physical activity such as walking should be encouraged in patients with mild to moderate HF to improve functional status and to decrease symptoms. Patients with CHF who are dyspneic at rest at a low work level may benefit from a formal cardiac rehabilitation program [125].

An implantable cardioverter-defibrillator (ICD) and cardiac resynchronization therapy (CRT) should be used according to ACC/AHA guidelines [101, 126–130]. Statins should also be used in these patients to reduce appropriate

Table 5 Class I recommendations for treating patients with current or prior symptoms of heart failure with reduced left ventricular ejection fraction

1.Treat underlying and precipitating causes of heart failure
2. Use diuretics and salt restriction in persons with fluid retention
3. Use angiotensin-converting enzyme inhibitors
4. Use beta-blockers
5. Use angiotensin II receptor blockers if intolerant to angiotensin-converting enzyme inhibitors because of cough or angioneurotic edema
6. Sacubitril/valsartan may be used instead of an angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker in patients with chronic symptomatic heart failure and reduced left ventricular ejection fraction class II or III to further reduce morbidity and mortality
7. Avoid or withdraw nonsteroidal anti-inflammatory drugs, most antiarrhythmic drugs, and calcium channel blockers
8. Recommend exercise training
9. Implant cardioverter-defibrillator in persons with a history of cardiac arrest, ventricular fibrillation, or hemodynamically unstable ventricular tachycardia
10. Implant cardioverter-defibrillator in persons with ischemic heart disease $\geq$40 days post-myocardial infarction or nonischemic cardiomyopathy, a left ventricular ejection fraction $\leq$30%, New York Heart Association class II or III symptoms on optimal medical therapy, and an expectation of survival of $\geq$1 year
11. Implant cardioverter-defibrillator in selected patients with heart failure at least 40 days after acute myocardial infarction or nonischemic cardiomyopathy with a LVEF of 30% or less and New York Heart Association class I symptoms on chronic guided directed medical therapy with a reasonable expectation of meaningful survival for more than 1 year
12. Use cardiac resynchronization therapy in persons with a LVEF $\leq$35%; New York Heart Association class II, III, or ambulatory IV symptoms on guided directed medical therapy; sinus rhythm; and left bundle branch block with a QRS duration of 150 msec or greater with or without a cardioverter-defibrillator
13. Add an aldosterone antagonist in selected patients with moderately severe to severe symptoms of heart failure who can be carefully monitored for renal function and potassium concentration (serum creatinine should be $\leq$2.5 mg/dl in men and $\leq$2.0 mg/dl in women; serum potassium should be $<$5.0 mEq/l)
14. Use hydralazine plus nitrates in patients self-described as African Americans with moderate to severe symptoms on optimal therapy with angiotensin-converting enzyme inhibitors, beta-blockers, and diuretics

Adapted from Yancy et al. [101]

cardioverter-defibrillator shocks and mortality [131, 132]. An aldosterone antagonist such as spironolactone [133] or eplerenone [134, 135] should be used according to ACC/AHA guidelines [101]. Isosorbide dinitrate plus hydralazine was very effective in treating Blacks with CHF in the African-American Heart Failure Trial [136, 137] and is now recommended in Blacks with New York Heart Association class II or IV symptoms on optimal medical therapy with a class I indication [136, 137].

ICD therapy has a class I indication in selected patients with CHF at least 40 days after acute myocardial infarction or nonischemic cardiomyopathy with a LVEF of 35% or less and New York Heart Association class II or III symptoms on chronic guided directed medical therapy with a reasonable expectation of meaningful survival for more than 1 year [101, 126]. ICD therapy also has a class I indication in selected patients with HF at least 40 days after acute MI or nonischemic cardiomyopathy with a LV ejection fraction of 30% or less and New York Heart Association class I symptoms on chronic guided directed medical therapy with a reasonable expectation of meaningful survival for more than 1 year [101, 129]. CRT has a class I indication for patients with CHF; a LVEF of 35% or less; class II, III, or ambulatory IV symptoms on guided directed medical therapy; sinus rhythm; and left bundle branch block (LBBB) with a QRS duration of 150 ms or greater [101, 127–130].

Since the 2013 ACC/AHA heart failure guidelines have been published, the PARADIGM-HF (Prospective Comparison of Angiotensin Receptor Neprilysin Inhibitor (ARNI) with Angiotensin-Converting Enzyme Inhibitors (ACEI) to Determine Impact on Global Mortality and Morbidity in Heart Failure) was reported [138]. This study showed that in 8442 patients with class II-IV CHF and a LVEF of $\leq$40% (later amended to $\leq$35%) at 27-month follow-up that compared to enalapril 10 mg daily, patients randomized to receive twice daily dosing of 200 mg of sacubitril (a neprilysin inhibitor) or valsartan in addition to standard medical therapy for CHF had a 20% reduction in death from cardiovascular causes or hospitalization for CHF [138]. Major limitations to this study include the following: (1) sacubitril has not been tested by itself in the treatment of CHF with a reduced LVEF and (2) the maximum recommended dose of valsartan for the treatment of CHF with a reduced LVEF was not used [139].

Table 6 shows the ACC/AHA class IIa recommendations for treating patients with current or prior symptoms of CHF with a reduced LVEF [101]. The serum digoxin level should be maintained between 0.5 and 0.8 ng/ml to avoid an increase in mortality [101, 140, 141]. CRT has a class IIa indication for patients with CHF, a LVEF of 35% or less, class III or ambulatory IV

Table 6 Class IIa recommendations for treating persons with current or prior symptoms of heart failure with decreased left ventricular ejection fraction

1. Angiotensin II receptor blockers may be used instead of angiotensin-converting enzyme inhibitors if patients are already taking them for other reasons
2. Hydralazine plus nitrates may be used if symptoms of heart failure persist despite angiotensin-converting enzyme inhibitors and beta-blockers
3. Implant cardioverter-defibrillator in patients with left ventricular ejection fraction (LVEF) of 30% to 35% of any origin with New York Heart Association class II or III symptoms on optimal medical therapy with a life expectancy of >1 year
4. Digoxin can be used in patients with persistent symptoms to reduce hospitalization for heart failure
5. Cardiac resynchronization therapy (CRT) can be used in patients with heart failure, a LVEF of 35% or less, class III or ambulatory IV symptoms on guided directed medical therapy, sinus rhythm, and a non-left bundle branch block (LBBB) pattern with a QRS duration of 150 ms or greater
6. CRT can be used in patients with heart failure; a LVEF of 35% or less; class II, III, or ambulatory IV symptoms on guided directed medical therapy; sinus rhythm; and a LBBB pattern with a QRS duration of 120 to 149 ms
7. CRT can be used in patients with heart failure, atrial fibrillation, and a LVEF of 35% or less on guided directed medical therapy if (a) the patient needs ventricular pacing or otherwise meets CRT criteria and (b) atrioventricular nodal ablation or pharmacological rate control will allow near 100% ventricular pacing with CRT
8. CRT can be used in patients with heart failure on guided directed medical therapy, a LVEF of 35% or less, and are undergoing placement of a new or replacement device with anticipated need for more than 40% ventricular pacing

Adapted from Yancy et al. [101]

symptoms on guided directed medical therapy, sinus rhythm, and a non-LBBB pattern with a QRS duration of 150 ms or greater [101, 128, 130]. CRT has a class IIa indication for patients with CHF; a LVEF of 35% or less; class II, III, or ambulatory IV symptoms on guided directed medical therapy; sinus rhythm; and a LBBB pattern with a QRS duration of 120 to 149 ms [101, 128–130, 142]. CRT has a class IIa indication in patients with CHF, atrial fibrillation, and a LVEF of 35% or less on guided directed medical therapy if a) the patient needs ventricular pacing or otherwise meets CRT criteria and b) atrioventricular nodal ablation or pharmacological rate control will allow near 100% ventricular pacing with CRT [101, 143]. CRT also has a class IIa indication in patients with CHF on guided directed medical therapy, a LVEF of 35% or less, and are undergoing placement of a new or replacement device with anticipated need for more than 40% ventricular pacing [101, 144].

In experimental studies, the recognition of factors enhancing the activation of the cardiac stem cell pool, their mobilization, and translocation, however, suggests that the detrimental effects of aging on the heart might be prevented in the future by the local stimulation of cardiac stem cells or the intramyocardial delivery of cardiac stem cells following their expansion and rejuvenation in vitro [2, 5, 7]. Cardiac stem cell therapy may possibly become a novel strategy for the devastating problem of CHF in the older population. The use of stem cell therapy in patients with ischemic heart disease is discussed elsewhere [145].

Normal Left Ventricular Ejection Fraction

Table 7 shows the therapy for older persons with CHF associated with a normal LVEF. Beta-blockers [123, 146], ACE inhibitors [147, 148], angiotensin receptor blockers [149], and aldosterone antagonists [150, 151] are efficacious in the treatment of these patients.

In older persons with CHF associated with a normal LVEF, pulmonary congestion is reduced by a low-sodium diet, diuretics, and nitrates.

Table 7 Therapy of patients with heart failure and normal left ventricular ejection fraction

1. Treat underlying and precipitating causes of heart failure
2. Avoid use of inappropriate drugs such as nonsteroidal anti-inflammatory drugs
3. Treat hypertension, especially systolic hypertension, hyperlipidemia, myocardial ischemia, anemia, obesity, and other comorbidities
4. Treat with cautious use of diuretics
5. Treat with beta-blockers
6. Treat with aldosterone antagonists
7. Treat with angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker if patient cannot tolerate ACE inhibitor because of cough, angioneurotic edema, rash, or altered taste sensation
8. Add isosorbide dinitrate plus hydralazine if heart failure persists
9. Avoid digoxin if sinus rhythm is present
10. Exercise training as an adjunctive approach to improve clinical status in ambulatory patients
11. Control ventricular rate in patients with atrial fibrillation

Sinus rhythm is maintained to increase the left ventricular filling time. The ventricular rate is slowed below 90 beats per minute by a β-blocker to increase left ventricular filling time. Myocardial ischemia should be decreased and is best achieved by giving a β-blocker. Elevated systolic blood pressure is decreased by diuretics and an ACE inhibitor. The left ventricular mass is reduced by an ACE inhibitor. Left ventricular relaxation should be improved by ACE inhibitors or β-blockers.

The Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT) trial randomized 3445 older patients with symptomatic CHF and a LVEF of 45% or more to spironolactone 15 mg to 45 mg daily or placebo [150–153]. Of these patients, 1767 patients were enrolled from the Americas, and 1, 678 patients were enrolled from Russia and Georgia. The primary outcome was a composite of death from cardiovascular causes, aborted cardiac arrest, or hospitalization for treatment of CHF. The mean follow-up was 3.3 years. In the Americas group, compared with placebo, spironolactone reduced the primary outcome by 18%, cardiovascular mortality 26%, hospitalization for CHF 18%, recurrent CHF 25%, and all-cause mortality 17%; increased the incidence of doubling of serum creatinine by 60%; increased the incidence of hyperkalemia ($\geq$ 5.5 mmol/L) 3.46 times; and reduced hypokalemia (serum potassium <3.5 mmol/L) by 49% [151]. In the Russia and Georgia group, all of these outcomes were similar for patients treated with spironolactone or placebo [151]. On the basis of these data, we recommend treating patients with CHF with a normal LVEF with an aldosterone antagonist.

Other Cardiovascular Disorders

In addition to age-related changes in cardiovascular function and deconditioning due to a sedentary life style, older persons also have a higher prevalence and incidence of cardiovascular disorders, which impair cardiovascular performance, than non-older persons. Table 8 lists the prevalence of some cardiovascular disorders in an older population in a long-term health-care facility [82, 154, 155].

Aortic Valvular Disease

Valvular aortic stenosis in older persons is usually due to stiffening, scarring, and calcification of aortic valve leaflets. Calcific deposits in the aortic valve are common and may lead to valvular aortic stenosis [28, 156–158]. Calcific deposits in the aortic valve were present in 22 of 40 necropsied patients (55%) aged 90–103 years [157]. Aortic cuspal calcium was present in 295 of 752 men (36%), mean age 80 years, and in 672 of 1,663 women (40%), mean age 82 years [158].

Calcific valvular aortic stenosis was present at autopsy in 18% of 366 octogenarians [159]. Valvular aortic stenosis was diagnosed by continuous-wave Doppler echocardiography in 463 of 2805 older persons (17%) with mean age 81 years [82]. Severe aortic stenosis was present in 2% of these 2805 older persons [82]. Severe aortic stenosis was also diagnosed in 3% of 501 persons aged 75–86 years in the Helsinki Ageing Study [160].

Aortic valve calcium, mitral annular calcium, and coronary artery disease in older persons have

Table 8 Prevalence of cardiovascular disorders in older persons in a long-term health-care facility

	Mean age	Prevalence	
Cardiovascular disorder	(years)	No.	%
Coronary artery disease [82]	81	1521/3624	42
Thromboembolic stroke [82]	81	1131/3624	31
Peripheral arterial disease [82]	81	1011/3624	28
40–100% Extracranial carotid arterial disease [154]	81	281/1846	19
Congestive heart failure [82]	81	978/3624	27
Hypertension [82]	81	2136/3624	59
Aortic stenosis [155]	81	463/2805	17
Mitral annular calcium [155]	81	1321/2805	47
$\geq$1 + Mitral regurgitation [155]	81	928/2805	33
$\geq$1 + Aortic regurgitation [155]	81	824/2805	29
Rheumatic mitral stenosis [155]	81	37/2805	1
Hypertrophic cardiomyopathy [155]	81	108/2805	4
Idiopathic dilated Cardiomyopathy [155]	81	29/2805	1
Atrial fibrillation [82]	81	495/3624	14
Pacemaker rhythm [82]	81	186/3624	5
Abnormal left ventricular ejection Fraction [155]	81	687/2805	24
Left ventricular hypertrophy [155]	81	1224/2805	44
Left atrial enlargement [155]	81	987/2805	35

similar predisposing factors for atherosclerosis [158, 160–166]. Older persons with extracranial carotid arterial disease [161] and with peripheral arterial disease [162] have an increased prevalence of aortic stenosis. Older persons with aortic stenosis [167–169] and with valvular aortic sclerosis [169, 170] have an increased incidence of new coronary events.

Many older persons with symptomatic severe aortic stenosis and comorbidities at high risk for mortality from surgical aortic valve replacement can now undergo transcatheter aortic valve replacement [171–175].

The prevalence of aortic regurgitation also increases with age [28, 176, 177]. Aortic regurgitation was diagnosed by pulsed Doppler recordings of the aortic valve in 526 of 1797 elderly persons (29%) with a mean age of 81 years [82]. Severe or moderate aortic regurgitation was diagnosed by pulsed Doppler recordings of the aortic valve in 74 of 450 elderly persons with a mean age of 82 years [178]. Margonato et al. [176] linked the increased prevalence of aortic regurgitation with age to aortic valve thickening.

Mitral Valvular Disease

Two degenerative aging processes – mitral annular calcification and mucoid (or myxomatous) degeneration of the mitral valve leaflets and chordae tendineae – can cause significant mitral valvular dysfunction [179–181]. Mitral annular calcification was diagnosed by two-dimensional echocardiography in 36% of 924 older men and in 52% of 1881 older women, mean age 81 years [82]. Mitral annular calcium was present in 11 of 57 persons (19%) 62–70 years of age, in 53 of 158 persons (34%) 71–80 years of age, in 190 of 301 persons (63%) 81–90 years of age, in 75 of 85 persons (88%) 91–100 years of age, and in 3 of 3 persons (100%) 101–103 years of age [182].

The breakdown of lipid deposits on the ventricular surface of the posterior mitral leaflet at or below the mitral annulus and on the aortic surfaces of the aortic valve cusps is probably responsible for the calcification [183]. Older men and women with mitral annular calcium have a higher prevalence of coronary artery disease [184–186], of peripheral arterial disease [186, 187], of extracranial carotid arterial disease [186, 188, 189], and of aortic atherosclerotic disease [186] than older men and women without mitral annular calcium.

Conduction Defects

The increased prevalence of conduction defects in older persons is due to age-related degeneration of the conduction system and to the development of cardiovascular disease. Aging is associated with regional conduction slowing, an anatomically determined conduction delay at the crista, and structural changes including areas of low voltage [190]. Impairment of sinus node function and an increase in atrial refractoriness occur with aging, predisposing to atrial fibrillation [190]. Table 9 lists the prevalence of conduction defects in 1153 older persons, mean age 82 years [191]. At a 45-month follow-up, older persons with second-degree atrioventricular block, left bundle branch block, an intraventricular conduction defect, and pacemaker rhythm had an increased incidence of new coronary events [191]. At a 45-month follow-up, elderly persons with first-degree atrioventricular block, left anterior fascicular block, or right bundle branch block did not have an increased incidence of new coronary events [191].

Table 9 Prevalence of conduction defects in 1153 older persons

Defect	Prevalence (%)
First-degree atrioventricular block	6
Left anterior fascicular block	8
Right bundle branch block	10
Left bundle branch block	4
Intraventricular conduction defect	3
Second-degree atrioventricular block	1
Pacemaker rhythm	4

Source: Adapted from Aronow [191]

Conclusions

Cardiovascular function in older persons is significantly affected by the aging process itself and by those acquired diseases of the cardiovascular system that are more prevalent with age. These physiologic and pathologic changes of the aging cardiovascular system must be taken into consideration during the clinical assessment and management of older patients who need to undergo surgical procedures and general anesthesia.

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15 Pulmonary Disease in the Older Adult

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Contents

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Abstract
A substantial proportion of the excess operative risk among elderly patients is attributable to respiratory complications. The excess risk is explained in part by structural and functional changes in the respiratory system associated with aging. These changes are progressive even in individuals who enjoy apparently good health and are most marked beyond 60 years of age.

Physiologic changes with age: pulmonary

Parameter	Change with age	Functional impact of change
Chest shape	↑ AP diameter	No significant impact
	Mild-mod kyphosis	
Conducting airways	Calcification	Insignificant ↑ deadspace
	Mild ↑ size	
	Mucus gland hypertrophy	Minimal significance
Lung parenchyma	Enlarged alveolar ducts	Similar to mild emphysema
	V/Q mismatch	**Decreased reserve**
	↓ Elastic recoil	
Bellows apparatus	↑ Chest wall rigidity	Increased work of breathing
	↓ Respiratory muscle strength	Highly individual
Ventilatory control	↓↓ **Response to hypercapnia and hypoxemia**	Impaired homeostasis under stress Signs of distress subtle

Most important messages in bold
AP anteroposterior, *V/Q* ventilation/perfusion

A substantial proportion of the excess operative risk among elderly patients is attributable to respiratory complications. The excess risk is explained in part by structural and functional changes in the respiratory system associated with aging. These changes are progressive even in individuals who enjoy apparently good health and are most marked beyond 60 years of age.

In youth, healthy individuals have a physiologic reserve (a marked excess of functional capacity over the amount needed to meet metabolic needs at rest or with stress). The respiratory system draws on this reserve as its function declines with age. Aged individuals thus become vulnerable to the stress, disease, and injuries that are weathered much more easily by the young.

The routine activities of healthy elderly persons are not limited by this decreasing respiratory system function. Thus, the effects of age may not be apparent until they need to draw on their physiologic reserves during stress, such as postoperative recovery or complications. An awareness of the inevitable, but possibly hidden, age-related changes in the respiratory system helps the surgeon anticipate and treat respiratory complications in elderly patients.

The purely age-related changes in the respiratory system are complicated by other accompaniments of aging. The lungs are exposed to a lifetime of environmental stresses, including tobacco smoke, respiratory infections, air pollutants, and occupational exposures to dusts and fumes. Elderly individuals also often have increasingly sedentary lifestyles and decreasing fitness.

As an introduction to the topics to be reviewed in this chapter, the various components of the respiratory system are shown in Table 1. Table 1 also contains introductory comments about structural and functional changes with age.

Airways and Lung Parenchyma Lung Shape

The lungs are closely applied to the chest wall, and their overall shape is determined by the chest wall shape. The increases in anteroposterior diameter of the lungs with age and the more rounded shape that results are presumably due to changes in the shape of the surrounding thoracic cage. These changes are not thought to have functional consequences.

Conducting Airways

The conducting airways consist of the air passages from the mouth to the level of the respiratory bronchioles. The volume of the conducting airways determines the anatomic dead space. Their size, shape, and branching pattern are the major

Table 1 Respiratory system and changes with aging

Functional division	Components	Function	Change(s) with aging
Conducting airways	Airways not involved in gas exchange	Transport gas to and from lung parenchyma	Calcification and other minor changes
Lung parenchyma	Respiratory bronchioles through alveoli and supporting structures	Exchanges gas between alveoli and pulmonary capillaries	Enlarged alveolar ducts; ventilation–perfusion mismatching
Bellows apparatus	Chest wall and respiratory muscles	Provides support for lung structure and applies force to lung	Increased rigidity of chest wall, some decrease in respiratory muscle strength
Ventilatory control	Respiratory control center; carotid and aortic bodies	Alters ventilation to match metabolic needs	Markedly decreased responses to hypoxemia and hypercapnia

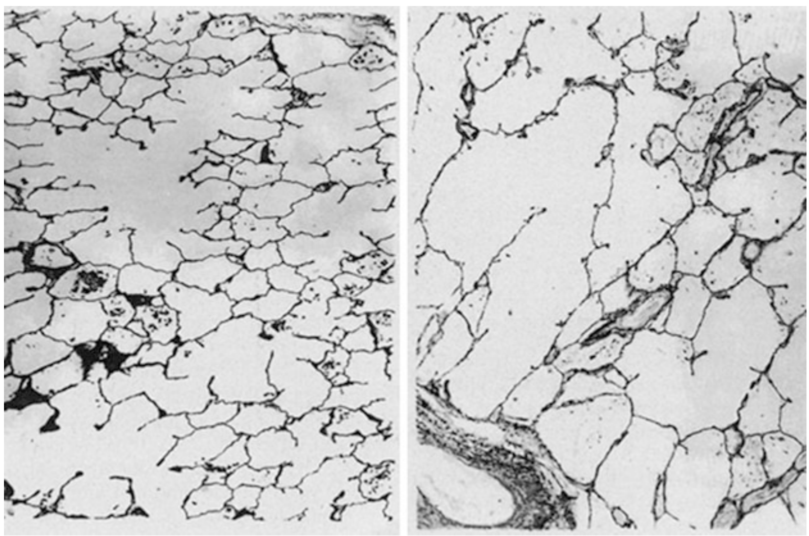


Fig. 1 Histologic changes in the aging lung. Normal lung of a 36-year-old woman (left). Lung of a 93-year-old woman (right). Alveolar ducts are dilated, and shortening of interalveolear septa is observed. (Photomicrographs courtesy of Charles Kuhn III, MD, with permission of the Mayo Foundation)

determinants of airway resistance. The large cartilaginous airways show a modest increase in size with age, resulting in slight but probably functionally insignificant increases in anatomic dead space [1]. Calcification of cartilage in the walls of the central airways and hypertrophy of bronchial mucous glands are seen during advanced age, but these and other changes in the extraparenchymal conducting airways appear to have little or no physiologic significance.

Lung Parenchyma

The respiratory bronchioles and alveolar ducts undergo progressive enlargement with age, beginning as early as age 30 or 40 but observable most prominently after the age of 60 (Fig. 1). The proportion of the lung made up of alveolar ducts increases, and alveolar septa become shortened, leading to a flattened appearance of the alveoli. The proportion of alveolar air decreases as the volume of air in alveolar ducts increases [2]. The distance between alveolar walls (the mean linear intercept, or MLI) increases, whereas the surface/volume ratio of the lung decreases. As a result of these changes, the alveolar surface area decreases by approximately 15% by age 70.

Superficially, the morphologic changes in the lung with aging are similar to those observed with mild pulmonary emphysema. To be classified as emphysema, however, the anatomic changes must consist of airspace enlargement in the gas-exchanging zone of the lung (distal to the terminal bronchioles) and must show evidence that the airspace enlargement is due to alveolar wall destruction, with fusion of adjacent airspaces [3]. For a time, there was considerable debate as to the cause and classification of the airspace enlargement seen with advanced age. Debate centered on whether the airspace enlargement was a "senile" form of emphysema.

Pump [4] and several early authors thought they could identify "emphysematous" lesions in aged lungs. However, Pump studied only two lungs (from 78- to 80-year-old men), one of whom had been a heavy smoker. Ryan and colleagues resisted the term "emphysema" and called the age-related structural changes "ductectasia" because of the prominent finding of enlarged alveolar ducts [5]. Significant alveolar wall destruction as a cause of emphysema appears to be unlikely, as Thurlbeck and Angus have shown that the number of alveoli per unit area remains constant in mature lungs [2]. The latter authors considered the changes to be a "rearrangement of the geometry of the lung." A National Heart, Lung, and Blood Institute Workshop on the definition of emphysema weighed the available evidence and decided not to include age-related changes in the lung parenchyma under the definition of emphysema [3]. To avoid confusion and to simplify the nomenclature, they recommended use of the term "aging lung" to apply to the uniform airspace enlargement that develops with increasing age.

Mechanical Properties of the Lungs

The lungs exert an inward force in the intact thoracic cage. The retractile force of the lungs, or "elastic recoil," can be measured during life by estimating the pleural pressure with an esophageal balloon. Measurements are taken at progressively decreasing lung volumes from total lung capacity (TLC) to functional residual capacity (FRC), when the airways are open and there is no airflow. The negative pleural pressure is generated by the lungs' elastic recoil forces.

Figure 2 compares the elastic recoil pressures of a young man, a normal elderly adult, and a patient with emphysema. The normal elderly individual and the patient with emphysema have a greater decrease in elastic recoil pressure than does a young person. This is reflected in the leftward shift of their pressure–volume curves [7, 8]. Emphysema produces a much greater loss of elastic recoil than is caused by aging alone.

There has been some disagreement as to whether aging changes lung compliance (the slope of the curve in Fig. 2) or, alternatively, is accompanied by a parallel leftward shift of the pressure–volume curve with aging (no change in compliance). There is general agreement if small changes in lung compliance do occur, they are not physiologically significant.

Changes in Lung Recoil Due to Surface Forces

The loss of surface area with age reduces the area of gas–liquid interface, resulting in a decrease in the surface tension forces. This ultimately causes a decrease in the lung elastic recoil. This change has important effects on lung function (especially on the function of small airways and expiratory flow).

Changes in Structural Macromolecules

Elastic fibers consist in large part of an extremely hydrophobic, highly cross-linked, and highly elastic macromolecule (elastin). They form a continuous skeleton that follows the airways and pulmonary vessels and extends to a fine mesh-work in the alveolar septa [9]. These fibers are thought to contribute substantially to lung elasticity. The amount of elastin in the lungs has been studied in an attempt to determine the cause of decreasing lung elastic recoil with age. Analysis of whole lungs has revealed that the elastin content actually increases (rather than decreases) with age [10]. More recent evidence indicates that the increase in lung elastin with age is accounted for by an increase in pleural elastin; parenchymal elastin does not change [9].

Careful studies of the elastic fibers in the lung parenchyma by two independent methods have

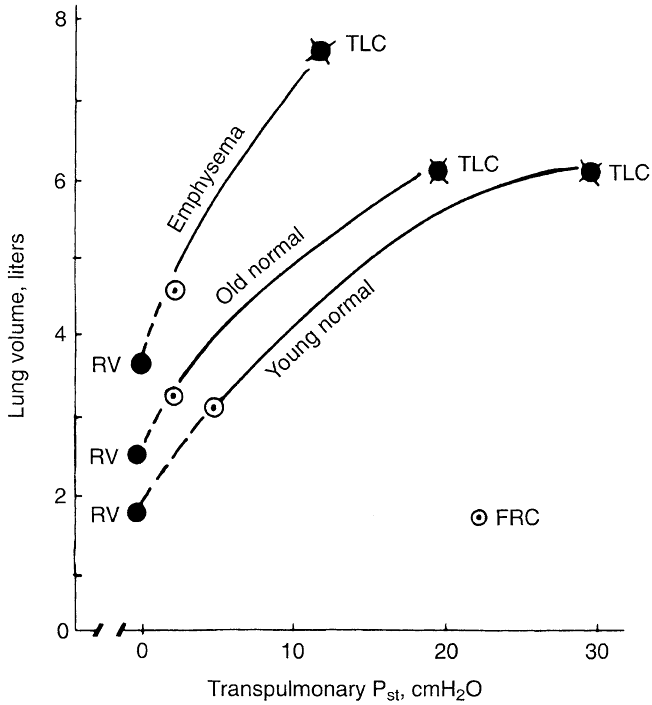


Fig. 2 Static pressure–volume curves of the lungs illustrating elastic recoil forces and compliance. To generate these data, transpulmonary pressure (which reflects lung elastic recoil) is measured at various lung volumes with an esophageal balloon. At any lung volume, the recoil pressure is less in the aged than in the young individual. This results in a pressure-volume relation that is shifted upward and to the left. A curve for a patient with emphysema is shown for comparison. With emphysema, recoil pressures are much less than in normal elderly individuals, and lung compliance (the slope of the curve) is markedly abnormal. (From Pride [6], with permission)

shown that they are remarkably stable following postnatal lung growth. Modeling of radiocarbon data [11] indicates that the "mean carbon residence time" in elastin is 74 years (Fig. 3). It is correct to consider that lung parenchymal elastin is stable over the human life span. These elastic fibers probably provide a metabolically inert scaffold for the structure of the lung. Thus, there are no age-related changes in lung elastin that provide an explanation for the decrease in elastic recoil forces observed in the elderly.

Although human studies have not been done, studies in rodents and birds suggest that lung collagen fibers, like elastic fibers, are long-lived. Finally, although some qualitative changes in collagen during aging have been described (decreases in solubility and increases in intermolecular cross-links), they appear to have no relation to changes in lung elastic recoil.

Chest Wall

The chest wall becomes more rigid with advancing age [8, 12]. As can be seen in Fig. 4, the static pressure–volume curve of the chest wall is shifted to the right and is less steep (indicating decreased compliance) with increasing age [13]. It is known that the articulations of the ribs with the sternum and the spinal column may become calcified, and the compliance of the rib articulations decreases with age. The changes in rib articulations may be compounded by the development of kyphosis due to osteoporosis. The decreasing compliance of the chest wall demands more work from the respiratory muscles. For example, in a 70-year-old person, approximately 70% of the total elastic work of breathing is expended on the chest wall, whereas this value is 40% in a 20-year-old.

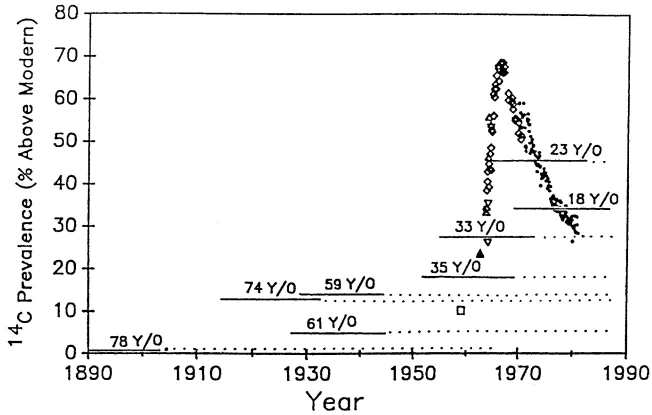


Fig. 3 Turnover of elastic fibers in human lung parenchyma. Radiocarbon (^{14}C) prevalence in lung elastin is shown on the ordinate, with zero being the level before atmospheric nuclear weapons testing began. Levels above zero reflect protein synthesis that has occurred since the 1960s (% Above Modern). The symbols are data from human tissues that exhibit rapid turnover, sampled during the years shown [11]. Each horizontal line represents an analysis of human lung parenchymal elastin from a single individual. The age at time of death is shown for each subject. The lengths and positioning of the solid portions of the lines correspond to timing and duration of fetal and postnatal lung growth, and the interrupted portions of the lines represent the remainder of the individuals' life spans. The vertical position of each line represents the ^{14}C prevalence measured in that sample. Note that the ^{14}C prevalence measured in the elastin samples reflects the ^{14}C prevalence in the biosphere during the period of lung growth. Individuals whose lungs had ceased growing before the nuclear weapons age had little nuclear weapons-related ^{14}C in their lung elastin, demonstrating that minimal lung elastin turnover occurred during adulthood. (From Shapiro et al. [11], with permission)

Muscles of Respiration

Age-related changes in nonrespiratory skeletal muscle include decreased work capacity owing to alterations in the efficiency of muscle energy metabolism, atrophy of motor units, and electromyographic abnormalities. Based on lessons learned with other skeletal muscles, it, at first, appeared likely that age-related abnormalities in respiratory muscles would also be found.

An early study by Black and Hyatt [14] appeared to confirm age-related decrements in respiratory muscle function by measuring maximal inspiratory pressure (PI_{max}) and maximal expiratory pressure (PE_{max}) in 120 normal individuals (both smokers and nonsmokers) between the ages 20 and 70. Maximal respiratory pressures in women were 65–70% of those in men. No significant age-related changes were observed in individuals under the age of 55. Trends toward reduced maximal respiratory pressure with age were seen for both sexes and with both PI_{max} and PE_{max} With the numbers of men studied, the change with age in PI_{max} was not statistically significant for the male gender.

More recently, McElvaney and coworkers [15] have come to a different conclusion in a similar study of 104 healthy individuals over the age of 55. They found large variation in maximal respiratory pressures from individual to individual (as had Black and Hyatt) but no significant correlation with age. In contrast, in a third population of 160 healthy individuals who ranged in age from 16 to 75 years, Chen and Kuo found significant gender differences in maximal respiratory pressures as well as trends toward decrements with age for both PI_{max} and PE_{max} in both genders [16]. The age-related change in PE_{max} in the male subjects was not statistically significant with the sample size studied. When the 40 individuals of both genders in the youngest age group (16–30 years) were compared with the 40 individuals in the oldest group (61–75 years), the decrement in PI_{max} was 32–36%, and the decrement in P^{e}max was 13–23%. Representative findings for maximal respiratory pressures in women are illustrated in Fig. 5.

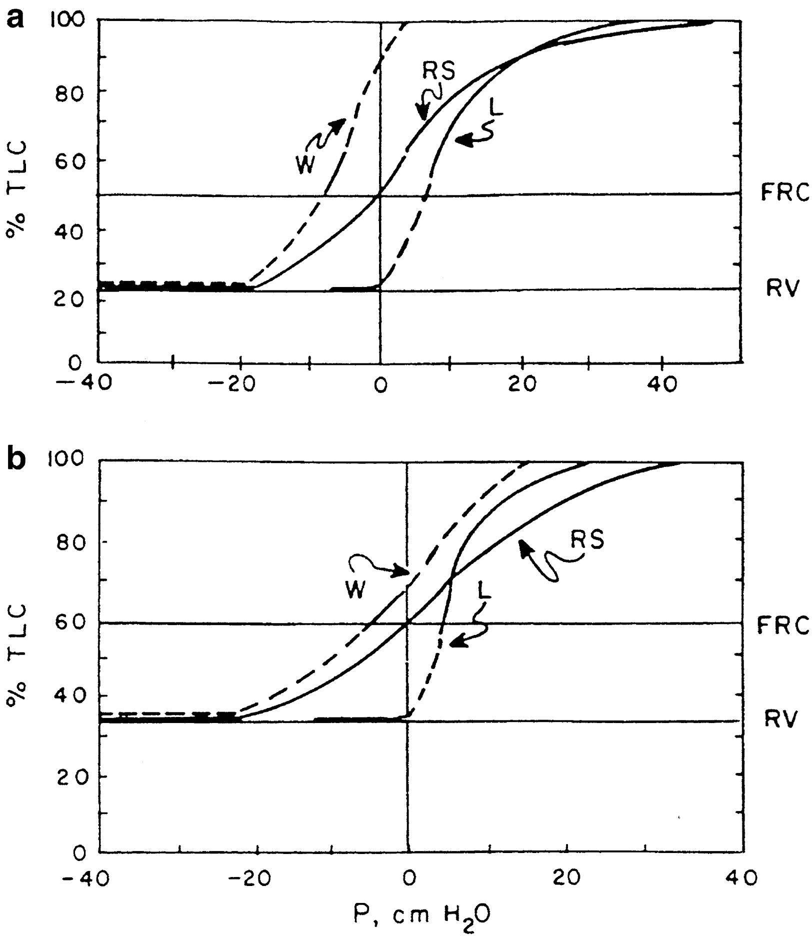


Fig. 4 Static compliance relations of the components of the respiratory system. *L* lungs, *W* chest wall, *RS* total respiratory system, *TLC* total lung capacity, *FRC* functional reserve capacity, *RV* residual volume, *P* pressure gradient, (**a**) A 20-year-old man; (**b**) A 60-year-old man. Note that the static compliance of the chest wall is substantially decreased (reduced slope) in the older individual, whereas FRC (resting volume of the respiratory system, or the point at which the pressure gradient across the respiratory system is zero) increases somewhat. Note again (compare with Fig. 2 of Chap. 35, "Parathyroid Disease in the Elderly") that the static recoil pressure of the lungs is reduced in the older subject

Chen and Kuo measured inspiratory muscle endurance against a resistive load and found significant decrements with age [16]. Physically active men had greater inspiratory muscle endurance than sedentary men.

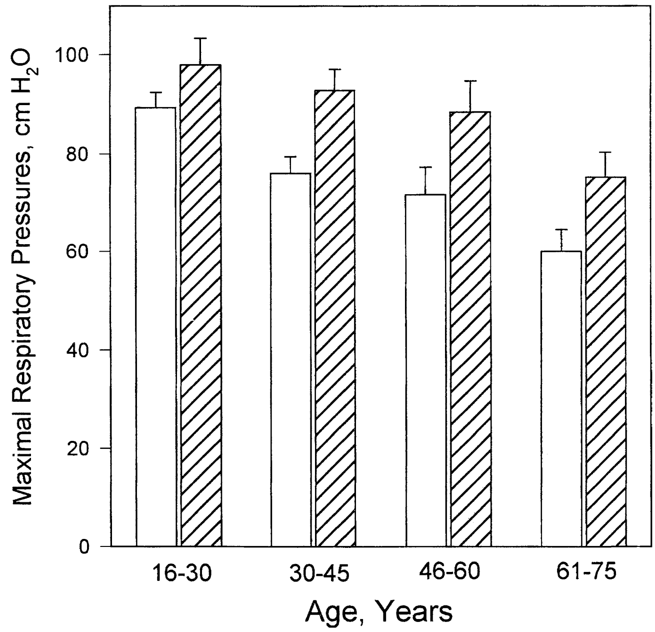
In summary, it appears that when populations of healthy individuals of widely differing ages are studied, moderate age-related decrements in respiratory muscle strength and endurance can be found. These studies usually define "healthy" only by the absence of disease and do not control for physical activity. They are complicated by marked interindividual variability, and longitudinal studies have not been reported. Respiratory muscle function may be better preserved with age than that of other skeletal muscles because of a straining effect of the continuous respiratory muscle activity. Finally, physical activity may have an additional straining effect that enhances inspiratory muscle endurance in all age groups.

Control of Breathing

Stanley and colleagues have found that elderly subjects (mean age 69 years) have a slower, more variable respiratory rate than a young control group [17, 18]. It is doubtful that this isolated observation has any functional significance, but it did suggest that ventilatory control changes with aging.

More important is that ventilation becomes much less responsive to stress in elderly individuals. It is well known that in young individuals sensitive ventilatory control mechanisms match minute ventilation closely to metabolic

Fig. 5 Representative variations in maximal respiratory pressure with age among women. Inspiratory and expiratory measurements were made at residual volume and total lung capacity, respectively. Open bars, maximal inspiratory pressure; hatched bars, maximal expiratory pressure. Error bars are standard errors of the mean. The variations with age were statistically significant but were small in magnitude. (From Chen and Kuo [16], with permission)



demands. As a result, arterial blood-gas values remain stable throughout a wide range of activities from rest to strenuous exertion, whereas oxygen consumption and carbon dioxide production vary widely. Similarly, when the efficiency of gas exchange is diminished by a variety of lung problems (e.g., atelectasis and pneumonia) or congestive heart failure, appropriate increases in minute ventilation minimize the potential for resulting hypercapnia or hypoxemia in healthy young individuals.

To compare old and young individuals, ventilatory control mechanisms have typically been tested by inducing either hypoxemia or hypercapnia while monitoring ventilatory parameters. Such tests have shown striking differences between young and elderly individuals in ventilatory and cardiac responses [19–22].

Diminished Ventilatory Response to Hypercapnia

Kronenberg and Drage [21] compared the ventilatory responses to hypercapnia while $PACO_2$ was allowed to rise to 65 mmHg. The elderly individuals had a significantly diminished ventilatory response to hypercapnia, measured as the slope of the relation between ventilation and $PACO_2$.

Diminished Ventilatory Response to Hypoxia

When these same authors [21] measured the ventilatory response to hypoxia, the contrasts between young and aged individuals were even more dramatic (Fig. 6). The ventilatory response to PAO_2 40 mmHg was uniformly smaller in the old subjects, and there was no overlap between the groups. The mean minute ventilation values at PAO_2 40 mmHg were 40.1 and 10.2 L/min in the young and old groups, respectively.

Diminished Occlusion Pressure Responses

Peterson and Fishman [23] showed that the differences in responses of elderly subjects to both hypercapnia and hypoxia are due to a lesser increase in tidal volume during stress, whereas the ventilatory rate increases normally. These authors also measured airway occlusion pressures, which are valuable indices of respiratory drive that are not affected by either respiratory muscle strength or respiratory mechanics. The measurements, called P_{100}, are the negative

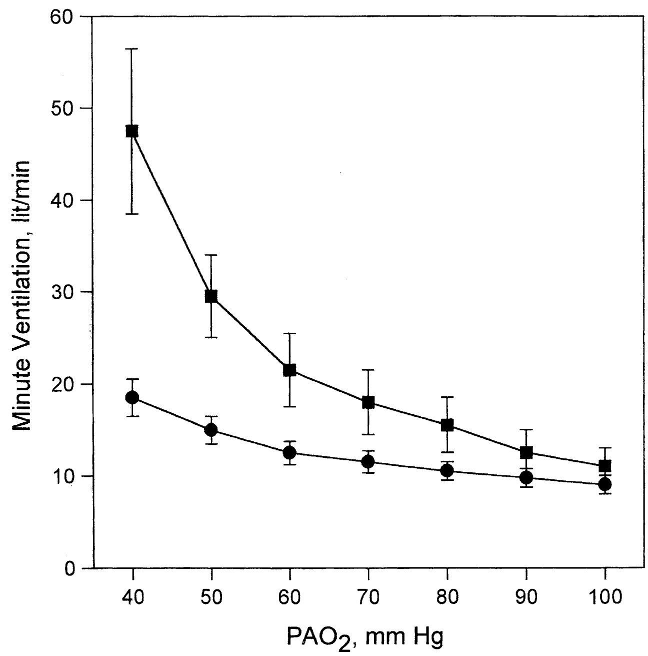


Fig. 6 Variations in ventilatory responses to hypoxia, with age. Eight normal men aged 64–73 years (mean 69.6 years) (circles) were compared to young controls aged 22–30 years (mean 25.6 years) (squares). Ventilation was measured while the subjects were exposed to isocapnic progressive hypoxia by a rebreathing method. Values are means ± SEM. Note that the ventilatory responses were strikingly attenuated in the older individuals. (From Kronenberg and Drage [21], with permission)

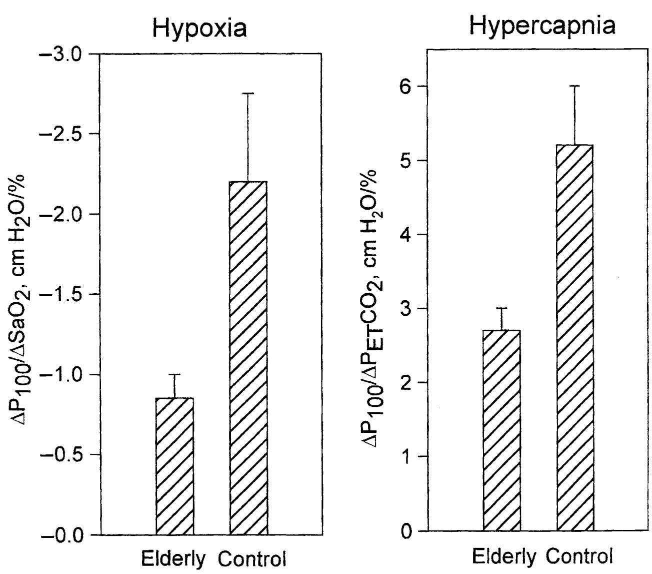


Fig. 7 Variations in occlusion pressure responses to hypoxia and hypercapnia, with age. Data are slopes of the relations between occlusion pressure responses and either SaO_2 or end-tidal PCO_2; error bars are the SEM. Occlusion pressure responses are an indicator of ventilatory drive independent of chest wall compliance and respiratory muscle strength. The elderly individuals showed significantly and strikingly diminished ventilatory drives in response to both hypoxia and hypercapnia. (From Peterson and Fishman [23], with permission)

pressures at the mouth when measured 100 ms after the start of inspiration against an occluded airway. The occlusion pressure responses to both hypoxia and hypercapnia (Fig. 7) were significantly reduced in ten elderly subjects (mean age 73.3 years) when compared to those of nine young control subjects (mean age 24.4 years) [22].

In summary, the compensatory change in tidal volume in response to either hypoxemia or hypercapnia is reduced (often strikingly) with age. The less-effective homeostasis is apparently due to reduced responsiveness of either the ventilatory drive or the neural output from the respiratory center. It has not been determined whether the diminished ventilatory drive results from altered chemoreceptor function or altered function of the respiratory center. Kronenberg and Drage favored altered receptor function based on their observation that elderly subjects responded to an alveolar oxygen tension of 40 mmHg with only an 11% increase in heart rate, whereas the young subjects responded with a 45% increase [21].

Respiratory Load Compensation and Dyspnea

Normally, when there is a change in the mechanical workload of the respiratory system (e.g., with lung disease, changes in posture, or mouth versus nose breathing), there is a reflex compensation that maintains the ventilation constant. To study the effects of aging, Akiyama and colleagues [24] measured responses to inspiratory flow-resistive loading in young and elderly individuals. In the young control group, inspiratory loading resulted in an increase in P_{100} at each level of induced hypercapnia, such that inspiratory loading did not change the ventilatory response to hypercapnia. In marked contrast, the P_{100} in the elderly group did not change when an inspiratory load was applied. Thus, ventilatory responses to hypercapnia were reduced during inspiratory loading in the elderly group.

At each level of PCO_2, the intensity of perceived dyspnea in response to inspiratory loading was higher in the elderly than in the control group. Thus, the sensation of dyspnea was intact or enhanced in the elderly subjects, while their compensatory responses were reduced.

Pulmonary Circulation

Pulmonary artery catheterization studies have typically been biased in that only subsets of patients have been reported. The reported studies were performed on individuals who had signs and symptoms that led to referral for heart catheterization. These individuals are probably not representative of "healthy" young and old cohorts. Furthermore, age-related changes in the pulmonary circulation are difficult or impossible to distinguish from changes due to heart disease or age-related changes in cardiac function. Even if they are real, the minor increases in pulmonary vascular resistance and age-related increases in pulmonary artery wedge pressure are probably not physiologically significant.

Pulmonary Function Tests

Several measurements of lung function and exercise capacity decline with age. However, descriptions of "normal" age-related changes are confounded by an increasing prevalence of disease, chronic illness, medication use, and an increasingly sedentary lifestyle. The influences of all of these factors are difficult to distinguish from each other. Superficially, it appears that longitudinal studies would provide the optimal design for distinguishing the effects of age from other influences. Longitudinal studies, however, have methodological problems and biases of their own, the most obvious being that the healthy elderly represent a healthy survival population. Regardless, it does seem that age alone has potentially important effects on lung function.

Lung Volumes

Figure 8 illustrates typical lung volume changes with aging based on cross-sectional studies. TLC, the volume of air in the lungs at the end of a maximal inspiration, is marked by the point at which the recoil pressure exerted by the respiratory system is exactly counterbalanced by the PI_{max} generated by the respiratory muscles. Cross-sectional studies of TLC summarized by the European Coal and Steel Community [25, 26], when combined, demonstrated no significant age coefficients for either men or women [25, 26].

Both slow and forced vital capacity (FVC) decline with age more rapidly in men than women. Average decrements in vital capacity per

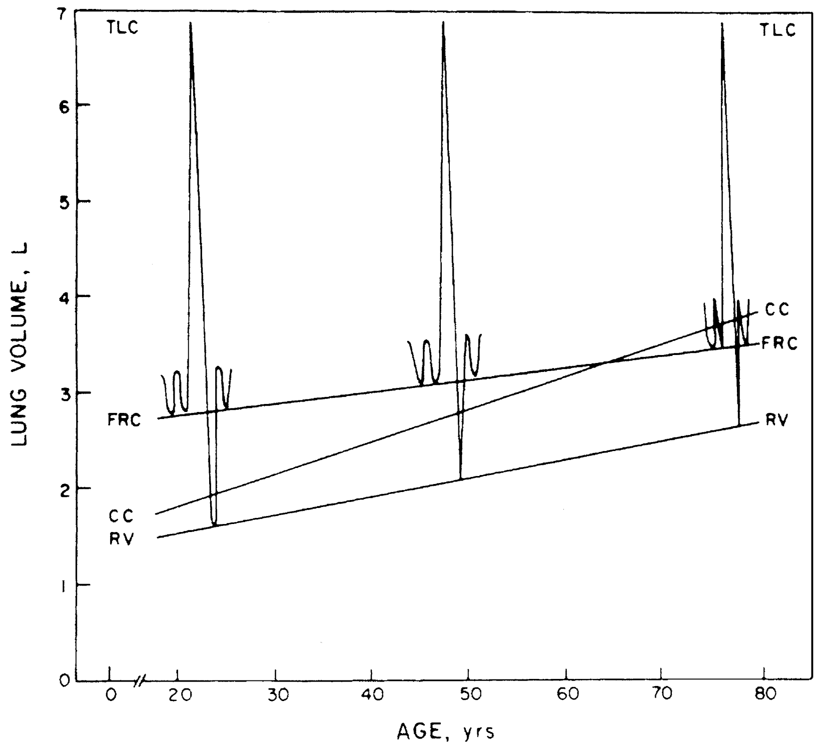


Fig. 8 Lung volume changes with age. *TLC* total lung capacity, *CC* closing capacity, *FRC* functional residual capacity, *RV* residual volume. Although not labeled, the vital capacity is TLC minus RV. The most consistent age-related changes are an increase in RV and a decrease in ventilatory capacity. (From Peterson and Fishman [23], with permission)

year vary considerably; in cross-sectional studies, declines range from 21 to 33 ml/year in men and 18 to 29 ml/year in women. Ware and colleagues [27], in a study containing both longitudinal and cross-sectional computations, found cross-sectional decreases in FVC for men and women to be −34 and −27.8 ml/year, respectively. Cross-sectional studies of residual volume (RV) and the RV/TLC ratio consistently show increases with age. In the young, RV (the volume of air in the lungs at the end of a maximal expiration) is the volume at which the outward static recoil pressure of the respiratory system is counterbalanced by the maximal pressure exerted by the expiratory muscles. In old subjects, the expiratory flow never completely reaches zero, and RV is determined in part by the length of time an individual can maintain the expiratory effort. Other factors leading to an increased RV with aging include loss of lung recoil, decreased chest wall compliance, decreased expiratory muscle force, and increased small airway closure (air trapping) in dependent lung zones [6].

FRC is also determined by the balance of the elastic recoil forces of the lung and chest wall, but in this instance, the equilibrium occurs at the end of a quiet (unforced) exhalation. Because lung recoil decreases and the chest wall stiffens with age, one would expect the FRC to increase. Cross-sectional studies, however, show inconsistent results, with most showing no change in FRC with aging. Studies that do find an increase in FRC with aging show a small positive age coefficient on the order of 7–16 ml/year. McClaran et al.'s longitudinal study found the FRC to increase 40 ml/year, but again the change was not significant [28]. Despite the conflicting data, it is generally believed that FRC increases somewhat with aging.

Loss of lung recoil also changes the volume at which airway closure occurs. When adults exhale fully, small airways close in the region of the terminal bronchioles in dependent lung zones. The lung volume at which this closure begins is measured as the closing volume or, if it is added to the residual volume, closing capacity. Closing volume increases linearly with age from about 5–10% of TLC at age 20 to about 30% of TLC at age 70. The loss of lung elastic recoil, a possible decrease in the recoil of the intrapulmonary airways, and decreases in small airway diameter probably explain most of the change in closing volume.

On average, closing volume encroaches on tidal volume by about age 44 when subjects are supine and at about age 65 when they are seated (Fig. 8). Airway closure during tidal breathing explains part of the decrease in arterial oxygen tension observed with aging.

Airflow

Although essentially all expiratory flows measured during a maximum expiratory maneuver decrease with age, the declines are most evident at low lung volumes (Fig. 9). Nunn and Dregg [29], in a study of 225 male and 228 healthy female nonsmokers, reported a modest decrease in peak expiratory flow (PEF) with aging. The rate of decline in FVC and forced expiratory volume at 1 s (FEV_1) with age tends to be more in (1) men, (2) tall individuals, (3) individuals with large baseline values, and (4) individuals with increased airway reactivity. Total airway resistance, measured at FRC, does not change with aging.

Gas Exchange

The carbon monoxide diffusing capacity (DL_{CO}) declines with age. Early cross-sectional studies reported a linear decline in DL_{CO} of about −0.1 ml CO/min/mmHg/year for men and −0.15 ml/min/mmHg/year for women [30, 31]. These declines are roughly 0.5% per year. In a large representative sample of US adult men, Neas and Schwartz [32] found an almost identical linear fall in DL_{CO}. In women, however, they found a nonlinear, quadratic decline in DL_{CO} with age. After age 47, the nonlinear component was not significant, and the decline in DL_{CO} was identical to that in the earlier studies. The decline in DL_{CO} with age did not vary with race.

The decline in DL_{CO} with age is not explained by increased nonhomogeneity of gas distribution. Measured DL_{CO} decreases as the alveolar PO_2 increases and the venous hemoglobin concentration falls. Neither alveolar PO_2 nor hemoglobin concentration varies enough with age to explain the aging-related decline in DL_{CO}. The magnitude of the decline in DL_{CO} corresponds fairly well to the magnitude of the known aging-related decrease in the internal surface area of the lung.

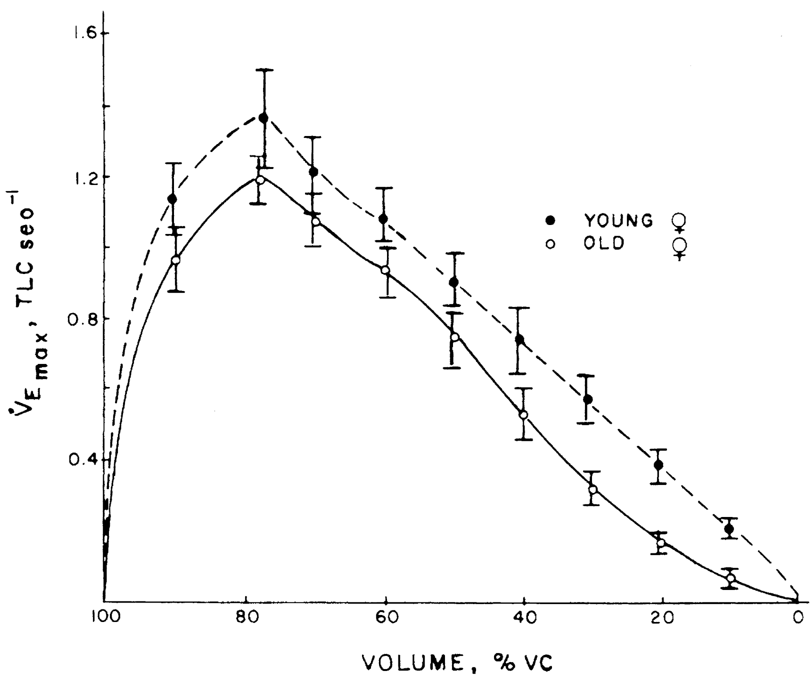


Fig. 9 Maximal flow-volume curves, showing the changes in expiratory flow rates with age. Data are for elderly women (mean age 63 years) and control young women (mean age 25 years). Although all flows tend to be reduced with aging, the reduction in flow is most evident at lower lung volumes, where the flow-volume curve is concave in regard to the volume axis. (From Peterson and Fishman [23], with permission)

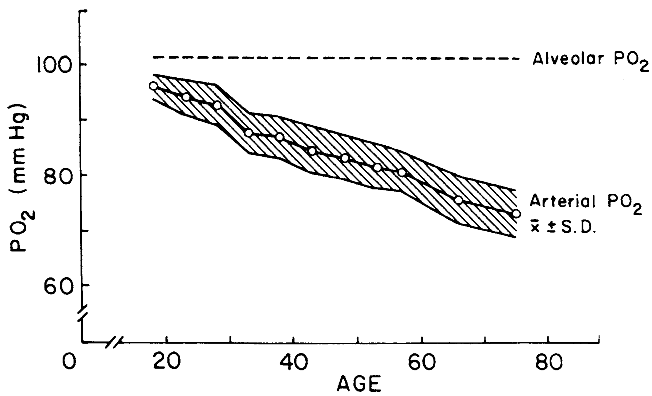


Fig. 10 Decreasing arterial oxygen tension (PO_2) with age. The lack of change in alveolar oxygen tension is also shown for comparison with PaO_2. The widening alveolar-arterial partial pressure difference for oxygen results from the development of basilar areas of low ventilation/perfusion ratios due to airway closure in the elderly. (Modified from Sorbini et al. [33], with permission)

Although alveolar oxygen pressure (PAO_2) remains constant with age, arterial PO_2 decreases, and the alveolar-arterial oxygen tension gradient ($PA\text{-}aO_2$) increases with aging (Fig. 10). The decline in PaO_2 with aging is more pronounced when subjects are studied in a recumbent as contrasted with an upright position. The most likely explanation for the decline in PaO_2 with aging is increased mismatching of ventilation to blood flow $\left(\dot{V}/\dot{Q}\right)$ as airway closure begins to occur during tidal breathing.

Summary and Implications for Geriatric Surgery

Aging is accompanied by readily measurable changes in respiratory system mechanics, gas exchange, ventilatory control, and respiratory muscle strength. Despite these changes, the activities of normal elderly individuals are not limited because they have substantial functional reserve of the respiratory system early in their lives. When anticipating operative morbidity and potential operative complications, however, the surgeon must be aware that elderly patients have lost much, or all, of their respiratory reserve. Operative stresses, pain, and bed rest are always less well tolerated by the respiratory system of elderly patients.

Changes in ventilatory control among geriatric patients deserve special attention. Because of changes in chemoreceptor function and respiratory center function, elderly individuals respond differently to hypoxemia and hypercapnia than their younger counterparts. Thus, an elderly patient who is developing respiratory failure may appear comfortable and may not be tachypneic or tachycardic. Vigilance and awareness on the part of the health-care team allow detection of respiratory complications early, through measurement of oxygen saturation and arterial blood gases. Such vigilance allows appropriate *nonemergent* interventions.

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16 Renal Disease in Older Adults

Jeffrey M. Turner and Deep Sharma

Contents

Abstract

Renal disease is common in older adults, and it is an important factor to consider in the surgical patient. Of particular concern is the fact that the perioperative period creates significant vulnerabilities to a number of organ systems, and renal disease can often magnify these risks. In addition, de novo injury to the kidneys is a common event in the perioperative period, and it is important that preventive measures are in place to reduce or minimize these events. This chapter reviews the unique management challenges associated with surgery in older adults with renal disease, including the importance of identifying specific sequelae that can present as a result of renal dysfunction and methods to optimize risk during the perioperative period.

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Assessing Renal Function in the Older Surgical Patient

The kidneys have several functions that are critical to maintaining health and survival. These include filtering plasma to regulate the body milieu, regulation of blood pressure via sodium handling, erythropoietin production to maintain red blood cell generation in the bone marrow, and vitamin D metabolism that promotes bone homeostasis. These functions are all interrelated, and kidney dysfunction typically includes abnormalities in all of these processes. However, it is the function of plasma filtration that has the most significant and immediate clinical implications and is most often of greatest concern to the clinician. The key anatomic structures involved in this process are the glomerulus, which is the filtering unit of the kidney that creates ultrafiltrate, and the tubule, which processes the ultrafiltrate by means of reabsorbing and secreting various electrolytes and organic substances to create the end product of urine.

The glomerular filtration rate (GFR) is an abstract parameter used to assess the kidney's filtering ability, and it is the key parameter by which global kidney function is assessed. The GFR in an individual with "normal" kidney function is greater than 100 ml/min/1.73 m^2. There are laboratory techniques to precisely measure GFR, and this includes the infusion of various exogenous biomarkers (inulin, ^{125}-iothalimate, and iohexol). However, these methods are not practical to perform in typical clinical settings. Measurement of endogenous biomarkers is therefore the standard method for calculating GFR in clinical laboratories. The most widely used biomarker is serum creatinine. Since the clearance of creatinine by the kidney closely associates with the GFR, quantification of the total creatinine in a 24 h urine sample can be used to calculate the creatinine clearance using the following formula: $C_{Cr} = (U_{Cr} \text{ x } V)/P_{Cr}$. Where C_{Cr} is the creatinine clearance over 24 h, U_{Cr} is the urine creatinine concentration, V is the urine volume over 24 h, and P_{Cr} is the plasma creatinine concentration. However, given the impracticality of having patients routinely submit a 24 h urine collection, various prediction equations have been developed to simply estimate the GFR based on the patient's measured serum creatinine value. These equations work under the assumption that both the production of creatinine from muscle cells and the removal of creatinine via the kidneys are occurring at a constant rate. For this reason, it is not appropriate to use these equations in the setting of acute kidney injury (AKI), as the GFR is not constant in this scenario. The Cockroft-Gault formula, the Modification of Diet in Renal Disease Study (MDRD) equation, and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation are all commonly used. The equations are listed below:

Cockroft-Gault formula:

$$\text{Male } C_{Cr}\ (\text{ml/min}) = (140 - \text{age}) \times \text{weight}/72 \times S_{Cr}\ (\text{mg/dL})$$

$$\text{Female } C_{Cr}\ (\text{ml/min}) = (140 - \text{age}) \times \text{weight} \times 0.85/72 \times S_{Cr}\ (\text{mg/dL})$$

MDRD equation:

$$\text{GFR}\left(\text{ml/min/1.73 m}^2\right) = 175 \times \text{standardized } S_{Cr}\ (\text{mg/dL})^{-1.154} \times \text{age}^{-0.203} \times 0.742\ (\text{if female}) \times 1.210\ (\text{if black})$$

CKD-EPI equation:

$$\text{GFR}\left(\text{ml/min/1.73 m}^2\right) = 141 \times \min\left(S_{Cr}/\kappa, 1\right)^{\alpha} \times \max\left(S_{Cr}/\kappa, 1\right)^{1.209} \times 0.993^{\text{Age}} \times 1.018\ (\text{if female}) \times 1.157\ (\text{if black})$$

Where κ is 0.7 for females and 0.9 for males, α is −0.329 for females and −0.411 for males, min indicates the minimum of S_{Cr}/κ or 1, and max indicated the maximum of S_{Cr}/κ or 1.

Note that the Cockroft-Gault formula requires inputting the patient's age, sex, and weight, in addition to the serum creatinine, while the

MDRD and the CKD-EPI equations require inputting the age, sex, and race, in addition to the serum creatinine. The Cockroft-Gault was the first equation that was developed. It actually predicts the creatinine clearance (a surrogate for GFR) rather than the actual GFR itself. Creatinine is secreted by the tubule in small amounts under normal conditions, in addition to being filtered by the glomerulus, so the creatinine clearance overestimates the GFR slightly, and this is one of the limitations of the Cockroft-Gault equation. The MDRD equation was more recently developed, and it is widely used in many clinical laboratories currently. The MDRD equation estimates the GFR, as opposed to the creatinine clearance, so it is more accurate than the Cockroft-Gault formula. However, the MDRD equation is less accurate in individuals with a GFR above 60 ml/min. The CKD-EPI equation is the most recently developed equation and is equally as accurate as the MDRD equation in individuals with a GFR < 60 ml/min/1.73 m^2; however, it has the advantage over MDRD of also providing accurate estimates of GFR in those with mild reductions as well as those with normal filtering function (GFR > 60 ml/min/1.73 m^2).

In the aging kidney, GFR declines on average by about 1.0 ml/min/1.73 m^2 per year after the age of 40 years old [1]. Therefore, older individuals will often have a lower GFR than younger individuals, irrespective of any disease-related injury. In addition, in those with CKD from chronic illnesses, the additive effect of the renal injury from their disease and the age-related changes can result in a higher severity of renal impairment than what might be seen in younger individuals with similar chronic comorbidities. This in part explains why the prevalence of CKD (defined as a GFR < 60 ml/min/1.73 m^2) is 38% among individuals over the age of 70 years old, as compared to only 8% in the general population [2].

As previously discussed, serum creatinine is a function of creatinine production by skeletal muscle and creatinine clearance by the kidney. As individuals age, muscle mass declines, and therefore creatinine production will decline as well. This results in a lower serum creatinine at any given degree of creatinine clearance in an older individual as compared to a younger individual. One can be misled by looking at the serum creatinine alone to assess renal function in an older individual, and this often results in an underappreciation for the degree of renal dysfunction. For this reason, most clinical laboratories now automatically report the eGFR with serum creatinine measurements (using one of the abovementioned formulas), and this has led to improvements in diagnosing CKD and referrals to a nephrologist [3]. As stated above, the prediction equations cannot accurately estimate GFR when the serum creatinine is not in steady state, therefore, they should not be used in settings of AKI. Given these points, we recommend using the eGFR when the serum creatinine is stable to establish the baseline kidney function in the preoperative period. However, during the perioperative period, when patients are prone to AKI, it is the change in serum creatinine from baseline that is more important to monitor as opposed to the reported eGFR. A doubling in the serum creatinine will roughly correlate to a 50% reduction in the GFR.

Specific Concerns for the Older Patient with Kidney Disease Undergoing Surgery

Volume Management

Impairments in volume regulation and blood pressure control can pose particular challenges in the older surgical patient with renal dysfunction. Kidney disease impairs the ability to excrete sodium and water, therefore, the excessive administration of fluids or blood products can result in severe hypertension and critical volume overload. For this reason, volume administration needs to be done in a thoughtful manner and guided by the clinical assessment of the patient. The volume of intravenous fluid administration, including during the fasting preoperative period, should be based on the clinical exam. Patients with kidney dysfunction are prone to hypertension and volume overload, therefore, it is not appropriate to reflexively order preoperative intravenous fluids irrespective of the clinical picture. In patients with obvious signs of volume overload (hypertension, elevated jugular venous pressure, edema in the extremities and lungs), fluids should be withheld. Intravenous loop diuretics can be used to treat volume overload in patients during the perioperative period, including those with acute kidney injury. Clinicians should appreciate that impaired kidney function results in the need for higher doses of loop diuretics to achieve similar natriuresis efficacy as those with normal kidney function [4, 5]. As a reasonable guide, in those with a GFR of less than 30 ml/min/1.73 m^2, an intravenous bolus of furosemide of at least 80–160 mg is typically necessary to achieve meaningful diuresis. In addition to increasing the dose of loop diuretics, other strategies for overcoming diuretic resistance include increasing the frequency of dosing (twice or three times daily or switching to a continuous infusion), adding a thiazide diuretic for additional sodium reabsorption blockade in the nephron, intensifying salt restriction in the diet, or coadministration of albumin in patients with severe hypoalbuminemia (typically less than 2.0 mg/dL) [6].

Hypertension

Given the kidneys are a critical organ for blood pressure control in the body, hypertension is nearly universal in patients with significant renal dysfunction. The prevalence of hypertension in advanced CKD is about 90% [7, 8]. Several pathophysiologies contribute to increases in blood pressure in the setting of kidney dysfunction, but none are as critical as sodium and water retention [9]. For this reason, diuretics are central to treating hypertension in patients with CKD. Loop diuretics have traditionally been the preferred diuretic agents in patients with advanced CKD (GFR $<$ 30 ml/min/1.73 m^2), and this sentiment is reflected in many guidelines that suggest avoiding thiazide diuretics except when used in combination with loop diuretics. These recommendations have been based on the dogmatic belief that thiazide diuretics are ineffective when the GFR $<$ 30 ml/min/1.73 m^2. However, it is worth appreciating that robust data is lacking to support these claims.

Activation of the renin-angiotensin-aldosterone system (RAAS) is another important pathophysiology of hypertension in patients with kidney failure [10]. Ample data have shown that angiotensin-converting enzyme inhibitors (ACEi) and angiotensin receptors blockers (ARBs) reduce proteinuria and slow GFR decline in CKD [11]. While these data are most robust in the setting of diabetic kidney disease, ACEi and ARBs should be considered first-line agents for the management of hypertension in all forms of CKD in the absence of refractory hyperkalemia. With that said, clinicians should be aware that controversy exists regarding the role of RAAS antagonists in perioperative period. These agents have the potential to exacerbate intraoperative hypotension while at the same time inhibiting renal autoregulation, so concerns exist whether they increase the risk for perioperative AKI. Data have shown that ACEi and ARB administration in the morning prior to surgery is associated with more frequent intraoperative hypotension events; however, these studies have not consistently shown increased risks for AKI, myocardial infarction, or death [12, 13]. To the contrary, some studies have suggested a myocardial protective effect of these agents in patients undergoing cardiac surgery [14, 15]. Given the mixed findings, there is currently no consensus on whether ACEi or ARBs should be held prior to surgery. Therefore, it is important to closely consider the risks and benefits of continuing RAAS blocking agents in each individual case.

Beta blockers and calcium channel blockers are effective agents for blood pressure lowering in patients with CKD; however, unlike diuretics and RAAS blocking agents, they do not offer unique benefits to this population. Second-line agents for the treatment of hypertension in CKD include mineralocorticoid inhibitors such as spironolactone, afterload reducing agents such as hydralazine, and alpha antagonists such as doxazosin and clonidine.

Hyperkalemia

Given the reduction in the kidneys' ability to excrete potassium, hyperkalemia is a common concern in patients with CKD, especially in the presence of high levels of potassium intake. While elevated serum potassium can cause severe muscle weakness and even paralysis, the most acute concern in hyperkalemia is the high risk of fatal cardiac arrhythmias. Small changes in the extracellular potassium concentration can lead to ventricular tachycardia and ventricular fibrillation due to destabilization of the resting membrane potential in the cells involved with cardiac conduction.

It is critical to review all sources of potassium intake in patients with hyperkalemia. Patients should be counseled to avoid foods high in potassium (Table 1), and daily intake should be restricted to less than 1000 mg in those with advanced CKD. In addition, intravenous fluid choice needs to be carefully considered in the context of the serum potassium. Balanced electrolyte solutions such as Ringer's lactate/acetate or Hartmann's solution contain 4 mEq and 5.4 mEq of potassium per liter, respectively. Under normal conditions this is not an excessive potassium load; however, in patients with moderate to severe hyperkalemia ($K > 5.5$ meq/L), these solutions should be avoided. It is also important to review medications that can cause hyperkalemia (Table 2). Renin angiotensin aldosterone system blockers such as ACE-I and ARBs are some of the most commonly used drugs that are associated with hyperkalemia, and the risk is particularly high when these are used in combination with a mineralocorticoid receptor antagonist. Unfractionated and low molecular weight heparin, which is commonly given in the perioperative period for deep venous thrombosis prophylaxis, suppresses aldosterone production in the adrenal glands, which can result in hyperkalemia [16]. This can be seen irrespective of dose, and with both intravenous and subcutaneous routes. In addition, succinylcholine has been well described as causing a rapid efflux of potassium from the muscle cells into the extracellular space, and predisposing risk factors for this include necrotizing pancreatitis, burn injuries, severe infections, and upper or lower motor neuron defects [17].

When evaluating a patient with hyperkalemia, an electrocardiogram (ECG) is essential to screen for peaked T-waves or prolonged QRS complexes [18], as these are early abnormalities that predict a high risk for the development of fatal arrhythmias. With that said, many patients with moderate or even severe hyperkalemia may not manifest ECG

Table 1 High potassium foods that may need to be restricted

Food	Potassium concentration (mg)
Baked potato	925
Clams, canned	535
French fries	470
Potato chips	465
Sweet potato	450
Dried beans	450
Banana	425
Spinach	420
Lentils	365
Milk	365
Prune	305
Fish (salmon, perch, haddock)	300
Tomatoes	290
Orange	240
Orange juice	235

Table 2 Medications commonly associated with hyperkalemia

ACE inhibitors
ARBs
Nonselective beta blockers (labetalol, propranolol, carvedilol)
Succinylcholine
Aliskiren
Potassium sparing diuretics (amiloride, triamterene)
Mineralocorticoid receptor antagonists (spironolactone, eplerenone)
Heparin
Trimethoprim-sulfamethoxazole
Ketoconazole
NSAIDs
Pentamadine
Calcineurin inhibitors (tacrolimus, cyclosporine)

NSAIDs nonsteroidal anti-inflammatory drugs, *ACE* angiotensin-converting enzyme inhibitor, *ARB* angiotensin receptor blocker changes, and it is often difficult to predict the risk of developing ventricular tachycardia or ventricular fibrillation in a given individual. Urgent treatment should be given in all patients with ECG changes attributed to hyperkalemia. In patients with serum potassium levels >6.0–6.5 meq/L, urgent treatment should always be considered irrespective of the presence of ECG changes or not. Treatment includes intravenous calcium gluconate to rapidly stabilize the membranes of cardiac conduction cells, followed by insulin, sodium bicarbonate, and beta agonists to promote cellular uptake of potassium. Diuretics (if the patient is not anuric) or dialysis (if the patient is anuric or if hyperkalemia persists despite other therapies) should be employed to remove potassium from the body. Sodium polystyrene sulfonate (e.g., Kayexalate) is a potassium exchange resin often given to promote potassium excretion in the stool; however, given it takes many hours to result in a meaningful lowering of the serum potassium [19], it offers little to no immediate benefit for patients presenting with severe hyperkalemia. Patiromer is a newer potassium exchange resin that is indicated for therapy of chronic hyperkalemia, but efficacy data for using it to treat acute hyperkalemia is lacking, and therefore it should be avoided or used cautiously in this scenario.

Metabolic Acidosis

The kidneys are critical in maintaining acid base balance as they are responsible for bicarbonate generation and conservation. Under normal physiologic conditions, the kidneys generate about 80 mEq of bicarbonate daily, which is critical for neutralizing acid loads. In addition, the kidney tubules must reabsorb approximately 4500 mmol of the bicarbonate that is filtered by the glomerulus daily [20]. Renal injury impairs the kidney's ability to perform these functions and results in the development of metabolic acidosis. In patients with CKD, the severity of metabolic acidosis is typically inversely associated with the level of GFR. Many patients will have mild to moderate levels of metabolic acidosis at baseline, and therapy with oral sodium bicarbonate is indicated when the serum CO_2 is less than 22 mmol/L. In the perioperative period, patients with CKD are particularly vulnerable to the development of hyperchloremic metabolic acidosis from sodium chloride infusion in the form of 0.45% and 0.9% saline infusion. This can lead to clinically significant degrees of metabolic acidosis which can lead to end organ dysfunction in the perioperative period. For this reason, balanced electrolyte solutions or other non-chloride-based solutions, such as sodium bicarbonate, should be preferred in patients with CKD and metabolic acidosis.

Preventive Strategies for Acute Kidney Injury in the Perioperative Period

The population of older patients undergoing surgery consists of an extremely heterogeneous group of individuals, ranging from the very healthy to the critically ill. The risk for AKI will vary significantly across this group depending on the underlying illness of the patient, the type of surgery they are undergoing, and what medications they are exposed to. The overall incidence of postoperative AKI has been estimated to be 1.2% [21]; however, this risk is much higher in certain at risk groups, such as those undergoing cardiac surgery, where the incidence of AKI has been reported to be as high as 50% [22].

Significant research efforts have focused on the diagnosis and treatment of postoperative AKI in recent years. Consensus criteria have been developed to standardize the diagnosis of postoperative AKI. The Kidney Disease Improving Global Outcomes (KDIGO) criteria define AKI as a 0.3 mg/dl (>26.5 mol/l) rise in serum creatinine from baseline within 48 h of surgery, or a 50% rise in serum creatinine from baseline within 7 days of surgery, or a decrease in urine output below 0.5 ml/kg/h for 6 h following surgery. In addition, efforts are ongoing to identify non-creatinine biomarkers to detect AKI earlier in patients undergoing surgery. These biomarkers include neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), interlukin-18 (IL-18), tissue inhibitor of metalloproteinases (TIMP-2), and insulin-like growth factor binding protein 7 (IGFBP-7). These agents have been most extensively studied in homogenous populations undergoing cardiac surgery, and data have demonstrated an association between elevated biomarker levels with AKI as well as nonrenal outcomes [23–26]. At this time these biomarkers are for the most part restricted to research use, and studies are ongoing to determine their role in routine clinical use to identify early onset of AKI before rises in serum creatinine occur, as well as differentiate functional causes of creatinine elevations from those that induce cellular injury.

Ischemic Kidney Injury

Acute tubular injury (ATI) secondary to ischemia is the most common cause of AKI in all hospitalized patients, and it accounts for 50% of cases of AKI in elderly hospitalized patients [27]. The aging process results in a reduction in renal plasma flow, a blunted ability to autoregulate blood flow within the kidneys, and poor renal reserve function in part due to reduced nephron number. These factors make older individuals more prone to developing ischemic ATI, especially in the perioperative period [28]. Data from animal models show that elevations in blood urea nitrogen and creatinine are more severe in older rats as compared to younger rats when exposed to similar degrees of ischemia, highlighting the increased vulnerability of aging kidneys [29]. In addition, there are impaired regenerative mechanisms in the aging kidney that result in a prolonged recovery period after ATI occurs [30].

Several strategies exist for preventing ischemic ATI in older patients undergoing surgery. It is critical to first identify those at high risk for perioperative AKI. Important variables for this include patient-related factors, operative characteristics, and pharmacologic exposures (Table 3). Since the kidneys receive about 20–25% of the blood flow from cardiac output, stable hemodynamics are a primary component to avoiding renal injury. Data have shown that the risk of AKI markedly rises with intraoperative mean arterial pressures (MAP) less than 60 mmHg [31]. To prevent renal ischemia, volume status should be closely monitored during the intraoperative period. Static parameters such as blood pressure, heart rate, pulse pressure, and peripheral arterial oxygenation are routinely used to guide fluid therapy. In high risk patients, the use of dynamic parameters of volume status, including transesophageal echocardiogram measured stroke volume, systolic pressure variation, and pulse pressure variation, may allow for earlier identification and correction of volume depletion, therefore reducing the risk of ATI. There is often a fine balance between volume resuscitating to achieve optimal cardiac output to prevent renal ischemia and giving too much fluid which puts the patient into overt volume overload. This is an important point, as overzealous fluid therapy resulting in volume overload can also contribute to AKI and impair renal recovery [32, 33]. Goal-directed volume therapies that aim to achieve a specific goal based on a hemodynamic parameter (e.g., giving 250 ml boluses of crystalloid solution when $>10\%$ declines in systolic blood pressure, stroke volume (as visualized by intraoperative transthoracic echocardiogram), or pule pressure occur during the intraoperative period) can lead to better renal outcomes by avoiding hypovolemia and hypervolemia in surgical patients [34]. These

Table 3 Factors associated with increased risk for perioperative acute kidney injury

Patient factors	Operative factors	Pharmacologic factors
Older age Male sex Underlying kidney disease Diabetes mellitus Infection Congestive heart failure	Emergency surgery Cardiac surgery Intra-abdominal surgery Prolonged duration of surgery Introperative bleeding Intraoperative hypotension	NSAIDs ACE inhibitors ARBs Antibiotics (aminoglycosides, penicillins, vancomycin) Calcineurin inhibitors Hydroxyethyl starch solutions Iodinated radiocontrast agents

NSAIDs nonsteroidal anti-inflammatory drugs, *ACE* angiotensin-converting enzyme inhibitor, *ARB* angiotensin receptor blocker strategies should therefore be favored over fixed volume therapies that are not guided by hemodynamic parameters.

Additional variables that may be important for renal protection against ischemic ATI in the older surgical patient include the choice of fluid composition used for volume management as well as the need for adjunctive vasopressor agents. Crystalloids, colloids, and blood products are all commonly used agents for replacing volume losses during surgery. Colloid solutions such as albumin are expensive and have not shown superiority over crystalloid solutions for volume resuscitation [35]; therefore, there is no renal benefit to routinely using albumin in the perioperative period. In general, blood transfusions should be used when significant intraoperative blood loss occurs. This will improve oxygen delivery to the kidneys and potentially improve renal outcomes in situations with significant hemorrhage. On the other hand, hydroxyethyl starch solutions should be avoided in surgical patients given its association with AKI and increased mortality [36, 37]. For individuals with hypotension refractory to volume resuscitation, vasopressors should be added to support blood pressure and renal hemodynamics. Although norepinephrine does result in renal vasoconstriction, this agent will have a net benefit of raising the MAP and favoring improved renal perfusion and oxygenation in patients with hypotension [38]. Therefore, this agent is an acceptable first-line vasoactive agent for addressing intraoperative vasodilatory shock. Overall, clinicians must remain diligent about optimizing hemodynamics before, during, and after surgery in older individuals. Close monitoring, thoughtful replacement strategies, and adjunctive vasopressor agents are important to reducing the risk for ischemic ATI in this population.

Avoiding Nephrotoxins

A number of medications can cause nephrotoxic ATI in the perioperative period. The most important culprits are nonsteroidal anti-inflammatory drugs (NSAIDS), antibiotics, and iodinated contrast exposure. Although NSAIDs are widely used in the general population and are readily available, these agents need to be thoughtfully considered when administered to older surgical patients. Renal prostaglandin production results in afferent arteriole dilatation that is essential for maintaining GFR in settings of reduced renal plasma flow. Use of NSAIDS (including cyclo-oxygenase-2 inhibitors) inhibits prostaglandin production and therefore impairs vasodilatory responses in the kidney. This results in ATI in high-risk subjects, especially those who develop hypotension or who are on RAAS blocking agents. This is especially problematic in the older surgical patient given the wide fluctuations in blood pressure that can occur during the perioperative period and the extensive use of RAAS blocking agents in this population. Thus pain management in the perioperative period needs to be approached thoughtfully. Tylenol or opiates can be used as alternatives to NSAIDs in those at risk for ATI.

Antimicrobial drugs are another class of medications that older surgical patients are commonly exposed to and that can cause AKI. These agents often reach high concentrations in the renal tubules as they pass down the nephron, and this magnifies their toxic potential to adjacent renal tubular epithelial cells and can result in ATI. Common culprits responsible for this include aminogylcosides, vancomycin, and pentamadine. Another mechanism of renal injury commonly seen with many antibacterial drugs is acute interstitial nephritis (AIN). AIN is a viscous inflammatory response in the renal parenchyma and tubular cells that is triggered by exposure to various agents. Penicillins, cephalosporins, and sulfa drugs are some of the most common medications that cause this. It is important that these agents are carefully administered to older surgical patients. Drug levels may need to be frequently monitored when gentamycin or vancomycin is being given, as their potential for injury is directly related to the plasma concentration level. In cases in which AKI is suspected from an antimicrobial medication, the offending agent should be discontinued immediately, and in some situations glucocorticoids are recommended.

Contrast-induced nephropathy (CIN) is another common cause of usually reversible AKI in the hospital setting. It typically manifests as a rise in serum creatinine within 1–3 days following iodinated contrast exposure. The incidence of CIN has decreased dramatically in recent years given the near ubiquitous use of low osmolar contrast agents as opposed to high osmolar contrast agents that were previously used [39]. The risk is highest in those with underlying kidney disease, diabetic nephropathy, high contrast volume exposures, and congestive heart failure [40–42]. In addition, older individuals, especially those over the age of 70, are at higher risk than younger individuals [43]. The exact pathophysiology is not completely understood, but evidence from animal studies suggests that ATI results from contrast-induced vasoconstriction and direct tubular cell injury [44, 45]. The best way to prevent CIN is to avoid contrast altogether. For this reason, careful consideration of the risks and benefits of contrast exposure should be made. Alternatives such as noncontrast computed tomography, ultrasound, and magnetic resonance imaging should be considered.

In those patients at high risk for CIN who must undergo contrast studies to obtain critical diagnostic information or to undergo important interventions, prophylactic measures should be employed. Pre- and post-contrast volume expansion with isotonic saline is one of the central measures to CIN prevention [46, 47]. A common protocol is to give 1 ml/kg/h for 12 h pre- and 12 h post-procedure. Diuretics typically should be held prior to the procedure as they negate the efforts for volume expansion. Newer studies have investigated novel methods to carefully guide fluid repletion. This includes using left ventricular end diastolic pressures to guide the rate of fluid administration post cardiac catheterization as well as the RenalGuard system in which volume replacement is closely matched to urine production from forced diuresis with furosemide [48, 49]. Older, small studies showed mixed benefits regarding the use of *N*-acetylcysteine for preventing CIN; however, a recent, large randomized control trial in which low osmolar contrast use was the standard of care has shown no overall benefit with this medication [50]. For this reason, many clinicians no longer routinely recommend *N*-acetylcysteine for preventing CIN.

Surgery in the Older Adult Patient with End-Stage Renal Disease on Dialysis

Timing of Dialysis Prior to Surgery

Patients with end-stage kidney disease on dialysis have a high burden of comorbidities; therefore, surgical procedures, both elective and nonelective, are common in this population. Not surprisingly, studies have shown that this group is at an increased risk for postoperative complications as compared to those not on dialysis [51, 52]. This includes a higher perioperative mortality. In a study of 1157 dialysis patients undergoing abdominal aortic aneurysm repair, the 30 day mortality for open repair was 16% and for endovascular repair it was 10% [53]. This compares to 30 day mortality rates of 1–5% for open repair and 1% for endovascular repair of abdominal aortic aneurysms in the nondialysis population [54]. The factors that contribute to higher perioperative morbidity and mortality in dialysis patients include increased risks for cardiovascular events, high rates of electrolyte abnormalities (namely hyperkalemia), frequent hemodynamic instability, and increased bleeding complications. There is sparse published data on how to best manage surgical risk in dialysis patients; however, most clinicians accept that a thoughtful approach is needed for presurgical dialysis treatments. For hemodialysis patients, it is common practice to perform dialysis the day prior to surgery. This means that Monday surgeries are not ideal, as it is standard practice for the vast majority of dialysis units to be closed on Sundays for routine treatments. Some situations may call for performing dialysis immediately before going to surgery (e.g., if moderate to severe hyperkalemia is present), but this is not necessary in most cases. For patients on peritoneal dialysis, there is variability in practice. Some nephrologists will increase the amount of dialysis by adding an extra exchange each day for 5–7 days prior to surgery, while other nephrologists will not make any changes to the peritoneal dialysis prescription prior to surgery. An important factor that may guide one strategy over the other for patients is the likelihood of not being able to perform peritoneal dialysis in the days following surgery. This situation arises in patients who are having intra-abdominal surgeries, such as catheter repositioning or hernia repairs, as the integrity of the peritoneum is disrupted and dialysis must be held until it heals. In such situations, increasing the number of daily exchanges prior to surgery will result in extra clearance and allow for the patient to better tolerate missing dialysis in the postoperative period for a limited time.

Protecting Vascular Access in Hemodialysis Patients

ESRD patients that undergo dialysis with a catheter have increased risk of mortality compared to patients that undergo dialysis with an arteriovenous access, either a fistula or graft [55, 56]. For this reason, it is critical that clinicians remain diligent about protecting the patency of vascular accesses in dialysis patients. There is particular concern in the older patient on dialysis as these patients are particularly prone to arteriovenous access failure [57]. Efforts to protect arteriovenous fistulas and grafts include performing needle sticks and blood pressure measurements only in the contralateral arm to the vascular access. In addition, the limb needs to be free of restraints to avoid occlusive pressure that may cause thrombosis of the access. Hypotension in the intra- or postoperative period can also cause thrombosis of the access, so this adds further emphasis for the need to carefully monitor hemodynamics and to promptly intervene if patients develop hypotension or hypovolemia. It is also important to examine the access frequently, in those patients who lack a thrill or bruit over the arteriovenous access, timely interventions for access declotting may need to be arranged.

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Traumatic Injury in Older Adults

17

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Contents

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Abstract

As the elderly population continues to grow, so does the number of injured older adults. The most common mechanisms of trauma in persons over the age of 65 include falls, motor vehicle collisions, and suicide. Physiologic changes associated with aging impair stress response to injury in the elderly. Regardless of mechanism or severity of injury, geriatric trauma patients consequently have increased morbidity and mortality. They also present unique challenges with respect to triage in the field, disposition postdischarge, and overall burden of healthcare costs. A full appreciation of the subtle differences surrounding geriatric trauma care is required in order to optimize treatment for these individuals and aim to return them to baseline functional status. Ethical considerations including patient wishes, goals of care, and end-of-life support are also highly relevant, even in the acute care setting.

Keywords

Geriatric trauma · Injury in the elderly · Falls · Geriatric critical care · Rehabilitation after injury

Introduction: Epidemiology of Injury in the Elderly

Injury is currently the leading cause of death for those under the age of 44, and the seventh leading cause of death in persons over age 65 [1] (Table 1). However, while some consider trauma to be a disease of the young, deaths associated with fall-related injuries (largely comprised of older adults) exceeds deaths due to motor vehicle traffic collisions or firearm-related injuries (Table 2). This highlights the fact that trauma is every bit a disease of the elderly. In fact, in 2013, approximately 6 million adults 65 and older were seen in US emergency departments for injuries, comprising 17% of all visits and costing over 30$ billion in medical care [2]. Furthermore, older adults are more likely than younger adults to be admitted to hospital for their injuries (24% age 65 and older admitted vs. 11% of those age 45–64) [2]. This is due in part to comorbid diseases and existing disabilities. Most importantly, older adults are consistently at a higher risk for death after injury, regardless of injury severity or mechanism of injury [3]. Decreased physical reserve, preexisting comorbidities, and a lack of provider understanding of the healthcare needs of older patients may all contribute to this finding.

This change in trends for trauma-related mortality is associated with changing population demographics. The elderly constitute one of the fastest growing segments of the US population. In 2013, the number of people 65 and older was 44.7 million, representing an increase of 25% over the previous 10 years [4]. By the year 2050, the number of persons over age 65 is projected to nearly double (83.7 million) [4]. The increase in the number of older adults is due in part to improved life expectancy. In 2013, the number of people in

Table 1 Leading causes of death in the United States, 2014

Ranking	Cause of death, all ages (# of deaths)	Causes of death, ages 65+ (# of deaths)
1	Heart disease (614,348)	Heart disease (489,722)
2	Malignant neoplasms (591,699)	Malignant neoplasms (413,885)
3	Chronic low respiratory disease (147,101)	Chronic low respiratory disease (124,693)
4	Unintentional injury (136,063)	Cerebrovascular disease (113,308)
5	Cerebrovascular disease (133,103)	Alzheimer's disease (92,604)
6	Alzheimer's disease (93,541)	Diabetes mellitus (54,161)
7	Diabetes mellitus (76,488)	Unintentional injury (48,295)

Data Source: National Vital Statistics System, National Center for Health Statistics, CDC, 2014 data

Table 2 Leading causes of injury deaths in the United States, 2014

Ranking	Cause of injury death, all ages (# of deaths)	Causes of injury death, ages 65+ (# of deaths)
1	Poisoning (42,032)	Falls (27,044)
2	Motor vehicle traffic (33,736)	Motor vehicle traffic (6,373)
3	Falls (31,959)	Suicide by firearm (5,367)
4	Suicide by firearm (21,334)	Unspecified (4,590)
5	Suicide by suffocation (11,407)	Suicide by suffocation (3,692)
6	Homicide by firearm (10,945)	Poisoning (1,993)
7	Suicide by poisoning (6,808)	Adverse effects (1,554)

Data Source: National Vital Statistics System, National Center for Health Statistics, CDC, 2014 data

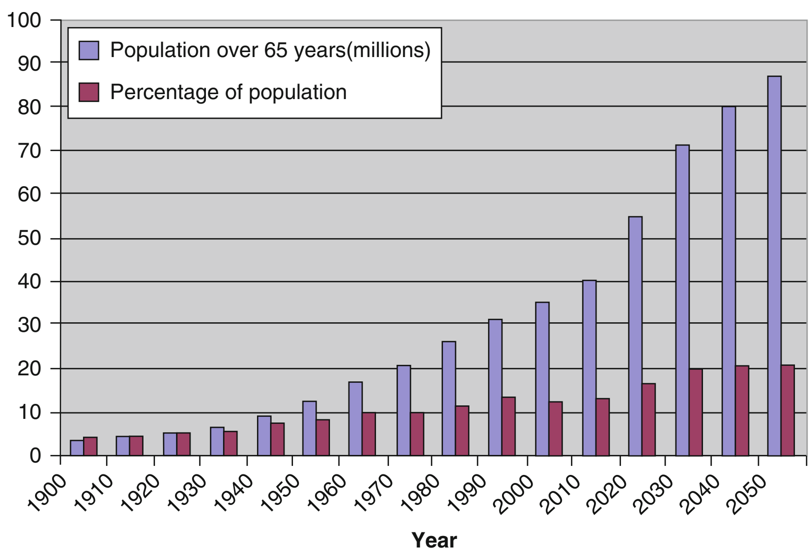

Fig. 1 Population growth over time (From original chapter)

the USA over age 85 was 6 million but is projected to be 14.6 million by 2040 [4] (see Fig. 1).

The most common mechanism of injury for older adults is fall-related injuries. An elderly person's risk of falling at least once in a given year is estimated to be as high as 27% [5]. Motor vehicle traffic collisions are the second most common cause of injury-related elder mortality. While blunt trauma is far more common than penetrating injury in the elderly, suicide by firearm is now the third-leading cause of injury-related mortality in older adults. Knowledge of the injury patterns common in older adults can help guide physicians caring for these patients. For example, physicians should consider social isolation, depression, and elder abuse in addition to risk for falls and safety behind the wheel.

The Impact of Altered Physiology and Comorbid Disease

Senescence affects all organ systems but does so to varying degrees and at variable times during the aging process. Lifestyle changes and advances in the treatment of debilitating medical conditions have enabled elders to live longer, healthier, and more active lives.

Accompanying this more active lifestyle is an increased risk for injury, including falls and motor vehicle crashes [6].

Despite overall improvement in quality of life moving into older age, functional decline is inevitable in all organs. There are many consequences to this process as it relates to injury. For example, increasing age can make assessing injury more challenging given the difficulty of understanding how dysfunction may relate to injury vs. underlying comorbid diseases. By age 75, over two-thirds of injured patients have one or more chronic medical conditions [7]. In those who reach the age of 95 years, the percentage is 82%.

Preexisting medical conditions also limit the ability of older persons to tolerate the increased physiologic demands associated with injury. Resting organ function often is preserved, but the ability to augment performance in response to stress is greatly compromised. Once injured, the elderly may have an increased rate of complications from preexisting conditions such as cardiovascular or liver disease, diabetes, chronic obstructive pulmonary disease, and renal insufficiency.

Finally, comorbid conditions may also have played a role in the risk for and severity of injury. An example of this is a patient with a cardiac condition on anticoagulants and beta blockers who becomes orthostatic and falls from standing, sustaining significant traumatic brain injury due to the acquired coagulopathy. It is imperative for an accurate history to be sought regarding the etiology of injury at the time of initial patient evaluation in order to accurately guide management and for secondary prevention. Treatment of comorbid illness will often be necessary in addition to that of the injury.

Changes in Physiology by Organ System

Central Nervous System

As we age, even the nondiseased brain experiences a slow, selective loss of brain parenchyma. Age-related brain atrophy between the 5th and 10th decade causes a reduction of approximately 15–20% of the cortical brain volume [8]. These findings are accelerated in patients with cognitive impairment [9]. For instance, patients with Alzheimer's disease have an additional 14–20% greater reduction in total cortical and forebrain brain volumes than expected during normal aging [8]. Another change is remodeling in cerebral vasculature. By age 45, 50% of vessels in the brain show intimal thickening [9]. Arterial wall stiffening leads to a decline in cerebrovascular autoregulation with age, making the brain more susceptible to injury during periods of systemic hypotension seen in trauma [10]. As a result of all of these changes, difficulties in cognition and memory are common in the elderly.

These changes have other implications in the setting of trauma. For one, determining mental status using tool such as the Glasgow Coma Scale (GCS) can be difficult. So can be distinguishing new neurologic findings from a patient's baseline neurologic function. Hearing loss and visual difficulty further complicate matters. Family members will often be the best source of information to determine if an elderly patient is at baseline mental status. Once admitted to the hospital, the elderly patient may experience episodes of delirium, agitation, and confusion, even in the absence of injury. This can further confound clinical assessments of a patient's recovery after injury.

Another consequence of decreasing brain parenchyma is an increase in the risk for extra-axial traumatic brain hemorrhage. As brain volume decreases, the dura remains adhered to the skull, causing an increase in the distance between the inner table of the skull and the outer surface of the brain. This lengthening causes the bridging veins to be pulled taut, thus rendering them more likely to sustain a shear-type injury during rotational stress, such as deceleration force in a motor-vehicle crash. Subdural hematomas are three times more common in the elderly.

In addition to cerebral-related injuries, changes in the cervical spine pose additional risks to the central nervous system. Degenerative disease of the bony cervical spine narrows the central spinal canal. Kato and colleagues demonstrated that these degenerative changes and spinal stenosis represent important risk factors for cervical spine injuries [11]. In addition, degenerative changes can limit mobility and strength.

Cardiovascular

With increasing age, structural and functional changes in the cardiovascular system alter the elderly patient's response to physiologic stress. Severely injured and critically ill patients over the age of 65 have a 32% incidence of depressed cardiac index and ejection fraction [12]. Cardiac imaging including MRI pulsed tissue Doppler echocardiography in the elderly confirm a limited ability of the heart to compensate in the setting of stress [13]. A dropping cardiac output may not be readily apparent given the fact that increasingly sclerotic arteries result in high blood pressure. The high blood pressure also increases afterload, resulting in hypertrophic remodeling of the left ventricle [14]. Similar stiffening of the right heart may be seen through increases in pulmonary arterial systolic pressures and vascular resistance. Diastolic relaxation and filling volumes can also be affected, predisposing the coronary vessels to alterations in perfusion. Due to worsening diastolic function, the atria enlarge to augment ventricular diastolic filling (the atrial "kick"). Patients in atrial fibrillation lose this kick and are more susceptible to hemodynamic compromise.

The aged heart also fails to respond appropriately to heightened endogenous or exogenous catecholamines. There is alteration in sino-atrial node conduction and decrease in beta-adrenergic response, lowering both intrinsic and maximal heart rates [15]. Maximum heart rate is reduced by about 30% between the age of 20 and 85 [16].

This decrease in chronotropy is often compounded in older adults taking beta-blockers, further masking physiologic response to hypotension or shock in injured patients, and predisposing to syncope.

As a result of these changes, older adults may present with a "normal" blood pressure and/or heart rate despite the fact they are in shock. Scalea et al. have demonstrated that as many as 50% of those who had "normal" blood pressure in fact had evidence of occult cardiogenic shock and a subsequent poor outcome [17]. In light of this, some have proposed the definition of hypotension in trauma for older adults be 10 points higher in older adults compared to younger adults [18].

Arrhythmias are another cardiac abnormality experienced frequently in the elderly. Arrhythmias can be elicited or exacerbated in response to shock, fluid, and electrolyte shifts and the mechanical atrial stretch from resuscitation [19]. One study specific to trauma patients demonstrated a 6% incidence of new onset atrial fibrillation in patients over 55 years, which was also an independent risk factor for mortality [20].

Coronary artery disease [21] is common in the elderly and may complicate the care for these patients. Wilson described a 5.6% occurrence of symptomatic CAD in a series of trauma patients over the age of 65. For those over 75 years of age, the incidence of symptomatic CAD was 12.9% [22]. In addition, CAD (especially right-sided coronary lesions) causes loss of autoregulation of coronary blood flow. Thus, as myocardial activity increases, the elderly can experience either occult or obvious cardiac ischemia with resultant pump failure.

Pulmonary

Decreases in respiratory function and reserve in the elderly are the result of changes in the chest wall and the lungs. After the age of 30, a 4% per decade decrease in alveolar surface area results in a negative effect on gas exchange as well as forced expiratory flow. Alveolar ducts enlarge, and the alveoli become flatter and shallower, reducing the area for gas exchange and leading to ventilation perfusion mismatch.

Decreases in chest wall compliance from anatomical changes such as kyphosis and a decline in respiratory muscle strength from muscle fiber atrophy lead to as much as 50% loss in maximal inspiratory and expiratory force [23]. Accessory muscles help to compensate for the decline in respiratory muscle atrophy. Lung elastance also progressively declines, causing a collapse of small airways and uneven alveolar ventilation (Tables 3 and 4).

Additionally, responses to hypoxia and hypercapnia are decreased. The aging mucociliary function worsens, with fewer cilia per square centimeter. Secretion clearance is also impaired. This, in addition to poor dentition, increased oropharyngeal colonization, swallow dysfunction, and a decreased lower esophageal sphincter tone, predisposes the elderly to aspiration pneumonia and pulmonary infection. Gram-negative organisms predominate in the oral flora, increasing the risk of pulmonary infection from aspiration.

Osteopenia of the thoracic cage may increase the rate of pulmonary contusions, rib fractures, and pneumo- and hemopneumothoraces as the bony thorax cannot absorb transmitted kinetic energy. In those with a flail chest, age has been shown to be the strongest predictor of poor outcome and is directly proportional to mortality [24]. As the number of rib fractures increases, so does the incidence of pneumonia and death [25], [26]. Mortality increases by 19% and the risk of pneumonia by 27% for each additional rib fracture in patients over the age of 65 (Fig. 2) [25]. Pain control is critical to allow deep breathing and prevent pulmonary complications.

Table 3 Factors predisposing the elderly to injury

Reduced ability to react to environmental hazards	Reduced hearing Presbyopia Degenerative joint disease Vertigo
Elderly placed in potentially dangerous situations	Dementia Cardiovascular accident Coronary artery disease
Increased consequences of injury	Osteoporosis Cirrhosis Chronic obstructive pulmonary disease Coronary artery disease Disabling central nervous system disorders

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Renal Disease

A number of structural changes occur in the kidney with age. Decrease in renal tubular length and thickening of basement membranes, as well as interstitial fibrosis and atherosclerosis of capillary beds, lead to ineffective secretion and reabsorption abilities of the aging kidney

Table 4 Physiologic changes associated with the elderly by organ system

Organ system	Changes associated with aging
Respiratory	Increased alveolar-arterial gradient, increased ventilation/perfusion mismatch, diminished ventilatory response to hypercapnea and hypoxemia, decreased lung and chest wall elasticity
Cardiovascular	Stiffened, calcified arterial vasculature, increased systolic pressure, increased afterload, widened pulse pressure, hypertension, atrial enlargement, lowered intrinsic and maximal heart rate, decreased coronary perfusion
Neurologic	Slow loss of brain parenchyma, intimal thickening of cerebral vasculature, susceptibility to cognitive disorders
Gastrointestinal and genitourinary	Decreased pharyngeal and lower esophageal tone, decreased glomerular filtration rate, decreased muscle mass, slower renal and hepatic clearance of drugs
Immunologic	Reduced T and B cell antibodies, impaired neutrophil function
Muscoloskeletal	Increased risk of osteopenia and osteoporosis, fractures secondary to falls

Original table

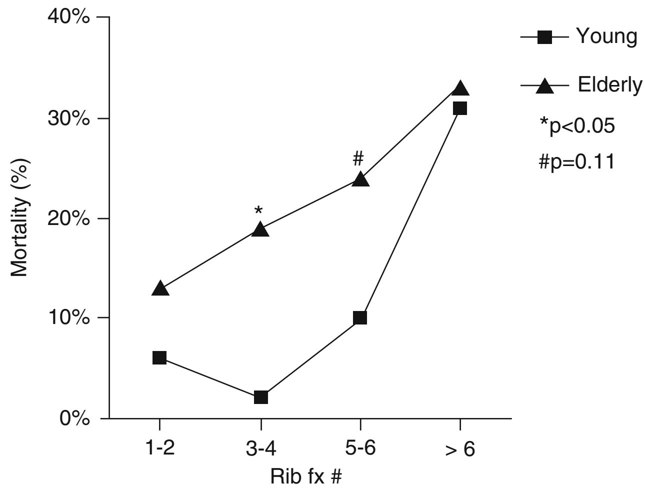

Fig. 2 Relationship between mortality and number of rib fractures (Reprinted with permission from Bulger et al. [24])

[27]. Between the age of 25 and 85, 40% of the nephrons become sclerotic and there is a decrease in renal mass, from renal cortical loss [28]. By age 80, the glomerular filtration rate (GFR) has decreased approximately 45%, but serum creatinine remains the same due to concomitant muscle mass loss [23]. Thus, serum creatinine for a given level of renal function is falsely low.

The lower GFR causes a diminished ability to concentrate urine in the aging kidney. A concomitant decrease in response to aldosterone and antidiuretic hormone further prevents the kidney from producing concentrated urine. Furthermore, diuretics prevent the aging kidney from concentrating the urine and make urine output a less reliable marker for renal perfusion in the elderly.

Once injured, the elderly who have renal insufficiency or failure may have additional problems. The platelet dysfunction commonly seen with renal failure may lead to prolonged bleeding even after minor trauma. Electrolyte disorders, most notably hyponatremia, hypo- or hyperkalemia, hypomagnesemia, and hypocalcemia, may cause dysfunctional neural transmission, cardiac dysrhythmias, seizures, mental confusion, muscular weakness, or syncope.

Drugs used to evaluate and treat the older trauma victim may further impair renal function. Extensive imaging with iodinated contrast may damage already impaired renal parenchymal and tubular system and lead to contrast-mediated nephropathy. Nonsteroidal anti-inflammatory drugs (NSAIDs) are frequently used to treat pain and avoid the sedative effects of narcotics, but use of these agents is associated with a significant risk of interstitial nephritis. Life-threatening infections with gram-negative organisms may require aminoglycosides, but such therapy may induce renal dysfunction despite seemingly acceptable drug levels. Despite renal replacement therapies, acute renal failure in trauma patients results in significantly increased mortality rate.

Musculoskeletal

Degenerative joint disease is common in the elderly and results in limited range of motion around major axial joints and puts the individual at high risk of injury. Lean body mass decreases by 4% every 10 years after the age of 25 and 10% every 10 years after the age of 50 [27]. Osteoporosis, with loss of up to 60% of trabecular bone and 35% of cortical bone, has been cited as a major factor contributing to the high incidence of fractures seen in elderly trauma patients [29].

Aging also influences the site of cervical spine fractures. In younger patients, the lower cervical spine region is more mobile and is the location of many cervical spine injuries. However, in the elderly, the lower cervical spine is less mobile due to degenerative changes, and the more mobile region of C1 and C2 is more often the site of injuries in the elderly [30].

Gastrointestinal

There is decreased hepatic function in the elderly due to a 40% hepatic mass loss by the age of 80 [23]. Preexisting liver dysfunction increases mortality after trauma [27]. Hepatic disease has the strongest effect on trauma mortality of all preexisting medical conditions and is associated with an increased mortality in elderly trauma patients with less severe injuries. Morris et al. demonstrated that cirrhosis, in trauma patients of any age, increased the risk of dying, with an odds ratio of 4.5 [31].

The elderly trauma patients are at an increased risk of intestinal infarction. Acute hemorrhage, neurogenic shock, or cardiac dysfunction from acute injury can all result in low flow states. In the elderly with underlying vascular calcification or mural thrombus, any decrease in flow can cause significant compromise to the bowel and result in intestinal ischemia.

Metabolic/Endocrine

By age 80, the elderly have lost almost 40% of their lean muscle mass [23]. During muscle breakdown for gluconeogenesis, critically ill patients lose a significant amount of muscle mass. As the elderly start with less muscle mass, the proportion of loss is greater. Thus after injury, the elderly quickly become severely malnourished, and nutritional support should begin early. Protein-energy malnutrition occurs in approximately 70% of the hospitalized elderly. A Cochrane review on nutritional supplementation in the elderly suggested that early nutrition reduced unfavorable outcomes, long-term complications, and days spent in rehabilitation [32].

The most notable endocrinopathy of aging is glucose intolerance. This hyperglycemia is a result of both decreased secretion of insulin and increased resistance to insulin. Increasing age is associated with an increase in serum glucose, but not an increase in insulin after mild or moderate trauma. There is also a decrease in thyroid function and responsiveness to metabolic stress in the elderly. Aging cause fibrosis of the thyroid gland with a decrease in the amount of T3 released, resulting in a lower basal metabolic rate. The elderly also lose their natural responses to cold and are at a higher risk of hypothermia. Warming, therefore, should be implemented as quickly as possible after injury.

Immunology

The aging adult experiences changes in both innate and adaptive immunity, thereby predisposing them to infections. These changes include impaired neutrophil function, a decline in T cells, as well as reduced B-cell antibody generation [33]. Conversely, there are elevations in levels of circulating inflammatory cytokines after relatively minor physiologic insult. A pertinent clinical example of this is seen in rib fractures in the elderly, where there is an increased risk of pneumonia and subsequent increase in mortality rate for hospitalized patients.

Common Injury Patterns in the Elderly

Falls

Falls are the most common injury in the elderly. The National Council on Aging states that one-third of Americans over age 65 fall each year [34]. In population-based analyses, fall-related injuries comprise over 50% of all injuries for individuals age 55 or older, and up to 80% of all injuries in the population over age 80. Most falls occur in or about the home, and most tend to be ground-level falls, while falls from great heights are uncommon. Between 30 and 40% of the population over 65 years of age who live in the community sustain a fall each year [35]. This is higher for persons living in long-term care facilities. Fractures occur in 4–6%, 25% being hip fractures, while other major injuries requiring hospitalization occur in an additional 2–10%. Elderly women are no more likely to fall, but sustain serious injury, usually fractures, more commonly than men. Men incur more CNS injuries and have higher mortality following falls. This may be from higher risk-taking and underreporting of less severe fall injuries in men. Inability to get up after a fall is common. Prolonged down time can cause decubitus ulcers, dehydration, and even rhabdomyolysis.

The elderly have numerous risk factors for falls. Debilitating chronic diseases such as Parkinson's, stroke, arthritis, dementia, and anemia are more prevalent in the population of elderly who sustain falls. Among the other factors are older age, Caucasian race, history of previous falls, polypharmacy (especially psychotropic agents, diltiazem, laxatives, and diuretics), dependence for activities of daily living, low body mass and impaired mobility, muscle strength, gait, balance, vision, hearing, and cognition. These factors have all been correlated with an increased risk of falls and fall-related injury. The role of exercise as a risk factor is not clear. Exercise may lead to increased coordination and strength. While some studies have shown significant decreases in the incidence of falls, exercise also increases the exposure of the elderly to possible fall scenarios.

Falls among the elderly result from complex interactions of structural and physiologic disabilities, as well as environmental factors. The consequences of a fall depend on such factors as the kinetic energy generated during the fall as well as the ability of the body structures to absorb and the fall surface to accept the energy. In addition, the protective responses, the garments of the faller, and the direction and body location of the impact will affect the outcome of the fall. Functional consequences of the aging process along with an alteration in cognition may lead to increased risk-taking. Lack of appreciation of their limitations also predisposes the elderly to falls. Loss of muscle mass and changes in body composition result in decreased strength. Combined with a limited range of motion due to degenerative joint diseases, the elderly are less able to absorb the kinetic energy during a fall. Thus, many falls that are categorized as accidents are truly interactions between identifiable environmental hazards and increased individual susceptibility to those hazards from accumulated effects of age and disease [35]. Therefore, management of the elderly fall victim must include an investigation into the cause of the fall, which can frequently be determined from a thorough history.

The extent of morbidity and mortality related to falls in the elderly is probably better captured when including discharge patterns from both hospitals and skilled nursing facilities (SNFs), as many elderly patients either have a prolonged recovery or progress to death in a SNF after ground level falls [36]. This reflects a "deferred mortality" associated with falls in older adults, as those who ultimately die do so after discharge but within 3 months.

The economic impact of falls in the elderly is huge. Direct medical costs totaled $616.5 million for fatal and $30.3 billion for nonfatal injuries in 2012 and rose to $637.5 million and $31.3 billion, respectively, in 2015. Fall incidence as well as total cost increased with age and were higher among women [37].

Motor Vehicle Collision

Motor vehicle collisions (MVC) are the second most common mechanism of injury in those 65 years of age and older. In 2012, there were 5,560 people age 65 and older killed and 214,000 injured in motor vehicle traffic crashes [38]. These older individuals comprise 17% of all traffic fatalities and 9% of all people injured in traffic crashes that year. Compared to the previous year, fatalities increased by 3% and injuries increased by 16%. Older drivers who are hospitalized after an MVC have significantly higher mortality rates, longer hospital stays, and are less likely to be discharged directly to their homes [39]. There is a greater frequency of intracranial hemorrhage and chest injury in the elder population, which also contributes to poor outcomes.

Elderly drivers appear to have lower crash rates compared with younger drivers, but they drive less often. When normalized for the number of miles driven, the >65 years group has the second highest crash rate after new drivers. The >85 years group has the highest per-mile-driven crash rate of all age groups. Reduced vision or hearing, impaired judgment, and reduced reaction times are well recognized as factors leading to

MVC in the elderly. Alcohol is less often involved in MVCs involving the elderly compared to younger drivers [40].

Pedestrian-Motor Vehicle Collision

The elderly are at risk to be involved in a pedestrian crash as a result of walking into oncoming vehicles, often due to confusion or impairment of visual or auditory acuity. Reduced gait speed of the elderly pedestrian may be inadequate to complete the crosswalk at time-controlled traffic intersections, leaving the elder in the street exposed to inattentive drivers. There is a demonstrated increased risk of pedestrian crashes and fatalities with increasing age [41].

Depression, Substance Abuse, and Suicide

Suicide is the third-leading cause of injury-related death for those 65 years of age and older [1]. Those over the age of 75 have the highest rate. The most common mechanisms of suicide in the elderly are by firearms, asphyxiation, or overdose. Only about 25% of the elderly who attempt suicide are actually successful. Risk factors for suicide in the elderly population include psychiatric disorders, especially depression; medical conditions, especially cancer or chronic lung disease; moderate to heavy alcohol use; and social isolation. Changes in behavior such as altering a will, new preoccupation with religion, or giving away life possessions may be warning signs of impending suicide.

There are approximately five million elderly suffering from depression, with higher rates in hospital settings [42]. In particular, up to 50% of nursing home residents may develop clinical depression within the first year of their stay [43]. Other risk factors for late-onset depression include social isolation, female sex, comorbid general medical conditions (in particular stroke, myocardial infarction and cancer), chronic pain, functional and cognitive impairment, and lower socioeconomic status.

Alterations in metabolism in the elderly require that particular attention be paid to the initiation and titration of antidepressant pharmacotherapy, which should be closely monitored in conjunction with a psychiatrist. SSRIs and mirtazipine are most commonly used for their safety profiles and efficacy. Electroconvulsive therapy ECT is a useful adjunct in patients refractory to medications or those with suicide risk, psychotic features, or Parkinson's disease. Psychotherapy is also effective in older patients.

Substance abuse, particularly alcoholism, is a rising problem in the elderly population. Nearly 15% of adults over age 65 consume more than the weekly recommended allowance of 7 drinks. Risk factors include loss of a spouse, depression, anxiety, disability or chronic pain, and prior history of alcohol use [44]. With age, the ability to metabolize alcohol is progressively impaired by a decrease in hepatic blood flow and enzymatic processing. Decreases in total body water and lean muscle mass also contribute to higher concentrations of blood alcohol per unit of alcohol consumed. Intoxication and withdrawal both carry an increased risk of delirium and impaired cognition in the elderly.

During the course of acute treatment of the elderly trauma patient, it is easy to overlook symptoms of depression or substance abuse. While stabilization of the patient takes priority, the clinician should also have a low threshold to screen for mood and substance disorders in patients presenting with repeated or suspicious falls or accidents. The surgical intensivist may use validated tools such as the Patient Health Questionnaire-2 and the Geriatric Depression Scale to screen surgical and trauma patients for signs of depression or dysthymia [45].

The American Geriatrics Society recommends routine questioning of elderly patients regarding the specifics of alcohol use, as well as incorporation of a modified version of the "CAGE" questionnaire to those with suspected trauma related to alcohol use [46]. In patients over 65, other forms of substance abuse involve polypharmacy, particularly with sedatives and hypnotics. These medication categories, as well as overuse of antidepressants and benzodiazepines, have been shown to significantly increase the risk of falls and traumatic injury in the elderly [47].

Burns

Deaths from burns are the eight most common cause of unintentional injury death in adults over age 65 [1]. In 2014, there were approximately 1151 fire/burn-related deaths in this age group. Diminished senses, impaired mentation, slower reaction time, reduced mobility, and bedridden states may decrease an elder's ability to identify fire and also to escape harm. Advances in burn care have improved mortality rates across all age groups including the elderly [48]. While long-term outlook for burn survivors is improving, the elderly still have a significantly higher morbidity and mortality rate for any size burn than their younger counterparts [49]. Overall mortality in those age 75 or older is between 45% and 60% [49, 50]. Risk factors are multifactorial, including premorbid conditions, decreased lean body mass, protein-energy malnutrition, decreased pulmonary reserve, and impaired response to infection. In addition to the standard management of burn victims, the burn victim may suffer hypoperfusion in the face of normal vital signs and adequate urine output. As older adults are more sensitive to large fluid shifts, a judicious approach to resuscitation is advised, titrating volume replacement calculations to physiologic parameters. Other pillars of modern burn care, including enteral nutrition, early wound closure, and aggressive rehabilitation, are also advised in the elderly, resulting in decreased length of hospitalization and decreased mortality. Early excision and grafting in the elderly yields fewer episodes of infection, resulting in a reduction in hospital stay and improved survival [48]. Long-term disability potential after discharge is greater in elderly burn patients, with fewer older adults returning home within a year of injury as compared to younger burn victims [51]. The management of burns in elderly patients remains a challenge from the clinical, rehabilitative, and psychosocial recovery process.

Elder Abuse

The US National Academy of Sciences defines elder abuse as: "(a) intentional actions that cause harm or create a serious risk of harm to a vulnerable elder by a caregiver or other person who stands in a trust relationship to the elder or (b) failure by a caregiver to satisfy the elder's basic needs or to protect the elder from harm" [52]. The abuse includes physical, psychological, sexual, and financial, as well as neglect. Such injuries can be subtle in their presentation compared with those from a physical assault.

Thomas estimated that the incidence of elder abuse ranges from 2% to 10% [53]. This number may underestimate the magnitude of the problem owing to the victim's reluctance to admit abuse for fear of loss of care, retribution from the abuser, or from being ashamed to be in an abusive relationship.

Risk factors should alert the healthcare provider to the diagnosis of abuse. Once suspicion is raised, the victim should be interviewed one-on-one to increase the likelihood of disclosure of the extent and details of the abuse. Victims may be embarrassed revealing such details to a group of health-care personnel. The details of the abuse should be documented completely in the medical record for the possibility of subsequent legal action. The physician who documents or suspects elder abuse is ethically obligated, and in most states legally bound, to report the case to an adult protective service agency.

The most important intervention is to protect the victim from danger. The victim may be reluctant to leave the care of their abuser because of ambivalence regardless of the perceived danger. Unless the victim lacks the cognitive skills to make informed decisions, individual liberty must not be compromised. The physician should interview the abuser in a nonconfrontational fashion to better understand the situation. The physician should acknowledge and empathize with the difficulty of shouldering the burden of elder care. Armed with this additional information, the physician is better prepared to intervene to break the abuse cycle.

Management of the Elderly Injured Patient

Triage

Triage for the geriatric patient should provide the appropriate intensity of medical care, taking into account factors including severity of injury, cost, availability, prognosis for functional recovery, and patient goals of care. This process begins in the prehospital setting when decisions must be made regarding the appropriate facility. The American College of Surgeons Committee on Trauma recommends that patients over the age of 55 years be considered for triage to a trauma center [54]. However, in reality, the elderly are the most undertriaged group [54]. A large multicenter study emphasized the importance of educating emergency medical services (EMS) personnel to recognize high-risk elderly trauma patients through an expanded set of triage guidelines [55].

Initial Management and Resuscitation

The first few minutes of resuscitation of the elderly trauma victims differs very little from that of younger patients. Early intubation in the multi-injured elderly trauma patient should be considered as it reduces the work of breathing and may avoid progressive respiratory failure and cardiovascular collapse. As the elderly have limited cardiovascular reserve, they are vulnerable to hypotension from induction agents, and reduced doses should be used. In addition, limited pulmonary reserve may make preoxygenation difficult, causing rapid desaturation during intubation.

A normal blood pressure for a younger patient may be a relative hypotension for an elderly patient with history of hypertension. Geriatric patients are more likely to present in shock than younger patients matched for trauma and ISS. Admission base deficit [56] levels correlate with mortality in the geriatric population, and the rate of serum lactate clearance after trauma correlates with survival [57].

Considerations for Specific Injuries in the Elderly

Head Injuries

In persons 55 years of age and older, more than 323,000 traumatic brain injuries (TBI) occur, the primary cause of which is falls [58]. Older age has been well recognized as an independent predictor of worse outcome after TBI, even with relatively minor head injuries. Older TBI patients also have been found to have longer length of stays, resulting in greater cost of care [59]. Large retrospective studies have shown that elderly patients with severe TBI (sustained Glasgow Coma Scale <9) have at least an 80% likelihood of death or major disability leading to placement in a long-term care facility [60].

As many as 73% of elderly TBI patients may have at least one comorbid condition as compared to only 29% of younger patients [61]. Treatment of some of these chronic conditions includes the use of aspirin and warfarin, which increases the risk of TBI in the elderly. Approximately 10% of the older patients with TBI are taking warfarin preinjury and this is associated with more severe TBI and a higher rate of mortality [62]. Urgent reversal of anticoagulation is advised, as the amount of bleeding is a major determinant of outcome. The Eastern Association for the Surgery of Trauma recommends that elderly patients taking warfarin presenting with intracranial hemorrhage should have their INR corrected (<1.6) within 2 h of admission [63]. Traditionally, fresh frozen plasma (FFP) has been used. However, large volumes of FFP are often required to fully reverse warfarin. This can cause pulmonary edema and volume overload in the elderly patient with compromised cardiac and/or renal function. Other alternatives include prothrombin complex concentrates [PCCs] as well as vitamin K and cryoprecipitate. A more complete and faster reversal time in patients on warfarin needing an emergent neurosurgical intervention using PCCs compared to FFP and vitamin K.

Hourly neurological exams, correction of coagulopathy, and repeat CT head every 6 h should be standard of care until clinical exam and radiologic findings stabilize. Even if the initial head CT scan shows no injury, the elderly patient on warfarin, with head trauma and a therapeutic INR, should be admitted and observed for a minimum of 12–24 h. A repeat CT scan should be done anytime for any change in the patient's neurologic exam.

There are several other management considerations in the elderly presenting with TBI. Well-validated practice guidelines regarding CT imaging in head trauma [NEXUS II, Canadian CT Head Rule] specifically excluded older populations from their studies. Brain atrophy allows for more space for intracranial blood to accumulate before causing symptoms, so clinicians should have a low threshold to image older patients. Intracranial pressure [ICP] monitoring and ensuring adequate cerebral perfusion pressure [CPP] are also altered because there is a decrease in the autoregulation mechanism in the elderly. Comorbidities may affect the responsiveness and perfusion needs of the cerebral vasculature in these patients, and guidelines for CPP management must be customized accordingly.

Spinal Injuries

Cervical fractures have a prevalence of 2–5% in patients older than 65 years, with low-energy falls being the most common mechanism [64]. Patients who are awake, alert, nonintoxicated, have no cervical tenderness, neurologic deficit, or distracting injury do not need further radiographic evaluation, regardless of age [65]. Although the three-view plain radiograph has been the traditional initial modality for cervical spine evaluation, many now use CT as the initial evaluation tool for cervical spine injury due to the high rate of missed injuries on plain films. If a neurological deficit is present, then magnetic resonance (MR) should be used to evaluate ligamentous and/or spinal cord injury. Clinicians should have a lower threshold to image the elderly with suspected cervical spine injury, given underlying risk factors such as cervical stenosis and degenerative osteoarthritis in this population. High cervical fractures, including odontoid fractures, are among the most common in the elderly. Cervical stabilization is the primary end point, be it with a cervical collar, halo, or operation.

Central cord syndrome (CCS), usually resulting from hyperextension, is more likely to occur in the elderly due to underlying cervical stenosis. Patients usually present with upper extremity motor weakness that is greater than lower extremity weakness, bladder dysfunction, and variable sensory loss below the level of injury. Younger patients with central cord syndrome typically regain independence in self-care of bladder and bowel function more frequently than elderly patients [66].

Thoracic Injuries

A number of studies have focused on rib fractures in the elderly and subsequent outcome. The elderly have a higher mortality from chest trauma as a result of the initial injury as well as secondary pulmonary insults. Major risk factors for mortality include age over 65 years, three or more rib fractures, or pre-existing cardiopulmonary disease. In 2000, Bulger et al. retrospectively evaluated patients over the age of 65 years with rib fractures compared to those younger than 65 [25]. Despite similar ISS and chest abbreviated injury score, the elderly fared significantly worse in all outcome measures. Morbidity and mortality increase as the number of rib fractures increased. With each additional fractured rib in patients over 65 years, mortality increases by 19% and the risk of pneumonia increases by 27% [25]. Close monitoring in a step-down or intensive care unit, appropriate pain control, aggressive pulmonary toilet, and early mobilization are all crucial in reducing complications in this patient population.

Traumatic blunt aortic injures (BAI) are often initially suspected by a widening of the mediastinum on a plain chest X-ray, and definitively diagnosed by CT angiography. Over the last 10 years, there has been a significant change in the management of BAI from the traditional, standard operative repair. Endovascular stent grafts were initially used for high-risk, multiply injured patients or those with comorbid disease, i.e., the elderly. However, many centers now use them as their initial treatment of choice for BAI. Nonoperative management, using aggressive blood pressure control (systolic <110), is successful in some high-risk elderly patients with small aortic tears [67].

Abdomen/Pelvis Injuries

Significant intra-abdominal injury occurs in approximately one-third of elderly patients with multisystem trauma. Although abdominal injury patterns are similar to the younger adult trauma population, abdominal wall laxity, alterations in pain fibers, and decrease in abdominal musculature may make the clinical abdominal exam more challenging in the elderly [27]. In addition, polypharmacy, dementia, or Alzheimer's disease can obscure the physical exam in the elderly, making the diagnosis of an intra-abdominal injury more difficult. As such, radiologic adjuncts may prove to be particularly helpful focused ultrasound is a reliable initial radiographic modality for evaluating for free fluid, but it cannot differentiate between a solid organ injury and a hollow viscous injury. CT scan can be used to evaluate a hemodynamically stable patient to identify the presence of intraabdominal injuries. IV contrast agent typically used to better identify vascular injuries, but can be problematic in the elderly for a number of reasons. Contrast-induced nephropathy can be as high as 25% in patients with preexisting renal dysfunction, diabetes, advanced age, and concurrent usage of nephrotoxic drugs. Patients at increased risk of contrast-induced nephropathy include those with a serum creatinine >1.5 mg/dL, or an estimated glomerular filtration rate [eGFR] <60 ml/1.73 m^2. Adequate volume expansion via isotonic intravenous fluids (isotonic bicarbonate or isotonic NaCl) pre- and post- procedure help minimize the risk of renal injury [68].

Nonoperative management of blunt splenic injuries has become standard of care, though there has been a change in thinking about how this applies to the elderly. Early studies showed a high failure rate for those over the age of 55 years. Recently, however, this has been challenged, and a number of studies have shown that age is not associated with increased failure rate [69] [70]. Thus, age over 55 years is no longer considered a relative contraindication to nonoperative management of splenic injuries.

Fractures

Overall, efforts to minimize fractures in the elderly should include fall-prevention programs and education around reducing osteoporosis risk. Fractures in the elderly can be due to force of impact from mechanical falls or other trauma, but the clinician must also consider the likelihood for the presence of a pathologic fracture from metastasis.

Hip fractures remain the most frequent cause of hospital admission after trauma in the elderly. Injuries can be intracapsular (femoral neck and head) or extracapsular (intertrochanteric and subtrochanteric). Unrevealing plain radiographs should be followed by a CT scan or MRI if clinical index of suspicion for fracture is high. In addition, factors associated with in-hospital death include sepsis, pneumonia, thromboembolism, and gastrointestinal disorders. The risk of dying after hip fracture is doubled in patients with cardiac disease, cancer, or cerebrovascular disease [71].

Complicated fracture-dislocation patterns in femoral neck fractures increase the risk of avascular necrosis due to the already tenuous blood supply to this area. While in younger patients, these injuries are usually secondary to a high-impact motor vehicle collision, similar patterns can be seen from a traumatic fall in the elderly.

Most hip fractures are treated surgically. Almost 40 years ago, Laskin et al. proposed a management scheme for intertrochanteric fractures in the elderly. This included early rigid fixation using compression hip screws to allow early mobilization and immediate weight bearing to assist with vigorous pulmonary toilet [72].The longer the elderly remain bedridden, the more likely they are to have complications, including atelectasis, pneumonia, need for mechanical ventilation, venous thrombosis, muscle atrophy, and skin breakdown, all leading to longer hospital stay and increase in mortality. Thus, early orthopedic consultation, fracture fixation, and physical therapy are warranted.

Pelvic fractures are also common in the elderly, including occult pelvic fractures of the pubic rami and sacral insufficiency fractures. A 2002 study by Henry et al. demonstrated that most elderly patients with pelvic fractures have lateral compression fractures, which are usually not associated with significant bleeding [73]. However, the authors found that the elderly are more likely than younger patients to have fracture-associated hemorrhage and require angiography. In addition, the outcome for older patients with pelvic fractures was significantly worse than for younger patients. Recognizing these differences in fracture and bleeding patterns in the elderly identifies those at high risk and helps guide resuscitation.

Rehabilitation and Disposition

The aim of rehabilitation is to restore an individual to his/her former functional environmental status or, alternatively, to maintain or maximize remaining function. Unlike younger patients in whom rehabilitative outcomes are more apt to be dramatic, the geriatric patient is likely to make subtle progress. The degree of independence the patient is able to attain can mean the difference between living at home and living in a long-term care facility. For many elders, maintaining functional independence is vitally important to having an acceptable quality of life. The physician caring for the injured elder must understand the importance of attaining or maintaining independence for their elderly patients and do whatever is necessary to achieve this. The elderly with chronic debilitating disease more frequently require rehabilitative services following trauma because of the limitations imposed by injury.

Multidisciplinary care of the trauma and critically ill geriatric patient is often required to facilitate the transition to home or a skilled nursing facility. Important considerations include whether the patient has the cognitive ability to execute his or her discharge instructions, and whether family and social supports are available.

There is an emerging body of evidence demonstrating that interventions addressing geriatric-specific conditions improve outcomes such as functional status, incidence of delirium, and hospital length of stay. Some hospitals incorporate care by geriatric trauma consultation teams (GTTs). Their involvement suggests improvements in pain management, medication counseling, advance care planning, and overall function prior to discharge. Similarly, the creation of geriatric trauma/ICU units shows reductions in length of stay and complication rates (urinary tract infections, respiratory failure, and pneumonia) [74]. As a quality improvement effort, the American College of Surgeons published a set of guidelines that can serve as checklist for surgeons [75]. By standardizing principles such as when to obtain geriatric consultation, medication management and delirium avoidance, the aim is to discharge geriatric trauma and ICU patients with better functional status, ADL performance, and lesser long-term morbidity.

Long-Term Outcome

It is generally accepted that both short-and long-term outcomes after injury are considerably worse in the elderly than in younger patients. Despite this, The Eastern Association for the Surgery of Trauma [EAST] practice guidelines recommend that age should not be used as a criterion for limiting care as with aggressive initial management because as many as 85% return to independent living [76]. Others have demonstrated somewhat less promising outcomes of the injured elderly. A study of 38,000 patients over the age of 65 demonstrated that 50% went home and that 25% were discharged to a skilled nursing facility [77]. Inaba et al. reported in a study of injured elderly that, at long-term follow-up, only 68% of patients were living independently as compared to before injury. Furthermore, an additional 20% required skilled home care [78].

Injury Prevention

The first step toward prevention of injury is to recognize the individuals who are most likely to suffer injuries, as well as the lifestyle factors contributing to injury. For active older adults, falls from a height or motor vehicle collisions are likely more common. In contrast, an inactive older adult may be at risk for falls from standing. As such, injury prevention efforts vary accordingly. Many of the factors that predispose the elderly to injury should be discovered on routine history taking in the elderly patient.

The most successful programs to date have been in fall prevention for frail elderly adults who experience a fall from their own height. These programs range from in-home safety inspections, exercise programs, gait training, and the use of devices such as hip protectors and other wearable technologies [79]. The American Geriatrics Society has published a clinical practice guideline that addresses the multifactorial nature of fall risk and prevention techniques including minimization of medications, exercise training, management of foot disorders, and modification of the home environment [80].

Similar prevention efforts directed toward identifying and reporting unfit drivers may help reduce rates of motor vehicle collisions. This includes persons with visual or hearing deficits, dementia, or disabling musculoskeletal disorders, and those using medications that decrease driving skills. In an effort to refresh skills and update traffic knowledge, the American Association of Retired Persons [AARP] and the National Retired Teachers Association have established driver education courses for adults over 55 years of age. Pedestrian accident-prevention programs can reduce fatal and serious injury occurrence through prolongation of traffic-light times to accommodate the decreased gait of the elderly, modifications of road and crosswalk signs, tighter speed-limit enforcement, and safety-education presentations at senior centers.

Decision-Making Capability

The process of informed consent and autonomous decision-making is often compromised in many trauma patients due to impaired cognition or life-threatening injuries. Older patients are particularly susceptible to alterations in mental status that would prevent them from making their own decisions regarding therapeutic interventions. The creation of advance directives or living will documents, as well as open communication with family members regarding goals-of-care wishes, are often helpful in guiding decisions when patients are not able to advocate for themselves.

In order for patients to make an informed decision, they must demonstrate an understanding of the diagnosis and proposed treatment plan, logically synthesize the information and be able to express a clear choice, with an understanding of how that choice will impact their lives. There are several validated assessment instruments at the clinician's disposal, including the MacArthur Competency Assessment Tool for Treatment [81] and the Assessment of Capacity for Everyday Decision-Making [82].

A patient who lacks capacity and does not advance directives in place requires a substitute decision-maker. Laws regarding the appointment of this individual vary by state; there are regions that seek out a next-of-kin, and others that select by ethics committee the person deemed most fit to act on behalf of the patient. Regardless of the differences in regulations, the role of the substitute decision-maker is to make decisions that would be most consistent with the patient's previously expressed wishes and best interest.

It is the physician's responsibility to provide realistic expectations regarding possible outcomes. If interventions such as CPR are clinically contraindicated by best professional judgment, the American Medical Association states that the physician may communicate the medical futility of certain interventions in the fatally ill and not deliver that intervention. The difficult nature of these conversations requires clear and ongoing communication, with a common ethical goal of acting in the patient's best interest.

End of Life/Withdrawal of Treatment

As injury is the fifth leading cause of death in adults over the age of 65, goals of care should be addressed early in the treatment of elderly trauma and surgical critically ill patients [6]. Documents such as advance directives or living wills are helpful in guiding the process, but not a substitute for clear and advance open communication between patients and their families, so as to guide care providers with respect to the patient's wishes. Despite every effort to avoid decision-making during acute decompensation or injury, trauma surgeons and surgical intensivists are frequently called upon to navigate these difficult conversations and must be adept at forming new, trustworthy therapeutic alliances with patients and their families.

Admission to a surgical intensive-care unit, and the aggressive interventions that accompany this, may not be consistent with the patient's best interest or their wishes. The discussion regarding end of life and withdrawal of care is often a multistep process. The decision not to perform cardiopulmonary resuscitation or to intubate is often the first decision that families or surrogates make. Often, it takes families some time to come to the reality that despite all medical advances, their loved will not survive. It is imperative to emphasize a clear and consistent message to all loved ones involved. Although there is a hierarchy of legal decision makers, having family members achieve cohesion on the direction of care can be invaluable in the coping process.

Early involvement of the palliative care team can help by providing resources and symptom management, as well as facilitate discussions between patients, families, and treating physicians without directing treatment to comfort only measures.

There are several models of palliative care available in most hospitals, and palliative care consultation may be appropriate for patients who: either has acute severe injury with poor prognosis or chronic and life-limiting critical illness, is greater than 80 years old, or for whom a specific medical intervention may be inconsistent with their desired goals of care.

If and when the decision is made by the family to withdraw treatment, the physician must ensure a smooth process. A patient-centered approach should be maintained at all times, whereby the patient and family's attitudes are respected. Some families may find closure from being present during the process of withdrawal of treatment. Adequate narcotics and sedatives help prevent any additional suffering. Turning off monitors and intravenous pumps and ensuring a quiet peaceful atmosphere for the patient and family enhances the family's experience.

Conclusion

With an increase in the number and lifespan of adults over the age of 65, care of the injured elderly has become an important component of the trauma surgeon's skill set. Resuscitation and specialized management of this patient population requires intimate knowledge of the numerous physiologic changes manifested in older adults. Furthermore, appropriate treatment decisions often call into balance consideration of goals of care and patient disposition. Early discussions with the patient, family, and decision-makers help to align expectations regarding expected treatment course and potential for recovery. With continuously expanding resources being made available, it is imperative to provide the best standard of care for geriatric trauma patients through a multidisciplinary approach.

Case Study

AB, a 78-year-old male, with past medical history of atrial fibrillation and hypertension, was a restrained driver involved in a motor-vehicle collision. The patient was t-boned on the driver side by a car traveling at approximately 50 miles/h. On arrival, he denies any loss of consciousness, complains of some left-sided hip pain, which is worse with movement. In addition, he complains of left-sided chest pain, which is worse with deep inspiration. He denies any abdominal pain or back pain.

Past medical history: atrial fibrillation, hypertension

Past surgical history: cholecystectomy

Medications: warfarin, aspirin, metoprolol, alendronate, and multivitamin

Allergies: none

Social history: denies alcohol, tobacco, or drug use

Physical Exam

Vital signs: Height – 75 inches, Weight – 85 kg, heart rate – 75 beats/min, blood pressure – 100/60 mmHg, respiratory rate – 30 breaths/min and shallow, oxygen saturation – 93% on 6 L by nasal cannula, EKG – rate-controlled atrial fibrillation.

On exam, there is a left-sided scalp hematoma and small laceration that is not currently bleeding. The patient has significant left-sided rib tenderness on palpation; no subcutaneous soft tissue air is appreciated. He also has notable hip and pelvis pain on palpation, though the pelvis does not appear to be unstable. Distal extremities are cool to the touch, but peripheral pulses are intact. All other aspects of the physical exam are normal.

Lab Work

Sodium – 139 mmol/L, Chloride – 109 mmol/L, Potassium – 4.0 mmol/L, Bicarbonate – 19 mmol/L, Glucose – 100 mg/dL, BUN – 35 mg/dL, Creatinine – 1.75 mg/dL, White blood cell count – 12,000, Hemoglobin – 10 g/dL, Hematocrit – 32.0%, Platelets – 175,000/mcl, INR – 2.2, PTT – 30s, PT – 19.5 s, Lactic acid – 4.5 mmol/L.

Serial cardiac enzymes are normal.

Arterial blood gas: pH 7.30, pCO_2 – 40 mmHg, pO_2 – 90 mmHg, O_2 saturation – 93%, base deficit – 6.5 mmol/L.

Radiographs

Chest x-ray: multiple left-sided rib fractures, no pneumothorax, no hemothorax.

CT head: scalp contusion, no intraparenchymal hemorrhage.

CT cervical spine: degenerative changes, no acute fractures or subluxations.

CT chest with IV contrast: left-sided rib fractures 5–10, no pneumothorax, small hemothorax, normal aorta.

CT abdomen/pelvis with IV contrast: left-sided inferior and superior rami fracture. Left-sided sacral fracture. Active extravasation in the pelvis. No solid or hollow viscous organ injury.

Things to Consider

1. Early intubation in an elderly person with multiple rib fractures and respiratory decompensation.
2. Optimize analgesia to assist with pulmonary toilet in the setting of multiple rib fractures, consider insertion of an epidural catheter.
3. Mild hypotension and normal heart rate in the setting of acute trauma may be related to medications the patient is taking (i.e., beta blockers)
4. Administration of IV contrast for CT scan in the elderly patient with a decreased GFR and creatinine clearance merits close observation of renal function and adequate IV hydration.
5. The need for warfarin reversal in lieu of active bleeding in the pelvis, and the method by which warfarin can be reversed.
6. The need for intensive care monitoring for this elderly patient with multiple rib fractures, unstable respiratory status, and pelvic fracture.

Hospital Course

AB received 2 units of fresh frozen plasma, which corrected his INR to 1.5. After consideration of his elevated INR and the fact that he has been on aspirin, he received a patient-controlled analgesia (PCA) pump to help with pain control, rather than an epidural catheter.

Due to AB's signs of hypoperfusion including cold extremities, acidosis, and base deficit, as well as the CT abdomen/pelvis imaging, it was clear that AB was developing signs of hemorrhagic shock. He was taken to interventional radiology for embolization. A bicarbonate infusion was started to protect his renal function in the setting of additional IV contrast load. Orthopedic surgery was consulted regarding the pelvic fracture.

After successful angioembolization of pelvic bleeding, AB returned to the intensive care unit with increased work of breathing. This was likely multifactorial in nature; including volume from the fresh frozen plasma and bicarbonate infusion, the supine position for the angiographic procedure, and the splinting due to multiple rib fractures. AB was intubated for airway protection and maintenance of adequate oxygenation and ventilation.

Five days into her hospital course, AB was hemodynamically stable and had weaned from the ventilator. He was subsequently extubated after an epidural catheter was placed for pain control. Unfortunately, 36 h later, he required reintubation for increased work of breath and dropping oxygen saturation. He became febrile and his white blood cell count was elevated, and chest x-ray revealed a right lower lobe consolidation consistent with pneumonia. He was started on broad-spectrum IV antibiotics and remained hemodynamically stable off vasopressors. On day 8 of hospitalization, after discussions with the family and AB, a tracheostomy was performed in order to improve pulmonary toilet and facilitate weaning from the ventilator. Five days later, he was off the ventilator and tolerating trach collar. Once transferred to the ward, he was able to pass a swallow study and eat. More than 2 weeks after admission, AB was transferred to a rehabilitation facility for further care.

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Ethical Issues in Older Adults

18

Margaret Drickamer

Contents

Abstract

Normative ethics addresses the criteria or standards by which we judge whether an action is considered to be right or wrong. Medical ethics is built on a utilitarian ethical structure; it bases what we *ought* to do on competing principles that are applied in the context of the clinical setting and not on overarching deontological moral imperatives. The guiding principles of American medical ethics are those of respect for autonomy, nonmaleficence, beneficence, and justice (Table 1).

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Introduction

Normative ethics addresses the criteria or standards by which we judge whether an action is considered to be right or wrong. Medical ethics is built on a utilitarian ethical structure; it bases what we *ought* to do on competing principles that are applied in the context of the clinical setting and not on overarching deontological moral imperatives. The

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Table 1 Definitions in medical ethics

Respect for autonomy	Maximize the individual's ability for self-determination
Nonmaleficence	Do no harm by direct action or negligence
Beneficence	The weighing of benefits, risks, and burdens for the greatest good
Justice	The fair and equitable distribution of resources, greatest good for the greatest number of people

guiding principles of American medical ethics are those of respect for autonomy, nonmaleficence, beneficence, and justice (Table 1). Autonomy is defined as the right to self-determination, the right to make one's own choices. The principle of nonmaleficence, often equated with the phrase primum non nocere, first do no harm, is better described as the obligation not to knowingly do harm by either an action or the omission of an action. Beneficence is the act of doing the most possible good; to take the action which will result in the most beneficial outcome for the patient. Justice, in the context of health care, refers to equality of medical treatment and the access to care. For any given clinical situation, the application of each of these principles may give different answers to what is right or wrong [1].

Weighing these competing principles in cultural, societal, and the individual contexts may lead to different actions. Not all cultures approach ethics in the same manner. For example, some religion-based cultures may feel that there are specific rules or god-given imperatives that may never be compromised and therefore all competing interests are secondary. The relative value of the four stated principles may be different for someone in a family-centered culture where individual autonomy may be less important than it is for American culture [2]. In this chapter, we discuss how these principles are applied in modern, mainstream American medicine with a special focus on the geriatric population.

Appropriate treatment of the geriatric patient involves a shift in perspective and priorities. The physician must recognize the multifactorial nature of illnesses, the need to fully understand the goals of care prior to initiating workup, and the need to continually review these goals as events unfold. Most illness states in older patients do not follow the paradigm of a unifying pathologic event. There may be many factors that need to be identified and addressed; factors that have predisposed the individual to the event, changes that have precipitated the event, and consequences of the situation. With age, the patient's perspective on the relative values of quantity and quality of life may change. A patient might wish to live a full, vital life to the age of 100, but may not want to merely survive that long in an incapacitated state. What is seen as a benefit, what weighs heavier as a burden, or what risks that individual is willing to take may change with time and experience.

Truth-Telling

The principle of nonmaleficence has, for millennium, been cited to justify the withholding of "bad news" from patients. The edict to withhold bad news was little challenged until the 1950s when the validity of this assumption came under scrutiny. In surveys conducted during the late 1950s and early 1960s, less than one-third of responding physicians stated that they always tell the truth to their patients about the diagnosis of cancer [3]; and in one survey 69% stated that they usually do not or never tell the patient the diagnosis of cancer [4]. By 1979, a similar survey revealed that 97% of responding physicians thought that a patient should be told the diagnosis of cancer [5].

This profound shift in practice in less than 20 years reflects both advances in medical knowledge and shifts in the emphasis in medical ethics. The development of treatment options for cancer initially drove this shift in communication. Patients could not undergo chemotherapy or irradiation unless they consented to the treatment and in order for them to be able to consent they needed to be informed of their diagnosis. In this case, recognizing the patients' autonomous right to choose treatments, or to forego treatments, was felt to be stronger than what was perceived to be the avoidance of the catastrophic harm that would be done by telling them their diagnosis (nonmaleficence). Interestingly, disclosure of information has not been found, in and of itself, to do harm. It does, in fact, allow the patient to discuss their goals and preferences more fully, as well as their emotional reactions, and to plan how they wish to approach this phase of their life.

Even when treatment options are still limited or nonexistent, as is the case with patients diagnosed with Alzheimer's disease, the weight of the argument is in favor of autonomy and therefore for truth-telling [6]. As we place an increasing emphasis on advance health care planning, the obligation to inform patients while they are capable of making decisions about their own future has become paramount. This is especially true when there is a risk of the patient becoming incapable of participating in decision-making, whether the patient is in the early stages of cognitive decline or facing the possibility of complications during surgery which might render them incapable of decision-making.

Older patients may have their right to know their diagnosis subverted by family members who feel that the patient would be unable to handle by knowing the information. On occasion, because of cultural values or for other personal reasons, a patient may not wish to be told a diagnosis. Patients may waive their right to be informed, but this must be an explicit decision between the patient and the physician [7]. Surveys have shown that 90–95% of elderly patients would want to know their diagnosis if they have cancer, which is not different than the percentages for younger patients.

Table 2 Principles of informed consent

Assess the patient's ability to understand the consequences of the decision
If the patient is incapable, identify an appropriate surrogate
Document the goals/values of the patient (or surrogate) expressed as the most important for the decision
Explain how the goals would be affected by the benefits/burdens/risks of the intervention
Document the decision and those present for the discussion

Table 3 Proposed communication skills for discussing evidence with patients

Ability to communicate complex information using nontechnical language
Tailoring the amount and pace of information to the patient's needs and preferences
Drawing diagrams to aid comprehension
Considering the values of the patient while weighing choices
Explanation for the probability and the risk for each option
Facilitative skills to encourage patient involvement
Evaluation of internet information that patients might bring to them
Creating an environment in which patients feel comfortable to ask questions
Giving patients time to take in the information
Declaration of equipoise when present
Checking patient understanding
Negotiation

Source: Adapted from [10] with permission from Elsevier

Informed Consent

Every adult patient who has decisional capacity has the right to accept or decline any treatment that is offered. Informing the patient of the benefits, side effects, and alternatives of even common and simple therapies (such as medications) is the first step toward the patient's consent as represented by their compliance with that therapy [8]. The process of informed consent when obtaining consent for invasive procedures is much more complex, but the same principles hold true (Table 2). The patient must understand the benefits of the procedure and the possible risks and burdens associated with it. The patient should also be informed of the benefits, risks, and burdens of all alternative therapies, including doing nothing. The quality of this discussion is as important as the content [9] (Table 3) [10]. Long lists of unlikely complications may not serve a useful purpose [11]. The discussion should be based on patients' values, fears, and goals and should inform them about the risks that either are common or, although rare, devastating. Documentation of the discussion should reflect the entire discussion, including the basis on which patients agreed or declined intervention and their ability to make the decision.

What information individual patients will want to know about their condition and possible treatments may differ with age. The 5-year prognosis may no longer be of as much significance as the quality of life to be had with different treatment options. The trade-offs between the burden of an intervention and its benefits will shift with different patient priorities [12]. An older person, or their surrogate, may wish to forego a diagnostic workup if they have already decided that they would not act on that information even if it was positive for disease. For example, a 90-year-old patient with multiple other medical conditions may decide to forego a biopsy of a lung lesion, having decided that she would not agree to surgery, radiation, or chemotherapy.

Many interventions other than those traditionally referred to as invasive are now requiring formal informed consent. The use of physical and chemical restraints in psychiatric and long-term care settings requires documentation of acceptance either by the patient or a surrogate. Appropriately informing patients of the meaning (i.e., positive and negative predictive value) of screening tests has been a recent focus, especially for cancer screening, in view of the patients' prognosis and preferences.

The corollary to a patient's right to informed consent is their right to decline treatment. In the 1991 case, *Cruzan v. the State of Missouri* the US Supreme Court ruled that patients have a right to refuse interventions and expanded this to include the right to refuse treatment for future care [13]. Chief Justice William H. Rehnquist wrote that a competent patient has a "constitutionally protected liberty interest in refusing unwanted treatment." The ethical conflict that the practitioners find themselves in is between the autonomous right of the patient to choose and practitioner's wish to do what they see as beneficent or nonmaleficent. This conflict often causes discomfort in the clinical setting. For example, a patient may choose to decline the repair of an abdominal aortic aneurysm despite what the physician knows is a very high risk of rupture and death.

The patient may decline a treatment before the intervention has been initiated or after it has been instituted. There is no legal or ethical distinction made between discontinuing and not initiating the same intervention [14], although frequently there is a stronger emotional component to the former. For example, if a patient has end-stage kidney disease and opts to forego dialysis, he or she will die from uremia. If patients who have been on dialysis for a period of time decide to stop dialysis, they too will die from their kidney disease.

Two areas often present a particular difficulty in the clinical setting: the discontinuation of ventilatory support and the discontinuing or non-initiation of artificial food or hydration. The discontinuation of ventilatory support parallels that of dialysis. The intervention has been instituted to maintain the patient through artificial means because of the failure of a vital organ to function. The patient will die from the effects of the underlying disease and resultant organ failure [15]. The conflicts cited in the case of discontinuation of ventilatory support are threefold: (1) that it is an active act (an act of commission) versus a passive act (act of omission) causing the demise of the patient; (2) that the proximity of the action to the death of the patient causes discomfort for the person stopping the ventilator; and (3) that the physician may not have a comfort level with palliation of the symptoms that may occur when ventilatory support is discontinued.

Much has been made of the arguments of "passive" versus "active" acts. Neither the legal nor the ethical literature supports it as a valid distinction [1], but it can make a major difference in the physician's level of comfort. Although the proximity of an action to the patient's death is uncomfortable for the physician, the need to discontinue invasive treatments for a patient who does not desire them is the more compelling duty. Being familiar with a routine of dignity and comfort care at the time of withdrawal of ventilatory support is crucial.

Discontinuing or foregoing artificial food or hydration in a dying patient also may cause discomfort on the part of physicians or patients' families, but not necessarily to the patients themselves [16]. Neither nutrition nor fluid support is necessary for comfort care, and there is evidence that fluids near the end of life cause discomfort by increasing secretions and suppressing the patient's endogenous endorphin responses. The duty to withhold artificial food and hydration if it is the patient's wish has been upheld in both state and federal courts and was confirmed in the *Cruzan* case. See the section below on "Decisions Near the End of Life" for more discussion of this topic.

Assessment of Decisional Capacity

Decisional capacity refers to the patients' ability to understand the consequences of the decision they are making, to make that decision, and to communicate the reasons for the decision. Understanding the consequences of the decision includes both the ability to understand the relevant information and to appreciate the situation and the impact of the decision [17, 18] (Table 4). Decisional capacity is decision specific, i.e., there are different standards of decisional ability needed to make different types of decisions (e.g., medical or financial) as well as different levels of complexity involved in the decision (e.g., simple procedure versus a complex procedure).

The ability to understand may be impaired because of temporary conditions such as delirium, transient coma, intoxication, or depression; or it may be permanently impaired by cognitive damage or psychiatric illness. Whatever the cause of the impairment, the key to the determination of capacity is the patient's ability to comprehend the advantages and disadvantages of treatment options and to make a decision. Whether we believe that the patient's decision is rational is not a determinant of capacity. Our society allows people to make what most would label as "irrational" decisions but, as part of our respect for autonomy, we cannot force what we would see as the right decision on others [19]. For example, we cannot prohibit alcoholics from drinking, even when it has been shown to impair their health or shorten their longevity. Patients' religious or ethnic beliefs may conflict strongly with our own beliefs, but they have the right to refuse any

Table 4 Legally relevant criteria for decision-making capacity and approaches to assessment of the patient

Criterion	Patient's task	Physician's assessment approach	Questions for clinical assessment[a]	Comments
Communicate a choice	Clearly indicate preferred treatment option	Ask patient to indicate a treatment choice	Have you decided whether to follow your doctor's (or my) recommendation for treatment? Can you tell me what that decision is? (If no decision) What is making it hard for you to decide?	Frequent reversals of choice because of psychiatric or neurologic conditions may indicate lack of capacity
Understand the relevant information	Grasp the fundamental meaning of information communicated by physician	Encourage patient to paraphrase disclosed information regarding medical condition and treatment	Please tell me in your own words what your doctor (or I) told you about: The problem with your health now The recommended treatment The possible benefits and risks (or discomforts) of the treatment Any alternative treatments and their risks and benefits The risks and benefits of no treatment	Information to be understood includes nature of patient's condition, nature and purpose of proposed treatment, possible benefits and risks of that treatment, and alternative approaches (including no treatment) and their benefits and risks

(continued)

Table 4 (continued)

Criterion	Patient's task	Physician's assessment approach	Questions for clinical assessment[a]	Comments
Appreciate the situation and its consequences	Acknowledge medical condition and likely consequences of treatment options	Ask patient to describe the views of medical condition, proposed treatment, and likely outcomes	What do you believe is wrong with your health now? Do you believe that you need some kind of treatment? What is the treatment likely to do for you? What makes you believe it will have that effect? What do you believe will happen if you are not treated? Why do you think your doctor has (or I have) recommended this treatment?	Courts have recognized that patients who do not acknowledge their illnesses (often referred to as "lack of insight") cannot make valid decisions about treatment Delusions or pathologic levels of distortion or denial are the most
Reason about treatment options	Engage in a rational process of manipulating the relevant information	Ask patient to compare treatment options and consequences and to offer reasons for selection of option	How did you decide to accept or reject the recommended treatment? What makes (chosen option) better than (alternative option)?	This criterion focuses on the process by which a decision is reached, not the outcome of the patient's choice, since patients have the right to make "unreasonable" choices

Source: Appelbaum [18]
[a]Patients' responses to these questions need not be verbal

treatment option they believe is in conflict with their beliefs.

On the other hand, understanding the patient's goals and preferences, their priorities as they age, is of fundamental importance to helping the physician to be comfortable and understand the decisions a patient may make as well as giving them the appropriate options from which to choose. Respect for each individual's unique point of view, needs, and desires is fundamental not just for respecting their autonomy, but for truly doing no harm with and maximizing the benefit of interventions.

Every physician obtaining informed consent should be able to do a basic assessment of decisional capacity. The physician should be able to diagnose delirium and, if needed, assess basic cognitive function. Tools focused on parietal lobe function, as do many of the commonly used cognitive mental status tests, are relatively poor predictors of the ability to make decisions, per se, but instruments that have a larger emphasis on frontal lobe or executive function, such as the clock drawing and other executive function examinations, may be more useful. What is most important is the physician's thoughtful discussion with the patient and the real-time assessment of the patients' understanding of the consequences of the decision they are making. Since the standard for decisional capacity is situation specific, it is important that one is able to assess their ability to understand the level of information needed for the decision at hand.

There are many other decisions that a patient may need to make other than informed consent where their capacity will need to be assessed and differing standards met. For example, a very high standard for decisional capacity must be met for a patient to agree to participate in a research study [20, 21], whereas a very low standard is applied to their ability to make a last will and testament. Of particular concern to the clinician is deciding whether patients retain the ability to decide on care options and whether they can return home

Table 5 Levels of decisional capacity

Medical decisions
Ability to understand relevant information
Ability to understand the consequences of the decision
Ability to communicate a decision
Research subject
Ability to understand the probability of a lack of benefit
Appreciation of risks and the uncertainty of the risks
Appreciate their right to withdraw from the study
Decisions of self-care
Ability to care for oneself *or*
Ability to accept the needed help to keep oneself safe
Finances
Ability to manage bill payment
Ability to appropriately calculate and monitor funds
Last will and testament
Ability to remember estate plans
Ability to express logic behind choices

Source: Modified from [24]

Table 6 Hierarchy of decision-making

Patient's current wishes
If the patient has decisional capacity, this ALWAYS takes precedence
Substituted judgment
Done by the surrogate decision maker only when the patient is not fully capable of making the decision
Based on the patient's prior values and wishes
Advance directive is used as a guide
Patient input is used when possible even if the patient is not fully capable of making the decision
Beneficence
Done by the surrogate decision maker when the patient lacks decisional capacity and evidence does not exist for substituted judgment
Weighing of benefits and burdens as based on the patient's present indications of pleasures and burdens
Input from caregivers is very important

Source: Modified from [24]

or need a more intense environment in order to remain safe [22, 23] (Table 5) [24].

If the physician is unsure of a patient's capacity, a psychiatric consultation may be requested if the question arises from a psychiatric illness; or a neuropsychologist or geriatrician may be consulted about cognitive or functional problems. The patient's decisional capacity at the time of any decision, whether they decide to accept treatment or to decline treatment, should be recorded in the medical record.

Competence is a term that has legal implications beyond what a physician judges on examination. Physicians should avoid using this term unless a court has ruled on the patient's competence. The court recognizes two major categories of competence; competence for financial decisions and competence to make decisions of person. Only if the court has ruled the individual to be incompetent *of person* should the individual be assumed to lack decisional capacity for medical decisions.

Decision-Making for Incapacitated Patients (Table 6)

If a patient is found to lack the capacity to make an informed decision, a surrogate decision maker must be identified. The principle of autonomy guides us to seek a surrogate who is the person most capable of representing the patient's wishes. If the patient has completed an Advance Directive that names a proxy decision maker, this is the person to whom questions should be deferred if the patient has lost decisional capacity. This designee may be variously referred to as the Durable Power of Attorney for Health Affairs or the Health Care Proxy, Surrogate, or Agent. It needs to be emphasized that this person can only make decisions for the patient if the patient no longer has decisional capacity. A patient may also choose a person in a less formal manner, and documentation of such a choice should help to guide the decision. A person who holds Power of Attorney for Finances does not, simply by having this limited power of attorney, have the ability to make other decisions for the person.

If the patient's choice of surrogate is not known, usually the next-of-kin is utilized. The hierarchy of authority is spouse, adult children, parents, siblings, nieces, or nephews. Adult friends may sometimes be able to act as surrogate if the relationship with the patient is such that they can act on his or her behalf. If it is thought that the person identified by this procedure cannot, in fact, act as an appropriate surrogate, if there is conflict about identifying a decision maker, if there is a lack of consensus among individuals, or if there is no one to take on this role, the court may need to decide who will act for the patient. In emergent situations, where the decision-making process is unclear, physicians should apply the "best interest rule" and proceed with any interventions necessary to save the patient's life or preserve function until the situation is clarified. Each institution may have different procedures for obtaining such permission to act, such as an agreement to act by the Chief of Staff. If there is time, emergency conservatorship from a court can be sought. As the situation and the patient's wishes become clear, and an intervention that had been started as an emergency procedure is found to be against the patient's wishes, then the intervention must be discontinued.

The task of making the decision for the incapacitated patient should honor the patient's autonomy by maximizing the individual's continued influence on the ultimate decision. If a patient gave explicit directives that apply to the situation at hand at a time when he or she was capable of decision-making, they must be followed. For example, if a patient with a terminal illness requests that no further interventions be done, including artificial food and hydration, a family member cannot reverse this directive once the patient is in a coma.

If patients have not been explicit about their wishes, the surrogate decision maker and the physician are then obliged to apply substituted judgment. This term is defined as "the application of the patient's preferences and values . . . trying to choose as the patient would have wanted" [25]. In studies comparing hypothetical decisions made by would-be surrogates and patients with decisional capacity, there is a 66% correlation. Previous discussions between the patient and the surrogate help to make these decisions much more representative of the patient's wishes [26]. Helping a family to understand that their obligation is to do what their relative would have wanted often relieves them of some of the burden of decision-making and helps clarify their thinking. Living Wills may be useful in this context. Living Wills may be formal documents executed by a lawyer, but they may also be readily available forms completed by the patient with or without assistance or simply a written statement or narrative. If patients are still capable of making decisions, all treatments must still be discussed with them even if they have a Living Will.

The Living Will is a "what if" statement – a hypothetical situation. The patient is saying, "*If* one of these conditions occurs to me (e.g., permanent coma), *then* do not attempt resuscitation." It does not necessarily mean that the patient does not desire this intervention in their present state of health. For example, a patient who is fully capable of making decisions has a Living Will that states that he or she would decline resuscitation if in a vegetative state. If this patient was to have a cardiac arrest in their present state, resuscitation should be attempted. If after the resuscitation the patient is found to be vegetative, the Living Will would take effect and no further resuscitation attempts should be made were the patient to arrest again.

Frequently, the exact circumstances outlined in a Living Will are not met, but it can still give a good indication of the patient's preferences and values, which then can be applied to the current situation [27]. Living Wills cannot cover all circumstances that may arise, and most patients wish to have a proxy decision maker to interpret their intent. State laws vary as to whether the Living Will or the proxy decision maker takes precedence when there is a conflict with the decisions. Encouraging the family to remember other health care decisions or comments the patient made when other family members were ill is also helpful in trying to define what someone "would have said."

If there is no information that helps the surrogate decision maker to reconstruct what the patient would have said, the guiding principle becomes that of beneficence, defined as weighing the benefits, risks, and burdens of an intervention in the context of the individual. With beneficence, although a patient may no longer be fully capable of making a decision, their voice can still be an important one. Their stated preferences and fears can be used to guide the decision about relative benefits and burdens [28]. This can be true for even markedly demented patients.

For example, the relative burden of an intervention in two patients, equally cognitively impaired, can be quite different. One patient may not become agitated when an intravenous line is started, and intravenous treatment would not be a great burden. Another patient may fight such an intervention, repeatedly pulling out the intravenous catheter and needing restraints. Although the second patient is not making an informed decision to forego intravenous therapy, the relative burden of the intervention is greater in this patient and therefore the relative benefit would need to be greater than other less noxious alternatives for the burden/benefit ratio to be the same.

There can, at times, be conflicting interests in adhering to this hierarchy as circumstances change and the patient's condition alters what is a burden and what is a benefit. Surrogate decision-making often uses a combination of substituted judgment and beneficence to arrive at a treatment decision [29]. What is most important is that these discussions occur as they can have major impact both on patients' quality of life and on the bereavement adjustment of the relatives [30].

As previously stated, decisional capacity is decision specific and capacity is often not black or white. Utilizing an Assent/Consent modal is commonly being accepted. This allows for different levels of patient involvement in the decision-making process. If the patient seems to be capable of making the decision but, due to memory problems or waxing and waning mental status, there is some question as to their ability to retain information, the family may be asked for their "assent," i.e., they agree that it is what the patient wants. If the patient cannot make the decision, the family may give the formal consent but the patient may need to "assent" in order to carry out the procedure. For example, a family may consent to chemotherapy but the patient must be willing to cooperate. The consent/assent modal balances the prior statements of the patient (future-looking autonomy) with beneficence for the person they are at this moment in time [31].

DNR Orders in the Operating Room

A patient's previously stated wish to forego intubation or attempts to resuscitate may be suspended at the time a patient undergoes surgery. Elective intubation in order to perform surgery or a cardiac arrest that occurs under general anesthesia where an immediate response is possible and where the cause may be readily reversible is different from a cardiopulmonary arrest under other circumstances. It may therefore be perfectly compatible with a patient's goals to have these procedures done in the operating room but not want them initiated in other circumstances. Indeed, intubation may be necessary if a procedure which the person does desire is to occur.

If a decision is made to reverse a do-not-resuscitate or do-not-intubate order during surgery, there must be a clear understanding prior to surgery of how postoperative events should be handled in case the patient is not then capable of making decisions. How long should an intubation continue if the patient is not quickly able to be extubated? If the patient does arrest and is resuscitated but has lost decisional capacity, what other treatment modalities would be an unwanted burden? Discussions with the patient, surgeon, anesthesiologist, and primary care physician can help safeguard against confusing and distressful situations [32].

Confidentiality

The Health Insurance Portability and Accountability Act (HIPAA) of 1996 has greatly enhanced the confidentiality of written records and communications [33]. It has also impacted verbal communication, but not to the same extent.

Sharing information with patients' relatives or friends is appropriate in only two circumstances: when patients have specifically stated that the physician may discuss their condition with the individual or when the patient has lost decisional capacity and a surrogate decision must be made. It is advisable to ask patients well in advance who they wish to have informed and how much they wish to have told.

The sharing of information among colleagues should be done in private and with respect for the patient's right to confidentiality. Casual conversations in public places, rounds in the hallways, and discussions in lobbies or waiting rooms with multiple families present can be a breach of a patient's right to privacy. Our sensitivity to this issue must be heightened, and the policing of each other should become everyone's responsibility.

Sharing medical information among health care providers without the patient's explicit authorization, if the clinical circumstances so require, is permitted. The use of clinical material for teaching purposes can be done only with sufficient safeguards to anonymity so the individuals involved are not identifiable. Other information can be released only with the patient's or surrogate's authorization unless it is required by law, as in the case of public health reporting of communicable and sexually transmitted diseases.

Limits to Autonomy and Choice (Futility)

The previous sections have dealt heavily with the respect for and safeguards of the patient's right to exercise autonomy. There are circumstances where this autonomy is tempered by other forces. Autonomy may be limited if the patient is a danger to others, a danger to self, or for the good of society. Laws may govern what procedures or interventions may be available to an individual. For instance, physician-assisted suicide is explicitly illegal in most states in the USA.

Although the US Supreme Court has affirmed an individual's right to refuse treatment, there is no corollary right to demand treatment [34]. In addition to the healthcare professionals' responsibility to understand the patient's goals of treatment and respect patient's own assessment of their quality of life, they also have the responsibility of knowing if an intervention is futile and not offering such treatments to the patient.

There are two perspectives on the definition of futility; referred to as quantitative and qualitative. An intervention is said to be quantitatively futile if it cannot achieve its physiologic objective. Because it is difficult to know what level of evidence is needed for what cut-off to call something physiologically futile, this concept has limited utility. A therapy is said to be qualitatively futile if it is unlikely to help patients achieve their primary goal even if it has a physiologic effect [35, 36]. An example is the foregoing of antibiotic therapy in a patient who is in the terminal phase of an illness. Although the antibiotics might have the physiologic effect of treating the infection, it would have no effect on comfort and a negative effect if it prolongs the patient's suffering. This concept, of futility in the light of the treatment goals, is paramount to the appropriate treatment of the geriatric patient.

If a procedure is judged futile, the physician does not have to offer the intervention to the patient or the surrogate. The very act of offering conveys the sense that there must be some benefit, some chance of success. Why else would it be offered? Therapies the patient and family might expect to have performed but that have become futile, such as an attempt to resuscitate a patient when circumstances clearly demonstrate that it would be futile, should be discussed in the context of their futility. For example, the patient or family should be told that where the patient's heart to stop, attempts to restart it would be futile and therefore would not be initiated. Simply ignoring the subject may engender mistrust, as most individuals are aware of the spectrum of treatments available. One in 20 patients who die in the ICU do not have a surrogate decision maker. The majority of the time physicians decide to cease life-sustaining interventions on the basis of their futility [37].

Defining a therapy as futile is simple under some circumstances and more difficult under others. The decision that someone is "not a surgical candidate" is frequently made when the relative risks and benefits clearly demonstrate that the treatment is not indicated. The decision to stop a therapy may also be made on the grounds of professional judgment. For example, if a tumor is not responding to chemotherapy, it can be unilaterally stopped by the clinician. The difficulty lies more in defining which therapies near the end of life still hold enough of an advantage for the patient that they should be offered.

Prognostication

In order for patients to be able to set goals, they need to be able to understand their prognosis and how interventions may or may not change that prognosis. Unfortunately, we are not very accurate in being able to prognosticate. Being able to predict short-term mortality in the acute care and intensive care unit setting has been explored through the SUPPORT Study [38] and through the use of the APACHE III instrument [39]. These instruments use a combination of diagnosis, cause of illness, and a scale for physiologic parameters to predict mortality risk, but the ability to apply them clinically remains a challenge [40]. The patients' physical and cognitive function prior to their hospitalization is the strongest predictors of outcome after an intervention [41].

Such legislative acts as the Medicare Hospice Benefits, and the Oregon Death with Dignity Act define the terminal phases of disease as the last 6 months of life. Our ability to accurately prognosticate this length of time is relatively poor, with only one-third of predictions being within 50% confidence intervals (i.e., if prognosis is 3 months, "accurate" would be from 1.5 to 6 months). Most physician prognoses are too optimistic [42].

Individuals in their eighth and ninth decades may define their goals similarly to patients with terminal diagnoses. Quality of life and relief from the burdens of illness and interventions may be more important than longevity per se. On the other hand, it should not be assumed that this is true for all individuals of advanced age. Although some elderly patients may look forward to more years of life, they may not wish to do so under any or all circumstances. In surveys of patients with and without terminal illnesses about why they might be motivated to avail themselves of physician-assisted suicide, fear of disability and dependence are the two most common motivators for wishing to end one's life. Predicting the risk or progression of disability is even more difficult than predicting death [43].

Decisions Near the End of Life

As has been emphasized in previous sections of this chapter, goal-oriented care is of the utmost importance to all geriatric care, but it is the sine quo non of end of life care. When a patient has a terminal illness or is faced with chronic, disabling, and progressive disease, decision-making must become very goal-focused. We have already discussed foregoing and discontinuing interventions when they no longer meet the goals of care. Treatment of suffering, physical, mental emotional or spiritual may lead to actions where the physician is seen as hastening death, either inadvertently or deliberately.

The potential for hastening the death of a patient is highest where there is a narrow therapeutic window between the dose of medication needed to control a symptom and the dose that could cause suppression of respiratory drive. The underlying ethical principle of "double effect" rests on the physician's intention and an acknowledgement that treatment may have two effects: one on symptoms and one on longevity. This is an acceptable risk to take if the physician and patient or surrogate have agreed that comfort is more important than longevity and the medication or treatment is given with the *intention* of relieving symptoms.

At some point in the patient's clinical course, interventions that we normally think of as prolonging life may have shifted to prolonging death. An example of this may be antibiotics for pneumonia. The symptoms of pneumonia can be treated (e.g., with scopolamine to control secretions and morphine for dyspnea) without treating the underlying pathophysiology of the pneumonia. Since every patient will, eventually, die of something, there comes a time when it makes sense to allow the clinical course to determine the mode of death. Aggressively treating the symptoms is often preferable to a prolonged dying process with the occurrence of increasingly hard-to-control symptoms.

Physician-assisted suicide and euthanasia (physician-assisted death) are instances when a therapy is prescribed, provided, or administered with the *intention* of ending that patient's life. The acceptability of such actions from both a moral and a practical point of view is under wide debate within the profession and in society in general. Those who argue for the practice of physician-assisted death point out that there are some symptoms that cannot be alleviated short of death (e.g., the discomfort and indignity of destructive head and neck cancer), and individuals should have the right to determine the time and mode of their death. Arguments against physicians assisting in suicide point out that the medical profession's obligation is to "care and to cure" and not to end life [44]. The four principles of autonomy, non-maleficence, beneficence, and justice are active parts of this debate. Some argue that out of respect for autonomy, individuals should be allowed to determine the time and mode of their death, especially if it is within the last 6 months of their "natural" lives. Others argue that if there is unbearable suffering that cannot be relieved by other means, then the principle of beneficence tells us that they should be allowed to end their lives. Many feel that physicians prescribing or acting with the intent of ending a patient's life would be professionally wrong because it would mean intentionally doing harm to the patient (non-maleficence). Finally, many fear that the practice will be a "slippery slope" leading to the premature death of certain segments of society such as the elderly and the disabled. As of now, physician-assisted dying is legal in two states in the USA (Oregon and Washington) and many countries in Europe. Although the debate remains open, the fear of abuse has not proven to be a reality in any locale where it is legal, where it has remained a small minority of patients (less than 5% of deaths) who decide to actively end their lives.

Conclusion

As an individual ages and the accumulation of both life experience and illness burden increase, decisions need to be made on the basis of the individual's goals and preferences. Patients need to be informed of their situation, their prognosis and their options as best we can define them. They have a right to decide their course of action within choices that are not futile and they have a right to influence decisions made for them if they have become incapacitated. Weighing autonomy and beneficence is often hard for the patient who has lost the ability to make decisions. Finding appropriate surrogate decision makers and helping them to understand their role is paramount to this process.

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Legal Issues in Older Adults

19

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Contents

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Abstract

The practice of surgery involving older patients is extensively regulated in the United States in a variety of ways. Besides direct government command and control ("Thou shalt" and "Thou shalt not") regulation and indirect regulation through Medicare and Medicaid reimbursement rules, a number of private entities contribute to the oversight of surgery practice through their standard-setting and disciplinary activities. A further source of regulation is the American judicial system, under which the courts may be used by individual patients who bring private civil malpractice lawsuits to seek financial compensation from particular surgeons and other health care professionals and institutions for harms that the defendants have wrongfully caused. Particularly egregious behavior, such as patient abuse, may even subject a health care professional to the possibility of criminal law prosecution. This chapter examines three specific areas of legal regulation affecting the practice of surgery for older patients. These foci are medical malpractice litigation, informed decision-making requirements and exceptions, and confidentiality protections. Additionally, general risk management considerations for the surgeon treating geriatric patients are outlined.

Keywords

Surgery jurisprudence · Surgery law · Surgery legal · Surgical malpractice · Informed consent for surgery · Decision making capacity · Advance medical planning · Surgery risk management · Geriatrics shared decision making

Abbreviations

ACS	American College of Surgeons
AHRQ	Agency for Healthcare Research and Quality
APS	Adult Protective Services
ASC	Ambulatory Surgical Center
CPG	Clinical Practice Guideline
CPR	Cardiopulmonary resuscitation
CPT	Cognitive Performance Test
DNAR	Do Not Attempt Resuscitation
DNR	Do Not Resuscitate
DPOA	Durable power of attorney
EHR	Electronic Health Record
HCQIA	Health Care Quality Improvement Act
HIPAA	Health Insurance Portability and Accountability Act
IEC	Institutional Ethics Committee
IRB	Institutional Review Board
MMSE	Mini-Mental State Exam
NPDB	National Practitioner Data Bank
PCORI	Patient-Centered Outcomes Research Institute
PDR	Physician's Desk Reference
PHI	Personal Health Information
POCD	Postoperative Cognitive Dysfunction
POLST	Physician Orders for Life-Sustaining Treatment
PPI	Pharmaceutical Package Insert
PSA	Prostate-specific antigen
SURPASS	Surgical Patient Safety System
UP	Universal Protocol for Preventing Wrong Site, Wrong Procedure, Wrong Person Surgery
WHO	World Health Organization

Introduction

The practice of surgery involving older patients is extensively regulated in the United States in a variety of ways. (Although this chapter focuses exclusively on surgical practice within the United States, many of the legal considerations discussed here apply to other countries as well) [1]. Under the US federal system, governmental regulation of surgery practice occurs for the most part at the state level, mainly through the activities of state medical boards that enforce the licensure and disciplinary provisions of their respective state Medical Practice Acts. The states regulate medical practice under their inherent police power, reserved to the states by the 10th Amendment to the US Constitution, to protect and promote the health, safety, welfare, and morals of the general population and also under the states' parens patriae (or parental) authority to protect individuals (including older patients) who are unable to protect themselves from harm.

Besides direct government command and control ("Thou shalt" and "Thou shalt not") regulation and indirect regulation through Medicare and Medicaid reimbursement rules, a number of private entities contribute to the oversight of surgery practice through their standard-setting and disciplinary activities. These private bodies include hospital medical staffs, specialty certification boards, and medical specialty societies.

A further source of regulation is the American judicial system, under which the courts may be used by individual patients who bring private civil malpractice lawsuits to seek financial compensation from particular surgeons and other health care professionals for harms that the defendants have wrongfully caused. Particularly egregious behavior, such as patient abuse, may even subject a health care professional to the possibility of criminal law prosecution.

This chapter examines three specific areas of legal regulation affecting the practice of surgery for older patients. These foci are medical malpractice litigation, informed decision-making requirements, and confidentiality protections. Additionally, general risk management strategies for the surgeon treating geriatric patients are outlined.

Medical Malpractice

In a typical malpractice lawsuit based on the tort theory of negligence, the plaintiff/patient must prove to the fact-finder (usually a jury), by a preponderance of the evidence (more than 50% likelihood), each of four essential elements in order for professional liability to be imposed by the court. The four elements of a prima facie (valid on its face) negligence claim are: (a) a duty owed, (b) breach or violation of that duty (negligence/fault), (c) damage or injury suffered, and (d) both factual and legal (proximate) causation.

Duty/Standard of Care

The surgeon owes a professional duty only to one with whom that surgeon has established a physician/patient relationship within the relevant time frame. Within that relationship, the legally enforceable duty owed is one of "due care" or "reasonable care under the circumstances." In the medical context, a combination of common law (judge-made law) tort doctrine, which is developed incrementally on a case-by-case basis, and applicable state statutes (legislative enactments) traditionally have required the physician to have and use the degree of knowledge and skill that is usually possessed and used by peer physicians in the same or similar circumstances. However, there is a significant current trend in many states to alter the traditional customary, peer-based professional standard of care in favor of imposing more objective, external standards of "reasonableness" against which the professional's behavior is to be evaluated. An objective standard of reasonableness may exceed (i.e., require more knowledge and sophistication than) the prevailing customary practice within the professional community at the time in handling a specific clinical challenge presented by a patient. Thus, it is possible that the state of the art in a particular area of care, required under a reasonableness standard, may not be synonymous with and satisfied by the current customary practice within the practitioner community.

Fact-finders (ordinarily a jury, but sometimes the judge acting in a fact-deciding capacity as well as a decider of legal questions) have the job of determining the applicable standard of care in any particular case. Fact-finders look to a variety of sources for that standard of care. Even in jurisdictions following a reasonableness standard, customary practice prevailing at the time of treatment among a majority or at least a "respectable minority" of the defendant's peers still carries substantial, but not necessarily conclusive, weight. Relevant statutes and regulations, especially those relating to professional licensure and discipline, are also a part of the equation, as are professional codes of ethics. Voluntary (but nonetheless potentially admissible into evidence at trial) standards of care may be created by private accrediting or certifying bodies such as the Joint Commission or the Accreditation Association for Ambulatory Healthcare. Guidelines issued by medical specialty societies (such as guidelines for structured training for surgeons performing robotic surgery created by the Society of American Gastrointestinal and Endoscopic Surgeons [2]) may influence a hospital's internal policies and procedures, which in turn may be introduced into evidence to help prove the standard of care to which physicians and others practicing within that hospital should be held legally accountable. Medical journal literature, textbooks (learned treatises), and informational materials for medical devices and drugs approved for physician use on patients by the Food and Drug Administration and contained in the Physician's Desk Reference (PDR) and pharmaceutical package inserts (PPIs) also may be introduced into evidence for the fact-finder's consideration.

Another source of the standard of care stems from the acknowledgement by leaders in health care delivery and financing that a good deal of routine medical practice has long been predicated more on habit and inertia than on solid empirical evidence establishing clinical efficacy. Out of a concern about both wasteful resource usage and the insufficient quality of patient care, over the past several decades there has been a concerted movement to rationalize medical practice. A central strategy for rationalizing medical practice is to develop, collect, and disseminate to practicing clinicians a variety of evidence-based Clinical Practice Guidelines (CPGs) or parameters to educate practitioners about whether a particular diagnostic or therapeutic intervention actually has been demonstrated to produce desired health benefits for patients. This movement has been led by professional organizations and specialty societies including the American College of Surgeons (ACS) and American Geriatrics Society, governmental agencies led by the federal Agency for Healthcare Research and Quality (AHRQ) and the Patient-Centered Outcomes Research Institute (PCORI) established by the Affordable Care Act, and individual institutions and agencies in the USA and elsewhere.

In a related matter, the American Board of Internal Medicine Foundation and Consumer Reports have partnered in a Choosing Wisely initiative designed to encourage and enable patients and physicians to share in making decisions about medical care that is supported by available medical evidence, not duplicative of other tests or procedures already tried, and necessary for that particular patient. Numerous medical specialty organizations have joined in this initiative, identifying common practices in their respective specialties for which physicians and patients ought to ask questions about the value obtained from routine use.

Unfortunately, the push toward more rational care through CPGs, Choosing Wisely, and other evidence-based best practice initiatives is impeded by physician perceptions of the arbitrariness of the courts in applying legal standards of care. Physicians often are afraid to reduce their ordering of screening tests and treatment interventions for fear of litigation if they act responsibly, but a bad outcome occurs nevertheless. One prominent example of legally induced overtreatment is the case of prostate cancer where, despite the US Preventive Services Task Force recommendation against routine prostate-specific antigen (PSA) screening for asymptomatic individuals, PSA screening has lessened only minimally [3]. This deviation from evidence-based prudence is exacerbated by the many subsequent prostate biopsies and surgeries that follow unnecessary PSA tests revealing conditions that should have been left alone [4].

Physicians' legal anxieties, especially in the geriatrics context, are generally overblown. Older persons have been underrepresented statistically as plaintiffs in medical malpractice lawsuits. Moreover, the legal ramifications of CPGs or practice parameters continue to evolve in a positive direction. There is an increasing tendency for the courts to admit into evidence, on behalf of either side to a malpractice dispute (i.e., for either inculpatory or exculpatory purposes), properly validated, scientifically supported contemporary CPGs on the issue of the standard of care to be applied under any specific set of circumstances. This development already has beneficial consequences, in that anecdotal reports indicate that most plaintiffs' attorneys consider physicians' compliance with, or deviation from, relevant CPGs in making decisions about whether to initiate malpractice litigation at all and how to conduct settlement negotiations for claims that are pursued. Compliance thus creates a kind of functional safe harbor for physicians while, even when the physician has deviated from a pertinent CPG, adequate documentation in the patient's record of the physician's reasons for alternative treatment in light of the particular patient's situation will justify the physician's conduct and preclude the imposition of liability.

Circumstances influencing the applicable duty of care under a reasonableness standard include the patient's age and related needs and capacities. The surgeon must be thoroughly sensitive to and knowledgeable regarding the patient's particular age-based characteristics that may affect diagnostic or therapeutic decision making and action for an older patient. For example, a patient's age is likely to exert an impact on which drugs are prescribed, the risks they may pose to the patient (especially polypharmacy), and the proper dosages and routes of administration. Further, the ability to factor the patient's age into calculating the risks of mortality and morbidity of proposed surgical interventions is part of the physician's duty of due care in advising the patient. Thus, for instance, the ACS as one of its Choosing Wisely recommendations urges physicians and patients to "avoid colorectal cancer screening tests on asymptomatic patients with a life expectancy of less than 10 years and no family or personal history of colorectal neoplasia" [5].

In a medical malpractice trial, each party ordinarily attempts to educate the lay (i.e., not medically trained) fact-finder about its respective version of the applicable standard of care through the testimony of expert witnesses. First, the judge determines as a matter of law whether a particular proffered witness possesses sufficient credentials to be allowed to testify as an expert and present a professional opinion. Usually, this means that expert testimony about the standard of care applicable to the performance of a particular type of surgeon may only be provided by a witness with credentials of the same type as the defendant surgeon. Potential expert witnesses may be drawn by either party from a national pool, since the standard of care is a national rather than a local one. Once a legal decision has been made to allow the jury to hear the expert testimony of a witness on the standard of care to which the defendant should be held accountable, then it is up to the fact-finder to decide how much weight or credibility to attach to the witness' testimony. The testimony of expert witnesses (mainly those testifying for plaintiffs) in medical malpractice trials sometimes is scrutinized for accuracy and honesty [6] by professional organizations and state medical boards.

Breach of Duty

The second necessary element the plaintiff must prove in a negligence-based malpractice lawsuit is a breach or violation of the applicable standard of care, that is, the element of negligence. The physician does not guarantee particular results, let alone perfection. By the same token, however, it is not enough for physicians to simply "do their best" if their conduct does not rise to the applicable level of care, even when the errors or omissions are unintentional. The concept that a defendant may be held legally liable only when shown to be at fault is fundamental to the traditional American tort system. Although there are proposals periodically made by academics and political lobbyists to move the handling of medically caused patient injuries toward some form of no-fault system, fundamental alteration of the existing tort system is unlikely.

Negligence is defined as unintentional, but blameworthy, wrongdoing that may occur in one of three categories. Nonfeasance is fault happening through inaction or omission, i.e., failing to do something that should have been done. Misfeasance consists of performing an act that should have been performed, but doing it in a substandard manner. By contrast, malfeasance is the wrongful performance of an act that should not have been done in the first place.

In the surgical context, this means that the surgeon is legally obligated to properly assess the patient before surgery, both in terms of the need for surgery in light of viable alternatives and in terms of the likely risks for that patient. Misdiagnosis or poor judgment may result in unnecessary surgery or, alternatively, delayed or foregone surgery [7]. Additionally, the surgeon is expected to perform the surgery competently in technical terms. The duty of due care extends to engaging in reasonable preoperative actions to reduce risks, as well as to competent handling of postoperative care involving routine checks for and recognition of somatic problems, infection, pain control, confusion, and other complications [8]. After hospital discharge, the patient is entitled to adequate follow-up care by the surgeon for a reasonable period of time.

Delineating the legally enforceable standard of care may become a particularly difficult matter in the murky area of surgical innovation or newly emerging techniques. At present, how surgical innovation is treated for malpractice litigation purposes depends on the specific case: as a species either of generally accepted and practiced therapeutic care, on the one hand, or of biomedical research involving human subjects (with its own extensive, distinct web of regulations), on the other hand.

A surgeon may be held personally liable for the consequences of his or her own negligent acts or omissions. The surgeon also may be held vicariously liable, under the doctrine of respondeat superior, for negligent conduct engaged in by an employee of the surgeon (such as a nurse or physician's assistant employed to assist in caring for patients in the physician's office) while acting within the scope of the individual's employment. The longstanding "captain of the ship" doctrine in the past was used to hold the surgeon responsible for the negligence of anyone participating in an operation, on the theory that the surgeon as "captain of the ship" ought to be in charge of – and precluded from delegating away responsibility for – everything occurring during the surgery; thus, for example, under this doctrine, liability would be imposed on the surgeon for retained instruments, sponges, and needles forgotten in the patient, even though the nurses (not the surgeons) were the ones who personally erred in counting. Although automatic application of the "captain of the ship" doctrine has been widely discredited today as unrealistic in light of the complexity of the modern operating room, courts will look at the surgeon's right of control over staff members and impose vicarious liability when such a right of control (whether or not control actually is exercised) is present.

Vicarious liability may also come into play when the surgeon is acting as the mentor/supervisor of a person in a medical trainee status, including medical residents, fellows, and students. Because the negligence of the trainee resulting in patient injury may be attributable to the surgeon based on the existence of a trainee/supervisor relationship even if the supervising surgeon was not personally at fault, surgeons in a formal teaching role should take care in assigning specific tasks to trainees, overseeing their trainees' performance in patient care, and evaluating trainees. In addition to vicarious liability exposure in the teaching role, the supervising surgeon may be exposed to possible direct liability for personal negligence in meeting the standard of care expected to be exercised by a reasonable surgeon in supervising a trainee.

Surgery occurs within a hospital or other corporate (either for-profit or not-for-profit) entity such as an ambulatory surgery center (ACS). Many patient injuries (including many of those leading to malpractice litigation) are caused by multifaceted health care delivery system failures, rather than by isolated deficiencies in the knowledge, skills, or character of an individual surgeon or other single members of the health care team. The entity within which the surgery takes place may be sued not just derivatively under a vicarious liability rationale for the acts and omissions of its employees, but also directly under a corporate liability theory for systemic negligence that causes patient injury. Health care institutional providers owe independent duties to their patients, including the duty to properly evaluate and supervise the physicians they employ or to whom they grant clinical admitting and treating privileges.

Institutional protocols should delineate operational procedures of their health care teams and the supervisory responsibilities of individual physicians. When there are multiple consultants for an individual patient, medical staff bylaws must spell out the continuing coordination and monitoring obligations of the identified attending physician; failure to do so unambiguously increases the liability exposure of all involved clinicians and the hospital in the event of a bad clinical outcome. Consultants who are not hospital employees must be credentialed to practice within the hospital according to criteria contained in the medical staff bylaws.

Damage or Injury

For the third requisite element of proof in a malpractice action, the plaintiff must produce sufficient evidence and persuade the fact-finder that some damage or injury has taken place. In the surgery context, virtually all filed claims involve an allegation of physical injury, with severity of injury being the most important single factor influencing the decision to sue. Particularly in claims involving older patients, frequently the patient's death is the injury claimed. Often, claims for emotional injuries, pain, and suffering are raised in conjunction with complaints about physical injuries.

If a meritorious malpractice claim has been established to the fact-finder's satisfaction (i.e., by a preponderance of the evidence), a judgment is entered by the court and the defendant is ordered to pay a specific amount of money damages to the injured plaintiff. Ordinarily, this financial payment is made by the defendant's liability insurance carrier on the defendant's behalf and must be reported to the National Practitioner Data Bank (NPDB), established under the Health Care Quality Improvement Act (HCQIA) of 1986, as an adverse action relating to that physician. Even if a malpractice claim is voluntarily settled by the parties without proceeding to trial and verdict (the most common way that cases get resolved), any payment made by or on behalf of the physician to settle the claim must be reported to the NPDB.

The overwhelming majority of malpractice lawsuits in which liability is found involves the awarding of compensatory damages. These dollars are intended to compensate the victim for his or her injuries, to make the victim "whole" again to the extent that money can accomplish that objective. Pecuniary (also called economic or special) compensatory damages encompass precisely measurable out-of-pocket expenditures or lost opportunity costs, such as extra medical bills, special equipment needs, and foregone wages. By contrast, nonpecuniary (also called noneconomic or general) damages encompass real – but more subjective and difficult to measure – losses, such as pain and suffering.

Punitive or exemplary damages are awarded over and above compensatory amounts. Such damages are rarely awarded in malpractice cases, because they are intended to punish defendants for egregious, malicious wrongs (such as patient abuse) and to set an example to deter others from engaging in similar conduct. Negligence is the theoretical basis for most medical malpractice lawsuits and, by definition, consists of unintentional wrongdoing. Therefore, punitive or exemplary damages would not make much sense in the negligence context. However, sometimes as a strategic maneuver a plaintiff includes a request for punitive damages in the complaint solely to be able to introduce before the jury evidence that otherwise would be inadmissible concerning the robust financial status of the defendant.

Causation

Frequently, the most important element to prove in a malpractice action is that the injury suffered by the patient was caused by the defendant's negligence. This is an especially big hurdle for many older patients to surmount, because often it can be counter argued by the defendant that any adverse results sustained are the product not of physician (or other health care professional) negligence, but rather the natural and probable consequence of the older patient's underlying morbidities.

To satisfy the causation requirement, showing mere possibility is insufficient. First, the patient must establish that the physician's negligence was a "cause in fact" of the injury. Under this requirement, it must be shown that either "but for" (sine qua non) the physician's negligence the injury would not have occurred or, alternatively, the physician's negligence was at least a substantial factor in bringing about the injury.

Moreover, the plaintiff is required to show that the physician's negligence not only was the factual cause of the injury suffered, but also that it was the most direct or proximate cause of the injury sustained. Put differently, there can be no intervening, superceding (i.e., unforeseeable) factors that occur to break the causal link between physician negligence and patient injury, or else the plaintiff's claim fails.

Take, for example, the case of a surgeon who performs an operation improperly. As a result of the surgeon's mistake, it is necessary for the patient to undergo additional surgery the next day. On the way from the patient's hospital room to the operating room, the patient falls out of the wheelchair in which he or she was not securely tied by an orderly, hits the floor, and suffers additional injuries. The surgeon's error the previous day in operating would be the "cause in fact" of the patient's injuries because "but for" the physician's negligence the patient would not have been in the process of being transported to the operating room and the fall and resulting harm would not have happened. However, in this scenario, the physician would not be liable for the additional injuries because the orderly's failure to transport the patient properly was an intervening, superceding (i.e., unforeseeable) event that broke the necessary proximate cause linkage.

Informed Consent

Under the ethical principle of autonomy or self-determination, every adult patient (with no upper age limit) has the right to make personal decisions regarding medical care, including decisions about which diagnostic and treatment interventions to undergo or decline. This ethical principle has been translated into the legal doctrine of informed consent. The substantive parts of the informed consent doctrine have evolved over time in the courts, on a case-by-case basis, as a product of state common law. Moreover, individual states have enacted statutes and promulgated regulations codifying a jurisdiction's specific details regarding informed consent.

It is important to note that although the adult patient has a right to decline a particular suggested diagnostic or therapeutic intervention, there exists no corresponding right for the patient or surrogate to demand medical tests, treatments, or procedures that the physician believes will be nonbeneficial or even harmful to the patient; rather, in such circumstances, the physician has an obligation to refuse to accede to the patient's demand. According to the ACS Statements on Principles [9]: "When patients agree to an operation conditionally or make demands that are unacceptable to the surgeon, the surgeon may elect to withdraw from the case."

Elements

For a patient's choice about any specific medical intervention to be considered a legally valid exercise of informed consent, three distinct but interconnected elements must be present. These elements are voluntariness, knowledge or information, and decisional capacity. Assurance that a patient's choice regarding medical alternatives is legally valid based upon these three elements is an imperative of the fiduciary or trust relationship between physician and patient.

Voluntariness

First, the patient's participation in the decision-making process and the final decision must be voluntary. This means it must take place free of force, fraud, duress, intimidation, or any other form of undue constraint or coercion. One aspect of voluntariness is that the patient is entitled to seek out independent opinions from physicians other than the original surgeon, although responsibility for payment for second and subsequent opinions may vary depending on the third-party payer involved.

Knowledge or Information

Second, the patient's medical choice or choices must be based on adequate knowledge or information. The physician has the responsibility to communicate in understandable, nontechnical terms material information about the patient's medical situation (material information being defined as information that might make a difference in the decision-making calculus of a reasonable patient in similar circumstances). Moreover, the physician additionally must be concerned with the flip-side of giving information to the patient, namely being certain that the patient understands the information conveyed [10]. Physicians should take care to assess whether the information they share is actually comprehended by the patient, since physicians often either overestimate patient comprehension or fail to consider it altogether [11]. A high prevalence of both health illiteracy and functional innumeracy within the general population poses serious obstacles to achieving meaningful patient comprehension [12].

In terms of specific data items that need to be shared with the patient, the ACS takes the position that the informed consent discussion conducted by the surgeon should include:

1. "The nature of the illness and the natural consequences of no treatment.
2. The nature of the proposed operation, including the estimated risks of mortality and morbidity.
3. The more common known complications, which should be described and discussed. The patient should understand the risks as well as the benefits of the proposed operation. The discussion should include a description of what to expect during the hospitalization and post hospital convalescence.
4. Alternative forms of treatment, including non-operative techniques.
5. A discussion of the different types of qualified medical providers who will participate in their operation and their respective roles."

The ACS further warns, "The surgeon should not exaggerate the potential benefits of the proposed operation nor make promises or guarantees" [9]. Managing patient expectations to keep them reasonable is an important part of the communication process from the surgeon's legal risk management perspective [7].

The AHRQ advises the consumer public to ask their physicians the following questions [13, 14]:

1. "What operation are you recommending?
2. Why do I need the operation?
3. Are there alternatives to surgery?
4. What are the benefits of having the operation?
5. What are the risks of having the operation?
6. What will happen if I don't have this operation?
7. Where can I get a second opinion?
8. What has been your experience in doing the operation? How many have you performed?
9. Where will the operation be done?
10. What kind of anesthesia will I need?
11. How long will it take me to recover?
12. How much will the operation cost?"

The ACS offers a similar set of queries for patients to pose before consenting to surgery [15]:

> "What are the indications that have led your doctor to the opinion that an operation is necessary?
>
> What, if any, alternative treatments are available for your condition?
>
> What will be the likely result if you don't have the operation?
>
> What are the basic procedures involved in the operation?
>
> What are the risks?
>
> How is the operation expected to improve your health or quality of life?
>
> Is hospitalization necessary and, if so, how long can you expect to be hospitalized?
>
> What can you expect during your recovery period?
>
> When can you expect to resume normal activities?
>
> Are there likely to be residual effects from the operation?"

The ACS Informed Consent statement for consumers [15] adds, at the conclusion of this list:

> "Of course, your surgeon may volunteer much of this information. However, if you still have questions, don't hesitate to ask. Remember, the operation is being performed on you, and you should seek any information that you need to improve your understanding. Your doctor should be willing to take whatever time is necessary to make sure that you are fully informed. No doctor can, or should, guarantee outcomes, because each operation is different, depending upon the individual condition and response of each patient. Nonetheless, your surgeon will be able to give you a good idea of what to expect."

For the older patient with multiple, serious comorbidities, the need for information about the whole health context is especially important. So, too, is accurate, honest discussion about what surgery can and cannot realistically be expected to accomplish and the possible outcomes of different approaches besides life versus death [16]. A surgeon should be sensitive to the fact that individual patients differ in terms of the amount and type of information they desire and that some older individuals want less information because they tend to defer to the physician's opinion [17]. However, the surgeon's presentation of, or at least offer to present, must be forceful enough to fulfill the surgeon's ultimate responsibility to assure the patient sufficiently understands the material considerations concerning the reasonable medical options presented.

Besides the essential informational items listed above, there are other potential items whose mandatory inclusion in the informed consent disclosure process is still being debated as we continue to figure out the best way to usefully inform and empower patients without overwhelming them with unhelpful data. Additional pieces of information in this evolving category include: complementary and alternative medicine options, which are increasingly popular with older individuals; the particular physician's success rate with the particular intervention being recommended [18]; other physician-specific information, such as a drug or alcohol dependency problem or the physician's age-related deterioration in physical and/or cognitive performance that might act as enhanced risk factors; the physician's financial or personal conflict of interests (e.g., consulting relationships with medical device makers [19]) or other incentives arguably impacting the patient's care [20]; the level of uncertainty in the medical community regarding the particular recommended intervention for someone in this specific patient's situation; and the role, if any, that defensive medicine considerations are playing in the health care professional's treatment proposal.

Further, one set of authors recommends the surgeon inform the patient when the surgeon has scheduled other surgeries to be done concurrently with that patient's surgery. The fact of concurrent surgeries, a detailing of who will do what parts of the patient's surgery, and an explanation of why concurrent surgeries have been scheduled should be shared with the patient as early as possible so the patient can use this consideration in making a decision about whether to have the surgery performed and by whom [21].

Live, in-person interaction directly between patient and physician is the most important modality of preoperative communication. However, this interpersonal interaction is increasingly being supplemented (but should never be supplanted) by the use of written literature and video modalities explaining proposed medical procedures, and such informational supplements have been shown to improve both patient knowledge and satisfaction [22]. The Internet and the easily accessible information it can convey to computer-savvy healthcare consumers and their families also has valuable potential as an effective decision aid for patients, as long as the medical profession helps patients to sort out authoritative, reliable from unreliable material available online [23].

Another increasingly important source of information, and not infrequently misinformation, is direct-to-consumer advertising in the popular media for specific medications, medical devices, and types of surgery. Patients no longer arrive in the surgeon's office as a blank slate in terms of knowledge and presuppositions, so it is incumbent on the surgeon to initially determine what accurate information or erroneous misinformation the patient already has at the outset of the informed consent conversation [24].

Meaningful communication with patients is especially challenging in the case of individuals with diminished proficiency in the physician's language. One study found that impaired language facility was associated with reduced patient comprehension even when written forms and other modes of information were translated for the patient, but the unanticipated result in that study may be explained more by the participants' educational level than their native language [25]. Federal law requires that health care institutions offer to make interpreters available for US patients with diminished proficiency in spoken English, but actual surgeon practice frequently entails deference to the wishes of the patient and family when they decline the presence of an interpreter, as well as differing thresholds before surgeons turn to professional or ad hoc (e.g., family) interpreters or attempt to rely upon themselves for the interpreter role. In terms of compliance with federal law, it is preferable that surgeons follow the hospital's adopted policy regarding the use of interpreters rather than try to handle the issue on a largely subjective, case-by-case basis [26].

Studies of the informed consent process point to substantial opportunity for improvement in the information communication part of that process, which ideally should serve an educational and bonding role. Physicians with all levels of educational background too commonly have a deficient understanding of their legal obligations in this arena and patients often very inadequately understand the information provided to them. There is some evidence that formal training improves surgery residents' ability to discuss treatment options with patients [11].

Among the strategies suggested by one Task Force for promoting shared decision making to achieve more goal-concordant care in seriously ill older patients with surgical emergencies has been a proposal for a structured approach to guide surgeons in communicating with patients [27]. The nine key elements in that proposed structured approach are: formulating prognosis, creating a personal connection, disclosing information regarding the acute problem in the context of the underlying illness, establishing a shared understanding of the patient's condition; allowing silence and dealing with emotion, describing surgical and palliative treatment options, eliciting patient goals and priorities, making a treatment recommendation, and affirming ongoing support for the patient and family.

Another set of authors has proposed a similar structured physician-older patient communication approach consisting of clarifying the patient's prognostic understanding and expectations for recovery, identifying the patient's priorities and goals for treatment, determining health states that the patient would find unacceptable, recommending palliative treatment alongside life-prolonging intervention as best aligned with the individual's personal goals and wishes, and affirming the clinician's commitment to the patient's well-being [28].

Decisional Capacity

Legally valid medical decisions require that there be a capable decision maker. A patient must be cognitively and emotionally able to weigh alternatives rationally; autonomous choices cannot be made by a nonautonomous person. The US legal system begins with a rebuttable presumption that every adult (with no upper age limit) is capable enough to make his or her own medical decisions if provided with sufficient information.

However, for some geriatric patients, this aspect of medical decision making may be factually problematic. It is "estimated that nearly half of U.S. adults near the end of life [are] unable to make decisions for themselves about whether to accept life-prolonging technologies" [29]. In particular, a substantial portion of the geriatric surgical population lacks adequate decisional capacity to make legally valid decisions about undergoing surgery [30].

There are a number of clinical factors that may interfere with an older patient's decisional capacity. There is a significant and increasing incidence of dementia, depression and other affective disorders, delirium, and other mental health problems such as psychoses among older individuals. However, the severity of mental illness, in terms of cognitive and behavioral impairment, and therefore the illness' impact on functional ability, varies for different patients at different times along a continuum. For that reason, there is not an automatic, precise correlation between an older person's clinical diagnosis and a simple, dichotomous determination that the individual definitely does or does not possess sufficient present capacity to personally make important decisions about medical care. Older individuals also are more likely to suffer sensory deprivations (such as hearing or sight deficits) that may interfere with the ability to understand and utilize information necessary for making medical decisions.

In each case, the attending physician needs to assess, either formally or informally, the particular patient's decisional capacity [31]. The literature suggests that physicians today often do an inadequate job of recognizing and properly investigating possible incapacity in patients [32]. One explanation for physicians frequently giving short shrift to the capacity issue is their tendency to avoid questioning the capacity of any patient who agrees with the physician's treatment recommendation, regardless of the patient's actual mental status.

Sometimes collaboration or consultation with a psychologist or psychiatrist in the capacity assessment endeavor can be very helpful. The conduct and documentation of such consultation can be a useful risk management practice for the surgeon, as the legal system affords mental health specialists a great deal (arguably an excessive amount) of deference as assessors of patients' decisional capacity.

A large amount of well-funded psychological and psychiatric research has been undertaken aimed at developing and disseminating new standardized instruments useful for the specific purpose of reliably measuring decision-specific capacity among older individuals. Despite this endeavor and the widespread incorporation of the Mini-Mental State Exam (MMSE) and the Cognitive Performance Test (CPT) into clinical practice for various diagnostic and treatment planning purposes, there exists no single, uniform, scientifically agreed upon standard of legal competence/decisional capacity for making medical decisions. Any capacity evaluation instrument should be relied upon only in conjunction with direct observation of the patient's ability to understand and manipulate information.

Assessment of decisional capacity should focus on function, rather than the patient's diagnosis or categorical label, since illnesses vary in severity and different people with the same clinical diagnosis may function at very different levels. Similarly, capacity assessment should not depend upon whether or not the assessor agrees with the particular choice made by the patient. Questions that should be included in the physician's tacit or explicit functional inquiry about a patient's decisional capacity are:

1. Can the patient make and communicate (in any manner) choices regarding medical interventions?
2. Can the patient articulate any reasons for the choices made (to indicate that some sort of reasoning process is taking place)?
3. Are the stated reasons given to explain the patient's choices rational in the sense that the patient starts with a factually accurate understanding of the medical circumstances and can reason logically from those circumstances to a conclusion?
4. Does the patient understand or appreciate the implications, including the foreseeable personal risks and benefits, of the alternatives presented and choices made?

Several considerations should guide the physician's assessment of a patient's decisional capacity. Most importantly, capacity is a matter of whether the patient has at least a minimally sufficient (not necessarily a perfect) degree of functional ability, regardless of the clinical diagnosis or whether the physician personally agrees or disagrees with the patient's decision. Second, capacity needs to be determined on a decision-specific, not a global or all-or-nothing, basis. A patient may be capable of rationally making certain kinds of decisions but not necessarily others; partial or limited capacity may be possible even when total capacity is not. A decision about undergoing surgery ordinarily involves an array of complex facets concerning significant potential risks, benefits, and alternatives and thus requires a relatively high level of cognitive/intellectual and emotional capacity on the patient's part.

Decisional capacity is variable, rather than static, over time in many older patients. It may wax and wane in particular cases depending on the environmental factors, such as time of day (for instance, the sundowning phenomenon in the elderly), day of the week, physical setting, presence of acute or transient treatable medical problems, other persons involved in supporting or interfering with the patient's decision, or the patient's reactions to medications. Physicians often can affect their patients' capacity, for better or worse, through the way they deliver care (e.g., through the choice and timing of medication administration). Physicians should endeavor to communicate with patients and, when possible, time the decision-making process around a patient's windows of lucidity.

Additionally, the presence of cognitive or emotional impairment, even if substantial, does not necessarily rule out the possibility of some level of involvement in decision making. Many older persons may be capable of engaging in shared or assisted consent with extra time and effort on the physician's part when the person has a supportive network of family and friends available. For instance, an older patient who cannot process information as swiftly or easily as a younger person still may be able to sufficiently understand the complexities of a proposed treatment plan and share in the decision making if afforded enough emotional support [31].

After surgery has taken place, there likely will be a series of postoperative treatment decisions that need to be made. The patient's decisional capacity may be an even larger issue at the postoperative stage. It has been reported that postoperative cognitive dysfunction (POCD), representing "a decline in a variety of neuropsychological domains including memory, executive functioning, and speed of processing," is a common clinical condition following major surgery in older patients, particularly in cardiac, vascular, urologic, and orthopedic surgery [33].

Exceptions to the Consent Requirement

The law recognizes certain exceptions to the usual informed consent requirement. The most relevant exception for surgeons concerns emergency situations. In the case of life-threatening emergencies, the law excuses noncompliance with the otherwise-applicable informed consent requirement on the rationale that we generally presume that a patient confronted with such an emergency would consent – if presently able to do so – to medical interventions necessary to preserve the person's life. Reliance on the emergency exception to dispense with obtaining the voluntary, informed, and capable consent of the patient prior to initiating an intrusive and risky medical intervention such as surgery should be strictly limited to situations containing all of the following characteristics: a true life-threatening emergency; time is of the essence and delay will greatly diminish the likelihood of success; the patient is unable at the time to make an autonomous decision about medical care; there is not enough time to identify, locate, and consult with a legally authorized surrogate decision maker; there is insufficient time to apply for a court order; and surgery is the least intrusive and risky alternative for accomplishing the goal of preserving the patient's life.

A more controversial exception to compliance with informed consent requirements is the doctrine of therapeutic exception or therapeutic privilege. The defense of therapeutic privilege to a claim of nondisclosure of material information about a patient's diagnosis, prognosis, or treatment is applicable when, in the physician's good faith professional judgment, disclosure would be likely to complicate or hinder necessary treatment, cause severe psychological harm, and be so upsetting as to render a rational decision by the patient impossible. The physician's desire to maintain a decent level of hope in a seriously ill older patient is understandable [34], but the courts have recognized the therapeutic privilege defense only very rarely and in extreme circumstances, lest this defense too readily become the exception that totally swallows the general rule.

Documentation of Consent

Although implied consent (implied by the patient's nonobjecting, seemingly acquiescing conduct) is sufficient for medical interventions that are not very intrusive or risky, surgery ought to be done only when the patient (or the patient's authorized surrogate) has indicated consent for the intervention expressly, and more specifically in writing. A signed, separate consent form does not by itself constitute compliance with legal requirements; the doctrine of informed consent ideally refers to a dynamic, authentic, shared decision-making process revolving around information provision and interactive communication between the physician and patient (or surrogate) [35]. A signed consent form does not by itself take the place of the requisite process of communication, but it does facilitate proving that the process took place, in the event that the sufficiency of informed consent is challenged after the fact. In addition, voluntary accreditation standards with which the physician's affiliated institution complies, such as those of the Joint Commission, may require the use of separate written consent forms for particular categories of medical interventions, certainly including surgery.

Research reveals that surgeon/patient conversations often deviate from the information on written consent forms the patient is asked to sign, with the conversations sometimes omitting information found on the forms and sometimes including information not found on the forms [36]. The information the patient receives should be consistent and coherent; hence, there is significant room for improvement both in the content of surgeon/patient discussions and in the drafting of consent forms.

Advance Medical Planning

Timely preoperative surgeon/patient conversations about the patient's goals for medical care are essential [37]. "The most important aspect of providing good end-of-life care to geriatric patients is having a discussion about the goals of care. Ideally, this conversation should include patients when they are at their normal functional status, as this allows them to express their desires as well as establish which family members they wish to be involved in the dialogue" [38]. These conversations happen [39], but not often enough [40]. Nonetheless, in anticipation of future circumstances in which decisions about surgery might need to be made but the patient would lack sufficient decisional capacity to give or withhold informed consent, there are several legal mechanisms available to maximize the patient's prospective medical autonomy. Best Practice Guidelines issued by the American College of Surgeons' National Surgical Quality Improvement Project and the American Geriatrics Society for "Preoperative Assessment of the Geriatric Surgical Patient" recommend that clinicians "determine the patient's treatment outcomes" and place advance directives in the patient's medical record [41].

Any adult may, while still capable, execute certain legal instruments that voluntarily delegate or direct the exercise of future medical decision-making power. While oral advance medical directives, theoretically, are completely legally valid, patients should be encouraged to execute written versions to maximize the likelihood that the directive ultimately will be respected by family members and health care professionals. Organizational providers are required by the federal Patient Self-Determination Act to initiate discussions with capable patients about the availability of advance medical directives opportunities.

The durable power of attorney (DPOA) consists of a written document in which an individual (the principal) appoints an agent, or attorney-in-fact, to make various kinds of decisions for the principal. Each state has enacted one or more statutes that explicitly authorize the use of a DPOA for health care to empower an agent (including a nonfamily member) to make medical choices on a patient's behalf, should the patient later lose decision-making capacity. A DPOA may be immediate in nature, meaning that it comes into effect as soon as the agent is named. In a springing DPOA, on the other hand, the legal authority transfers (springs) from the patient to the agent only upon the occurrence of some specified future event, like a declaration of the principal's incapacity by a designated number of examining physicians. The patient should be notified by attending health care professionals when they have decided to act as though decision-making authority has sprung to the designated agent, so the patient can utter a protest, if desired, to the agent's exercise of power.

The DPOA is a proxy directive, and thus distinguishable from a living will, which is an instruction-type directive. In an instruction directive, a presently capable patient documents his or her wishes regarding future medical treatment (e.g., "no extraordinary measures" or "keep me alive forever no matter what pain or expense") rather than naming an agent to make future treatment decisions in the case of eventual incapacity. The two kinds of legal devices are not mutually exclusive; indeed, patients may be encouraged to execute them in tandem because the living will can help an agent named under a DPOA to exercise the patient's autonomy rights more accurately.

The latest innovation in advance health care planning is the Physician Orders for Life-Sustaining Treatment (POLST) Paradigm. (The precise title for this concept may vary among different jurisdictions.) A POLST is a mechanism that converts a patient's treatment wishes into the tangible form of a physician's order. Because physicians and other health care professionals (including emergency responders) are accustomed to carrying out medical orders, there is evidence that when treatment instructions are expressed in the form of a POLST they are substantially more likely to be honored and implemented in practice than are wishes expressed only in the form of a patient's prior expression or a surrogate's current representation of the patient's inferred preferences. Unlike an advance directive that is advisable for any adult, a POLST is appropriate only for a patient who is so seriously ill that a physician exercising sound judgment would not be surprised if that patient died within the next year. Individual states are at different points concerning the degree of POLST penetration in medical practice. Some states have enacted statutes and/or regulations specifically authorizing POLST, while other states are in earlier stages of legal recognition, although in no state are there any laws that prohibit either physicians from writing a POLST for an appropriate patient or emergency medical personnel or other health care professionals from following a POLST.

The POLST Paradigm builds on the Do Not Resuscitate (DNR) mechanism that has been utilized for appropriate patients for several decades. The DNR – also known as Do Not Attempt Resuscitation (DNAR) or No Code – order instructs health care professionals to refrain from initiating cardiopulmonary resuscitation (CPR) for a particular patient who suffers a foreseeable, even anticipated, cardiac arrest. The prevailing law is that a physician may write a DNR order if the decisionally capable patient decides that the likely burdens of CPR (a Code) would seriously outweigh any expected benefits (e.g., mere continued existence until the next, probably fatal, cardiac arrest).

DNR orders may be relevant to the surgery context in at least a couple of important respects. First, several studies have found that the preexisting presence of a DNR order is independently associated with a higher mortality rate among geriatric patients undergoing emergency surgery. This DNR versus non-DNR mortality discrepancy is due mainly to the greater incidence of renal insufficiency, heart attacks, organ/space surgical site infections, and pneumonia among postsurgical patients with preexisting DNR orders.

The authors of these studies uniformly conclude that the informed consent process should include patient and family counseling on surgical expectations because the risk of perioperative events are significantly elevated when a DRN order exists and that prognostic data may be material to patient/surrogate decisions about undergoing the surgery [42, 43]. Potential explanations for this risk elevation are that: patients for whom DNR orders have been written are likely to be sicker in the first place; physicians may be less aggressive in treating DNR patients postoperatively (although there is no evidence to confirm this theory); and/or that patients with DNR orders and their surrogates may be less willing to accept aggressive postoperative treatment [42]. It has been speculated that some patients with DNR orders might consent to emergency life-sustaining surgery but then resist aggressive postoperative interventions for complications, on the theory that after surgery when serious complications occur, patients adopt a different, more realistic perspective on the balance of potential benefits and burdens of various medical treatments [43].

Second, the American College of Surgeons, American Society of Anesthesiologists, and Association of Operating Room Nurses have published guidance to their members relating to the status of DNR orders as a part of operative and anesthesia care. According to this policy statement, "The best approach for these patients [who are considering surgery but have a DNR order already in place] is a policy of 'required reconsideration' of the existing DNR orders. Required reconsideration means that the patient or designated surrogate and the physicians who will be responsible for the patient's care should, when possible, discuss the new intraoperative and perioperative risks associated with the surgical procedure, the patient's treatment goals, and an approach for potentially life-threatening problems consistent with the patient's values and preferences" [44].

In recommending required reconsideration, the ACS policy statement rejects an automatic rule either requiring DNR enforcement during surgery or always revoking it as a precondition of surgery, leaving the resolution of the resuscitation issue ultimately up to the informed choice of the patient or surrogate. Nevertheless, because surgeons ordinarily anticipate and insist upon the need for aggressive postoperative care of patients undergoing high risk operations, many of them decline to operate altogether on patients who have advance directives that limit aggressive postoperative treatment [40]. This may occur because "surgeons seem to rely on assuming that patients understand surgery is high risk and assent that they require difficult postoperative care after a major procedure. This may account for the perception that surgeons are overly aggressive in prolonging life in postoperative care, because a surgeon has had a discussion with a patient and told the patient what to expect intraoperatively and postoperatively, and the patient agreed to pursue the intervention." [45]. Another way of interpreting surgeons' avoidance of patients with treatment-limiting advance directives is that many surgeons experience difficulty in moving from a curative medical treatment model to a more palliative mode of care, and we need to ask how physicians generally, and surgeons, particularly, can learn to negotiate acceptable accommodations with their patients centered around the patient's goals of care [37].

Surrogate/Proxy Decision Making

Even when a patient is determined by the medical team to lack sufficient present capacity to autonomously make specific necessary decisions about recommended interventions, informed consent principles still apply. What is different in the case of patient incapacity is that decisions must be made for that patient by a surrogate or proxy (terminology sometimes varying by jurisdiction).

The modern trend pertaining to all of the various mechanisms of surrogate decision making has been toward the substituted judgment standard. Under this approach, the surrogate is expected to make the same decisions that the patient would make, according to the patient's own priorities and values to the extent they can be ascertained, if the patient were presently able to make and express his or her own authentic decisions. The subjective substituted judgment standard is most consistent with respect for autonomy. When it cannot realistically be ascertained what the now-incapacitated patient would have decided if imbued with adequate present capacity, the surrogate is expected to act in a fiduciary or trust agent role and rely on the traditional best interests standard. The best interests test mandates that decisions be made in a manner that, in the surrogate's considered judgment, would confer the most benefit and the least burden on the incapacitated individual.

Formal designation of a person with legal authority to act as the patient's surrogate for medical decision-making purposes may be accomplished through several different channels. These surrogate designation mechanisms are described below.

Advance Planning

As was discussed earlier, a person may take steps, while still decisionally capable, to anticipate and prepare for his or her eventual incapacity. Advance directives may be executed by a presently able individual and the resulting DPOA may be used to designate a decision-making agent. Under a DPOA as described earlier, the principal may give the agent general or specific instructions to direct future medical decision making or may make an unrestricted grant of authority and in either case may make the delegation of authority effective immediately or on a future, springing basis.

The DPOA is distinguishable from the regular or ordinary power of attorney. The latter device ordinarily is used to delegate authority to make arrangements and take actions regarding the principal's financial or property affairs, and the agent's authority expires automatically when the principal becomes decisionally incapacitated. In the medical decision-making sphere, therefore, an ordinary POA usually is inapplicable.

Guardianship

Creation of a guardianship or conservatorship (precise terminology varying among different jurisdictions) is the most legally definitive means of transferring decision-making power to a surrogate without the patient's permission. It entails appointment by a state court of a surrogate (the guardian/conservator) who is empowered to make certain decisions on behalf of an incapacitated person (the ward). This legal process is initiated in response to a petition filed by the family, a health care facility, a financial institution, the local Adult Protective Services (APS) agency, or any other interested party. The legal proceeding involves review by the court of a sworn affidavit or live testimony of a physician who has examined the alleged incapacitated person and offers a professional opinion about the individual's present capacity. Most courts strongly prefer to appoint a family member who is willing and able to act as a guardian/conservator; in the absence of a willing and able family member, however, the court may appoint someone else (such as a close friend) or a public (governmental) or private guardianship program if those options are locally available. There are also professional guardians who are available for court appointment if the ward has money the court can order be used to pay for the guardian's services.

Creating total or plenary guardianship entails an extensive deprivation of an individual's fundamental personal rights. When a deprivation of rights (such as the right to make one's own medical decisions) is involved, the legal policy is that society should intervene only in the least restrictive or least intrusive manner possible consistent with accomplishing the legitimate purpose of the intervention. On the basis of the least restrictive alternative doctrine, limited or partial guardianship/conservatorship is preferred whenever feasible over the plenary variety. In every American jurisdiction, courts have been given the statutory authority to limit a surrogate's power in terms of duration and the types of decisions (e.g., surgery) covered.

Because the official legal process of guardianship/conservatorship ordinarily entails significant financial, time consumption, and emotional costs, it should not be initiated unless and until less formal approaches, like consultation with an Institutional Ethics Committee (IEC) or ethics consultation service, have been exhausted in an effort to reach an accommodation that all the involved parties (including the patient's physicians) can tolerate.

Default Authority Statutes

In the absence of judicial appointment of a guardian/conservator or the patient's prior formal designation of an agent, the longstanding medical custom has been for physicians to turn to family members (when available) to function as surrogates for their incapacitated relatives. This next-of-kin practice has been codified in the large majority of states by legislative enactment of "family consent' statutes that expressly authorize specific relatives, listed in a priority order, to make particular kinds of decisions (including medical decisions) for their incapacitated family members. This statutory codification of common practice is based on the presumption that family members generally know best the basic values and preferences of their relatives (thus making substituted judgment realistic) or, at the least, will act as trustworthy advocates for their relatives' best interests. However, physicians and other health care professionals must be alert to possible troublesome conflicts of interest – financial, emotional, or otherwise – that can render a family member inappropriate to act as a surrogate decision maker for the patient.

In the absence of any family member willing and able to act as surrogate decision maker for an incapacitated patient, state default authority statutes name certain others (e.g., friends) who are empowered to make decisions for the patient. Physicians should carefully avoid stepping into the surrogate decision maker role themselves, in order to avoid creating the appearance, let alone the reality, of a conflict of interest.

"Unbefriended" Patients

A challenging set of issues concerns the burgeoning number of incapacitated *unbefriended* older individuals who lack willing, available family or friends to advocate or engage in substitute decision making for them. This population group arises because of a combination of demographic and family structure changes in American society, namely older individuals today outliving their own decisional capacity and either never marrying or having children or, alternatively, outliving their spouse, children, and other relatives.

A few program models exist as a starting point to develop efficient processes to deal with situations involving treatment decisions for the unbefriended group. For example, programs have experimented with such options as internal institutional committees, public guardianship offices, professional guardians (when the ward has sufficient assets to pay for this arrangement), and volunteer guardianship projects. The health care system and the law need to continue clarifying theoretical matters and operational details pertaining to decision making for this population group. The surgeon should consult hospital legal counsel to determine acceptable local sources of surrogate decision making for the incapacitated patient without relatives or friends. In 2016, the American Thoracic Society and the American Geriatrics Society jointly established a Task Force charged with developing a relevant policy statement.

Nonbeneficial Surgery

There are times when a patient, or more usually the patient's family, may insist on initiating or continuing medical treatments ("doing everything possible"), including treatments relating to surgery [45], that the clinician believes are clinically and ethically inappropriate in terms of patient benefit. Neither patients nor families possess a legal right to demand, nor does a physician owe a duty to provide, nonbeneficial medical treatment. On the rare occasions when courts have become involved prospectively with this issue because families have asked a judge to order health care professionals to provide specific medical treatments, the judicial opinions generally have been confusing, inconsistent, and poorly reasoned. However, no court has ever held a health care professional or institution liable after the fact for failure to begin or perpetuate futile interventions for a critically ill patient, even when the family was insisting on doing everything technologically possible.

In practice, clinicians usually seem to take the path of least resistance in such circumstances and "treat the family," often out of misapprehension about potential liability exposure. Other factors that may contribute to the provision of nonbeneficial emergency surgery for older patients are the difficulty of making and communicating an accurate prognosis in light of insufficient data, problems in assessing whether and how much the patient is suffering, the patient's and family's image of surgery as an effort to "do something" to give the patient at least a chance to live and recover, and the surgeon's belief that offering nonbeneficial surgery gives the family time to cope with an overwhelming, emotional situation [46, 47]. In the vast majority of cases, better physician–family communication, perhaps supplemented with formal or informal dispute resolution mechanisms such as IECs, in which the realistic (i.e., negative) implications of "doing everything possible" are clearly delineated, can avoid or resolve serious disagreement over how to proceed [48].

Research Context

The requirements relating to informed consent in the diagnostic and therapeutic contexts all apply with full force in the context of biomedical research, including surgical research, involving the use of human participants as research subjects [49]. Besides common law doctrine, particular aspects of informed consent for human subjects research are governed by federal regulations (the Common Rule in all cases, 42 Code of Federal Regulations Part 46, and regulations of the Food and Drug Administration when investigational drugs or medical devices are involved) and state statutes. Under the federal regulations, research protocols enrolling human subjects as data points must be approved by an Institutional Review Board (IRB) before subject enrollment may commence. One of the primary responsibilities of the IRB is to assure that enrollment occurs only when subject or surrogate consent is given voluntarily, knowledgeably, and by a decisionally capable person, and separate written consent forms usually are required. The other main IRB tasks are assuring that risks to the subjects are minimized, the ratio of risks to potential benefits is ethically tolerable, and that subject selection is equitable.

Confidentiality

Because of the physician/patient relationship, surgeons constantly come into the possession of information about patients and their families. Health care professionals owe patients a fiduciary responsibility to hold in confidence all personal patient information entrusted to them as a consequence of the professional/patient relationship. This ethical obligation, founded on the patient's important interest in maintaining personal privacy and avoiding the social stigma and potential discrimination that breach of one's medical privacy might implicate, is enforceable under both state and federal law.

Every state, both within its respective professional Practice Acts and in separate statutes pertaining to particular health care delivery settings, has enacted statutory provisions delineating the confidentiality duties of health care professionals and institutions. Often, state agencies publish accompanying regulations to implement these statutes. Moreover, a strong common law health care confidentiality doctrine has been enunciated over time by state court decisions. Violation of state common law or statutory or regulatory requirements regarding the confidentiality of patient information may subject erring health care professionals to civil damage suits brought by or on behalf of the patient whose privacy was improperly infringed; additionally, violation of state Practice Act provisions may subject the violator to administrative sanctions by the state, including license suspension or even revocation.

However, numerous exceptions to the general confidentiality rule have been recognized, either by the courts as part of the common law or embedded in state legislation or regulation. The most prominent exception occurs when a patient, expressly or impliedly, voluntarily, and knowingly waives, or gives up, the right to assert that particular information be kept confidential. These waivers take place daily to make information available to third-party payers (for instance, Medicare claims processors and private health insurers), quality of care auditors (such as Joint Commission surveyors), and other public and private entities like health care surrogates authorized to make medical decisions on behalf of a decisionally incapacitated patient. Also, because the modern delivery of health care most often is a team endeavor, each patient implicitly gives permission for the sharing of certain otherwise private pieces of information among the members of the treatment team. Internal information sharing of this nature is essential to optimal care, especially for accomplishing coordination and continuity of surgical care for older patients. Indeed, failures in communication among the multiple professionals involved in the care of a patient needing such coordination and continuity may form the basis for negligence liability claims when harm results.

Second, the patient's reasonable expectation of privacy must give way when the health care professional is mandated by state statute or regulation to report to enumerated public health or law enforcement authorities such as APS the professional's reasonable suspicion that certain conditions or activities have occurred or are occurring. Such reportable conditions or activities may include elder mistreatment or neglect (in many states including cases of self-neglect within that definition), domestic violence, infectious diseases, births, and deaths. Some states that have declined to mandate the reporting of particular situations to public authorities nonetheless encourage voluntary reporting; a few states have pursued this approach regarding cases of suspected elder abuse or neglect. Those states supply an incentive for voluntary reporting by expressly providing legal immunity against any form of civil, criminal, or administrative liability for covered persons making good faith reports to public authorities. Mandatory and voluntary reporting statutes embody the state's exercise of either its inherent police power to protect and promote the general health, safety, welfare, and morals of the community or its *parens patriae* power to step up and safeguard individuals (such as persons with serious cognitive or emotional disabilities) who are not capable of protecting themselves.

Further, a health care professional may be compelled to reveal otherwise confidential information about particular patients by the force of legal process, namely, by a judge's issuance of a court order requiring such release. This is a possibility in any civil or criminal lawsuit involving a factual dispute about a patient's physical or mental condition. A court order (as opposed to a subpoena or subpoena *duces tecum*, which is issued simply as an administrative, nondiscretionary matter by the court clerk rather than by a judge) requiring one to produce personally identifiable patient information may overrule the state's professional/patient testimonial privilege statute that ordinarily would prohibit the professional from testifying in a legal proceeding regarding private patient information. Every state testimonial privilege statute provides for judicially compelled testimony on the part of the health care professional when, for example, the patient has placed his or her own health condition and medical treatment in issue in a lawsuit.

Besides state statutes, regulations, and common law provisions, there are a variety of federal statutes and regulations imposing on health care professionals and institutions particular confidentiality obligations when care is provided within specific types of health care settings, including federal penal institutions, veterans affairs facilities, military institutions, federal community health centers, and facilities specializing in the treatment of persons having drug and alcohol addiction. Violation of these laws may result in substantial civil fines. Statutes and regulations setting the conditions for receipt of Medicare and Medicaid payments contain confidentiality provisions, situated within general patients' rights standards. Noncompliance with those provisions could trigger a range of regulatory sanctions, at the extreme including decertification of the institutional provider from participation in federal health care financing programs.

Federal regulations codified at Title 45, US Code of Federal Regulations Parts 160 and 164 implement the Health Insurance Portability and Accountability Act (HIPAA) of 1996 (Public Law No. 104–191, title XI, Part C). These regulations, published in the form of a Privacy Rule and a Security Rule, impose on covered health care entities (defined in part as any health providers who transmit any patient-related information electronically) an extensive set of requirements regarding the handling of personally identifiable medical information contained in patient records. These regulations impose severe criminal and civil sanctions for unauthorized disclosures of protected health information (PHI). Substantively, HIPAA and its implementing regulations in essence codify preexisting state statutory and common law protections for patients, with the addition of provisions making it clear that patients now have the right to access the information contained in their own medical records. (Previously, state law had varied or was unclear regarding the issue of patient access to records.) HIPAA contains provisions authorizing covered entities to transmit PHI to certain others for purposes of "treatment, payment, and health care operations" such as quality assurance or marketing. These and other exceptions explicitly contained in HIPAA basically track the preexisting state statutory and common law exceptions.

The physician must guard against the unauthorized disclosure of protected PHI. The person who has the authority to give or refuse consent for medical treatment (the patient or a surrogate) usually controls the release of identifiable medical information to third parties, unless there is a court order or government regulation demanding something different. All questions about the release of medical information to third parties in specific cases should be directed to the institution's medical records department or legal counsel.

Patient Safety and Risk Management

A number of strategies are available to individual surgeons and the institutions within which they practice to reduce the risks of negative legal entanglements to which they are exposed. Effective risk management is integrally tied to the cultivation of a preventive safety culture within the health care institution [50]. The institution's risk management program (designed to identify, mitigate, and avoid potential injuries and other types of problems that could result in legal, and therefore financial, loss to the institution) should incorporate specific activities designed to address patient safety and associated legal risks prevalent in the surgery context. For instance, prior to surgery, an effective prevention strategy for POCD would identify risk factors in patients in terms of age-related physiological changes, comorbidities, and lifestyle, history, alcohol consumption, smoking, and the use of various medications [33].

This chapter section briefly outlines a few of the most salient patient safety/risk management strategies relevant to surgical care of geriatric patients. The surgeon should become knowledgeable about his or her own institution's risk management program and cooperate with institutional risk managers to ensure appropriate sensitivity to surgical practices and potential problems and their avoidance or mitigation. The surgeon should view the risk manager as a partner in pursuit of the common goal of providing, and if necessary proving after the fact that the surgeon provided, quality patient care.

Safety Checklists

Surgical complications represent a significant cause of mortality and morbidity in geriatric patients. Some of these complications are associated with human errors by individuals or teams, such as wrong patient/procedure/site surgery, equipment malfunctioning or availability problems, unanticipated blood loss, nonsterile equipment, and surgical items such as sponges or instruments left inside patients. It has been credibly estimated that medical error is the third leading cause of death in the USA [51]. Surgical checklists can potentially prevent errors and complications that may occur during surgery or perioperatively [52]. Checklists may reduce errors by, among other things, increasing the probability that all critical tasks have been done, facilitating a respectful team approach, encouraging communication, identifying and preventing near misses, and pushing the care team to prepare systematically for both anticipated and unanticipated complications. Checklists are useful in both hospital settings and in ambulatory surgical centers (ASCs) [53]. Ideally, checklists should be tools that support clinical practice without substituting a rigid formula in place of professional judgment [53].

A number of specific surgical checklists have been developed and disseminated. These include the: World Health Organization (WHO) Surgical Safety Checklist; Joint Commission Universal Protocol (UP) for Preventing Wrong Site, Wrong Procedure, Wrong Person Surgery; and Surgical Patient Safety System (SURPASS) checklist [52], as well as those incorporated in the Safe Surgery Saves Lives program [53]. Additionally, many individual institutions have developed their own surgical checklist versions.

Hospital Credentialing

In order to admit a patient to a hospital or ASC and/or treat them in that facility, a surgeon must be credentialed by the facility. Health care facilities grant admitting and treating privileges to physicians and other health care professionals based on a review of the applicant's training and experience by the facility's organized medical staff, with the facility governing board ultimately granting the credentials in response to the medical staff recommendation. In the past, privileges were often granted on a very broad, even unlimited basis. Today, by contrast, privileges are granted on a limited basis, restricted based on the medical staff's evaluation of an applicant's personal experience and qualifications regarding particular medical services. For example, a facility has the discretion to grant a surgeon privileges to perform surgery using traditional methods, but not extend those privileges to innovative new techniques such as the da Vinci Surgical System unless the surgeon can demonstrate particular expertise and experience in using the innovative technique.

Health care facilities owe their patients a legal duty to credential their physicians and other health care professionals in a nonnegligent manner, by using due or reasonable care in the credentialing process. Exercised judiciously, the legal authority and responsibility of health care facilities to credential practitioners can act as a powerful patient safety and quality assurance tool [2].

Documentation

Creating and maintaining accurate records of patient care is an integral part of the duty that a physician owes a patient. Good documentation is imperative to providing competent patient care and avoiding unexpected bad outcomes and thus is wise risk management practice. Moreover, in the event the surgeon is accused of providing substandard care, the surgeon's best (and sometimes only) defense will lie in the quality of documentation created to explain and justify decisions made and actions taken. In addition, institutional accreditation and third-party payment turn heavily on information drawn from medical records.

The quality of medical records is especially important in surgery, where patient conditions are subject to rapid change and many different professionals may be involved as members of the surgical team. The watchwords of documentation from both medical and legal perspectives are completeness, legibility, accuracy or truthfulness, timeliness, corrections made in a clear and unambiguous fashion, and objectivity. Dedicated training can make a positive, albeit fairly modest, impact on surgeons' documentation performance [11].

The ongoing evolution toward adoption of electronic health record (EHR) systems in health care institutions holds the strong potential for improving the quality and efficiency of patient care documentation. One of many problems that need to be solved, though, is the lack of interoperability among different EHR systems among different health care facilities and even within the same facility. The advent of EHR also implicates a number of HIPAA compliance and other information confidentiality concerns of the sort discussed previously.

Special attention should be directed to proper documentation of informed consent in the surgery arena. The role of informed consent documents has been discussed previously.

Error Disclosure and Apology

The disclosure of adverse events to patients, including adversities related to medical errors, is a vital component of a complete patient safety and quality improvement program [54]. The magnitude of medical errors committed in the USA is substantial [51], with many of those errors taking place before, during, or after surgery on older patients. The surgeon may be faced with the dilemma of whether to explicitly admit to a patient or surrogate that a problem being experienced by that patient may be related to the occurrence of a medical error. The immediate temptation may be to cover up the fact that an error has taken place.

Disclosure of errors to patients or surrogates is difficult for surgeons for several reasons [54, 55]. For one thing, often there is a relational distance between the surgeon and the patient, whom the surgeon may have met only once prior to the surgery. There rarely is a longstanding, mature relationship. For another thing, interactions between surgeons and patients or surrogates frequently take place in information-poor environments. Third, since surgical error may cause direct physical injury to the patient, the patient's or family's reaction to the error may be quite emotionally intense; anticipation by the surgeon of an intense, negative encounter may increase the surgeon's anxiety and potentially make the surgeon more averse to facing these disclosures. In addition, empathy does not come naturally to most surgeons, and many need to learn how to do better at engaging in empathic behaviors.

Of course, a major impediment to a vigorous assault on the medical errors problem is the fact that many physicians and other health care professionals persist in equating the admission of error with legal suicide. As explained below, physician anxieties about adverse legal consequences, while sincere, are mainly exaggerated or erroneous.

Another obstacle is the traditional shame-and-blame culture of medicine. Individual actors have been singled out for making mistakes, rather than an environment in which errors are recognized as a complex systematic phenomenon requiring broader solutions. In the shame/blame environment, where errors are seen as a form of personal moral failure that shatters the pervasive aura of infallibility, the physician's fear of losing face in front of one's peers seriously impedes efforts to encourage a more forthright response to medical errors.

Indulging the temptation to cover up errors in medical care, besides violating basic ethical principles, probably constitutes ineffective or even counterproductive legal risk management [1]. For one thing, modern medical care has become such a complex enterprise involving so many different professionals potentially interacting with the patient, the medical record, and external evaluators (including attorneys) that, pragmatically speaking, it is unlikely that a cover up of essential facts about a medical error relating to serious patient harm could be sustained for very long. Moreover, the majority of patients and surrogates expect and respect honesty on the physician's part; patients who feel they have been communicated with candidly are more likely to trust than sue the physician. Patients tend to approach plaintiff attorneys with an eye toward filing a malpractice lawsuit when they are angry at the physician [56], and nothing makes most patients angrier that believing that the physician has not been truthful with them, particularly when serious harm for which the patient was not prepared occurs.

When a patient has been injured by a medical error, placing the focus on patient welfare (i.e., working to remedy or mitigate the patient's medical problem, even though that might entail admitting the error), rather than on concealing the error from the patient, is the most constructive defensive practice. Error disclosure has not opened up a floodgate of new litigation that otherwise would not have happened [57]. Even when litigation occurs, the disclosure of an error by the physician ordinarily is not harmful to the physician's defense. Many states have enacted *I'm Sorry* statutes that prohibit or greatly limit the admissibility into evidence at trial of an apology by the physician made to the patient. In addition, the federal Patient Safety and Quality Improvement Act affords protections to those who report errors to certified data collection organizations by shielding the content of reported patient safety information from legal discovery and disclosure. Unfortunately, many physicians are not aware of these statutory protections and hence remain reluctant to participate in the kinds of patient safety initiatives that the Patient Safety and Quality Improvement Act intends to encourage [58].

Transparency and apology regarding medical errors is likely to be positive in another respect as well, even if litigation were to occur despite the disclosure and apology. In medical malpractice litigation alleging negligence, technically the focus is on whether the physician deviated from the standard of reasonable care under the circumstances in that specific case. In reality, however, the jury usually must be convinced (i.e., angered) that the defendant physician was a bad person who treated the patient not just improperly but cavalierly and uncaringly. It assists the plaintiff to satisfy that unwritten but real burden of proof when the physician has tried to conceal a medical error to protect the physician's own legal and financial interests even though concealment of the error may have interfered with the patient's recovery. At the same time, a defendant physician can favorably impress the jury with his or her positive character by demonstrating that the error was quickly acknowledged so that full attention could be devoted to improving the patient's medical condition (and the care of future patients) in light of the error.

Expectations for disclosure of errors are now codified into regulatory requirements and guidelines published by medical professional organizations. Joint Commission standards mandate that patients be informed about all outcomes of care, including unanticipated outcomes.

In examining the issue of admitting medical errors, one must distinguish between admitting the fact that something has gone askew, on one hand, and volunteering the opinion that one or more members of the healthcare team were negligent, on the other. Not all mistakes fall to the level of a deviation from professionally acceptable standards of care; deciding whether negligence has taken place, let alone whether that negligence proximately or directly caused a financially compensable injury, requires legal determinations by a jury or judge and is a set of questions beyond the competence of a physician to make unilaterally. Hence, the physician's obligation to be truthful extends only to acknowledgment that a mistake has happened and a show of empathy for the patient's situation ("I am sorry that you have to go through all this hassle"), not to personally concede or accuse others of being at legal fault.

Physicians should make themselves aware of the disclosure support resources of their institution or malpractice insurer and take advantage of these supports. Institutions can support physicians and other health care professionals through methods such as just-in-time disclosure coaching, role modeling by senior physicians, skills training, simulation, and offering clinical coverage and support [54]. The federal AHRQ has created and made available, http://www.ahrq.gov/professionals/quality-patient-safety/patient-safety-resources/resources/candor/index.html, a Communication and Optimal Resolution kit as a process designed to open lines of communication between clinicians, patients, and their families after harm occurs.

Conclusion

Surgeons and other health care professionals, plus the institutions and organizations within which they serve older patients, continuously and inevitably interact with law and the legal system. These interactions may concern a wide slew of pertinent subjects. This chapter has surveyed a few broad areas within which such interaction is likely to occur and directly affect every physician who cares for older patients. For personalized attention and advice in particular situations, especially for questions pertaining to the detailed law of a specific jurisdiction, specialized legal consultation should be secured from knowledgeable attorneys in private practice, risk managers employed or retained by the institutional health care provider, the physician's professional liability insurance carrier, or an IEC.

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20 Physiologic Responses to Anesthesia in the Elderly

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Contents

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Abstract

Older adults undergo age-related physiologic changes that are important to consider in anesthetic management. Key cardiovascular

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changes include left ventricular hypertrophy and changes in autonomic responses. Key pulmonary changes include changes in lung structure, blunted responses to hypoxia and hypercapnia, and increased risk of aspiration. Older adults are also more susceptible to postoperative cognitive changes. The interaction of anesthetic drugs with changes in cardiac, pulmonary, and neurological systems must be anticipated. Pharmacokinetic and pharmacodynamics properties of individual anesthetic drugs will also be altered in older adults. The anesthetic plan should be tailored to the needs and physiology of older adults, keeping in mind important principles of geriatric care.

Keywords
Anesthesia · Physiology · Geriatric

Introduction

This chapter focuses on the *interaction* of anesthesia and age-related physiologic changes that are likely to increase perioperative complications. The reader is encouraged to consult relevant chapters contained in this textbook on preoperative assessment and specific organ systems for a comprehensive discussion of general physiologic changes with aging.

A Patient

An 85 y/o man presents for emergency exploratory laparotomy. He recently underwent ankle surgery subsequent to a fall, and in the setting of postoperative opioid administration, developed ileus with concern for bowel ischemia. He has a high level of education, but his wife has noticed some cognitive decline recently. He is independent with his acts of daily living at baseline and can climb one flight of stairs. He has moderate aortic stenosis, a history of paroxysmal atrial fibrillation, and was a former smoker. In talking to the patient, he does appear mildly confused. His heart rate is 98 and his blood pressure is 160/74. He is afebrile.

In this patient, as with all older adults, anesthetic drug choice and dosing need to be considered carefully. Physiologic changes in older adults and the interaction of these changes with both co-morbidity and anesthetic agents are also critically important. Specifically for this patient, key anesthetic goals include: safe induction in light of aortic stenosis and volume fluctuations, optimizing hemodynamics in a patient with both aortic stenosis and paroxysmal atrial fibrillation, avoiding pulmonary complications, and minimizing the risk of postoperative delirium. Although fundamental principles of anesthetic care clearly apply, there are unique aspects to consider in the geriatric population. This chapter will provide an overview of these important anesthetic considerations for safely taking care of older adults, generally organized by organ system and anesthetic drug. Table 1 summarizes important organ-specific considerations in anesthetizing older adults.

Cardiovascular Implications of Anesthesia in the Elderly

Cardiovascular Changes with Aging that Affect Anesthetic Physiology

Characteristic changes in the cardiovascular system occur with age and affect the response to anesthesia and to perioperative stress. These changes include systolic and diastolic dysfunction, left ventricle hypertrophy, increased arterial stiffness, altered conduction systems, altered autonomic responses, and cardiovascular disease. Each of these changes will be discussed in more detail.

Left Ventricle Structure and Function

Structural changes occur in the aging heart, including decreases in myocyte number and size

Table 1 Organ-specific considerations in anesthetizing older adults

	Key physiologic effects of aging	Clinical anesthetic implications
Cardiac	Left ventricle hypertrophy and diastolic dysfunction Conduction abnormalities and autonomic dysfunction High prevalence of coronary and valve disease	Preload dependent, but susceptible to volume overload. Labile hemodynamics with blunted compensatory mechanisms. Evaluate for coronary artery disease and aortic stenosis
Pulmonary	Increased V/Q mismatch Decreased response to hypoxia and hypercarbia Loss of lung elasticity and decreased chest wall compliance Decreased cough reflex	Increased A-a gradient Risk of respiratory failure, especially in the setting of anesthetic agents Increased work of breathing Increased aspiration risk
Neurologic	Increased brain sensitivity to anesthetic agents	Increased postoperative delirium and cognitive dysfunction
Renal	Decreased renal mass	Decreased drug clearance; Susceptible to acute renal failure
Hepatic	Decreased blood flow during anesthesia	Decreased clearance of drugs with high hepatic extraction ratios
Endocrine	Impaired glucose tolerance	Hyperglycemia: Infection
Thermoregulation	Decreased muscle mass and blunted thermoregulatory mechanisms	Hypothermia, which can lead to increased infection, coagulopathy, risk of arrhythmia, and postoperative myocardial infarction

and an increase in the amount of connective tissue [1]. These changes result in decreased systolic function of the heart. Decreased intrinsic contractile function may be partially compensated for with increasing muscle mass and subsequent left ventricular cardiac hypertrophy.

Left ventricle hypertrophy may also result from vascular changes that are common in older adults. Arterial stiffening is highly related to age and occurs through a variety of mechanisms, including loss of elastic lamina, increase in collagen, inflammation, and calcification [2]. As shown in Fig. 1, the consequences of vascular stiffening are profound, with increased pulse wave velocity resulting in aortic pressure waves that are reflected back towards the heart during systole. This in turn causes an increased afterload during late systole, which can lead to compensatory left ventricular hypertrophy.

Left ventricle hypertrophy is associated with important physiologic changes, including diastolic dysfunction. Diastolic dysfunction is thought to occur when low cardiac output results from a ventricle with thick walls but a small cavity

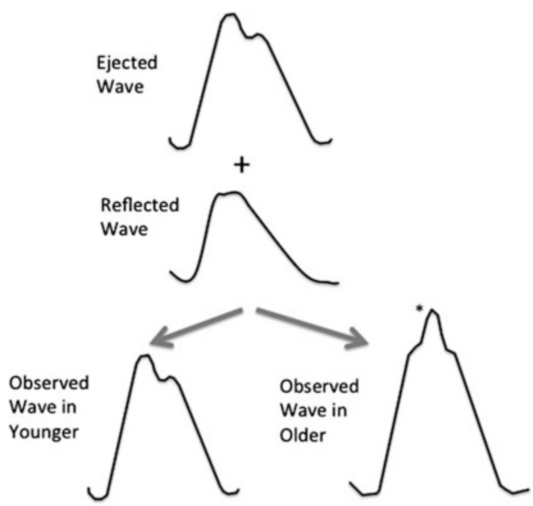

Fig. 1 The observed wave is composed of the *ejected* wave (due to ventricular contraction) and a *reflected* wave, which propagates backwards after reflection at points of vascular branching. Due to increased vascular stiffness, the reflected wave returns earlier and faster in older adults compared to younger counterparts. This results in characteristic changes in the observed wave in older adults, including systolic hypertension (*)

[3]. In this physiologic state, delayed relaxation impairs early diastolic filling [4] and enhances the importance of late diastolic filling in maintaining cardiac output [5]. Late diastolic filling, however, must now overcome ventricular stiffness and that requires higher atrial pressures. To boost cardiac output in the setting of increased ventricular stiffness, elderly patients depend on higher diastolic filling pressures and are often preload-dependent. Additionally, the atrial contribution to ventricular filling becomes critical and creates greater susceptibility to hypotension should atrial fibrillation occur. Adequate preload and normal rhythm are critical given the reduced ability of older adults to augment cardiac contractility during periods of increased demand.

Another factor that affects diastolic filling of the ventricle is the relative time the heart spends in systole versus diastole. In the aging heart, length of diastole is shortened and systole is lengthened as a compensatory mechanism to maintain ejection fraction [6, 7]. Increased left ventricular filling does increase inotropy by means of the Starling forces, but the compensation for the systolic function is at the expense of higher diastolic pressures and greater time in systole [8, 9]. Shortened diastolic time also affects coronary perfusion [10, 11].

Stiffening of the vessel walls occurs in the venous system with aging, with the implication that rigid veins fail to function as a preload buffer. The venous system normally contains 80% of blood volume, so low venous capacitance means that the aging venous system cannot accommodate excess volume or adapt to low volume states without a comparatively large change in filling pressure [12].

Conduction Abnormalities

Conduction abnormalities are common in the elderly. Dilation and fibrotic change in the atria predispose the elderly to atrial fibrillation. Bradycardia is the second most common initiating rhythm after premature atrial contractions [13] and may increase the incidence of new onset atrial fibrillation. The high incidence of sinus bradycardia may be related to drop-out of sinus node pacemaker cells to as little as 10% of levels seen in young adults [7]. New onset atrial fibrillation during the perioperative period in the elderly frequently results in significant blood pressure changes. The cell populations in the aging AV node are maintained. AV conduction slows with aging, however, resulting in lengthened P-R interval [14, 15].

Autonomic Responses

The aging of the autonomic nervous system is characterized by progressively limited capacity to adapt to stress. In particular, cardiovascular responsiveness in the elderly is impaired. For instance, maximal heart rate decreases with aging and can be estimated by the formula: maximum predicted heart rate = 220 – age [16]. As a consequence, the ability of older adults to increase cardiac output by means of an increase in heart rate is limited. There is also reduced adrenergic responsiveness [17], affecting both the β-adrenergic absolute heart rate response [18, 19] and inotropy [20] and alpha-adrenergic mediated arteriolar tone [21].

Rapid response to hypotension is mediated by baroreceptor function. The stiffening of arterial walls in the elderly may contribute to the well-documented decrease in baroreceptor response. There is a decrease in baseline vagal tone [22] and consequently diminished carotid sinus baroreceptor response to hypotension in the elderly [23, 24].

Cardiac Disease

In addition to physiologic changes associated with "normal" aging, older adults are at high risk for cardiovascular disease. The prevalence of coronary heart disease, myocardial infarction, congestive heart failure, and valvular calcification increases markedly with age [25]. Optimal perioperative evaluation of a patient's cardiac status according to established guidelines [26] is crucial, and a high index of suspicion for cardiovascular disease is required in older adults. In contrast to pulmonary complications, in which age is the primary risk factor, the degree of cardiovascular disease appears to be more predictive of cardiac complications than age alone.

The Interplay of the Aging Cardiovascular System and the Effects of Anesthesia

Individual Anesthetic Drugs

Although anesthetic drugs have different mechanisms of action and effects on the cardiovascular system, an important point is that most anesthetic drugs can be used safely without hemodynamic compromise in the elderly population if several principles are kept in mind. Anesthetic dose requirements of both intravenous induction agents and inhalational agents decrease with age. In addition, slower titration of medication as opposed to bolus administration may be warranted because changes in body composition alter the pharmacokinetics of intravenous agents. The so-called greater "sensitivity" of aged patients to the bolus administration of certain drugs has been related to a reduction in either the initial volume of distribution or the initial distribution clearance. In elderly patients compared to younger ones, the same bolus dose will generate a markedly higher plasma concentration and thus a greater pharmacologic effect.

As far as individual anesthetic agents, there is no one "best" agent to optimize cardiac physiology in older adults. Rather, the individual physiology of the patient must be considered with respect to cardiovascular effects of anesthetic agents. It is useful to consider effects on heart rate, rhythm, preload, contractility, and afterload. Indeed, the cardiovascular effects of anesthetic agents are pleiotropic and affect most of these variables to varying degrees.

Specifically, it is clear that decreased ventricular contractility occurs with intravenous anesthetic agents. Propofol is the most common induction agent used today and is generally thought to be a direct myocardial depressant. The negative inotropic effect of propofol is mediated by a decrease in intracellular calcium [27]. In fact, propofol is a greater myocardial depressant than the inhalational anesthetics [28]. Even ketamine, which produces a sympathetically mediated increased heart rate and blood pressure, causes some direct myocardial depressant effect [29, 30]. It appears that opioids have minimal effects on contractility [29]. It has been suggested that etomidate is the induction agent of choice in elderly patients with limited cardiovascular reserve. However, hemodynamic instability after induction with this agent in severely compromised patients can be remarkable. In comparison to the intravenous agents, inhaled anesthetic agents are associated with less myocardial depression. Volatile anesthetics decrease inotropy by means of their effects on the L-type calcium channels, the sarcoplasmic reticulum, and the contractile apparatus [31]. Cardiac output is generally maintained under the modern agents because the myocardial depression is accompanied by afterload reduction [32].

Most anesthetic agents also reduce afterload by decreasing arteriolar tone. Propofol is a potent vasodilator [33]. Opioids are also vasodilators, though this effect is small when compared to propofol or the inhalational agents [34]. Reduced afterload is a common effect of anesthetic agents and is often treated with small doses of alpha-agonist drugs. However, it is important to consider that alterations in preload and contractility may also be important factors and need to be addressed.

Anesthetic agents blunt baroreceptor function. The degree of inhibition depends on the anesthetic agents administered. As a result, tachycardia may not be observed in response to hypotension. Inhalational agents blunt baroreceptor function in a dose-dependent manner [35]. Although both opioids and propofol alter baroreceptor function, the effect is much less than observed with the inhalational agents [28]. Significant bradycardia can occur, however, because of the direct vagotonic effect of the opioids, especially fentanyl.

General Interactions of Cardiovascular Aging with Anesthetic Management

The most frequent cardiovascular problem that occurs with anesthesia in the elderly is hemodynamic instability, which manifests itself primarily as hypotension. The broad differential diagnosis of hypotension in the perioperative setting includes changes in cardiac rate, rhythm, preload, contractility, and afterload. In terms of heart rate, elderly patients may tolerate tachycardia poorly due to decreased time for filling during diastole, as well as imbalances in oxygen supply and demand. Thus, the anesthetic depth and sympathetic stimulation must be carefully titrated. Preload may be reduced due to anesthetic-induced vasodilation as well as decreased intravascular volume from fasting, blood loss, and insensible losses. Older adults with diastolic dysfunction may be highly dependent on adequate preload [7]. However, older adults are also at increased risk of fluid overload. Indeed, the balance of euvolemia is more delicate in the elderly than in the younger patient, as the clinical range between hypovolemia and fluid overload is narrowed. Anesthetic agents also decrease contractility and inhibit baroreceptor responses. Furthermore, older adults have diminished inotropic stimulation to β-receptor stimulation. This makes the aging heart with diastolic dysfunction more dependent on adequate preload to maintain cardiac output. Finally, anesthetic-induced sympatholysis may result in decreased systemic vascular resistance.

Perioperative congestive heart failure in the elderly occurs in a bimodal type of time frame. It may first appear in the immediate recovery phase after anesthetic emergence. It is most likely to occur when sympathetic tone reappears and may be the result of pain or fluid shifts from the peripheral vasculature to the heart. It may next appear on postoperative days two to three and likely occurs with mobilization of extravascular fluid. Late postoperative congestive heart failure is exacerbated by underlying renal dysfunction, and its prevention requires physician attentiveness and diuresis.

Mode of ventilation during anesthesia can have significant cardiovascular effects in the elderly. Positive pressure ventilation decreases venous return via an increase in intrathoracic pressure. Similarly, hyperventilation can cause hypotension via impairment of venous return. An additional mechanism of hypotension is the decrease in sympathetic tone associated with hypocapnea [36, 37]. Spontaneous ventilation is associated with less hypotension in the elderly patient with diminished cardiovascular reserve, because venous return is augmented during inspiration.

The prone position can be associated with a significant reduction in the cardiac index secondary to vena cava compression [38]. Both the sitting position and reverse Trendelenburg position decrease venous return and can worsen hypotension in severely preload-dependent elderly patients. Trendelenburg augments venous return. Lateral position is generally not associated with significant hemodynamic effects. Although right lateral decubitus has improved venous return over the supine and left lateral decubitus positions, the effect is probably minimal except in patients with congestive heart failure [39].

Laparoscopic insufflation causes decreased venous return. This, coupled with the depressant effect of anesthetic drugs, can result in hypotension. It is typical for $PaCO_2$ to slowly rise after 30 min of laparoscopy. This results from the increased CO_2 load and the decreased ability to eliminate CO_2 secondary to pneumoperitoneum. The hypercapnea and its associated increase in sympathetic tone [40] may cause hypertension and ectopy. Correction of hypercapnea requires ventilatory changes such as increased respiratory rate, tidal volume, and peak airway pressures, which may further impair venous return.

Elderly patients frequently take cardiovascular medications, which interact with anesthetics. For instance, bradycardias are apt to occur in anesthetized patients being treated with β-blockers and calcium channel blockers. Bradycardia may also be associated with anesthesia-specific medications such as high-dose narcotics, acetylcholinesterase inhibitors for reversal of neuromuscular junction blockade, and with a rare acetylcholine-like effect of succinylcholine (a short-acting neuromuscular relaxant). Under rare instances, heart block can occur; the risk increases with preexisting bundle branch block. Preoperative use of ACE inhibitors [41] and angiotensin receptor blockers [42] has been closely associated with increased risk of hypotension in anesthetized patients. It is controversial, however, whether discontinuing these medications preoperatively will decrease the incidence of perioperative hypotension.

Regional Anesthesia: Spinal and Epidural

Spinal and epidural anesthesia cause significant afterload reduction due to blockade of sympathetic fibers. Because the sympathetic fibers are small in diameter, they are highly susceptible to local anesthetic blockade. The sympathectomy associated with regional anesthesia has greater effects in the elderly because of limited ability to mount a compensatory response and possibly greater propensity to obtain a higher spinal anesthetic level [43]. With epidural anesthetics, the decreased compliance of the epidural space in the elderly is associated with achievement of a higher dermatome level of anesthesia with the same dose of local anesthetic in comparison to younger patients. A decrease in blood pressure with neuraxial blockade is nearly universal and often heralds the onset of motor and sensory blockade (Fig. 3). Preload reduction contributes to hypotension as well as afterload reduction. Tachycardia is the normal compensatory response but may be impaired in the elderly. With a very high sensory level (T1 to T4), the cardioaccelerator fibers may be blocked, thus precluding the tachycardia response and predisposing the patient to severe hypotension and reduction in cardiac output. When hypotension occurs after administration of spinal anesthesia in the elderly, volume loading is generally insufficient to correct the hypotension, and vasopressors are generally required [44]. Furthermore, excessive volume loading can be associated with ventricular dysfunction [45].

It should be noted that the careless use of spinal anesthesia in a hypovolemic patient with limited cardiac reserve will likely result in cardiovascular collapse. These events are associated with profound bradycardia, resulting from activation of the Bezold-Jarisch reflex. When patients are hypovolemic and spinal anesthesia is to be used, it may be best to use a continuous catheter technique. This allows slow titration of drug so that hemodynamic changes have a slower onset and can be treated in a timely manner. Epidural anesthesia also can be administered slowly via a catheter so that the hemodynamic response can be gradual and controlled. Even with gradual administration, there is a risk of rapid hemodynamic changes if the patient is not closely monitored.

Spinal and epidural anesthesia can be desirable modes of anesthesia in the elderly in order to attenuate the stress response to surgery, avoid central nervous system depressants, avoid airway manipulation and its associated pulmonary complications, and assist in postoperative pain management.

Pulmonary Implications of Anesthesia in the Elderly

Pulmonary complications are a major cause of postoperative morbidity in the elderly. Postoperative respiratory complications are associated with 40% of the perioperative deaths in patients older than 65 years of age [46]. The aging of the pulmonary system and anesthesia interact to increase the likelihood of these events.

Pulmonary Changes with Aging that Affect Anesthetic Physiology

Normal structural changes account for some of the increased risk of respiratory compromise in the elderly. There is a loss of elasticity of the lung tissue, and the chest wall becomes less compliant. The result is increased residual volume of the lung. Total lung capacity remains unchanged or slightly decreases, but the increase in residual volume causes a decrease in vital capacity [47]. The effect is increased work of breathing for given level of gas exchange and increased shunt and dead space.

The geriatric patient is more susceptible to hypoxia stemming from increased closing capacity of the small airways. As the aging lung loses elasticity, the smallest airways are no longer stented open by elastic tissue but instead rely on some minimal amount of lung inflation, or closing capacity, to maintain small airway patency. As lung volumes decrease with active expiration, there comes a point when the summation of intra-airway pressure and elastic forces stenting open distal air passages become insufficient to overcome the tendency of these distal airways to collapse. There is a general trend toward increased closing capacity with aging. By age 66, closing capacity exceeds functional residual capacity (FRC) in the sitting position [48]. When closing capacity exceeds FRC, some portion of the lung will be ineffective in gas exchange during at least part of the respiratory cycle. This mechanism leads to increasing V/Q mismatch in the elderly and a gradual decrease in blood oxygenation. On average the PaO_2 decreases 0.31 mmHg per year of age [47].

The loss of muscle mass with aging does not spare the muscles of respiration. Decreased muscle strength in the intercostals and accessory muscles of respiration impairs the ability to perform maximal ventilatory maneuvers and impairs the ability to mount a strong cough. Clearance of secretions is in part dependent on the patient having sufficient strength to perform the maneuver. Elderly patients are less able to maintain adequate tidal volume and generate sufficient inspiratory or expiratory force. If the weakness is severe enough, it may interfere with extubation and weaning efforts.

Other changes in the elderly that are of importance to anesthetic physiology include a blunting of the response to hypoxia and hypercarbia [49, 50]. In addition, aging leads to dysphagia, decreased esophageal motility, and decreased cough reflex.

The Interplay of the Aging Pulmonary System and the Effects of Anesthesia

During spontaneous ventilation, the inhalational agents decrease tidal volume and minute ventilation [51, 52]. This is associated with an increase in $PaCO_2$ and respiratory rate. In the absence of opioids or other respiratory depressants, profound tachypnea can occur. Despite the increase in respiratory rate, however, the net effect on the alveoli is a decrease in ventilation. In the anesthetized state, spontaneous ventilation in the supine position results in decreased functional residual capacity due to cephalad displacement of the diaphragm and inward displacement of the ribcage [53]. The work of breathing [54] is increased because the weight of the abdominal contents must be displaced with inspiration. Decreased functional residual capacity means less oxygen reserve prior to any apneic interval.

Ventilation-perfusion (V/Q) mismatching occurs during anesthesia and is caused largely by atelectasis [55] and impaired hypoxic pulmonary vasoconstriction. Atelectasis commonly forms in dependent regions of the lung shortly after induction of anesthesia and progresses as gas is absorbed from poorly ventilated regions [56]. Positive end-expiratory pressure can reduce atelectasis formation, but large tidal volume recruitment maneuvers are generally necessary to reverse shunt [57]. Hypoxic pulmonary vasoconstriction reduces blood flow to underventilated regions, but this mechanism is partially inhibited by anesthetic agents [58].

These physiologic changes mean that an A-a gradient is likely to occur in older adults under anesthesia. Impaired oxygenation is secondary to the anesthetic effects of decreased minute ventilation, increased atelectasis, and the aging effect of increased closing capacity. In addition, hypoxic pulmonary vasoconstriction is impeded by the aging effect on pulmonary vascular rigidity and by anesthetic inhibition.

Normal ventilatory drive depends on central and peripheral chemoreceptor response to hypercapnea, hydrogen ion concentration, and pH. The response to hypercapnea is independent and synergistic with the response to hypoxia. The carbon dioxide response curve is shifted to the right under anesthesia requiring higher CO_2 [59] for a given minute ventilation. Likewise, there is impaired response to hypoxia with even minimal residual inhalational anesthetic levels [60]. Ventilatory failure may occur secondary to the combined effects of anesthesia and aging to decrease minute ventilation, depress hypoxic and hypercarbic respiratory drive, and increase the work of breathing in the face of decreased muscle mass. This is particularly important in older adults.

Other anesthetic effects on the pulmonary system include impairment of bronchial mucociliary clearance in intubated patients [61] and impairment of swallowing reflex from pharyngeal dysfunction and risk of aspiration at subhypnotic concentrations of anesthetic [62]. Decreased pharyngeal tone results in upper airway obstruction. The incidence of apnea due to upper airway obstruction is increased in obese individuals.

The pulmonary implications of residual anesthetic effects after emergence are a serious issue in the elderly. Of primary importance are the effects of muscle relaxants. Age-related pharmacokinetic and pharmacodynamic changes interact with the decrease in muscle mass to potentiate the effects of these drugs, thus increasing the risk of respiratory compromise in the early postoperative period [63, 64]. The respiratory depressant effects of sedative agents, narcotics, and inhalational anesthetics are prolonged. As a special case, the inhaled anesthetics are eliminated primarily by the lung. Decreases in minute ventilation and cardiac output, as well as V/Q mismatch, will prolong the elimination of inhaled anesthetic agents [65, 66].

Laparoscopic surgery deserves special mention. The insufflation pressure during laparoscopy displaces the diaphragm cephalad; this reduces tidal volumes toward that of the dead space volume. In this case, adequate ventilation is maintained either by increasing the airway pressure to maintain adequate tidal volume or by decreasing insufflation pressures. Under these conditions, atelectasis develops at an accelerated rate. Low levels of PEEP may be used in this setting as long as intrathoracic pressures do not impair venous return so as to cause hemodynamic compromise.

Regional Anesthesia and Pulmonary Implications

With spinal or epidural blockade of sufficient dermatomal height for abdominal procedures, the musculature of the thoracic cage will be anesthetized, eliminating the contribution of the intercostal muscles to respiration. Spontaneous ventilation is still possible, however, because the diaphragm is the major muscle of respiration. In these circumstances, loss of accessory muscle function may be an issue in patients with limited pulmonary reserve. Protective airway reflexes are maintained although cough may be impaired.

Spinal and epidural anesthesia have been advocated as a means of decreasing postoperative pulmonary complications. Epidural anesthesia continued into the postoperative period may help in promoting early mobilization, cough, and deep breathing by relieving postoperative pain. In theory, spinal or epidural anesthesia helps to minimize the administration of central nervous system depressants during the perioperative period, thereby maintaining protective airway reflexes. It is common practice, however, for sedation to be administered during spinal and epidural anesthetics. Therefore, it is important to identify at-risk patients and verify recovery of protective reflexes in the elderly after an anesthetic, including sedation for spinal.

Physiologic Response to Anesthesia in the Aging Nervous System

Age-related decreases in central nervous system functional reserve lead to alterations in pharmacodynamics and increased susceptibility to postoperative cognitive dysfunction and delirium.

Altered Pharmacodynamics

Brain sensitivity to most anesthetic agents increases with age, as shown in Fig. 2.

This necessitates decreasing the drug dose in the elderly. The minimum alveolar anesthetic concentration (MAC) decreases by 5–6% per decade of age [67]. There is also a significant sensitivity to the common induction agent propofol [68]. Many opioids, including fentanyl, are more potent in older adults due to increases in brain sensitivity [69]. However, the pharmacodynamics of muscle relaxants do not appear to be altered with age. The underlying mechanism to explain altered brain pharmacodynamics is unclear at present. Altered brain pharmacodynamics may result from age-related changes in the receptors, signal transduction, or homeostatic mechanisms. Within

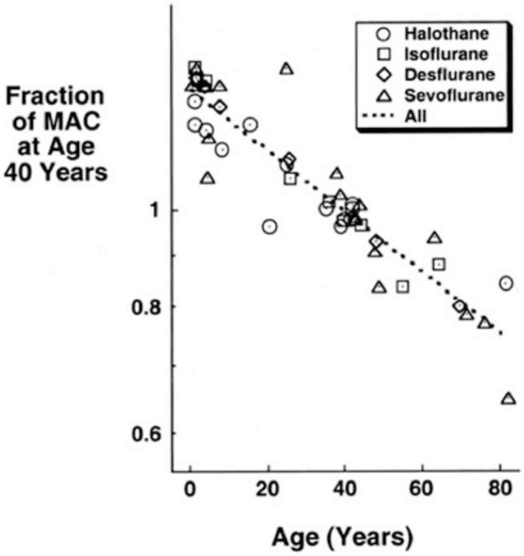

Fig. 2 Aging influences MAC in humans for desflurane, isoflurane, halothane, and sevoflurane. One MAC equals the minimum alveolar concentration at which 50% of subjects age 40 would not move in response to a surgical stimulus. MAC is at its peak in humans less than 1 year of age and decreases by approximately 40% in older adults.

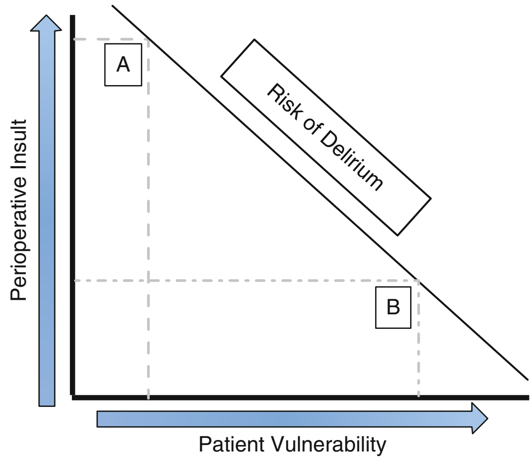

Fig. 3 Conceptual model of risk of delirium based on patient vulnerability and perioperative insult. Patient "A" has low vulnerability, so the perioperative insult leading to delirium is likely high. Patient "B" has high vulnerability, so the perioperative insult leading to delirium may be much lower

the central nervous system, aging is associated with decreases in dopaminergic and cholinergic neurons and receptors as well as a decrease in the number of synapses [70]. There are also alterations in brain phospholipid chemistry associated with changes in second messengers such as diacylglycerol [71]. A definitive association between these changes and age-related brain pharmacodynamics has yet to be established. Some components of the elderly drug response can also be explained by pharmacokinetic changes associated with aging [71]. These responses are specific to each drug and are highly related to drug distribution and clearance.

Increased Susceptibility to Postoperative Delirium and Cognitive Dysfunction

Sensitivity to anesthetic agents may manifest as neurologic dysfunction after surgery. The incidence of postoperative delirium and postoperative cognitive dysfunction has been reported to exceed 50% in certain surgical populations [72] and seems to be highest after cardiac surgery and hip fracture repair [73, 74]. Thus, postoperative delirium and postoperative cognitive dysfunction are two of the most common postoperative complications in the elderly, with an incidence that is higher than that of myocardial infarction or respiratory failure [75].

Postoperative delirium is thought of as an acute confusional state, characterized by changes in cognition, attention, and consciousness [76]. The pathophysiology of delirium is not well defined, but it generally results after an acute insult in a vulnerable patient. The degree of surgical or physiological insult required to precipitate postoperative delirium or postoperative cognitive dysfunction varies from patient to patient. As shown in Fig. 3, in patients with a high degree of preoperative cognitive reserve, a substantial insult is required for postoperative delirium and/or postoperative cognitive dysfunction to occur. Conversely, in patients with a lower degree of cognitive reserve, a relatively minor stress is all that is necessary for postoperative delirium and/or postoperative cognitive dysfunction to develop [72]. Several validated risk models for postoperative delirium have been developed in both cardiac

[74] and noncardiac [77] surgery. Important risk factors include patient age, education, baseline cognitive status, history of cerebrovascular disease, and other comorbidities.

The anesthetic contribution to delirium is unclear, but certain key anesthetic decisions may be important. A wide variety of drugs are associated with delirium, many of which are used frequently in the perioperative period. These include benzodiazepines, anticholinergics, opioids, corticosteroids, anticonvulsants, antidopaminergic, antiemetics, and H_2 antagonists [78]. In particular, the use of benzodiazepines has been strongly linked with delirium in the intensive care unit [79], although the evidence during surgery is less rigorous. Recent large trials have suggested a potential benefit for dexmedetomidine for perioperative sedation [80], even in extubated patients [81].

The benefit of regional compared with general anesthesia to reduce delirium has been investigated, with the hypothesis that sparing of general anesthesia would reduce the incidence of postoperative delirium. However, studies to date have not consistently supported that hypothesis [82]. One potentially confounding factor is the depth of anesthesia, since patients receiving a regional anesthetic may in fact have a level of consciousness consistent with general anesthesia [83]. Indeed, several trials have suggested that avoidance of excessively deep levels of anesthesia may result in less postoperative delirium [84–86]. An observational study further suggested an association between burst suppression and postoperative delirium [87].

Variation in intraoperative blood pressure has been proposed as a modifiable risk factor for delirium, with the hypothesis that inadequate cerebral perfusion may contribute to postoperative delirium [88]. Importantly, both low blood pressure and high blood pressure have been associated with delirium [89, 90]. However, the results have been inconsistent and there is no clear consensus on optimal blood pressure goals for older adults during surgery [91].

Pain may be an important risk factor for postoperative delirium [92, 93]. As a class, opiates are not associated with postoperative delirium, except for meperidine [94]. This may be because of its atropine-like structure and influence on brain cholinergic activity.

In the postoperative period, it is important to recognize that postoperative delirium may be the presenting symptom of a number of complications, including sepsis, urinary tract infections, myocardial infarction, stroke, and pneumonia [95]. Thus, the first step in managing postoperative delirium is to identify and treat underlying medical and/or surgical causes.

Changes in cognition that continue well beyond the perioperative period are commonly labeled as postoperative cognitive dysfunction (POCD). However, the definition of POCD is not clear, and the incidence of POCD varies dramatically according to the methodology used [96, 97]. Nevertheless, well-done studies have suggested an incidence of 6–33% in the early weeks after surgery, with declining incidence between 1 and 12% in the 3–12 months after surgery [96, 98].

Similar to delirium, the etiology of POCD is likely to be multifactorial, and the mechanism is unclear. POCD may even be independent of surgery and anesthetic, with a similar reported incidence of POCD among patients undergoing angiography with sedation, total hip replacement, and cardiac surgery [99]. However, in vitro and animal studies do suggest that inhalational and intravenous anesthetic agents alter neuronal function after exposure [100, 101]. Neurons exposed to anesthetics in vitro have increased oligomerization and cytotoxicity of β-amyloid, the protein associated with Alzheimer disease [102, 103]. In aged rats, exposure to anesthetic agents causes long-term declines in cognitive function [104, 105]. POCD is also highly related to underlying patient comorbidities, cognitive status, and cerebrovascular disease.

There is currently no standard of care for POCD prevention. However, an intriguing association has been reported between postoperative delirium and subsequent cognitive decline [106, 107], suggesting that prevention of delirium may be one strategy to prevent longer-term cognitive change.

Renal Implications of Anesthesia in the Elderly

Anesthesia decreases renal perfusion and glomerular filtration rate. When a patient receives an anesthetic, glomerular filtration rate may be acutely decreased by hypotension, redistribution of blood flow away from body core, or a specific pressure effect of laparoscopy. The potential for postoperative acute renal injury is greater with preexisting renal disease.

Drug excretion and metabolism by the kidney is proportionately decreased with aging. Many anesthetic drugs depend on renal elimination. Dose adjustment of most medications should be anticipated in the elderly. Of special note, many of the commonly used opioids and muscle relaxants have some component of renal elimination, and their effects are prolonged in the elderly. Fortunately, there are alternate drugs, with little or no dependence on renal elimination. Inhaled anesthetics are eliminated primarily by the respiratory route. Serum enzymes degrade certain drugs such as cisatracurium, remifentanil, and chloroprocaine. Due to the blood stream degradation of cisatracurium, this agent may be of special value in the elderly patient with renal impairment who requires muscle relaxation.

Hepatic Implications of Anesthesia in the Elderly

Hepatic functional reserve is fairly well maintained with healthy aging. As a result, anesthetic drug binding to serum proteins produced by the liver is not significantly affected. One potential effect of anesthesia is decreased hepatic blood flow. Hepatic blood flow parallels cardiac output and correlates with the rate of elimination of drugs with high hepatic extraction ratio [108, 109]. Commonly administered anesthetic agents with high hepatic extraction ratios include fentanyl, sufentanyl, lidocaine, meperidine, ketamine, and propofol. Drugs with lower hepatic extraction ratios are less impacted by hepatic blood flow.

Endocrine Implications of Anesthesia in the Elderly

Hyperglycemia is a frequent issue during surgery in the elderly patient. Inhalational anesthetics impair glucose tolerance. The mechanism is unclear but may be secondary to direct inhibition of insulin secretion [110]. Thus, hyperglycemia occurs in the anesthetized state with or without surgery. Insulin resistance and prevalence of diabetes is increased in the elderly. This effect is compounded in the face of obesity.

Thermoregulation

Normal human thermoregulation allows only small fluctuations in core temperature within the narrow interthreshold range of 0.2 °C; this range can be extended to 2–4 °C under the effects of anesthesia [111]. Multiple inputs from the core and periphery contribute to the detection of temperature variation. Peripheral sensation tends to contribute largely to behavioral aversion to unpleasant environments, while core sensing mechanisms have a relatively larger impact on autonomic responses [111]. The response to decreased temperature begins when the threshold of vasoconstriction is reached. Beyond the vasoconstriction threshold lies the threshold for the energy intensive shivering mechanism. Non-shivering thermogenesis, although important in neonates, is negligible in adults. The response to elevation in core temperature begins when the threshold for sweating is reached. With extremes of temperature elevation, active vasodilation can also occur [111].

During anesthesia, hypothermia is a common challenge as a consequence of several colluding factors. Preparations for surgery entail exposing large surfaces of the patient's skin. Operating rooms are traditionally kept very cool. Under anesthesia, vasodilation occurs as a direct anesthetic effect. This results in an immediate decrease in core body temperature from a redistribution of body heat from the core to the periphery and eventually results in greater dissipation of heat to the environment. By central mechanisms, anesthesia decreases the threshold temperature for vasoconstriction and shivering, allowing drift of the core temperature.

The elderly are predisposed to hypothermia [112] as a result of decreased muscle mass and neural and hormonal mechanisms. Thyroid function and overall metabolic rate decrease with aging. Decreased muscle mass leads to greater heat loss and less heat generation. The neural thermoregulatory mechanisms [112] are altered with a lowered threshold for vasoconstriction, decreased maximum vasoconstriction response, decreased α-adrenergic response [113], and decreased thermal perception.

These changes with aging compound the tendency, present among all patients, to develop hypothermia during both general and spinal anesthesia. The effects occur across a wide spectrum of anesthetic techniques and agents [114].

Complications of hypothermia include possible coagulopathy [115], increased risk of surgical wound infection [116], and increased cardiac risk [117] secondary to hypermetabolism if shivering occurs after emergence from anesthesia.

Anesthetic Drugs in Older Adults

As a general rule, using the shortest acting, most reliably cleared drugs in the geriatric patient population is an important strategy to overcome the increased sensitivity and potentially prolonged clearance of drugs used in anesthesia [118]. Further, it is important to recognize that delayed time to peak effect and increased sensitivity associated with aging can lead to "dose stacking" – a dangerous overshooting beyond the desired effect. To avoid dose stacking, slow, gentle titration of intravenous anesthetics such as propofol, with a dose that may be 50% of the weight-based dose in younger adults, is necessary. Hypotension should be anticipated and treated [119]. Further, polypharmacy and drug interactions must be considered, particularly when multiple drugs cleared by a common pathway are used, potentially leading to increased drug half-life.

Pharmacokinetic Considerations

Most intravenous anesthetic and analgesic drugs are cleared by Phase I and II metabolism in the liver [120]. Phase I reactions are mediated by the cytochrome p450 reductase family of enzymes and are a source of drug-drug interactions in daily life and in the perioperative period. Phase II reactions are rarely rate limiting steps and do not appear to be significantly affected by aging. The data are mixed as to whether cytochrome p450 (CYP) activity decreases with age [121, 122]. However, decreased hepatic blood flow, loss of hepatic mass, and changes in expression of CYP are likely contributors to delayed clearance of drugs used for anesthesia [120]. Further, pharmacogenetic variation in CYP isoenzymes may further influence individual variability in metabolism elderly patients [123].

Specific Anesthetic Drugs

Anxiolytics

Benzodiazepines are commonly used for anxiolysis and amnesia. In general, midazolam is the shortest acting benzodiazepine available and is the primary drug in the class considered for anesthetic purposes in the elderly patient. It is metabolized via hepatic hydroxylation by cytochrome p450 3A4 and 3A5 to its major metabolite l-hydroxymidazolam and is subsequently conjugated and excreted. Pharmacodynamic changes with aging result in increased sensitivity to midazolam and the starting dose should be reduced to 0.25–1 mg and titrated gently if needed [124]. When used alone, hemodynamic effects of midazolam are usually minimal. However, hypotension has been observed when midazolam is combined with fentanyl, propofol, or other anesthetic agents. The use of midazolam is controversial in older patients primarily because benzodiazepines have been associated with delirium in the ICU [125]. However, midazolam in small doses can be a useful adjunct during monitored anesthesia care with procedural sedation, especially when remifentanil, ketamine, or dexmedetomidine are the primary agents. Of note, benzodiazepines are reversible with flumazenil, a unique feature of this class of sedative/anxiolytic drugs.

Overall, the elimination half-life of midazolam appears to be moderately increased in elderly patients. Further, midazolam clearance has been shown to be prolonged by the simultaneous administration of propofol, as well as calcium channel blockers such as diltiazem, likely through interactions with CYP3A [126, 127].

Diazepam and lorazepam are longer acting benzodiazepines that have also been associated with delirium. Further, diazepam has active metabolites that can result in unpredictable clearance. In general, these longer acting benzodiazepines should be avoided in frail geriatric patients, except perhaps when treating seizures or withdrawal syndromes.

Remimazolam is an ultra-short acting benzodiazepine that is under Phase III investigation. It is rapidly cleared by tissue esterases with a half-life of approximately 8 min and remains reversible with flumazenil [128]. While the pharmacokinetics may be very attractive in the aged population, if it is approved further studies in the elderly will be needed.

Induction Agents

Propofol is the most commonly used intravenous anesthetic agent, providing excellent hypnosis, relatively rapid recovery after bolus dosing, and some protection against nausea. As discussed previously, propofol also causes significant vasodilation and potential hypotension that is exaggerated in older patients, especially in the presence of hypovolemia. In general, older patients require less drug (20–60% reduction) to achieve the same level of anesthesia. The initial propofol dose in the older patient is distributed in a smaller central volume of distribution, and the peak concentration may be more pronounced and prolonged compared with a younger patient in whom the redistribution occurs rapidly after the bolus dose. This translates to an increased sensitivity of older patients to smaller bolus doses and a delay to peak effect, including delayed peripheral vasodilation. Thus in the elderly patients, it is important to reduce the bolus and increase the interval between repeated doses to avoid dose-stacking. When continuous infusions of propofol are used, the context sensitive half-life can be prolonged and unpredictable, particularly in elderly patients, and this variability must be accounted for.

Etomidate is frequently used to induce anesthesia, especially in elderly patients, trauma victims, and emergency situations. Etomidate has less significant hemodynamic effects at typical induction doses compared with propofol because it tends to increase the SVR; thus, it requires less rescue with vasopressors [129]. However, in the elderly patient, it may still cause a reduction in cardiac output and hemodynamics may still need additional support. In general, the induction dose should be reduced by 25–50% in the elderly patient. Etomidate is associated with adrenal suppression. In retrospective studies, etomidate has been associated with increased mortality in hospitalized patients, but it is unclear if this is due to selection bias or causation [130].

Ketamine is an NMDA blocker that produces dissociative anesthesia. Ketamine causes the least respiratory depression of any sedative agent, has significant analgesic effect, and is synergistic with other anesthetic agents, including propofol, midazolam, and opioids. In the elderly patient, small doses of ketamine can reduce opioid requirements and offset the hypotensive effects of higher doses of propofol. While its use has been associated with psychomimetic effects and agitation in younger patients, this appears to be less of a problem in elderly patients, especially when administered with benzodiazepines or propofol. Preemptive low-dose ketamine infusions in the postoperative period have been used to treat significant pain that is resistant to traditional medications [131]. The opioid sparing effects of ketamine can be very useful in the older compromised patient. At these lower doses, there has been no evidence of any increased cognitive problems. Further, ketamine has been shown to have anti-inflammatory effects and may have cerebroprotective effects [132].

Opioids

Elderly patients exhibit increased sensitivity to central respiratory effects of opioid medications, and this may lead to an increase in the risk of unrecognized postoperative hypoventilation and apnea. In general, all initial opioid doses should be reduced in older patients and careful monitoring of both oxygenation and ventilation is required.

Fentanyl is a synthetic opioid, about 50–100 times more potent than morphine. It is lipid soluble and has a rapid onset of approximately 5 min, relatively short duration of effect and relative hemodynamic stability. Fentanyl does not cause histamine release. During induction of anesthesia, fentanyl has been shown to block the adverse hemodynamic effects of intubation [133, 134].

Remifentanil is another highly potent synthetic opioid that is becoming increasingly popular for short, stimulating procedures, especially in elderly patients in whom significant perturbations of the cardiovascular system can be deleterious. Remifentanil is metabolized by nonspecific esterases in the blood and tissue and is suitable for infusion. In older patients, the initial dose and infusion should be reduced by about 33%. When larger doses are administered bradycardia (that can be profound) and respiratory depression may occur, limiting use [69].

Hydromorphone is a semi-synthetic morphine derivative that causes less histamine release than morphine with similar duration of effect and half-life to morphine, but without significant active metabolites. In elderly patients, the volume of distribution and clearance are decreased and the half-life is increased. Thus, reduced dosing in elderly patients is important [135].

Morphine is the prototypical opioid for postoperative pain [136, 137]. Older patients show an increased sensitivity and decreased clearance. In the elderly patient, especially in the presence of renal failure, active metabolites can complicate the pharmacological profile and make the activity and duration of effect unpredictable. Several studies have suggested that the initial postoperative requirements of morphine are similar in old and young patients, but the maintenance doses should be reduced [138]. Further, morphine can cause significant histamine release.

Meperidine is no longer recommended as an analgesic, as its metabolite normeperidine can accumulate and cause seizures, and it has been implicated as a cause of delirium in elderly patients.

Neuromuscular Blocking Agents

Muscle relaxation during surgery is critical for exposure and to prevent patient movement and is generally achieved through the administration of nondepolarizing drugs such as vecuronium, rocuronium, and cisatracurium. These drugs are competitive antagonists of acetylcholine at the motor end plate. The most important anesthetic concern for the elderly patients is the complete reversal of these agents at the end of the surgery. Any residual drug effect could result in significant respiratory impairment in the recovery room, especially when combined with residual anesthetics and analgesic medications. For this reason, the longer acting muscle relaxant pancuronium should be avoided altogether in the elderly.

Sugammadex is a noncompetitive reversal agent that binds rocuronium and vecuronium, leading to reversal of neuromuscular blockade. While it has been used worldwide for several years, it was approved in the United States in December, 2015. Sugammadex appears to take longer to reverse neuromuscular blockade in elderly patients, but appears to be quite effective. Sugammadex is not currently indicated for patients with renal failure and has been associated with bradycardia and anaphylaxis. While it is promising, further studies in elderly patients are needed [139].

Inhalational Agents

General anesthesia usually includes the addition of a volatile anesthetic agent: the agents currently in use in the United States are sevoflurane, desflurane, and isoflurane. It is well documented that older patients require less volatile anesthetic to attain a suitable depth of anesthesia. The amount of inhalational agent decreases linearly with aging so by age of 80 years a patient requires 2/3 of that needed in a 20-year-old patient.

Other

Dexmedetomidine is an alpha 2 agonist that is more selective than clonidine. It is approved for sedation and has gained popularity as a sedative and anesthetic adjunct. Dexmedetomidine has analgesic properties and can be used in small bolus doses or continuous infusion. In addition to providing sedation and analgesia, dexmedetomidine is also a hemodynamic depressant and can cause hypotension and bradycardia and can be used in withdrawal syndromes. In general, the cardiovascular side effects must be considered and mitigated by patient selection, adequate volume resuscitation, and inotropic or vasopressor support. Recent studies have shown promise that dexmedetomidine may be beneficial in reducing the rate of postoperative delirium in elderly patients in both cardiac surgery and non-cardiac surgery [81, 140].

Acetaminophen is frequently overlooked as a useful opioid sparing analgesic in the immediate postrecovery phase. For the older patient without liver impairment, scheduled dosing is recommended and frequently combined with multimodal approach that includes low doses of NSAIDs or opioids [141].

Ketorolac is a NSAID available for intravenous administration. It can be a useful adjunct for pain relief and results in significant opioid sparing. Ketorolac, like all NSAIDS, must be used cautiously in elderly patients, especially in patients with dehydration or renal failure, a history of gastrointestinal bleeding, or anticoagulant or antiplatelet therapy. Postoperatively ketorolac should be administered for short duration, and in older patients the dose should be reduced by 50% starting at 15 mg and not exceeding total 60 mg/24 h.

Gabapentin is an anticonvulsant that has analgesic properties [142]. The mechanism of action of gabapentin is not fully understood, but involves binding to voltage-gated calcium channels. Single preoperative doses of gabapentin have been found to reduce pain intensity and opioid use in the first 24 h postoperatively. In addition, gabapentin administration is associated with a reduced incidence of postoperative nausea and vomiting, constipation, and urinary retention, although an increase in sedation has been noted, especially at higher doses.

Conclusion

Aging affects every body system, so the interplay between anesthesia and aging is necessarily complex. It is crucial to specifically consider age-related changes in the cardiac, pulmonary, and neurologic systems. Labile hemodynamics and potential for diastolic heart failure are important cardiovascular issues in older adults. The risks of postoperative ventilatory failure and pneumonia are increased in the elderly. Postoperative cognitive dysfunction is a common entity after all types of major surgery. Because of decreases in hepatic and renal reserve, pharmacodynamics and pharmacokinetic changes must also be taken into account. At this time, it is difficult to define the optimal anesthetic for the elderly. Rather, the anesthesiologist must understand age-related changes, important comorbidities, and the planned surgery to design an anesthetic that accounts for all of these factors and is based on fundamental principles of geriatric anesthesia.

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Part III

Perioperative Care

Management of Acute Postoperative Pain in the Geriatric Patient

21

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Contents

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Abstract
Arguably more than any other community, the care of the geriatric surgical patient draws on the full breadth of a physician's skills, interweaving a sophisticated understanding of age-related physiology, advanced therapeutics, and vigilant humanitarian concern for an at-risk and often neglected patient population. Seldom is this more evident than in the geriatric surgical patient in acute post-operative pain. In their review, Brennan, Carr, and Cousins note that "because pain management is the subject of many initiatives within the disciplines of medicine, ethics, and law, we are at an 'inflection point' in which unreasonable failure to treat pain is viewed worldwide as poor medicine, unethical practice, and an abrogation of a fundamental human right" (Brennan et al. Anesth Analg 105:205–221, 2007).

Introduction

In their review, Brennan, Carr, and Cousins note that "because pain management is the subject of many initiatives within the disciplines of medicine, ethics, and law, we are at an 'inflection point' in which unreasonable failure to treat pain is viewed worldwide as poor medicine, unethical practice, and an abrogation of a fundamental human right" [1].

Clearly this right to receive adequate pain management extends to the postoperative surgical patient of any age, and yet fear of uncontrolled postsurgical pain continues to be among the primary concerns of patients about to undergo surgery [2]. This fear is not unfounded since, despite increasing research and clinical attention, many adult surgical patients continue to experience moderate to severe pain, while less than half who undergo surgery report adequate postoperative pain relief [3, 4]. These findings are even more concerning when extrapolated to the elderly, who enter the surgical arena with higher levels of uncontrolled pain, particularly those who are cognitively impaired [5, 6].

The elderly are also more likely to have multiple comorbidities with less physiologic reserve, which compounds their risk for postoperative complications. For instance, uncontrolled acute pain in the postoperative setting leads to increased sympathetic activity which in turn leads to tachycardia, hypertension, and increased myocardial oxygen demand [7]. In elderly patients with coronary artery disease, the risk of myocardial infarction increases. Inadequate postoperative analgesia in the elderly has been linked to longer hospitalizations, lengthier rehabilitation, frequent readmissions, and the aforementioned cardiopulmonary morbidity. Less well recognized is the fact that inadequate acute postsurgical pain management can lead to chronic pain syndromes [8–10]. Chronic neuropathic pain states are difficult to treat once established and can affect the future quality of the patient's life through a constellation of maladaptive physical, psychological, family, and social consequences [11] (Fig. 1).

In addition to the objective physiologic implications, pain exists simultaneously as a subjective psychological phenomenon. Many factors combine to form a patient's concept of pain, including previous pain experiences, cultural background, coping styles, social supports, the degree of control felt over the pain/disease, fear, anxiety, and depression [12]. This subjectivity extends to those

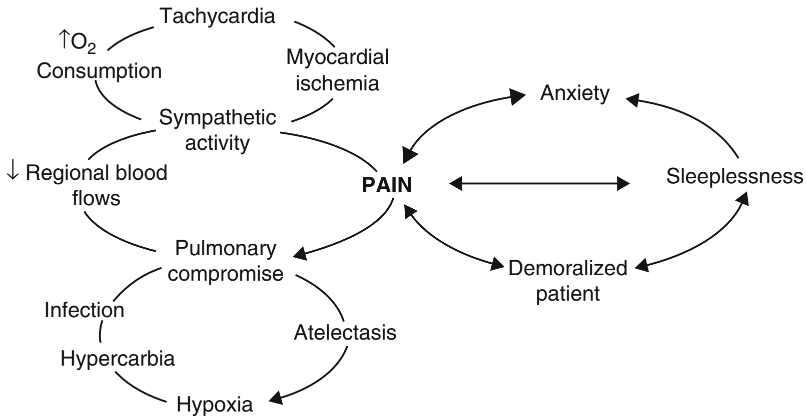

Fig. 1 Harmful effects of unrelieved acute pain (reprinted from Sinatra [7], with permission from Elsevier)

caring for the elderly patient as well, subtly influencing behavior and care patterns.

The global population is aging due to parallel declines in mortality and fertility rates [13]. By the year 2050, there will be a fourfold increase in the elderly population compared with only a 50% global population increase, and at that time 25% of the elderly will be over the age of 80 [14]. The US geriatric population is quickly growing, with 10,000 individuals reaching the age of 65 every day. In 2007, adults 65 and older comprised only 13% of the US population but represented 43% of all inpatient hospital days [15]. Elderly patients have surgery four times more frequently than the younger population, and these tend to be more painful, including elective joint replacements, emergent reductions of fall-related fractures, and complex surgeries for cancer [16].

However, there is little merit in considering the treatment of acute pain in the elderly population unless it differs from that provided to younger patients [14]. This begs the questions of whether elderly patients perceive pain differently from younger patients; are there changes in nociception that occur with aging, and do elderly patients process and respond to nociception differently?

Nociception Is Not Pain

Activity induced in the nociceptor and nociceptive pathways by a noxious stimulus is not "pain," which is always a psychological state. Although we appreciate that pain most often has a proximate physical cause, especially acute pain, activity in nociceptor systems is not equivalent to the "experience of pain" [17]. The recognition that pain serves an important biologic function related to survival raises the important question: to what extent do age-related changes in nociception impact on the capacity of the pain experience to fulfill an "enteroceptive" function such as thirst, hunger, and thermoception that constitute sensory indexes of the health of the body? [18].

Assessment and intervention for pain in the elderly should therefore begin with the assumption that all neurophysiologic processes subserving nociception are intact [19]. In fact Gagliese and Melzack demonstrated that age did not affect the rating of pain by postsurgical patients [20]. That is to say, tissue injury produces the same experience of pain in an elderly person as in a young person.

There are data to suggest, however, that some impairment of Aδ fibers occurs with aging and therefore impedes the early warning of tissue injury [18]. There are also data that suggest that widespread and substantial changes in structure, neurochemistry, and function occur in the dorsal horn of the spinal cord and CNS with aging [18].

Multiple studies report reductions in the descending inhibitory modulating systems for nociception in the elderly [18, 21]. Gibson and Ferrell conclude that the reduced efficacy of endogenous analgesic systems might be expected to result in a more severe pain experience following prolonged noxious stimulation [18]. It is also possible that the documented decline in afferent transmission pathways could be offset by a commensurate reduction in the endogenous inhibitory mechanisms of older persons, with a net result of little or no change in the perceptual pain experience [18]. They further conclude that any deficit in endogenous analgesic response (which is stimulus intensity dependent) will become critical, thereby making it more difficult for persons of advanced age to cope with severe or persistent clinical pain conditions [18].

Evidence suggests that as age advances, pain threshold increases, but pain tolerance decreases [22]. The net effect may be that elderly patients experience acute surgical pain in the same way as younger patients. It is clear that if a surgeon was to make a skin incision with a scalpel in an elderly unanesthetized patient, then the patient would most certainly scream with pain. Yet silent myocardial infarctions are more common in the elderly, and the bowel must be more distended before the elderly sense pain, often delaying the diagnosis of such conditions as a bowel obstruction [22, 23].

With respect to the heart, the complete absence of "the perception of pain" that can occur in the presence of myocardial ischemia, arteriolar occlusion, myocarditis, early acute endocarditis, valvular ulceration, etc. makes it difficult and yet extremely important to assess for pain in elderly patients recovering from surgery [24].

But while there is controversy over whether the number and integrity of nociceptors decreases with age, the clinical position that age dulls the "sense of pain" is untenable [18]. It is the processing and transmission of the nociceptive information that may be altered in the elderly, and the elderly may be more sensitive to the side effects of medications that are used to treat pain. These observations thereby give the impression that the elderly are less sensitive to pain. But no physiologic changes in pain perception in the elderly have been demonstrated according to a five-state study by Cleeland [23]. This is supported by the observation that age does not affect the success of traditional interventions for the treatment of pain [19].

Again one would not assume that a surgical incision in an elderly patient will "hurt" less and therefore does not need to be treated. Likewise, anyone who has observed an elderly patient with acute herpes zoster certainly can attest to the excruciating pain that these unfortunate patients report. If given adequate preoperative teaching, assessed preoperatively for any impediments to the use of patient-controlled analgesia (PCA), e.g., dementia, elderly patients were successfully started on PCA in the postanesthesia care unit after general anesthesia once they were awake and responsive enough to receive a loading dose of opioids titrated to comfort [19].

Pharmacodynamics/Pharmacokinetics, Organ Function, and Aging

The aging process is characterized by a progressive functional decline in all organ systems as well as compromised organ reserves, which can negatively affect the ability to deal with perioperative stress. Even the fit elderly patient's ability to compensate for perioperative stress is compromised. These physiologic changes impact the pharmacodynamics and pharmacokinetics of anesthetic and analgesic medications [25]. Because baseline cardiac, hepatorenal, and neurologic functions are typically adequate in the absence of acute challenges, it can be very difficult to predict the effect of perioperative stress on the older patient [26].

In general, the pharmacodynamic actions of drugs (what the drug does to the patient) are unaffected in the normal aging process, although dose requirements to produce the same effect may change with age, and the therapeutic window between intended effect and side or adverse effects may be narrowed in the elderly [27–29].

The pharmacokinetic actions of drugs (what the patient does to the drug), on the other hand, are more greatly affected by the reduced cardiac output and organ blood flow of aging. These pharmacokinetic changes may complicate medication management [30], as demonstrated by Woodhouse and Mathur who studied the 24-h cumulative PCA opioid administration as a function of age. Morphine and fentanyl both showed an expected reduction in dose by 50% in the elderly, while meperidine was more variable due to a more complex pharmacology [31].

A general slowing of the CNS and alterations in drug metabolism and excretion account for much of the increased sensitivity to analgesics in the elderly [32]. There is decreased cerebral blood flow, decreased cortical mass, and as noted above altered perception and affective expression of pain. Similarly decreased blood flow to peripheral nerves can combine with common comorbid conditions such as diabetes to cause peripheral nervous system dysfunction manifesting as decreased sensitivity to pain, temperature, and pressure.

The liver exhibits decreased hepatocyte mass and blood flow, decreased cytochrome p450 function, and prolonged drug metabolism [33]. There is an age-related decrease in basal metabolic rate of the liver and a decline in albumin production of about 10% [34]. Although most tissues have some enzymatic metabolism, the majority occurs in the liver. Patients with impaired liver function will therefore have altered metabolic capacity for drug elimination, particularly demethylation. Drugs that are administered simultaneously and that are metabolized by the p450 system of enzymes will compete for binding sites leading to altered blood levels [35].

With aging there is a decreased lean body mass and total body water and an increased proportion of body fat; these alter the volume of distribution and redistribution of drugs and alter their rates of clearance and elimination [26]. Renal blood flow is compromised, approximately 10% per decade of life after the age of 50 with a concomitant loss of renal parenchyma, demonstrated best by decreasing glomerular filtration rate (GFR) rather than blood urea nitrogen/creatinine ratios [36]. Anesthetics, surgical stress, pain, sympathetic stimulation, and renal vasoconstrictive drugs may all compound subclinical renal insufficiency [26]. Impaired renal clearance may lead to accumulation of metabolites, increasing the half-lives of renally cleared drugs. Similarly, decreased plasma binding increases blood levels of active drugs such as opioids and NSAIDs [even the specific cyclooxygenase 2 (COX-2) inhibitors, such as celecoxib (Celebrex®)] [37]. Taken together these factors account for the increased incidence of medication side effects, iatrogenic overdosing, and drug-drug interactions in the elderly.

Perioperative Cognitive Impairment and Pain

Pathologic perioperative CNS dysfunction, as distinguished from physiologic CNS changes of aging, is a common phenomenon in elderly surgical patients and can complicate pain management [38]. Postoperative cognitive dysfunction (POCD) is a postoperative memory or thinking impairment that has been corroborated by neuropsychological testing [39], while postoperative delirium (POD) is defined as an acute change in mental status, with inattention and altered level of consciousness throughout the course of the day [40].

POD is typically transient and acute, while POCD is a more persistent problem of a change in cognitive performance, often noticeable to the patient and/or family. Preoperative confusion is a predictor for POD, which can occur in 5–15% of elderly patients undergoing noncardiac surgery, and up to 60% of cardiac and orthopedic procedures. POCD has been found to occur in 10–13% at 3 months and can have significant socioeconomic and medical implications including increased risk of death in the first year after surgery [18, 41, 42].

Little is known of the neurophysiological relationships between pain- and age-related degenerative brain diseases. The elderly patient with cognitive impairment is at a greater risk than cognitively intact patients for undertreatment of pain [43]. Studies indicate that individuals with cognitive impairment maintain normal pain perception thresholds [44]; however, altered central processing of pain stimuli at the cortical level where neurodegeneration is present can alter the patient's expression of pain. This is above and in addition to the physiologic CNS changes of aging but similarly impacts the affective component of pain primarily. Significant pain may therefore go unrecognized in the cognitively impaired, as clinicians and nurses assess pain in large part based on affect and pain behavior. It has been shown as well that the type of pain with which a patient presents may harbor bias toward undertreatment [45].

Various interventions have been studied to attempt to decrease the occurrence of POCD, including multimodal analgesia techniques and perioperative vitamin supplementation, though no clear effective strategy has been proven [46, 47]. As uncontrolled postoperative pain is a primary contributor to POD/POCD, the best course of action appears to be adequate analgesia along with anticipatory perioperative support should the inevitable CNS dysfunction occur.

Perioperative Pain Management Planning

As with any surgery, a complete history and physical exam prior to admission is paramount in obtaining a good postsurgical outcome. Acute pain in the perioperative setting can be compounded by preexisting chronic pain, which has been documented to exist in 25–73% of older people in the community and skilled-nursing facilities of Western nations [48]. Assessment and documentation of preexisting pain should be thorough with reference to location, intensity, aggravating/relieving factors, quality, and radiation. Comorbid psychological, emotional, and cognitive factors are predictors of postoperative side effects including pain, nausea, and fatigue and should be well documented as well [49].

Approximately 40% of elderly patients take at least 5 drugs per week, and 12–19% use at least 10 [50]. Thorough documentation of medications including the preoperative analgesic regimen will help anticipate post-op pain requirements as well as medication interactions. Consideration should be given to continuing adjuncts and anxiolytics throughout the perioperative period albeit at a reduced dose, particularly if the patient is physically dependent on them despite being generally contraindicated in the elderly. This may include centrally active muscle relaxants such as carisoprodol and common benzodiazepines. Antidepressants should be continued with consideration for any interactions with anesthetic and analgesic medications.

Education, Counseling, and Forming a Plan

The American Pain Society recommends preoperatively providing individually tailored programs of education and support for patients and families with more intensive needs such as the elderly and cognitively impaired. Such a strategy may provide for reduced postoperative opioid consumption, less preoperative anxiety, fewer requests for sedative medications, and reduced length of stay after surgery [51].

Meeting with patients and their families preoperatively is an important opportunity to educate them about their care while simultaneously dispelling commonly held notions which may hinder pain control. For example, older patients may endure pain longer, waiting until it is severe before reporting to the nursing staff [52]. Men in particular may fear being viewed as weak if they report their pain [53]. Older generations often acquiesce to the opinions and beliefs of family members which may in turn prevent them from being honest about their own pain [54]. It has been suggested that older people fear a loss of independence and may play down their pain in an attempt to maintain autonomy [55].

These sociological biases extend to medical practitioners as well. Common misconceptions include pain being a normal part of the aging process, perception of pain decreasing with age, older people using pain as a means of seeking attention, and opiates as dangerous or addictive to the elderly [56–59]. Patients, families, and practitioners alike may benefit from pertinent information and education relating to analgesia in the pre- and postoperative period [60].

During the perioperative planning, every attempt should be made to minimize or negate the elderly patient’s hospital stay entirely. Bed rest can induce functional decline in elderly patients after only 2 days of hospitalization. The worse the patient's functional status is preoperatively, the greater the expected benefit of avoiding hospitalization [61]. Elderly patients are less able to adapt to unfamiliar environments and routines and recover faster in their familiar home environment. Avoiding hospitalization in the elderly undergoing minor surgery has been shown to result in less POCD at 1 week, as well as reduced respiratory events, nosocomial infections, and early postoperative complications [62].

Along these lines, Launay-Savary et al. [63] recently reviewed the evidence as to the feasibility and efficacy of enhanced recovery after surgery (ERAS) programs in the elderly, finding them overall beneficial for patients over 70 undergoing colorectal surgery. These multidisciplinary care protocols target specific perioperative goals such as analgesia, re-feeding, drains, surgical approach, and postoperative care in an attempt to minimize perioperative morbidity and mortality. While no longer questioned in younger patients, the increased frailty and age-related morbidity of the elderly warrants special adaptation of the endpoints to this population. Examples include returning to the same domicile, maintaining a certain quality of life the patient is accustomed to, and avoiding loss of autonomy. While morbidity remained increased and compliance to such protocols decreased when compared to younger patients, the reduced duration of hospital stay and overall morbidity when compared to age-matched non-ERAS patients attest to the efficacy of ERAS versus traditional management.

Methods of Post-Op Pain Assessment

Adequate pain management would be impossible without accurate and reliable methods of measuring pain. Established methodology breaks down into self-reported and behavioral/physiologic methods, each offering different efficacies depending on the cognitive state of the patient. Common self-report scales used to measure pain intensity include the visual analogue scale (VAS), verbal rating scale (VRS; using familiar words such as none, slight, mild, moderate, and severe), numeric rating scale (NRS; 0 = no pain; 10 = worst imaginable pain), and facial pain scale (FPS) [64, 65]. In the postoperative setting, the VRS and the NRS are most validated as well as preferred by elderly populations [66, 67]; however, they require the patient to have minimal to no cognitive dysfunction.

In those with mild to moderate cognitive dysfunction, the VRS stands out as the preferred tool though patience and persistence may be required to obtain answers [68]. For those with severe cognitive dysfunction as in dementia or POD, behavioral methods are necessary and assessment of the patient's pain by family or caretakers may be helpful. The Doloplus and Doloplus-2 are batteries of assessments taking into account somatic, psychomotor, and psychosocial elements to render a pain level. They have been validated for elderly postoperative populations, but can be time-consuming to obtain [69]. The Algoplus is a more recent behavioral acute pain scale validated in elderly patients unable to communicate [70], and may be obtained by briefly observing the patient with regard to face, gaze, body, behavior, and auditory indices. Two or more positive signs out of the five categories indicate pain.

Whichever method is ultimately chosen, it is important to consistently reassess not only for pain but for efficacy of interventions and side effects, with adjustments to the pain management plan following accordingly. In the postoperative period "dynamic pain relief" or the patient's ability to ventilate deeply, cough, and ambulate without pain are important indices of adequate analgesia as well.

Multimodal Therapy

As we have seen the elderly present a heterogeneous mix of physiological changes, comorbid conditions and medication regimens for which broad generalized pain management strategies are difficult. Each case presents a unique challenge.

With that in mind, we will now start developing our toolbox with which to treat acute postoperative pain. The analogy is appropriate, for the role of pharmacologic adjuvants and nonpharmacologic techniques in postsurgical analgesia has been greatly expanded over the past years in part because of increasing awareness of the morbidity attributed to opioids [71]. The concept of balanced or multimodal analgesia was developed to both improve analgesic efficacy and reduce side effects [72]. Targeting different receptors and pain mechanisms with smaller individual amounts of medications creates an opioid-sparing synergy which may work to decrease postsurgical morbidity and mortality in geriatric populations. Appropriate selection is critical; however, a contraindicated tool will potentially cause more harm than good.

Systemic Pharmacologic Therapy

Opioids

Despite the cautionary rhetoric, opioids remain the closest drugs we currently have to an ideal analgesic. They exhibit no ceiling effect and can produce profound analgesia by progressive dose escalation. They are the most effective agents for the relief of any type of acute pain because of their predictable dose-dependent response, which is only altered in the elderly by their increased dose sensitivity. Their versatility is unmatched. They are effective when given orally, parenterally via provider bolus or patient-controlled analgesic (PCA) formulations, or neuraxially via epidural (infusion or patient controlled epidural analgesia [PCEA]) or intrathecal routes.

Opioids have been shown to produce a greater incidence of respiratory depression, cognitive depression/delirium, constipation, and sedation in the elderly; but the elderly seem to be less sensitive with respect to nausea and vomiting [73]. Opioids have no significant long-term organ toxicity and can be used for years [74]. Addiction is negligible when opioids are used appropriately in the context of medical care [75].

Morley introduced a concept of "Broad Spectrum Opioids" versus "Narrow Spectrum Opioids" [76]. The narrow spectrum opioids have analgesic actions limited to the Mu, Kappa, and Delta opioid receptors. For purposes of acute postoperative pain management, we are primarily dealing with Mu opioid agonists. The broad spectrum opioids find more usefulness in chronic pain and neuropathic pain with their Mu opioid action enhanced by actions also as *N*-methyl d-aspartate (NMDA) receptor antagonists. In addition, some have central neuromodulating effects through inhibition of reuptake of serotonin and norepinephrine similar to many antidepressants. Some broad spectrum opioids have all three properties (e.g., methadone).

When opioids are used in a fixed oral dose mixed with a nonopioid analgesic, their efficacy is limited by the maximal safe dose for the adjuvant (acetaminophen, aspirin, or NSAID typically). A list of the common combination oral opioids is shown in Table 1.

The concept of "start low and go slow" is paramount with opioid use in the elderly. Many oral formulations are scored for use as half-doses. Patients experiencing moderate pain should be started on a weak opioid. Strong opioids are used for more severe pain such as postsurgical. They have a wide therapeutic window and no ceiling effect, with higher doses producing an increasing level of analgesia. They are the agents of choice for parenteral administration [77].

Weak Opioids

Codeine, an alkaloid of opium, is the prototype "weak" analgesic. Although a parenteral preparation is available, it is nearly always given orally and often in a fixed mixture with a nonopioid analgesic. It is 10–20% less efficient than morphine; a 200 mg dose is equipotent to 30 mg of morphine. The half-life of codeine is 2.5–3.0 h [77]. Codeine is often combined with acetaminophen with or without caffeine in doses of 300 mg acetaminophen, 30 mg codeine, and 15 mg caffeine (e.g., Tylenol 3™). Codeine is converted to Codeine-6-glucuronide, a renally excreted metabolite with activity equal to the parent compound. This will prolong activity and toxicity in patients with renal insufficiency; doses should be halved and spaced out accordingly [69].

Table 1 Combination opioids available for oral administration. The dose is limited by the adjuvant and not the opioid component. The maximum doses should be reduced in the elderly or in the presence of liver and renal insufficiency

Trade name®	Opioid component	Dose of opioid (mg)	Adjuvant drug	Dose of adjuvant (mg)	Tabs/caps per day
Advil			Ibuprofen	200	12
E.S. Tylenol			Acetaminophen	500	8
Tylenol-3	Codeine	30	Acetaminophen	300	13
Tylenol-4	Codeine	60	Acetaminophen	300	13
Darvon	Propoxyphene	65			NL
Darvocet	Propoxyphene	65	Acetaminophen	325	13
Darvocet N-100	Propoxyphene	100	Acetaminophen	325	13
Vicodin	Hydrocodone	5	Acetaminophen	500	8
Vicodin ES	Hydrocodone	7.5	Acetaminophen	750	5
Lortab Elix	Hydrocodone	7.5	Acetaminophen	500	8
Lorcet 10/650	Hydrocodone	10	Acetaminophen	650	6
Norco	Hydrocodone	10	Acetaminophen	325	13
Vicoprofen	Hydrocodone	7.5	Ibuprofen	200	12
Percodan	Oxycodone	5	Aspirin	325	6
Percocet	Oxycodone	5 10	Acetaminophen	325	13
Tylox	Oxycodone	5	Acetaminophen	500	8
Oxycodone	Oxycodone	5			NL

Hydrocodone is a codeine derivative, available in the USA in combination with acetaminophen, aspirin, or ibuprofen. It is more potent than codeine, although good data are lacking [77].

Codeine (Tylenol™ 3 or 4), dihydrocodeine (Synalgos™ DC), and hydrocodone (Vicodin™, Lortab™, Norco™, etc.) do not have opioid action until they undergo metabolic conversion to morphine or hydromorphone respectively by the action of the enzyme CYP2D6, one of the P450 group of enzymes [78]. Eight to thirty percent of the population is reported to be deficient in this enzyme and therefore will have a poor to absent response to these medications [79]. In addition, there are a number of drugs common in elderly populations which will depress the action of CYP2D6 leading to decreased analgesic efficacy, such as amiodarone (Cordarone®), fluoxetine (Prozac®), haloperidol (Haldol®), paroxetine (Paxil®), propafenone (Rythmol®), quinidine, ritonavir (Norvir®), terbinafine (Lamisil®), and thioridazine (Mellaril®) [78].

Oxycodone is a semisynthetic derivative of the baine, an opium alkaloid. Because of its high bioavailability (>50%), it is suitable for oral administration and is 1.5 times more potent than morphine by this route and 10 times more potent than codeine [80, 81]. When administered parenterally, its intensity and duration of analgesia are 25% less than those of morphine [81]. However, in the USA, oxycodone is exclusively an oral medication. Oxycodone given orally has a half-life of 2–3 h and duration of action of 4–5 h. It is metabolized like codeine: demethylated and conjugated in the liver and excreted in the urine [81]. Oxycodone has been considered a "weak" analgesic because of its use in a fixed combination with acetaminophen and aspirin, e.g., Percocet® (oxycodone 2.5, 5, or 10 mg with acetaminophen 325 mg) or Percodan® (oxycodone 5 mg with aspirin™ 325 mg) which limits its dose. When oxycodone is used alone, it has no ceiling effect for analgesia. It is more potent than morphine, and there are reports suggesting that it might have fewer side effects [82, 83]. Its availability in 5 mg tablets permits careful titration in patients with a narrow therapeutic margin. It is also available in extended-release preparations with doses of 10, 20, 40, and 80 mg without acetaminophen, which can be used for q12h dosing or occasionally q8h dosing.

Oxycodone is therefore a versatile and flexible oral medication that can be used to treat pain of any intensity requiring an opioid analgesic [77]. It is also interesting that patients who report poor analgesic effect from codeine- and hydrocodone-based opioids will report excellent analgesia from oxycodone-based analgesics. This is a result of enzymatic metabolism of oxycodone by CYP2D6. Therefore, the patients who are deficient in this enzyme cannot convert codeine or hydrocodone to morphine, but also will not metabolize oxycodone quickly and therefore have a prolonged effect from oxycodone [78]. The reverse would also be true in that those patients who genetically have high levels of CYP2D6 will get excellent analgesia from codeine or hydrocodone, but oxycodone although effective will have a shortened duration and require more frequent dosing.

Tramadol (Ultram®) is weak opioid analgesic that also inhibits the reuptake of serotonin and norepinephrine while providing some NMDA-antagonistic properties. It has about one-tenth the potency of morphine and is effective for mild to moderate pain. Unlike other opioids, tramadol exhibits an analgesic ceiling, which limits its use for severe pain syndromes. Tramadol appears not to be associated with physical dependence but does have a relatively high incidence of associated nausea compared with that of other opioids [84]. Similar to codeine, it depends on CYP2D6 for production of its main active metabolite, O-desmethyl-tramadol, which is renally excreted and may accumulate in patients with renal insufficiency. Those without CYP2D6 activity will be resistant to the analgesic effects of Tramadol. It can be given IV with less respiratory depression and constipation than morphine [68]. Tramadol is also available as a combination drug with acetaminophen (Ultracet® 37.5 mg tramadol/325 mg acetaminophen) or as a sustained-release tramadol of 100 or 200 mg (Ultram® ER).

Tramadol should be used with caution in patients with epilepsy or taking seizure-lowering medications. Additionally, it is contraindicated with monoamine oxidase inhibitors (MAOI) for fear of serotonin syndrome. Use with serotonin-reuptake inhibitors (SRI) should be monitored [85]. A maximum daily dose of 300 mg is suggested for healthy individuals, with a reduction to 200 mg in patients with other risk factors [86].

Tapendatol (Nucynta®) is an oral, centrally acting synthetic mu-agonist with norepinephrine reuptake inhibiting properties. In the USA, it is approved for moderate-severe pain. In orthopedic postsurgical musculoskeletal pain, 50–100 mg every 4–6 h was equivalent to oxycodone 10–15 mg every 4–6 h with decreased incidences of nausea, vomiting, and constipation [87].

Strong Opioids

As described by Morrison et al., *morphine* is the prototype strong opioid agonist [77, 88]. Like other “strong” opioids, there is no ceiling to the analgesic effect, although side effects, particularly sedation and confusion, may intervene before optimal analgesia. Morphine is metabolized in the liver, where it undergoes glucuronidation at the 3- and 6-positions. Morphine-3-glucuronide (M3G) and morphine-6-glucuronide (M6G) accumulate with chronic morphine administration [89]. M6G binds to Mu receptors with affinity similar to morphine but also binds to delta receptors, which may account for its higher analgesic potency [75, 90].

M6G appears to be 20 times more analgesic than morphine when administered directly in the periaqueductal gray, but only 0.077% of this metabolite crosses the intact blood–brain barrier following oral or parenteral administration [90, 91]. With single-dose morphine studies, the relative parenteral/oral potency ratio is 1:6 [92]. After chronic use, the ratio changes to 1:3 as a result of the accumulation of active metabolites [93]. There is experimental [94] and clinical [95] evidence that M3G, which has negligible affinity for opioid receptors and does not produce analgesia, has excitatory effects on neurons and can cause myoclonus and rarely a hyperalgesic state [90]. It is thought that the myoclonus and hyperalgesia precipitated by M3G are mediated by different receptor mechanisms [96].

The half-life of morphine is about 2 h but the onset time for analgesia from a bolus dose can be as long as 90 min [97]. Shafer and Flood comment that this slow onset of analgesia should make it difficult to titrate morphine [30] even though Auburn showed that titration of small morphine doses every 5 min was safe and effective in the elderly [28, 97].

Extended-release oral preparations of morphine have been available for many years in many different doses permitting q8h, q12h (MS Contin™), and once daily dosing (Kadian™ and Avinza™). Slow-release preparations should be used only after dose titration with morphine sulfate and only if the pain is expected to continue [77]. Morphine metabolites are eliminated by glomerular filtration and can accumulate in patients with renal insufficiency, leading to an increased incidence of side effects [98]. Opioids with fewer or no active metabolites are preferable in frail patients and those with renal disease [x].

Hydromorphone (Dilaudid®) is a potent semisynthetic phenanthrene-derivative opioid agonist [24]. When single doses are administered parenterally, 2 mg of hydromorphone is equipotent to 10 mg of morphine. Hydromorphone is somewhat shorter acting than morphine but has a higher peak effect. Its bioavailability is 30–40% with an oral to parenteral ratio of 5:1 [99]. It has a half-life of 1.5–2.0 h, and active metabolites may accumulate during renal failure [100]. Because hydromorphone is highly water soluble, continuous subcutaneous infusion and intravenous infusions of hydromorphone result in similar analgesia and side effects [101].

Fentanyl is a synthetic phenylpiperidine-derivative opioid agonist that interacts primarily with Mu receptors [102]. It is 80–100 times more potent than morphine and highly lipophilic [30]. The onset time for analgesia when administered intravenously is 2–3 min making it an ideal agent for analgesic titration, intra-op, and in the post-anesthesia care unit (PACU).

Fentanyl is also available in both a transdermal (Duragesic™) form and oral transmucosal (Actiq™) form. The transdermal form is not recommended, however, for the treatment of postoperative pain because the titration is lengthy and it lacks the flexibility, which is the cornerstone of treatment for acute and evolving pain. Oral transmucosal fentanyl is being used for severe breakthrough pain requiring rapid onset without intravenous access (e.g., at home). Its inherent safety is that the patient can discontinue administration with the onset of analgesia without having to use the entire dose; however, Actiq™ is only FDA approved for cancer pain.

Methadone is a synthetic diphenylheptane-derivative opiate mu agonist with serotonin/norepinephrine reputake inhibition at the level of the spinal cord, as well as NMDA antagonistic properties [103]. It is an inexpensive and effective analgesic, but its use is limited by the need for a carefully individualized dose and interval titration. When administered to opioid naive patients, especially the elderly, the risk of overdose is high. It should therefore be used only for selected patients and only by individuals experienced with its use [104]. The oral bioavailability is high, ranging up to 100%, and it is rapidly absorbed from the gastrointestinal tract with measurable plasma concentrations within 30 min after oral administration [104, 105]. It has no active metabolites and its clearance is not affected by hepatic or renal disease [105].

When administered in single parenteral doses to opioid naïve patients, methadone is equipotent to morphine, with duration of analgesia of 4–6 h [106]. Its plasma level declines in a biexponential manner with a half-life of 2–3 h during the initial phase and 15–60 h during the terminal phase [107]. This biexponential decline accounts for the relatively short analgesic action and the tendency for drug accumulation with repeated dosing. A reduction in dose and interval frequency is often needed during the first few days of treatment to prevent side effects from overdosage [108]. The rare patient allergic to morphine and intolerant to fentanyl might benefit from methadone because of its different chemical structure. Furthermore, since methadone is cleared almost exclusively by the liver, it can be a useful medication in patients with renal failure [109].

Given its NMDA antagonism, patients with neuropathic pain or opioid tolerance can often obtain relief when changed to methadone.

However, methadone must be started at a much lower dose and increased slowly, with a frequency of not less than every 3 days. Breakthrough doses of the present opioid must be maintained during this transition period [103]. Another interesting recent finding concerning methadone is the report that it is a potent inducer of cell death in leukemia cells and inhibited proliferation of these cancer cells [110].

Principles of Dosing and Delivery Methods

After most major surgical procedures opioids are first-line treatment for post-op pain. While tenet of "start low go slow" still applies, immediately after surgery is a time to be more aggressive as uncontrolled pain may drive delirium, particularly in the cognitively impaired [111]. The addition of nonopioid adjuvants will provide a synergistic effect and decrease overall opioid requirement.

Shafer and Flood describe several concepts that must be considered when treating the elderly with opioids by bolus intravenous administration or by continuous infusions as is commonplace in the postoperative period [30]. They state that "the calculation of the equianalgesic dose is complicated by the relative intrinsic potency of the opioids, the different pharmacokinetic profiles, and the large differences in the rate of blood–brain equilibration." Further, because of these stated differences in the properties of the opioids, the equianalgesic dose also becomes a function of the time after the injection was made, and they give an example of fentanyl (50 μg), which has a rapid onset and will have the same effect at 10 min as 5 mg of morphine which has a slow onset time. However, at 60 min postinjection, 50 μg of fentanyl will have the same effect as 1 mg of morphine [30]. Thus, one must be careful in titrating morphine with frequent bolus doses since it may result in stacking the effect which may not become evident until 60 min later. It may be better to load a patient to comfort with fentanyl while starting a PCA with morphine or hydromorphone, in order to allow enough time for the longer acting and slower onset opioids to reach peak effect and steady state.

For patients with severe acute postoperative pain, parenteral morphine has classically been the opioid of choice [77]. Today, at least in the well-monitored site of the postanesthesia recovery room, hydromorphone and fentanyl have become more common. Whichever the initial choice of opioid is, a good rule of thumb is to reduce the starting dose by half compared with that in a younger patient and maintain the same dosing interval [112]. After the initial dose determination, drugs are titrated based on the analgesic effect. Opioids should be titrated until one of the two endpoints is reached: adequate analgesia or the development of intolerable side effects [113].

PCA is a safe, effective modality for the delivery of opioids for pain that is expected to resolve (e.g., postoperative pain). The patient self-delivers fixed doses of an opioid by pressing a button. Post-op bolus opioid titration to comfort must be accomplished before beginning PCA. In the experience of the authors, one can utilize the total dose required to obtain comfort as a measure of the 3-h patient requirement in setting up a PCA. Estimated morphine consumption by age in the first 24 h after major surgery is: 100 – patient's age ≈ mg of IV morphine [12]. Basal infusion rates are not recommended for the elderly as accumulation of dose can occur during periods of sleep. But the lockout period must also be adjusted so that the patient has adequate time to experience the effect of the analgesic but short enough that the patient can "catch up" with his/her pain.

With PCA an overdose is infrequent because the patient must be alert to press the button, and there is a lockout time between delivered doses during which pressing the button does not result in the delivery of medication. Family members must be cautioned not to press the button for their loved ones while the patient is sleeping in response to a groan or grimace. The usual PCA starting dose for morphine is 1 mg and for hydromorphone is 0.2 mg. The usual lockout time is 8, 10, or 15 min, although this should be adjusted for the individual patient depending on the severity of pain, the age of the patient, and whether there is a basal rate. Some advocate a low-dose basal infusion of opioid at night (e.g., morphine 0.5 mg/h or hydromorphone 0.1 mg/h) to avoid frequent awakenings because of pain, especially for the first 2–3 nights after surgery, although this may increase the daily morphine consumption [114]. Others feel that in the elderly it is better that the patients be allowed to awaken and press the PCA button on their own [115]. However, when PCA was compared with the more traditional "as-needed" administration of intramuscular opioids in a randomized trial involving postoperative pain control in elderly men, PCA using morphine without a basal rate was clearly found to result in better analgesia, fewer complications, less sedation, and higher patient satisfaction than intramuscular opioids [116].

For patients unable to operate PCA or in situations where PCA is not available, a continuous opioid infusion (e.g., morphine 0.5–1.0 mg/h or hydromorphone 0.10–0.25 mg/h) could be started and the patient observed for excessive sedation (reduce dose) or behavioral cues of pain (increase dose). This may be necessary for intubated patients or patients treated in end-of-life care. Frequent behavioral assessments focusing on face and body language that may indicate pain are essential, particularly during the first 24 h following surgery [77]. However, most hospitals might require an intensive care setting in order to provide a continuous infusion of opioid analgesia which the patient's condition may not warrant. It has also been shown that round the clock bolus dosing of intravenous opioids can provide good pain control if the patient is unable to use the PCA machine. This could be in the mode of "nurse-controlled analgesia" and would probably be safer than the continuous infusion.

For patients in whom pain is difficult to control, it has been shown that optimum pain control with minimal side effects could be obtained using PCA with a combination solution of 1 mg/ml morphine and 1 mg/ml ketamine, with a lockout period of 8 min [117]. This takes advantage of the ability of ketamine to block NMDA receptors and enhance the opioid analgesic effect of morphine.

When venous access is problematic, the subcutaneous route can be used. The infraclavicular area is generally the best site when a continuous infusion, PCA, or both are used. A 27-gage butterfly needle is well tolerated and can be maintained for 3–5 days, after which the site must be rotated. When intermittent dosing is required, an insulin syringe is used to minimize trauma. Doses for subcutaneous administration are equal to intravenous doses, and hydromorphone is the agent of choice because of its high potency and lipid insolubility. It is best to avoid the intramuscular route because of erratic absorption and pain from the injection [77]. One must remember, however, that the subcutaneous tissue site can only accommodate <2 ml volume per hour and so solutions must be concentrated. Hydromorphone being more soluble and more potent than morphine is suitable for concentrating.

With all opioid modalities, anticipation of side effects and treating them accordingly is preferable to stopping treatment altogether. Coadministration of stool softeners and antiemetics helps to prevent the common side effects of constipation and nausea [10].

Systemic Nonopioid Adjuvants

Acetaminophen

A nonspecific centrally acting cyclooxygenase inhibitor with few peripheral effects, acetaminophen has been a useful analgesic for mild to moderate pain for some time. Despite fears of dose-dependent hepatic necrosis, in recommended doses (1000 mg every 4–6 h; max 4000 mg/24 h) it is well tolerated in the elderly [118]. In the absence of significant renal impairment, there is evidence that no dose reduction is required for the elderly at all [68]. Hypovolemic surgical patients, as well as those with compromised liver function (malnourished, alcohol abusers, hepatitis), should have reduced doses of 2000 mg/24 h.

Acetaminophen is very effective when given intravenously where it exhibits higher CNS concentrations than oral or rectal routes [119] and may be used as such for the first 24–48 h post-op before switching to oral formulations. Given its opioid-sparing effects, scheduled dosing of acetaminophen should be the core component of a multimodal analgesic regimen [120, 121].

NSAIDs

To understand the cascade of renal effects of NSAIDs, it is necessary to look at the beneficial effects of the enzyme cyclooxygenase 1 (COX-1) on converting arachidonic acid to various prostaglandins. These prostaglandins are necessary for maintaining good renal blood flow, adequate glomerular filtration rate, and homeostasis of potassium and sodium retention through appropriate secretions of renin, aldosterone, and antidiuretic hormone (ADH). When the conversion of arachidonic acid to prostaglandins is inhibited by NSAID inhibition of COX-1, then the kidney comes under risk and loses its ability to regulate salt and water balance. This detrimental effect of NSAIDs on the kidney is potentiated by renal hypoperfusion states [122]. All NSAIDs can result in renal insufficiency; and with the exception of salicylsalicylic acid and choline magnesium trisalicylate, for which the risk is less, they can inhibit platelet aggregation and cause dyspepsia and gastric ulceration [77].

NASIDs have peripheral and central effects [123]. The "Constitutive" effects of the prostaglandins resulting from the actions of COX-1 also include protection of the stomach and intestinal lining and preservation of platelet function [124]. The "Inducible" effects of COX-2 on conversion of arachidonic acid to prostaglandin E-2 leads to inflammation and pain. Blockade of the action of COX-2 reduces inflammation and pain without affecting the good effects of the prostaglandins that are COX-1 dependent [124, 125]. In the presence of inflammation, COX-2 can be found elevated in the CNS. The common NSAIDs are nonspecific because they have variable effects on blockade of COX-1 and COX-2. The most common oral NSAIDs used in clinical practice are shown in Table 2.

There is a ceiling dose effect to all of the NSAIDs, above which no further analgesia is obtained; and although the dose may vary, it usually falls below the maximal recommended dose of the manufacturer [126]. In general, for elderly patients, agents with short half-lives (e.g., ibuprofen) are most appropriate; for patients with a history of dyspepsia, ulcer disease, or bleeding diatheses, either salicylsalicylic acid or choline magnesium trisalicylate should be used if a traditional NSAID is indicated [77]. NSAIDs, when combined with opioids in the PCA setting, both decrease overall opioid consumption and decrease pain intensity [127].

Parenteral NSAIDs are being used increasingly for postoperative pain as sole analgesic agents and in conjunction with opioids as opioid-sparing agents [128]. The efficacy of ketorolac has been well established with 30 mg being equianalgesic with 10 mg of parenteral morphine [128]. Intravenous ketorolac has been shown to reduce opioid requirements for knee and hip replacement surgery by 35–44% and by 50–75% for thoracotomy and upper abdominal surgery [129, 130]. While

Table 2 Common oral NSAIDs by chemical class [222]

Propionic acids	Salicylates	Fenamates	Oxicams	Acidic acids	Benzine-acidic acid
Ibuprofen (Motrin®)	Aspirin	Meclofenamate sodium (Meclomen®)	Piroxicam (Feldene®)	Tolmetin sodium (Tolectin®/DS)	Diclofenac sodium (Voltaren®) (Voltaren® XR)
Naproxen (Naprosyn®)	Diflunisal (Dolobid®)			Indomethacin (Indocin®) (Indocin® SR)	
Fenoprofen calcium (Nalfon®)	Salicylsalicylic acid Disalcid®			Sulindac (Clinoril®)	
Ketoprofen (Orudis®)	Choline magnesium trisalicylate Trilisate®				

ketorolac can reduce opioid requirements, it is not potent enough to be used as a sole analgesic after major surgery such as intraabdominal surgery [131].

Peak analgesia from ketorolac is typically seen 1–2 h after administration, and the half-life is approximately 6 h, although it may be prolonged in patients with reduced renal function or in the elderly. The manufacturer's recommended dose for elderly individuals or those with renal insufficiency is 15 mg every 6 h following a 30 mg loading dose, and doses as low as 7.5 mg q6h have been found to significantly reduce opioid requirements in such painful surgeries as spinal fusion [132].

Ketorolac has a side-effect profile similar to those of other NSAIDs. There appears to be a significantly increased risk of gastrointestinal bleeding in the elderly, particularly with high doses and with the duration of use of more than 5 days [133–135]. But when used in doses of 15 mg or less q6h for less than 3 days, toxicity seems to be minimal. A recent meta-analysis of randomized controlled trials found no increased risk of postoperative bleeding related to ketorolac use, despite fears of platelet inhibition [136].

Recent development of intravenous ibuprofen (Caldolor®) has given practitioners another parenteral tool for multimodal analgesia. Perioperative administration of 800 mg every 6 h in abdominal surgery decreases morphine requirements and pain scores, while being generally well tolerated [137].

Parecoxib is a specific COX-2 inhibitor that is available in Europe for intravenous administration. In a study of parecoxib 40 mg IV administered on induction of general anesthesia, and then q12h for 24 h, improved postoperative analgesia without increased bleeding for total hip arthroplasty was observed. It is well known that COX-2 is responsible for the synthesis of prostaglandins, which sensitizes the nociceptor and acts as excitatory neuromediators in the CNS and in the periphery [125, 138].

In another study, parecoxib was found to be an effective analgesic in acute postoperative pain at 20 or 40 mg over placebo given either intravenously or intramuscularly. The number needed to treat (NNT) for parecoxib 20 mg IV for at least 50% pain relief over 6 h was 3.0 and for 40 mg was 2.2 [139]. This compares favorably with other analgesics, e.g., morphine 10 mg where the NNT was 3, ibuprofen 400 mg where the NNT was 2.7, and acetaminophen 1,000 mg where the NNT was 4.6 [140]. Ibuprofen was actually more effective than morphine at these doses. In direct comparison of 4 mg of intravenous morphine with 30 mg of intravenous ketorolac or 20 mg of intravenous paracoxib, the times to remedication were 3 h for morphine versus 5.5 h for both the ketorolac and paracoxib at the specified doses [141].

Impairment of wound healing has been attributed to the use of NSAIDs in the postoperative period. Studies have shown that there was no effect on epidermal wound healing with selective COX-2 and nonselective COX inhibitors in a mouse model. The authors propose that this was probably due to redundant mechanisms for wound repair, most of which are not influenced by the COX-2 inhibitors [142].

Power indicates in his review article that the data is conflicting with respect to bone healing and nonunion when these agents are used in orthopedic procedures [143]; but much of the adverse data come from animal studies which may not have clinical significance in humans [144, 145]. Short-term use of COX-2-specific inhibitors may play an important role in preventive analgesia for postoperative pain management [138, 146].

It is important to remember that COX-2-specific inhibitors do not affect platelet aggregation [125, 138] and therefore may pose a risk for myocardial infarction (MI) if the patient is taken off aspirin therapy. Since low-dose aspirin is increasingly being used for cardioprotection, it is important to note that coadministration of selective COX-2 inhibitors does not alter this protective effect [147]. It has recently been shown that celecoxib (Celebrex™) does not appear to be associated with an increased risk of serious cardiovascular thromboembolic events and it is the only remaining oral COX-2 inhibitor available in the USA [148]. It could therefore be used as a preoperative medication and continued postoperatively through healing (e.g., $<$10 days) as part of a multimodal preventive analgesic regimen, if the patient is able to take oral medications and does not have an allergy to sulfa-containing medications.

Gabapentinoids

A relatively new nonopioid adjuvant in the treatment of postsurgical pain, gabapentin and pregabalin bind to the alpha-2-delta subunit of neuronal calcium channels and decrease neuronal pain transmission. They have been extensively studied and shown to have opioid-sparing effects in a wide variety of surgical procedures including spine surgery, orthopedics, and hysterectomy [149–151].

Opioid-sparing effects of gabapentin occur after a single preoperative oral dose, and this is thought to be protective against postoperative delirium [152]. 300–400 mg doses are reasonable in the elderly. Larger doses may be used but could cause dose-dependent sedation. Gabapentin exhibits no metabolism and is completely renally excreted. Other side effects include dizziness, visual disturbances, and swelling of lower extremities. The uptake of gabapentin is less predictable than that of pregabalin, which is more potent and bioavailable. Pregabalin causes less sedation.

Ketamine

Ketamine is an N-methyl-D-aspartate (NMDA) receptor blocking agent which exhibits dose-dependent analgesia, amnesia, unconsciousness, and akinesia, while avoiding respiratory depression [203]. Lower concentrations and doses predominately block the closed form of the NMDA channel leading to analgesia rather than anesthesia [204]. Due to the potential for hallucinations, patients with psychiatric or substance abuse (alcohol, amphetamines) comorbidities should not receive ketamine [153]. Despite fears of ketamine's undesired dissociative and dysphoric side effects, more recent research points to the many advantages of perioperative use including effective opioid-sparing postoperative analgesia, attenuation of the acute analgesic tolerance to opioids, and prevention of rebound pain that occurs following opioid usage [203, 204].

Bell et al. retrospectively studied the efficacy and tolerability of ketamine for perioperative control of acute pain in adults and found reduced pain intensity, reduced rescue pain medication requirement, or both perioperatively. Ketamine in the first 24 h after surgery reduced morphine requirements and decreased incidences of postoperative nausea and vomiting [154]. Though many forms exist, the most common perioperative analgesic dosing ranges from 0.2 to 0.5 mg/kg IV and 0.5 to 1.0 mg/kg IM in adults, with continuous IV infusions usually starting at 0.1–0.2 mg/kg/h [155, 156]. As with most analgesics in elderly populations, it is recommended to decrease this by 10–30% with careful consideration given to administering in the cognitively impaired. An antisialogogue may be required with infusions.

Glucocorticoids

Glucocorticoids given both preoperatively or postoperatively have been shown to reduce postoperative nausea and vomiting and to decrease pain [157, 158]. A single dose of glucocorticoid steroid can reduce pain following ambulatory surgery without increasing postoperative bleeding risk in the elderly [159]. Less than 8 mg of dexamethasone or 150 mg of methyprenisolone intravenously seems to be adequate.

α2-Agonists

Preoperative oral administration of clonidine, an α2-agonist, reduces pain and postoperative analgesic requirement, provides sedation, and facilitates emergence from anesthesia [160]. Analgesia from intrathecally administered morphine was enhanced by oral clonidine premedication after total abdominal hysterectomy [161].

Antidepressants

Antidepressants that have been used in pain management are listed below (Table 3) along with starting doses and tolerability [162]. In summary,

Table 3 Antidepressants in clinical practice. Tricyclic antidepressants: The dosages are low (adjusted for the elderly patient). The antidepressants that are effective in pain management are those that have both serotonin and norepinephrine reuptake inhibition effects. The tricyclic antidepressants all have these effects but their side effect profiles determine the tolerability of these drugs particularly by elderly patients, e.g., anticholinergic effects, sedation. The non-tricyclic antidepressants that are effective in pain management tend to be less sedating and have a faster onset of effect with respect to decreasing neuropathic pain after initiation of therapy than the tricyclic antidepressants that can require several weeks of treatment to become effective

Tricyclics	Anticholinergic effects (sedation)	Dose range	Tolerability
Amitriptyline (Elavil®)	Least effect	10–25 mg qhs	
Desipramine (Norpramin®)	Least effect	10–25 mg qhs	Best
Doxipin (Sinequan®)	Most effect		Most sedating
Imipramine (Tofranil®)	Intermediate	10–25 mg/day	Best
Nortriptyline (Pamelor®)	Intermediate	10–25 mg/day	Best
Non-tricyclics			
Venlafaxine (Effexor®)		≥150 mg/day	
Duloxetine (Cymbalta®)		30–120 mg/day	Best
Bupropion (Wellbutrin®SR)		150–300 mg/day	
Trazadone (Deseryl®)	Sleep aid in women	50–300 mg/day	Risk of priapism in men

amitriptyline is probably the most studied in pain management and its efficacy is well established. Of the newest antidepressants that have been studied in pain management, duloxetine (a non-Tricyclic) is well tolerated with a fast onset of effect after the initiation of treatment [162].

Regional Analgesic Techniques

Many regional techniques exist to provide perioperative anesthesia and analgesia ranging from neuraxial administration (epidural, intrathecal) of medications to peripheral perineural deposition and combinations of both. Indwelling catheters may additionally be placed to prolong analgesic effect with sustained administration of medications perineurally or into the epidural space. When studied versus conventional parenteral administration of analgesics, regional techniques are clearly superior for postoperative pain relief, particularly dynamic pain relief [163]. However, lack of consistency within regional anesthesia studies and protocols remains an important factor that has limited the ability to portray firm indications, guidelines, and recommendations about any advantageous or optimal technique in the geriatric population [164]. When compared to general anesthesia regional techniques have failed to show significant long-term variation in morbidity and mortality, except reduced incidence of deep vein thrombosis and reduced blood loss when regional is utilized [165].

As part of a multimodal anesthetic/analgesic however, regional techniques provide excellent pain relief as well as opioid-sparing capacity which shortens care stays, allows for earlier ambulation and return of bowel function, and improves mental status post-op [86]. Compared to parenteral analgesia, better outcomes have been consistently shown using epidural and peripheral nerve blockade in rehabilitation after major surgery in the elderly, though these same studies often note increased complication rates as well with use of epidurals [68].

While regional is no panacea, when instituted as part of a multimodal technique in appropriate patients, the reduced postoperative neurological, pulmonary, cardiac, and endocrine complications may outweigh the potential downsides.

Neuraxial Analgesia

The epidural route of administration for opioid, local anesthetic, or a combination provides superior analgesia for dynamic or rest pain in comparison with systemic opioids [166] and may be used for continuous infusion with or without patient-controlled epidural analgesia (PCEA). Most of the benefits of epidural analgesia stem from the opioid-sparing effects of the local anesthetic and the abolition of the surgical stress response in the spinal cord. Benefits to bowel motility are limited to epidurals placed at the thoracic level, and local anesthetics alone alter bowel motility and stress responses; epidural opioids do not [167].

Carli et al. in a study of 64 patients for elective colon surgery randomized to an IV PCA group or epidural group found that epidural analgesia enhanced functional exercise capacity and health-related quality of life indicators after colonic surgery [168]. The results indicated that the epidural group had improved outcomes for pain control, mobilization, gastrointestinal motility, and intake of protein and calories. This may be a function more of the local anesthetic, facilitating bowel function, thereby causing less nausea, and more willingness to eat. Decreased pain can also result in the same benefits, not just at rest but also with mobility, and less pain may ameliorate insulin sensitivity and hypercatabolism and maintain muscle protein better. These benefits seemed to carry out to 6 weeks in the study of health-related quality of life indicators, leaving little doubt that epidural analgesia is even better than systemic opioids in the elderly [168].

Neuraxial opioid injections can play a role in multimodal pain management, particularly in abdominal, pelvic, and thoracic surgery. Intrathecal morphine ensures good postoperative analgesia for several hours and reduces the rescue dose of intravenous opioids [169]. A smaller dose of intrathecal morphine may minimize the incidence of adverse events in the elderly, though dose-related urinary retention, hypotension, and respiratory depression still occur [69]. Doses of 100 micrograms were reported to provide optimal balance between analgesia and adverse effects [170], while 50 μg still afforded good results in the extremely elderly [171].

Due to the stenotic spine with smaller intervertebral foramina for medication to escape through, the elderly are at increased risk for respiratory depression with neuraxial opioids. A single intrathecal dose of hydrophilic opioid (morphine) remains in the CSF longer, is absorbed systemically slower, and travels more rostrally to brainstem respiratory centers [172]. Hydrophobic opioids (fentanyl, hydromorphone) may be more preferable as they will exhibit less rostral spread. Fentanyl tends to be sequestered in the fat tissue of the epidural space and absorbed rapidly by epidural vascular structures, reaching systemic plasma levels within 2 h of commencing an epidural infusion that would equal the same infusion rate given intravenously [173, 174]. Care must therefore be taken with fentanyl during the initial phases of the infusion, whereas the respiratory depressive effects of morphine or hydromorphone tend to be more delayed if they are to occur. As with IV dosing, a reduction of 25–50% of any neuraxial opioid in the elderly is wise.

Pruritis is a common side effect of morphine administered either parenterally (intravenous or intramuscular) or spinally (intrathecal or epidural) [175]. However, the mechanisms and therefore effective treatments are different. Parenteral morphine results in histamine release in a dose-dependent manner and can be treated with antihistamines such as promethazine or dyhenhydramine. Epidural or intrathecal morphine also produces pruritis through a central stimulating effect mediated through the mu opioid receptor. It is treated most effectively not with antihistamines but with a naloxone infusion at a low enough dose to ameliorate the pruritis without reversing the analgesic effect [175].

Combination of low-dose opioid and local anesthetic limits the toxic effects of each drug. Various combinations of opioid and local anesthetic can be used to meet the needs of individual patients. Today ropivacaine/hydromorphone 0.2%/0.02 mg/ml has become very popular as an epidural infusion. Local anesthetic side effects include orthostatic hypotension, numbness/weakness, and urinary retention. Opioid side effects include sedation, urinary retention, and pruritis [176].

The local anesthetic/opioid ratio is adjusted based on the type and severity of side effects that develop. Complications of epidural infusions include accidental subarachnoid puncture with postdural puncture headache (generally benign and self-limiting), epidural hematoma, and epidural abscess. Side effects and complications are minimal if the catheters are inserted and monitored by those experienced with the technique [77].

When compared to continuous epidural infusions, self-adjustment provided by PCEA allows for a reduction in analgesic consumption and a decrease in adverse events [177]. PCEA reduces analgesic requirements compared with continuous epidural infusion after major abdominal surgery [178]. No standard protocol has been validated specifically in the elderly. Several studies advocate a combination of local anesthetic with an opioid as background infusion from 3 to 6 ml/h, a bolus of 2–3 ml, and a lockout period from 15 to 20 min [179, 180].

Concomitant use of the epidural and parenteral routes is not recommended because (1) it makes titration of drugs overly complicated and (2) it becomes difficult to determine the origin of side effects if they develop. Generally, it is not advisable to maintain an epidural catheter for more than 8 days even if the site of insertion is without evidence of inflammation or infection. The source of epidural infection from continuous catheters is not well known, but skin flora is considered the primary source [181]. If the epidural route is still needed, the catheter can be replaced with a new one at the segmental level above or below the insertion of the old catheter.

An additional benefit of spinal anesthesia has been suggested, although not yet proven. The perioperative period is characterized by a state of immunosuppression, which was shown in animal studies to underlie the promotion of tumor metastasis by surgery [182]. Bar-Yosef and his associates demonstrated that spinal anesthesia when added to general anesthesia reduced tumor recurrence in an animal model. They propone that as the immunosuppression of surgery is partly ascribed to the neuroendocrine stress response, it is hypothesized that spinal blockade, known to attenuate this response, may reduce the tumor-promoting effect of surgery. They therefore conclude that the addition of spinal block in their model had an advantage over the use of general anesthesia alone, and they suggest that it acts by reducing the neuroendocrine response to surgery [182].

These authors further state that since in clinical practice, an epidural block can be carried over into the postoperative period, it is reasonable to assume, but certainly proof is needed, that the favorable effect of prolonged epidural block on immune function and tumor metastasis will exceed the effect they found using short-term spinal block. This study provides the first experimental evidence that neuraxial anesthesia may reduce postoperative metastatic development [182]. Controlled clinical studies are necessary to confirm this result in humans. We believe it is important to note that regional anesthetic and analgesic techniques have benefits that go beyond just pain control in order to encourage surgeons and primary care physicians to request such techniques where appropriate from the anesthesiologists.

Peripheral Perineural Analgesia

While epidural analgesia has been the gold standard for postsurgical analgesia for many years, the disadvantages as noted have spurred interest and utilization of peripheral nerve blocks, both single-shot and continuous (CPNBs) peripheral catheter techniques. Infiltration of local anesthetic around a peripheral nerve or plexus, proximal to the desired site of action allows for several hours of analgesia with the option of threading a catheter for continued blockade utilizing electronic infusion or disposable elastomeric devices. These blocks allow for unilateral analgesia, facilitating movement, and rehabilitation without the necessity of a Foley catheter, which can be a cause of delirium post-op. In addition, patients can safely be sent home with continuous elastomeric catheters, pulling the catheters out themselves when the disposable pumps are empty [183].

With the interscalene technique, blockade of the shoulder is possible. The upper extremities below the shoulder are easily blocked with supraclavicular or infraclavicular techniques. And the lower extremities including the hips can be blocked with a combination of sciatic with lumbar plexus or the so-called 3-in-1 femoral block. The transversus abdominis plane (TAP) block procedure is increasingly used after major abdominal surgery in the abdomen. It is easy to provide and has few complications and greater acceptability [184]. The rectus sheath block can be used for abdominal surgery with mid-line incisions above the umbilicus [185]. Thoracic surgery is amenable to paravertebral blockade. The use of ultrasound needle guidance in addition to nerve stimulation techniques has made these procedures more accurate and less risky [186]. The aim will always be to provide good analgesia without significant motor blockade.

Of significance is that in a recent report woman undergoing mastectomy for tumor removal had one-fourth the risk of metastatic recurrence when surgery was performed with a continuous paravertebral catheter [187]. The catheter was placed at T2-3 through which a bolus of local anesthetic was given followed by a continuous infusion of local anesthetic. These patients also received general anesthesia with intravenous propofol. This group of patients was compared with a group that received general anesthesia alone [188]. The paravertebral catheters were removed after 2 days.

Compared to general anesthesia-neuraxial anesthesia, peripheral nerve blocks reduce pain, opioid consumption, PONV incidence, and PACU stay and provide "fast-track" recovery with increased patient satisfaction, particularly after CPNBs [189]. After a peripheral plexus block, the elderly exhibit increased sensory and motor blockade which is significantly correlated with age [69]. Peripheral blocks are associated with minimal hemodynamic effects compared to neuraxial local anesthetic administration. CPNBs are utilized extensively in orthopedic surgery, allowing for prolonged analgesia, quicker mobilization, and rehabilitation in relative comfort [69, 190]. They reduce economic impact by decreasing parenteral analgesic need and the associated postoperative morbidity therein [191].

CPNBs are not without fault however. In a national survey, the incidence of catheter dislocation was 4.7% [192], which was an even greater problem if the patient was given no parenteral analgesics as backup. In a large prospective study, 4% of patients receiving CPNBs could not move their arm or hand for 16 h after surgery [193], and a 0.7% chance of falling following total knee arthroplastly with a femoral CPNB was reported by Feibel et al. [194].

Perineural blockade techniques are generally low risk in older patients, though may be more technically challenging in some situations. The elderly lose muscle mass and have poor tissue echogenicity under ultrasound, and obesity in older adults is prevalent causing difficulty in utilizing surface landmarks and nerve stimulator techniques. Patients with acute trauma such as hip fractures may be difficult to position for blocks, and the risk-benefit ratio of giving parenteral sedation/analgesia to facilitate positioning must be assessed. In these situations, utilizing ultrasound to obtain a femoral nerve block with fast-acting mepivacaine or lidocaine+bicarbonate while the patient is supine and relatively comfortable may facilitate positioning for lateral neuraxial administration of a spinal anesthetic.

Older adults with cognitive dysfunction require special consideration if they are to be discharged home with blocks and indwelling catheters. Caregiver and familiar education is important. They must be ready to supervise the patient so that the catheter does not get pulled out prematurely. Leaking catheters may agitate or cause skin breakdown at the catheter site, while motor blockade of the lower extremity can lead to falls. Should the catheter migrate or be removed unexpectedly, oral analgesics and emergency contact numbers should be provided.

Special mention is required for local anesthetic toxicity in the elderly, who have lower serum protein levels leading to higher local anesthetic concentrations in the plasma. Cardiac, hepatic, and renal end-organ disease should be documented and considered as these will decrease the ability to metabolize the medication and decrease the toxic threshold. When multiple catheters and blocks are utilized, the total volumes of anesthetic should be noted and subsequent infusion doses reduced accordingly. Ropivacaine seems most appropriate for long-term infusion, as it causes less cardiac and CNS toxicity than bupivacaine.

Unfortunately, unlike epidural analgesia which can in fact provide complete analgesia without the need for supplemental intravenous or oral opioid analgesia (since opioids are administered spinally), peripheral nerve blockade cannot be used to completely eliminate the need for supplement opioid analgesics. Patients should be discharged home with some form of oral analgesic should complications with the catheter arise.

Nonpharmacologic Therapies

It is advantageous to utilize all nonpharmacologic therapies as they have little to no side-effect profile and are often cost-saving. Transcutaneous electrical stimulation (TENS) and transcutaneous acupoint electrical stimulation (TAES) produce opioid-sparing effects [195]. Psychological techniques include guided imagery, cognitive-behavioral techniques, and mindfulness training. Reynolds [196] found that patients who believed such nonpharmacological treatments could be effective benefited from their use for managing pain.

Cold application decreases skin and joint temperature, decreases blood flow, and has a direct analgesic effect. Distraction (music, television, reading) is beneficial in the cognitively dysfunctional and intact alike. Deep breathing exercises can be discussed and utilized perioperatively. These techniques require no formal training to implement.

Transitioning to Outpatient Care

Once pain is controlled and bowel function restored, analgesics should be changed to the oral route. This conversion should be made prior to discharge, and it is recommended that at least 24 h of observation be allowed so that an adequate oral regimen can be established and tested prior to discharge. Depending on individual variability and the type of surgery, this transition should occur 3–8 days after the surgery. Standardized equianalgesic dose tables are available to aid conversion, but they present average data based on single-dose studies of the drugs in opioid naive patients. There may be individual differences in patient absorption, metabolism and response, and as such tables should be used for guidance only [197]. A good rule of thumb is starting at a lower than equianalgesic dose in the first instance and titrated upwards as required [198].

Occasionally patients require parenteral or epidural opioids for a more prolonged period, usually because of intervening complications. Typically, patients require oral opioids for 5–10 days after parenteral or epidural opioids are discontinued. A certain percentage of patients, especially after more painful surgeries, require oral opioids for 2 weeks or longer [77].

For example, for conversion from intravenous or oral morphine to a fentanyl transdermal patch, one only needs to remember that 60 mg/day of intravenous morphine or 180 mg/day of oral morphine will equal a 100 mg/h transdermal fentanyl patch. As with all sustained-release opioids, this is for continuous pain that is opioid responsive. One still needs to consider breakthrough pain medications, fast onset, and short duration, for activity-based pain. Since hydromorphone is about 4–5 times as potent as morphine, a similar conversion can be made from intravenous hydromorphone of 15 mg/day to a 100 mg/h transdermal fentanyl patch. Once patients have been receiving intravenous opioid medication for several days, the equianalgesic relationship between intravenous and oral doses changes from 1–6 (IV to oral) to closer to 1–3.

Oral analgesics such as oxycodone or codeine are appropriate choices for a patient with mild-to-moderate pain [199]. Fixed combinations with nonopioid analgesics can be useful, but they sometimes limit the careful individualized titration that is the basis of therapeutic success. The oral transmucosal route may prove effective for rescue doses, but absorption is probably inadequate for more sustained relief. This latter statement also holds for the rectal route, which, additionally, is often uncomfortable for the patient and the caregiver.

One example of the difficulty with combination medications is conversion from intravenous PCA to oral. As seen in Table 4, the oral

Table 4 Equianalgesic doses of common intravenous and oral opioids. Notice that the oral equivalent for 10 mg of intravenous morphine is 30 mg of oral hydrocodone. But when hydrocodone is combined with acetaminophen, the ratio is such that a toxic dose of acetaminophen would be taken with the hydrocodone. It is better to convert to a pure opioid agonist until such time that a reasonable dose of a combination medication can be given safely as shown in Table 2

Drug	IV (mg)	Oral (mg)
Morphine	10 mg	30 mg
Hydromorphone (Dilaudid®)	1.5 mg	7.5 mg
Methadone[a]	10 mg	12 mg
Fentanyl	0.1 mg (100 ug)	N/A[b]
Meperidine (Demerol®)	100 mg	300 mg
Codeine	N/A	200 mg
Oxycodone (Percodan®) (Percocet®)	N/A	20 mg
Hydrocodone (Vicodin®) (Lorcet®)	N/A	30 mg (5 mg/tab Vicodin® with 500 mg acetaminophen)

[a]Not recommended for acute titration; ratio depends on presence of prior opioid tolerance
[b]Oral transmucosal fentanyl is available in 200 μg, 400 μg, 800 μg, 1600 μg doses, and the transmucosal absorption depends on the duration of contact with the mucosa but will maximize at about 25% of the total dose with the remainder being swallowed and subject to a small degree of gastric absorption. An effervescent lozenge is also available in similar doses with a reported absorption of about 50%

equivalent of hydrocodone to 10 mg of intravenous morphine is 30 mg. The usual combination of hydrocodone with acetaminophen is 5 and 325 mg, respectively. Therefore, six tablets of this combination drug would be necessary to equal 10 mg of intravenous morphine.

Special Considerations

Some surgical procedures are associated with a higher risk of postoperative pain syndromes such as phantom limb pain syndrome after amputation. Regional anesthetic techniques offer the greatest protection; however, some patients either decline to have a regional blockade or the blocks are contraindicated for various reasons, and general anesthesia must be administered. General anesthetics alone do not protect the spinal cord from undergoing central sensitization leading to chronic neuropathic pain [200, 201]. But a polypharmaceutical approach, although not proven yet, seems to offer an advantage over traditional anesthetic and postoperative management techniques.

The following recommendations for the example of phantom limb pain prevention with amputation surgery are based on the author's experience, supported by the available evidenced-based medicine, which although limited in this regard, aims to target polypharmacy in such a way to help the brain modulate neuropathic pain [202]. The recommendations given below for this presented scenario of an amputation without the benefit of regional anesthesia is similar to the multimodal polypharmaceutical therapeutic recommendations of power, in which he reviews the uses of both opioid and nonopioid analgesics, anticonvulsants, and antidepressants in postoperative pain management [143].

As indicated above, in these authors' experience, agents that have NMDA receptor blocking action like ketamine [203, 204], drugs with Mu opioid agonist action, tetrodotoxin resistance (TTXr) sodium channel blockers such as the local anesthetics, serotonin and norepinephrine reuptake inhibitors such as antidepressants [205–207], neuronal calcium channel blockers such as the anticonvulsants gabapentin or pregabalin [208–213], and anti-inflammatory drugs if not contraindicated (see above) can all contribute to CNS protection. In such a case, preoperative oral gabapentin (Neurontin®) 300–1,200 mg [72, 79, 208–215] or pregabalin (Lyrica®) 75–150 mg, and if available a COX-2 inhibitor celecoxib (Celebrex®) 200 mg, can also be given orally which would alleviate the need for intraoperative ketorolac. It is true that COX-2 inhibitors are controversial with respect to patients at risk for stroke or myocardial infarction which makes up a large percentage of the elderly population. But there does not seem to be evidence that a single preoperative dose of 200 mg of celecoxib would pose a significant risk versus the benefit of preemptive analgesia [216].

Low subanesthetic doses of ketamine (0.10–0.2 mg/kg IV intraoperative preincision) can be used for as part of the intravenous induction, and repeat doses q2h intraoperative can provide additional inhibition of activation of spinal cord NMDA receptors. As previously stated, if the patient is unable to take a COX-2 inhibitor (celecoxib), then ketorolac 7.5–15 mg should be given prior to amputation intraoperatively and continued q6h intravenously for 48 h. Lidocaine 1.5 mg/kg IV at the time of skin incision and repeated during the amputation as a general sodium channel blocker can all be helpful.

Intraoperatively, the anesthesiologist (again in these authors' experience) can administer several adjuvants that will also assist in protecting the spinal cord from excessive nociceptive input. Methadone would be a good choice for an opioid because of its NMDA receptor antagonist effect, but it is often unavailable and its slow onset of action is not suitable for intraoperative administration. Fentanyl would therefore be a logical choice since it is potent and more easily titrated due to its rapid onset of action when administered intravenously.

Although the data are not conclusive, there is data to show that magnesium amplifies the analgesic effects of low-dose morphine in conditions of sustained pain [217]. Lysakowski et al., in a meta-analysis study of magnesium, concluded that the trials reviewed did not provide "convincing" evidence that perioperative magnesium has a favorable effect on postoperative pain intensity and analgesic requirements. Nevertheless, it may be worthwhile to further study the role of magnesium as a supplement to postoperative analgesia, since this molecule is inexpensive, relatively harmless, and the biological basis for its potential antinociceptive effect is promising [218]. There is a possibility that magnesium might have an additive or even synergistic effect with other NMDA antagonists, specifically ketamine although the optimum dose is not established [219, 220].

Considering the good tolerability of magnesium, these findings may have clinical application in neuropathic and persistent pain. Again the appropriate dose of magnesium is not known, but 30 mg/kg IV intraoperative administered prior to skin incision seems to be safe even in the elderly population. In combination with low-dose gabapentin, significant improvement in the effectiveness of morphine is observed in a rat model of nerve ligation neuropathic pain [214]. Referring to the above-stated preoperative dosing of gabapentin, the two should enhance the protective analgesic effect of the opioid used.

Postoperatively, the antineuropathic regimen should be continued until the wound (stump) has healed in terms of continued gabapentin or pregabalin (100–300 mg tid or 50 mg tid, respectively) along with an appropriate opioid, anti-inflammatory, and antidepressant (for serotonin and norepinephrine reuptake inhibition action).

The Elderly Chronic Pain Patient

Initial opioid doses are much higher for patients on chronic opioid therapy. For these patients, the presurgical opioid dose must be converted to a continuous infusion, and the as-needed PCA dose should be set equal to the hourly infusion dose. When converting oral opioids to parenteral opioids refer to an opioid conversion chart (Table 3). A patient receiving 180 mg of oral morphine every 24 h prior to surgery, for example, should be started postoperatively on 60 mg of morphine intravenously in 24 h (2.5 mg/h) and a PCA dose of 2.5 mg every 15 min. If the pain is severe, the continuous infusion rate should be increased. Patients on chronic opioid therapy have almost always developed tolerance to the respiratory suppressant and cognitive side effects of opioids, and so it is rare for these patients to develop these symptoms, even after receiving doses substantially higher than their baseline [77].

Oxycodone is not available for intravenous administration and so the oral dose must be converted to a morphine or hydromorphone equivalent to convert to an intravenous dose. Since oxycodone is about 1.5 times more potent than morphine, 120 mg/day of oxycodone (extended-release oxycodone) would be equivalent to 180 mg/day of oral morphine or 60 mg/day of intravenous morphine [77]. This equivalency can then be used to set up a PCA of morphine or hydromorphone (15 mg/day hydromorphone = 60 mg/day morphine).

Addiction, Dependence, Tolerance, Pseudoaddiction

The fear of addiction or psychological dependence is one of the major barriers to the appropriate management of pain in the USA. Psychological dependence is the development of drug-seeking behavior that persists despite harm to the patient or others. Such drug-seeking behavior includes the hoarding of medication, use of medication for purposes other than control of pain, and obtaining opioids from multiple sources. It is important to distinguish true psychological dependence from "pseudoaddiction" [221], which can develop in patients who are undermedicated for their level of pain. Pseudoaddiction is drug-seeking behavior motivated by a need to obtain enough analgesia to control pain. When pain is appropriately managed and adequate analgesia provided, the behavior disappears. Although further research is needed, it appears that the incidence of psychological addiction in patients without a history of substance abuse and treated with opioids for control of pain is rare [75]. Fear of addiction should never limit the use of opioids for pain control in the elderly patient who has no history of substance abuse [77].

Conclusion

As aptly stated by Morrison, Carney, and Manfredi, in the first edition of this book, "good pain management in the elderly surgical patient is a complex, challenging undertaking of critical importance. Ensuring adequate analgesia requires an understanding of age-related changes in pharmacokinetics and pharmacodynamics, pain physiology, the appropriate use of analgesic agents, and knowledge of these agents' limitations and side effects. Unfortunately, few studies have focused on the assessment and treatment of pain in elderly individuals, and guidelines for analgesic therapy are often based on the experiences of young and middle-aged adults. Further research involving pain in the elderly is critically needed given the evolving changes in population demographics (persons over 65 represent the most rapidly growing segment of the US population) and the increasing rates of surgery in this population. Until such research is completed, clinicians must continue to interpret the available data in the

Table 5 Choosing the best option for postoperative pain control in the elderly. Continuous epidural or peripheral nerve block techniques offer the best control of postoperative pain in the elderly patient; however, if not appropriate or contraindicated, then intravenous administration must be utilized. Transition to oral medications must be adequate to control pain prior to discharge. When intravenous access is not available and the oral route cannot be used, the subcutaneous route is better than the intramuscular route. When the subcutaneous route is used, the absorption is less erratic with hydromorphone (more lipid-soluble) than with morphine. For intermittent dosing, it is best to use an insulin syringe. For continuous infusion, a 27-gauge butterfly needle can be used. Postoperative orders for pain medication should be standing rather than PRN. The remarks "hold for excessive sedation" and "patient may refuse" add a safety valve to the order. PCA, patient-controlled analgesia. Modified from Morrison et al. [77]

Cognitively intact	Cognitively impaired
More painful procedures (e.g., thoracotomy, complex abdominal/pelvic surgery)	
Epidural: lipophilic opioid (e.g., fentanyl) plus local anesthetic as a continuous infusion with or without epidural PCA *or*	*Epidural:* opioid plus local anesthetic as a continuous infusion without PCA *or*
Intravenous: strong opioid as an intravenous infusion with intravenous PCA	*Intravenous:* strong opioid as a continuous infusion without PCA, or nurse administered "PCA" without a basal rate based on patient assessment
Less painful procedures (e.g., lower abdominal surgery, hip/knee replacement)	
Intravenous: strong opioid via PCA or given intravenously every 4–6 h	*Epidural:* opioid plus local Anesthetic as a continuous infusion without PCA *or*
	Intravenous: strong opioid as a continuous infusion without PCA
If appropriate for the surgery, continuous peripheral nerve blocks with supplemental oral medications	If appropriate for the surgery, continuous peripheral nerve blocks with supplemental oral medications

context of their knowledge of age-related physiologic changes, medication effects, side effect profiles, and clinical experience. This approach is summarized in Table 5 and results in appropriate pain management for most elderly surgical patients" [41]. The increased use of regional and peripheral nerve block techniques holds much promise for acute postsurgical pain management in the elderly population, as does our increasing knowledge of the pathophysiological mechanisms of pain translating into advances in the polypharmaceutical multimodal approach to pain management.

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Postoperative Delirium

22

Michelle Humeidan and Stacie G. Deiner

Contents

Abstract

Postoperative delirium (PD) is one of the most common complications in geriatric patients after surgery and is linked to significantly increased morbidity and mortality in affected patients. An acute change in consciousness along with inattention and disorganized thinking are key characteristics of PD, which typically occurs in the first 24 to 72 h after surgery. This chapter provides a detailed discussion of modifiable and non-modifiable risk factors for PD in the preoperative, intraoperative, and postoperative phases of care. Being able to risk stratify geriatric surgical patients and quickly recognize symptoms of PD is important for prevention and timely intervention. A brief discussion of PD pathophysiology is presented; however, much more research is needed to better understand the mechanisms

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and modulators of PD. A review of the current best practice guidelines from the American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults is provided highlighting several pharmacologic and nonpharmacologic interventions for the treatment of PD.

Keywords
Postoperative delirium · Postoperative complications · Geriatric · Confusion assessment method

Introduction

A significant increase in health-care consumers over the age of 65 years and the associated rise in demand for surgical procedures [1] highlight the importance of understanding postoperative complications in elderly patients. Postoperative delirium (PD) is common after major surgery in the elderly and presents in the first 1–3 recovery days. PD manifests with a dynamic change in consciousness with key features of attention deficit and disorganized thoughts. As many as 65% of patients undergoing high-risk procedures such as hip fracture repair and cardiothoracic surgeries experience PD. Even low-risk surgeries such as elective outpatient procedures have an incidence of PD of 4–7% [2, 3]. PD can have serious consequences, including increased mortality. Billions of healthcare dollars are spent annually on the costs of PD, including increased postoperative morbidity and loss of function and independence [4–7]. This chapter will provide a fundamental overview of patient and procedural risk factors for PD, only some of which are modifiable, and will discuss the most widely utilized and accessible diagnostic tool, the Confusion Assessment Method (CAM). In addition, pathophysiology and important considerations for differential diagnosis of PD are discussed. The American Geriatrics Society (AGS) has published specific guidelines on the management of patients at high risk for PD, which form the basis of the current best practices for perioperative optimization and treatment strategies presented in this chapter [8].

Risk Factors for Postoperative Delirium

Risk factors associated with the development of PD can be categorized as preoperative, intraoperative, or postoperative. Pre-existing factors are inherent to the patient or situation, in contrast to risk factors that develop during the perioperative period (i.e., triggering risk factors). Additionally, risk factors may be considered amenable to optimization or nonmodifiable.

Preoperative Factors

Aging patients with neurobiological dysfunction at baseline are at increased risk for PD. Patients with systemic illness, reflected by higher American Society of Anesthesiologists (ASA) physical status scores and poor functional status, are also high risk for development of PD. Preoperative risk factors for PD can be recognized broadly as decreased cognitive reserve, burden of physiological and cognitive-behavioral comorbidities, and substance exposure and abuse (Table 1).

As older patients undergo a wide variety of surgeries, the risk of PD appears to go up starting at approximately 60 years [9–17]. Insult to the physiology and function of the central nervous system is associated with PD. Cerebrovascular disease [17–19], history of dementia [20] or delirium [21], subjective reporting of memory complaints [22] or objective performance below a standard reference score on cognitive tests [13, 20, 21, 23–26] are all surrogates for decreased

Table 1 Preoperative risk factors for postoperative delirium

Risk factor	Study	Population
Advanced age	Katznelson et al. [9]	Cardiac surgery patients
	Krzych et al. [10]	Cardiac surgery patients
	Norkiene et al. [11]	Cardiac surgery patients (CABG)
	Gao et al. [12]	Spinal surgery patients
	Böhner et al. [13]	Vascular surgery patients
	Fineberg et al. [14]	Spinal surgery patients (lumbar)
	Ushida et al. [15]	Spinal surgery patients (cervical)
	Miyazaki et al. [16]	Cardiac surgery (CABG)
	Smulter et al. [17]	Cardiac surgery
History of stroke, TIA, or dementia	Shah et al. [20]	Major head and neck cancer surgery
Subjective reporting of memory complaints	Veliz-Reissmüller et al. [22]	Cardiac surgery (elective)
MMSE score	Kazmierski et al. [18]	Cardiac surgery
	Rudolph et al. [26]	Cardiac surgery
	Saczynski et al. [106]	Cardiac surgery
	Osse et al. [59]	Cardiac surgery
	Veliz-Reissmüller et al. [22]	Elective cardiac surgery
	Schoen et al. [27]	Cardiac surgery
Cognitive impairment per IQCODE-SF	Juliebø et al. [23]	Hip fracture repair surgery
Pre-existing cognitive impairment	Litaker et al. [21]	Major elective surgery
	Kazmierski et al. [18]	Cardiac surgery patients
	Shah et al. [20]	Major head and neck cancer surgery
	Freter et al. [24]	Orthopedic surgery (elective)
	Greene et al. [25]	Major, elective noncardiac surgery
	Böhner et al. [13]	Vascular surgery
History of delirium	Litaker et al. [21]	Major elective surgery
Poor sleep/sleep disruption	Leung et al. [96]	Major noncardiac surgery
Pre-existing diabetes	Kazmierski et al. [18]	Cardiac surgery
	Smulter et al. [17]	Cardiac surgery
Peripheral artery disease	Kazmierski et al. [18]	Cardiac surgery
	Otomo et al. [29]	Cardiac surgery (CABG)
Cerebrovascular disease	Kazmierski et al. [18]	Cardiac surgery
	Loponen et al. [19]	Cardiac surgery (CABG)
Atrial fibrillation	Bucerius et al. [30]	Cardiac surgery
	Miyazaki et al. [16]	Cardiac surgery (CABG)
Heart failure	Loponen et al. [19]	Cardiac surgery (CABG)
	Katznelson et al. [9]	Cardiac surgery
Obstructive sleep apnea	Flink et al. [31]	Knee replacement surgery
Renal failure	Sasajima et al. [32]	Arteriosclerosis obliterans with lower limb ischemia patients undergoing bypass surgery
Carotid stenosis of 50% or greater	Miyazaki et al. [16]	Cardiac surgery patients
Atherosclerosis in the ascending aorta	Otomo et al. [29]	Cardiac surgery patients

(continued)

Table 1 (continued)

Risk factor	Study	Population
Increased number of medical comorbidities, often measured by the Charlson Comorbidity Index (CCI)	Robinson et al. [33]	Noncardiac, nonneurological major surgery requiring postop ICU
	Guenther et al. [34]	Cardiac surgery
	Tan et al. [35]	Cardiac surgery
	Pol et al. [36]	Vascular surgery
	Lee et al. [37]	Hip fracture repair
Higher preoperative pain scores	Smulter et al. [17]	Cardiac surgery
	Tan et al. [35]	Cardiac surgery
	Behrends et al. [52]	Noncardiac major surgery
Lower regional oxygen saturation levels in the brain	Schoen et al. [27]	Cardiac surgery
	Morimoto et al. [28]	Abdominal surgery
Depression (presenting with ongoing depressive episode)	Kazmierski et al. [18]	Cardiac surgery
Depression (presenting with depressive symptoms)	Böhner et al. [13]	Vascular surgery
	Leung et al. [47]	Noncardiac elective surgery
History of depression	Stransky et al. [48]	Cardiac surgery
Alcohol use	Litaker et al. [21]	Major elective surgery
	Shah et al. [20]	Major head and neck cancer surgery
	Patti et al. [50]	Colorectal surgery for carcinoma
Drug abuse	Fineberg et al. [14]	Spine surgery (lumbar)
Smoking history	Benoit et al. [51]	Abdominal aortic aneurysm repair surgery
	Miyazaki et al. [16]	Cardiac surgery (CABG)
Decreased functional capacity/preoperative frailty	Juliebø et al. [23]	Hip fracture repair surgery
	Pol et al. [36]	Vascular surgery
	Brown et al. [39]	Cardiac surgery patients
Increased ADL dependence/reduction in ADLs	Leung et al. [40]	Noncardiac surgery
	Hattori et al. [41]	Vascular, orthopedic, and GI surgery
Poor preoperative nutritional status	Ganai et al. [42]	Abdominal surgery
	Tei et al. [43]	Colorectal cancer surgery
Dehydration	Harasawa and Mizuno [44]	Cerebrovascular surgery
Fluid fasting	Radtke et al. [45]	Surgery
Low BMI	Lee et al. [37]	Hip fracture repair surgery
	Juliebø et al. [23]	Hip fracture repair surgery
Benzodiazepine use	Do et al. [49]	Orthopedic surgery
Psychoactive medications	Benoit et al. [51]	Abdominal aortic aneurysm repair surgery
Polypharmacy	Goldenberg et al. [57]	Hip fracture repair surgery
	McAlpine et al. [58]	Gynecologic malignancy surgery

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cognitive reserve. Low baseline regional oxygen saturation level in the brain is also a risk factor for PD [27, 28]. Amount and severity of systemic disease likewise correlates with development of PD. Diabetes [17, 18], peripheral artery disease (PAD) [18, 29], cardiovascular disease (atrial fibrillation [16, 30], heart failure [9, 19]), obstructive sleep apnea [31], and renal failure [32] have all been linked to risk for PD. Similar to the ASA physical status score used preoperatively, the Charlson Comorbidity Index (CCI) is more broadly utilized to quantify the comorbidity load a patient carries. Higher CCI scores are strong predictor of PD risk [33–37]. Additionally, decreased functional capacity and preoperative frailty are risk factors for PD [23, 36, 38, 39]. High level of dependence on care givers as measured by Activities of Daily Living (ADLs) [40] and lower overall quality of life [41] are associated with PD. More robust patients are at decreased risk for PD compared to those with poor preoperative nutritional status [42, 43], dehydration [44] and fluid fasting [45], and low BMI [23, 37].

Psychosocial factors should be elicited as part of the patient's history as they may modify the patient's risk for PD. An optimistic attitude and positive expectations have been shown to be protective against PD [46], while patients with depressive symptomatology [13, 18, 47] or a history of depression [48] are at increased risk for PD. PD is seen more commonly in patients dissatisfied with their degree of preoperative social support [49], and patients with a history of substance abuse are more likely to develop PD including alcohol [20, 21, 50], drugs [14], and tobacco [16, 51]. The experience of pain can increase risk for PD as higher baseline pain scores reported before surgery predict increased likelihood of developing PD [17, 35, 52].

Drugs can greatly impact physiology and cognition in geriatric patients. The American Geriatrics Society has published the Beers Criteria List, a comprehensive assessment of medications best avoided in elderly patients [53] [54], and Beers Criteria medications like benzodiazepines, nonsteroidal anti-inflammatories (NSAIDS), antihypertensives, and sliding scale insulin are routinely given to surgical patients. Used perioperatively for their antihistamine, antispasmodic, and anti-emetic properties [55, 56], anticholinergic compounds found on the Beers Criteria List should be avoided in geriatric patients. Administration of corticosteroids and meperidine has been linked to development of PD and should be avoided as well [8, 54]. Avoidance of specific medications and decreasing polypharmacy are good strategies for lowering risk of PD [57, 58].

Intraoperative Factors

Risk for PD has been associated with a number of intraoperative variables. Hemodynamic instability is linked to increased risk of PD, and medication-specific risks are seen intraoperatively as well as preoperatively (Table 2).

After invasive surgery [14, 59–62] and emergency surgery [10, 60, 63], patients have increased likelihood of developing PD. Surgical time has been positively correlated with incidence of PD [20, 37, 64]. Intraoperative hypotension and hypothermia are risk factors for PD [50, 65, 66], as well as blood loss [67], blood transfusion [12, 68], and increased fluid administration [17]. Increased embolic load to the cerebral vasculature during cardiopulmonary bypass (CPB) is hypothesized to be a mechanism of PD [69, 70].

Contributions of anesthetic medications to the risk of PD have been investigated in several studies, but overall the two major approaches to surgical anesthesia, general and regional techniques, have not been shown to differ in risk for PD [71–73]. Identified as a potentially modifiable factor, depth of anesthesia is being studied for impact on PD risk. Exposure to episodes of deep anesthesia was shown in one study to increase PD [74], and deep sedation with propofol infusion (Bispectral Index Score (BIS) of 50) has been associated with significantly higher prevalence of PD compared to light sedation (BIS of 80) [75]. Midazolam can be desirable for its amnestic properties and for its hemodynamic stability, but its use (at least as an infusion) is associated with PD [49]. Likewise, administration of long-acting [45] and short-acting opiates during surgery increases risk of PD [45–77].

Table 2 Intraoperative risk factors for postoperative delirium

Risk factor	Study	Population
Emergency surgery	Krzych et al. [10]	Cardiac surgery
	Kalisvaart et al. [63]	Hip surgery
	Koebrugge et al. [60]	Endovascular aortoiliac surgery
Longer duration of surgery	Shah et al. [20]	Major head and neck cancer surgery
	Norkienė et al. [64]	Cardiac surgery
	Lee et al. [37]	Hip fracture repair surgery
Invasive surgery	Fineberg et al. [14]	Spine surgery (lumbar)
	Koebrugge et al. [60]	Endovascular aortoiliac surgery
	Salata et al. [61]	Aortic aneurysm repair surgery
	Hudetz et al. [62]	Cardiac surgery
	Osse et al. [59]	Cardiac surgery
Fentanyl use	Radtke et al. [45]	Surgery
	Andrejaitiene and Sirvinskas [76]	Cardiac surgery
	Burkhart et al. [77]	Cardiac surgery
Midazolam use	Do et al. [49]	Orthopedic surgery
Greater intraoperative volume loads	Smulter et al. [17]	Cardiac surgery
Low intraoperative body temperature	Detroyer et al. [66]	Cardiac surgery
Blood loss	Marcantonio et al. [67]	Major elective noncardiac surgery
Blood transfusions	Whitlock et al. [68]	Cardiothoracic surgery
	Gao et al. [12]	Spine surgery
Intraoperative hypotension	Patti et al. [50]	Colorectal surgery
	Tognoni et al. [65]	Urological surgery

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Postoperative Factors

Several characteristics of postoperative management, in addition to various postsurgical complications, are associated with onset of PD (Table 3).

Paradoxically, both poorly controlled pain and use of opioids [78–80], such as meperidine [81–83] and tramadol [84], have all been associated with increased PD risk. Intravenous administration of opiates with patient-controlled analgesia (PCA) is associated with more risk of PD than oral opioids [40, 78]. Lumbar plexus block plus PCA has been shown to significantly reduce the risk of PD compared to PCA alone in hip arthroplasty patients [85]. Ideally, a plan for analgesia is developed by the surgeon and anesthesiologist for any major surgery in a geriatric patient. Incorporation of opioid-sparing techniques like adjunctive medications (e.g., acetaminophen, gabapentin) and regional analgesia (e.g., peripheral nerve blocks and epidurals) should be part of the analgesia plan. A prophylactic pharmacologic bowel regimen should be started if opiates are necessary to decrease problems associated with decreased bowel motility [86].

Postoperative complications have a significant impact on the risk for PD. Critical illness requiring postsurgical admittance to the ICU [36] and longer duration of mechanical ventilation [64, 77] have been associated with PD, along with pneumonia [19, 87] and low cardiac output syndrome [11, 64]. Anemia [67] and blood transfusion increases risk for PD [67], as does low postoperative oxygen saturations [88]. PD is more frequent in the setting of markedly abnormal postoperative levels of sodium, potassium, or glucose [89]. Systemic inflammatory response syndrome (SIRS) [34], elevated levels of CRP [77, 90], and increased

Table 3 Postoperative risk factors for postoperative delirium

Risk factor	Study	Population
Pain	Vaurio et al. [78]	Major elective noncardiac surgery
	Leung et al. [79]	Major noncardiac surgery
	Nie et al. [80]	Hip fracture repair surgery
Administration of meperidine	Adunsky et al. [81]	Hip fracture repair surgery
	Marcantonio et al. [82]	Major elective noncardiac surgery
	Morrison et al. [83]	Hip fracture repair surgery
Benzodiazepines	Marcantonio et al. [82]	Major elective noncardiac surgery
	Leung et al. [40]	Noncardiac surgery
	Takeuchi et al. [87]	Esophageal cancer surgery
Tramadol	Brouquet et al. [84]	Major abdominal surgery
Pneumonia	Loponen et al. [19]	Cardiac surgery (CABG)
	Takeuchi et al. [87]	Esophageal cancer surgery
SIRS	Guenther et al. [34]	Cardiac surgery
Low cardiac output syndrome	Norkiene et al. [11]	Cardiac surgery (CABG)
	Norkienė et al. [64]	Cardiac surgery
Higher postoperative body temperatures	Smulter et al. [17]	Cardiac surgery
Postoperative blood transfusion	Marcantonio et al. [67]	Major elective noncardiac surgery
Low postoperative hematocrit	Marcantonio et al. [67]	Major elective noncardiac surgery
Low postoperative oxygen saturations	Wang et al. [88]	Major head and neck surgery
Markedly abnormal postoperative levels of sodium, potassium, or glucose	Yildizeli et al. [89]	Thoracic surgery
Elevated levels of C-reactive protein	Burkhart et al. [77]	Cardiac surgery
	Dillon et al. [90]	Major elective surgery
Admittance to ICU	Pol et al. [36]	Vascular surgery
Significantly longer time on mechanical ventilation	Norkienė et al. [64]	Cardiac surgery
Significantly longer time on mechanical ventilation	Burkhart et al. [77]	Cardiac surgery

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postoperative body temperature have been associated with increased risk of PD.

Features, Etiology, and Diagnosis of PD

Features

The Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM V) diagnosis of delirium requires that symptoms must have an acute onset and be fluctuating in their course. Decreased orientation to the environment, cognitive disturbances like altered memory, language, perception, and visuospatial abilities, along with inattention are necessary to diagnose delirium. A comprehensive evaluation for conditions in the differential diagnosis of PD should commence quickly in geriatric patients, initiating with prompt intervention for life-threatening conditions like hypoglycemia, hypoxia, and ischemia (Table 4).

Table 4 Differential diagnosis for postoperative delirium

Emergence from anesthesia drugs (polypharmacy, withdraw, anticholinergics, antihistamines, barbiturates, and benzodiazepines)
Endocrine and metabolic disturbances (hypoglycemia, hypothyroidism, hyponatremia, Hyperammonemia, etc.)
Mental disorders (dementia, depression, and anxiety)
Hypoxia and ventilation disturbances
Infection
Sensory deprivation or overload
Ischemia (TIA, CVA)
Intracranial neoplasm
Seizure disorder (postictal state)

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The duration of dysfunction and the activity level of the patient are used to identify subtypes of PD. Acute PD (hours to days) and persistent PD (weeks to months) can manifest with hyperactivity, hypoactivity, or mixed activity. Mood lability, agitation, and/or refusal to cooperate with medical care are often seen in hyperactive delirium. Sluggishness and decreased psychomotor activity are features of hypoactive delirium. Delirium tends to wax and wane over a patient's clinical course, and individuals may display mixed characteristics of both extremes of activity in PD [91]; however, the majority of patients will be one or the other. The hypoactive subtype has the worst overall prognosis [92].

Etiology

Significant preclinical and translational research efforts are focused on elucidating potential mechanisms of PD, though clear targets for the prevention and modification of PD outside of clinical risk factors are currently lacking.

Immune activation can lead to CNS dysfunction and is a promising field of study [93] . Markers of immune activation can be measured in a variety of tissues including plasma, urine, and CSF, and investigations in delirious patients have reported elevated levels of C-reactive protein (CRP), interleukins (IL), tumor necrosis factor-α (TNF-α), and cortisol to name a few [93, 94]. Pro-inflammatory cascades are initiated by important perioperative events like surgical trauma and/or infection, but just the process of aging can prime the immune system and CNS of geriatric patients for exaggerated and pathologic inflammatory response to stress [93–95]. Oxidative stress is important to immune function, but can also be detrimental if the burden of reactive oxygen species overwhelms metabolism. Energy imbalances and local ischemia associated with oxidative stress can have significant downstream effects on CNS function.

Sleep hygiene is an important part of optimizing care for geriatric patients as sleep-deprivation impairs cognitive function. Both major and minor surgery can disrupt circadian rhythms resulting in diminished postoperative sleep quality, slowed recovery, and possibly a predisposition for PD [96]. Although endogenous melatonin dysregulation is seen after major surgery [97] and patients with PD have been reported to have low melatonin levels [98], postoperative melatonin supplementation for prevention of PD in ICU patients after major elective surgery has not shown benefit [99].

A variety of disruptions in neurotransmitter regulation have been implicated in PD, including altered acetylcholine, dopamine, norepinephrine, glutamate, serotonin, histamine, and g-aminobutyric acid (GABA) [93, 94]. A cholinergic mechanism is central to the pathophysiology of Alzheimer's disease and may be an important mechanism contributing to increased risk of PD in patients with pre-existing dementia [100, 101].

Diagnosis

Once various metabolic, physiologic, and pharmacologic reasons for delirium have been excluded, PD can be screened for using a variety of validated assessment tools like the Delirium

Symptom Interview (DSI), NEECHAM Confusion Scale, Intensive Care Delirium Screening Checklist (ICDSC), and Nu-DESC (Nursing Delirium Screening Scale). As per the AGS Guidelines, health professionals caring for post-surgical patients should be recognizing, evaluating, and documenting signs and symptoms associated with delirium [8]. Likely the most utilized delirium assessment tool – the CAM – was developed as a bedside assessment for delirium that could be administered quickly by non-psychiatrists. The CAM is validated as a sensitive, specific, reliable, and easy to use tool for delirium identification [8, 102]. The CAM has been modified for use in different patient populations. Recognizing the communication difficulties inherent to ICU patients secondary to mechanical ventilation, presence of orogastric tubes and exposure to psychoactive medication, the brief 4-question CAM-ICU was created [103].

Treatment of PD

Prevention efforts targeting PD should involve awareness of factors important for identification of high-risk patients, followed by attempts to impact any modifiable characteristics of the patient, surgery, and anesthetic plan. Despite best practices for prevention, PD will develop in some geriatric patients, and environmental adjustments, appropriate diagnostic testing, and addition of consultants to the care team are recommended by the AGS Guidelines as part of a comprehensive treatment plan for PD (Table 5).

Both nonpharmacologic and pharmacologic approaches can be used for treatment of PD. Based upon the Yale Delirium Prevention Program, the Hospital Elder Life Program (HELP) has been the most studied treatment strategy for delirium in hospitalized medicine patients. Pre-existing cognitive impairment, sleep deprivation, immobility, visual impairment, hearing impairment, and dehydration are targeted by a standardized protocol, which has been associated with a 14.4% decrease in delirium and an estimated cost savings of >$1.2 million per year in a 500-bed community teaching hospital [104]. Additional focus on early mobilization, nutrition optimization, and cognitive activities in abdominal surgery patients has shown promising ability to decrease PD [105]. In general, non-pharmacologic interventions for the effective treatment of PD include increased physical activity and cognitive stimulation, constant access to hearing and visual aids, good sleep hygiene, and adequate nutrition and hydration. Engaging a full range of team members from nursing to geriatric medicine consultants for the optimal care of the delirious postoperative geriatric patient is important.

According to the AGS Guidelines, only patients that are severely distressed or agitated and pose a threat to themselves or others warrant pharmacological treatment with antipsychotics. Antipsychotics are not indicated for prophylaxis against delirium. Daily face-to-face evaluation of patients with PD should be completed, ensuring that the lowest effective dose and shortest possible duration guides administration of psychoactive medications to geriatric patients.

Conclusion

PD is one of the most common complications after surgery in geriatric patients. The impact of PD on postoperative recovery is significant, putting patients at risk for loss of function and mortality, while adding tremendous costs to healthcare. Knowledge of key risk factors is important to give perioperative providers an awareness of patients at risk for PD. Screening patients for risks can identify modifiable factors and bring attention to those patients that may require enhanced services as part of their care. The most encouraging approach to preventing and treating PD employs a multidisciplinary team of providers to optimize perioperative care of geriatric surgical

Table 5 Summary of best practices in the prevention and treatment of postoperative delirium [8]

Perioperative phase of care	Best practice	Strength of recommendation	Quality of evidence
Preoperative (prevention)	Educational programs to improve understanding of epidemiology, assessment, prevention, and treatment	Strong	Low
Preoperative (prevention)	Multicomponent nonpharmacologic intervention program (e.g., cognitive reorientation, sleep enhancement, early mobility, adaptations for sensory impairment, nutrition, fluid repletion, pain management, adequate oxygenation, prevention of constipation)	Strong	Moderate
Postoperative (management/ treatment)	Multicomponent intervention program (cognitive reorientation, mobility/exercise/physical therapy, therapeutic activities/cognitive stimulation, sensory adaptation, nursing education, and geriatric consultation)	Weak	Low
Postoperative (management/ treatment)	Perform medical evaluation, make medication and/or environmental adjustments, order appropriate diagnostic tests, and obtain appropriate clinical consultations to identify and manage underlying PD contributors	Strong	Low
Preoperative/ postoperative (prevention)	Provide regional anesthetic at the time of surgery and postoperatively to improve pain control	Weak	Low
Postoperative (prevention)	Optimize postoperative pain control with nonopioid medications if possible	Strong	Low
Postoperative (prevention)	Avoid medications that induce delirium (e.g., benzodiazepines, anticholinergics, sedative-hypnotics, meperidine)	Strong	Low
All (prevention and management)	Avoid newly prescribing cholinesterase inhibitors to prevent or treat PD	Strong	Low
Postoperative (management/ treatment)	Use antipsychotics at lowest effective dose for the shortest possible duration to treat severely agitated or distressed patients (only if behavioral interventions have failed) – evaluate ongoing use daily	Weak	Low
Postoperative (management/ treatment)	Avoid benzodiazepines as first-line treatment of agitated patient except when specifically indicated (i.e., treatment of withdrawal)	Strong	Low
Postoperative (management/ treatment)	Avoid antipsychotics and benzodiazepines in older adults with PD who are not agitated (e.g., hypoactive PD)	Strong	Low

Table excludes practices for which the American Geriatrics Society Expert Panel did not issue a recommendation for or against and/or practices lacking sufficient evidence of efficacy

patients with both pharmacologic and nonpharmacologic approaches. Early recognition of PD is of paramount importance, and all care providers for geriatric surgical patients should be able to recognize PD symptomatology. Protecting the cognitive function of geriatric patients should be a primary goal of geriatricians, surgeons, anesthesiologists, and nursing working through collaborative strategies to provide optimal care to the aging surgical population.

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Models of Care

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Abstract

The science of health care targeting the unique needs of older adults has evolved tremendously during the last 30 years including the development of several geriatric models of care across all health care settings. This chapter describes the most prominent geriatric hospital models of care, including their objectives, unique strategies, and outcomes. All geriatric care models aim to prevent complications and address hospital factors that can contribute to complications. Although each may differ in their approach, all incorporate the principles of comprehensive geriatric assessment: physical health, functional status, psychological health, and socio-environmental parameters. The overall objectives of the models are similar: educate health care providers in core geriatric principles, target risk factors for complications, incorporate patient or family choices and treatment goals, employ evidence-based interventions, promote interdisciplinary communication, and emphasize proactive discharge planning (or transitional care). Geriatric models of care usually include institutional approaches that address workforce issues as well as how the evidence-based geriatric care processes are embedded within the organizational structure of the hospital or health system. Specific models of care described include the consultative service or mobile ACE unit, NICHE, and HELP as well as evolving surgical specialty models of care.

Keywords

Acute care · Geriatrics · Outcomes · Implementation · Sustainability · Geriatrics · Care models · Interdisciplinary · Patient/family centered

Introduction

Models of care addressing the unique needs of older hospitalized patients can be traced to the comprehensive geriatric assessment (CGA) programs first developed in the 1970s [1]. CGA programs screen older patients at high risk for geriatric specific problems, assess for modifiable risk factors, and implement evidence-based strategies consistent with the patient's treatment goals. Over the last 35 years, changes in the health care system, coupled with the increasing older adult population, has led to development of several geriatric models of care across all health care settings. In general, the goals of these geriatric models of care in the hospital focus on (1) prevention of complications that occur more commonly in older adults and (2) address hospital factors that contribute to complications. This chapter provides an overview of complications that are more frequently found in older patients, care delivery issues that are addressed by geriatric models of care, and a description of the most commonly employed hospital models.

Complications of Older Hospitalized Patients

Although patients aged 65 and over represent about 14.5% of the US population, they account for 55% of those undergoing surgical procedures in American hospitals [2]. In addition to the high proportion of older patients, the most troublesome finding is that older patients also represent a higher complication rate for certain conditions which subsequently lead to higher health care costs and account for three-quarters of postoperative mortality [2]. Older adults are more likely to experience additional types of complications that, in addition to reducing survival, can result in loss of independence and lead to hospital readmission, increased usage of rehabilitation services, and new placement in a nursing home. The physiologic changes with aging coupled with the higher likelihood of physical frailty and cognitive impairment (either chronic dementia and/or delirium) all contribute to the older person's vulnerability to complications during hospitalization [2–4]. The complex challenges of those adult patients with cognitive impairment are often not adequately addressed. Table 1 provides examples of common behaviors of cognitively impaired persons that can lead to complications. The resulting increased length of stay, increased risk of posthospital complications, and higher costs are well documented [6, 7].

Although geriatric models of care can improve the overall outcomes and experiences of hospitalization, [8] in general, these programs are designed to target those adverse events that occur more commonly in older patients. Table 2 provides a summary of these complications and the clinical and related cost outcomes associated with these complications. These complications are often referred to as "geriatric syndromes" that are further described in ► Chap. 5, "Geriatric Syndromes."

The Inpatient Prospective Payment System that the Centers for Medicare & Medicaid Services (CMS) uses to reimburse hospitals instituted provisions in October 2008 for eight preventable hospital-acquired conditions that would not receive payment [9, 10]. Three of these eight are complications are known to occur most frequently in older inpatients and have been found to be reduced when geriatric models of care are employed [8, 11]. These three complications (fall-related injury, pressure ulcer, and catheter-associated urinary tract infection) are among the six adverse events or complications specifically associated with hospitalization of older adults.

Table 1 Behaviors of cognitively impaired patients contributing to high complication rate (Silverstein and Maslow [5])

Behaviors	Example	Potential complication
Inability to follow directions	Does not use call bell to ask for assistance and gets out of bed without needed assistance	Fall-related injury
Removal of treatments	Pulls out central lines	Hemorrhage
		Infection
		Physical restraints and associated complications
Not able to communicate needs	In pain but not able to verbally communicate this to nurse	Functional decline
Wandering	Leaves unit and exits hospital in gown	Hypothermia
		Other injuries
		Use of physical and chemical restraints that increase likelihood of delirium, falls, fall-related injury, and nutritional problems
Misinterprets visual and auditory cues	Resists staff attempts to assist the patient to get out of bed which is perceived as an assault and then hits staff	Agitation-related injury
		Overuse of psychoactive medication that increase likelihood of delirium, falls, and fall-related injury
Decreases inhibition of inappropriate behaviors	Removes clothing and walks down the hallway nude	Agitation-related injury
		Overuse of psychoactive medication that increases likelihood of delirium, falls, and fall-related injury

Table 2 Complications in the older surgical patient[a]

Complication	Hospital factors[b]	Clinical outcome	Cost implications
Functional decline	Immobility Bed rest without medical/surgical indication Physical restraint Inappropriate medication prescribing New psychoactive drug use Obstacles in the hospital physical environment	Reduced/loss of independence in function (activities of daily living) Reduced/loss of ambulation Pain Increased rate of pressure ulcers, falls, fall-related injuries, and development of contractures	Longer length of stay (LOS) Increased rate of institutional or home-based rehabilitation Nursing home placement
Fall-related injury	Immobility Physical restraint Inappropriate medication prescribing New psychoactive drug use Obstacles in the hospital physical environment	Pain Fracture requiring surgical intervention Reduced/loss of independence in function (activities of daily living) Reduced/loss of ambulation	Medicare will not pay for treatment[c] Surgery Longer LOS Institutional or home-based rehabilitation Nursing home placement
Under/malnutrition	Immobility Inattention to oral care Lack of feeding assistance for those with physical or cognitive impairments	Reduced wound healing Discomfort due nasogastric tube placement Percutaneous enteral access procedures (gastrostomy) Delirium Physical restraint to prevent tube removal Aspiration Functional decline	Longer LOS Surgery Institutional or home-based enteral nutrition therapy
Pressure ulcer	Immobility Physical restraint Under/malnutrition Dehydration	Immobility Sleep deprivation Pain Sepsis Septicemia Surgical debridement Surgical techniques (direct closure, flaps, and skin grafting)	Medicare will not pay for treatment[b] Longer LOS Institutional or home-based skilled nursing treatment

Urinary tract infection (UTI: secondary to catheter use or CAUTI)	Emergency room placement without indication Incontinence treatment No postsurgical monitoring of catheter use	Immobility Pain Delirium Acute pyelonephritis Bacteremia Sepsis Prosthetic joint infection Higher risk for death	Medicare will not pay for treatment[b] Longer LOS Rehospitalization
Delirium	Physical restraint Inappropriate medication prescribing New psychoactive drugs Urinary catheterization CAUTI Immobility Under/malnutrition Dehydration	Functional decline Persistent cognitive impairment Falls, injuries Undetected infection Sleep deprivation	Longer LOS Rehospitalization Nursing home placement Death

[a]Geriatric syndromes refer to conditions highly associated with aging such as frailty, sleep disorders, self-neglect. For the purpose of this review, these syndromes and potential complications are more narrowly defined
[b]Hospital factors. There is a myriad of patient and hospital factors that contribute to each complication; however, this list provides examples of those specific hospital practices that place the older adults at high risk and which are the focus of geriatric care model interventions
[c]As of October 2008, hospitals no longer receive payment for eight hospital-acquired conditions; three of these eight indicated in the table are complications known to occur most frequently in older inpatients and are reduced when geriatric models of care are employed (fall-related injury, pressure ulcer, and catheter-associated urinary tract infection)

Although there are other geriatric syndromes (e.g., incontinence) and other potential complications associated with older inpatients (e.g., sleep deprivation, inadequate pain management, dehydration, adverse drug effects), many of these syndromes and complications are either risk factors or outcomes of these three and/or functional decline, under/malnutrition, or delirium. More details about each of these can be found in other ▶ Chaps. 7, "Frailty," ▶ 8, "Function and Prehabilitation," ▶ 22, "Postoperative Delirium," and ▶ 24, "Nursing Issues in Older Adult Surgery Patients."

The occurrence of each of these complications leads to interventions that can often prolong the hospital stay. Following hospital discharge, they frequently contribute to death, institutionalization as well as disproportionately high pre-hospitalization rates, high emergency department usage, and increased need for rehabilitation therapy services. As illustrated in Table 2, the *inter-relationships* among these various complications during hospitalization are obvious. The data supporting the importance of prevention, early detection and treatment of these complications in older surgical patients is well documented [8, 11, 12]. This led, in 2012, to the American College of Surgeons (ACS) partnering with the American Geriatrics Society (AGS) and the John A. Hartford Foundation to develop the American College of Surgeons National Surgical Quality Improvement Program (NSQIP)/American Geriatrics Society (AGS) Best Practices Guidelines: Optimal Preoperative Assessment of the Geriatric Surgical Patient. This guideline was updated rereleased in 2016 [4].

Although patient characteristics, especially multiple comorbidities, frailty, and cognitive impairment, may increase vulnerability of older inpatient to negative consequences, the hospital environment plays an independent and significant role in determining staff practice and subsequent patient outcomes such as iatrogenic complications [13]. Thus, geriatric models of care are meant to address these hospital-based or institutional factors that are likely to contribute to complications among older patients. Effective resolution of these negative consequences is dependent on geriatric models that target both patient and environmental (institutional) risk factors.

Geriatric Care Model Objectives

Although geriatric models of care differ in their approach to prevent complications and address care delivery problems that can contribute to complications, all share a common set of general objectives [14, 15]. Although these objectives could be applied to any patient regardless of age, it is how geriatric care models apply these that are age-specific. Table 3 provides examples of processes and interventions to meet these six general objectives.

The six general objectives of geriatric care models are:

Educate Health Care Providers in Core Geriatric Principles

The complications most frequently encountered among *o*lder patients are often due to system-level problems. These include inadequate educational preparation of health care providers to recognize age-specific factors that increase risk of complications [16, 17]. All geriatric care models require a coordinator or clinician with advanced geriatric education, however, the implementation of any model depends on direct care staff with the knowledge and competencies to deliver safe and evidence-based care to older patients. Thus, the coordinator or other geriatric clinician role includes teaching of other staff through rounds, journal clubs, conferences, and other internal institutional educational venues [18].

Target Risk Factors for Complications

Given the disproportion of certain complications or geriatric syndromes among hospitalized older adults, the clinical focus of all geriatric models is prevention via risk factor reduction and early detection of these problems. Some models may focus on

Table 3 Geriatric care models: objectives, processes, and interventions

Objective	Examples of processes	Examples of interventions
Educate health care providers in core geriatric principles	Resident training includes required geriatric rotation *or* mandatory geriatric rotation for residents Institutional continuing education includes geriatric-specific training *or* geriatric-specific interdisciplinary continuing education programs Geriatric specialist responsible for geriatric training initiatives	Hospital intranet includes geriatric programming Journal club includes geriatric journals and/or articles focusing on geriatric outcomes Medical, surgical, nursing, and interdisciplinary rounds include geriatric case studies
Target risk factors for complications	Policies, protocols, and documentation system includes assessment tools and practices that identify older adults at risk for complications Assessment tools prompt providers to consult geriatric specialists for evaluation of high risk problems Geriatric specialist provides individual evaluation of risk factors	Electronic medical record (EMR) provides alerts for medications prescribed that are known to increase fall risk EMR prompts providers to document daily cognitive testing results Hospital policy for daily cognitive assessment of at-risk patients Cognitive assessment indicates delirium that leads to geriatric specialist consultation
Incorporate patient (family) choices and treatment goals	Policies and protocols support and documentation system includes forms that elicit patient choices as well as family involvement in care Geriatric nurses are prepared to coordinate an interdisciplinary evaluation and promote development of *informed* patient/family treatment goals and plan of care Palliative care is consulted and provides informed choices to patients/families in situations of life-threatening illness	Admission history includes evaluation of patient's preferences for postdischarge rehabilitation Unlimited visiting hours and bedside recliners encourage family participation in recovery Patient and family preferences for type and degree of family involvement is documented Patient with Alzheimer's disease who is unable to verbally indicate needs is evaluated by palliative care specialist for pain evaluation/treatment
Employ evidence-based interventions	Policies and protocols integrate geriatric specific implications Education and training for all clinicians include core geriatric content	Hospital protocol for urinary catheter removal within 2 days postsurgery Unit-based mobility program Physical environment reduces injury risk for nonambulatory patients with dementia such as low-height beds and bedside mats
Promote interdisciplinary communication	Medical record facilitates patient information across disciplines Processes in place to encourage face-to-face interaction among disciplines Unit-based and hospital-wide committee includes geriatric specialist representation	Interdisciplinary team rounds held biweekly Programmatic initiatives include all applicable disciplines, for example, physical and occupational therapy in unit-based mobility program Comanage patients across specialties such as geriatric oncology Collaborate with other programs such as palliative care in providing symptom management
Emphasize discharge planning or transitional care	Documentation system provides comprehensive hospital course information to primary care provider and other postdischarge providers (home care, nursing home, etc.) as well as elicits pertinent information *from* other providers	Patient and caregiver receive comprehensive documentation of hospital treatment, changes in treatment plan, and postdischarge instructions Understanding of instructions is evaluated before discharge Phone follow-up postdischarge to evaluate patient condition and needs

a particular syndrome; however, the interrelationship of these complications and their shared risk factors often result in a reduction of the other geriatric syndromes. Targeting risk factors requires standardized assessment tools known to be valid and reliable for older adults. See the 2015 Best Practices Guideline from ACS NSQIP/American Geriatrics Society [4], and the Portal of Geriatrics Online Education (http://www.pogoe.org/) for examples of assessment instruments. Implementation of geriatric care models often includes institutionalizing these practices such as incorporating these tools in the medical record as well as hospital policies, procedures, and protocols.

Incorporate Patient (Family) Choices and Treatment Goals

All health care decision should be guided by the patient's choices. Choices range from decisions about activity level and medication use to more complex issues including advance directives. Decisions regarding life-sustaining treatment are often influenced by quality of life considerations balanced by the potential length of life. For family members acting in the best interests of patients who can no longer participate in decision-making, this can be a complicated dilemma. Life-sustaining treatments are often employed with very old patients who die in the course of hospitalization although most prefer comfort care. Geriatric models are meant to address this lack of congruence by supporting efforts to provide care that is more consistent with patients' preferences [19]. For this reason, many geriatric models work collaboratively or in conjunction with palliative care programs [20]. See also the ▶ Chap. 18, "Ethical Issues in Older Adults."

Employ Evidence-Based Interventions

Given that most physicians, nurses, and other health providers have received minimal content in their training regarding geriatrics, it is not surprising that there is a higher complication rate for older hospitalized patients. Advances in geriatric science, similar to other research-based approaches, are not readily employed in hospital care. Problems with polypharmacy, inappropriate medications (e.g., overuse of psychoactive), overuse of restraints, inadequate detection of delirium, depression, and undermanagement of pain are some of the many hospital factors that can contribute to poor outcomes. Thus, geriatric models promote the use of standardized evidence-based guidelines [4].

Promote Interdisciplinary Communication

Since geriatric syndromes are not just medical problems but represent a complex interaction of medical, functional, psychological, and social issues, other disciplines such as nursing, pharmacy, social work, physical and occupational therapy are needed. Geriatric care models all include interdisciplinary teams, i.e., an approach that facilitates communication among disciplines, which is known to improve patient outcomes [21]. Examples of successful strategies include interdisciplinary rounds and standardized communication (e.g., SBAR) [22].

Emphasize Discharge Planning (or Transitional Care)

Many older patients will require rehabilitation or skilled nursing services following surgery. Older adults are more likely to experience problems associated with discharge planning that can lead to delays in discharge and greater use of emergency service use and hospital readmission. Hospital readmission for older patients is most likely associated with medical errors in medication continuity, diagnostic workup, or test follow-up. These poor outcomes are attributed to a lack of coordination among health care providers that can result in unresolved medical issues and deficient preparation of patients and their caregivers to carry out discharge instructions [23]. Geriatric models not only focus on the inpatient experience but also the post-hospital care environment and the care transition following hospital discharge.

Two of the six models consider the care transition a primary focus of their programs.

Geriatric Models

There are several types of geriatric models that are currently employed in hospitals throughout the United States. In addition to incorporating the original tenets central to comprehensive geriatric assessment (screen for those at high risk for geriatric specific problems, assess for modifiable risk factors, and implement strategies consistent with the patient' treatment goals) all also strive to deliver quality care for older adults in a cost-effective manner. Comprehensive geriatric assessment assumes that the systematic evaluation of a frail older person by a multidisciplinary health care team will uncover actual or potential health problems. The considerable advances in geriatric health care science over the last 35 years can then be applied in treating or preventing these conditions and thus result in better health outcomes.

Although the specific mode of intervening may differ among the models, they all address both common health problems and care delivery issues. The geriatric model may consider all geriatric syndromes or target specific ones such as delirium or functional decline. Similarly, a geriatric model may be employed as a hospital-wide approach, unit-based intervention, or focus on specific processes of hospitalization such as admission screening or discharge planning. Geriatric care may also be integrated within surgical specialty services. Regardless of the structure of the geriatric model, all facilitate the general objectives listed in Table 3. Table 4 provides a summary of the clinical foci, unique features, coordination, and interventions for each of the six most commonly employed geriatric models of care.

Geriatric Consultation Service

Older hospitalized patients are vulnerable to adverse events and certain medical conditions in the acute care setting or following hospitalization. Their multiple comorbidities and reduced physiological reserves place these individuals at risk to develop certain hospital-acquired geriatric syndromes such as hospital-associated deconditioning, delirium, pressure ulcers, falls, hospital-acquired infections among other geriatric syndromes. These geriatric syndromes in hospitalized older adults can increase morbidity, mortality, and resource utilization. Further, these adverse events can change the trajectory of recovery for a person and decrease the quality of life for the patient and family caregiver.

The geriatric consultation service focuses on early identification and treatment of vulnerable hospitalized older adults who develop geriatric syndromes. Nursing leaders and the interdisciplinary team are essential to providing the best care for this vulnerable population. Increasing awareness and timely recognition of common geriatric syndromes in older adults can significantly impact the outcomes in this particular population.

The geriatric consultation service and the multidisciplinary team provide input to other specialties that focus on preserving functional mobility, minimizing iatrogenic events, preventing the use of potentially inappropriate medications in hospitalized patients. The geriatric medicine consultation service works with other medical and surgical specialties to comanage complex cases. Often geriatricians will take the lead when addressing common conditions such as delirium, malnutrition, depressed mood, behavioral and psychological symptoms of dementia, frailty, pain, sensory impairment, and sleep disorders. The geriatric consult service can impact length of stay, readmission rates, complications, hospital costs, and mortality rates. The consultation service integrates other disciplines such as social services, physical therapy, occupational therapy, pharmacist, speech therapy, and dietitian services. The geriatrician's role on this team is to coordinate this comprehensive evaluation of the patient's medical and geriatric functional needs. Geriatric medicine also pays particular attention in delineating the patient's goals of care and determining post-acute care needs. The key approach to this model is to assess the patient's cognitive

Table 4 Core components of six geriatric care models

Model type	*Clinical outcome focus*[a]	*Unique features*	*Program/team coordination*	*Interventions*[b]
Geriatric consultation	Primary focus can vary depending on composition of consult team and may be specific to a surgical specialty or procedure	Employed by primary provider request	Individual consultant (geriatrician, geropsychiatrist or geriatric nurse specialist) *or* Interdisciplinary team that is coordinated by geriatric medicine or psychiatry fellow, geriatric nurse specialist or an administrative director	Comprehensive geriatric assessment: medical, psychiatric, functional, and social Recommends interventions based on consultant discipline (medicine, psychiatry or team that includes nurses, social workers, and others) Primary provider chooses which recommendation to employ
Acute Care for the Elderly (ACE)	Functional decline	Dedicated unit with explicit admission criteria Requires interdisciplinary team and Redesign of physical environment to accommodate physical and cognitive needs	Unit directed and/or team coordinated by geriatrician, geriatric nurse specialist, administrator or comanaged by clinician-manager	Physical environment to promote patient mobility, orientation, and staff observation Interdisciplinary rounds facilitate care coordination and thus: Identify modifiable risk factors for geriatric syndromes and complications Prevent avoidable discharge delay Promote timely referrals to disciplines or specialists
NICHE: GRN/ACE	Nursing processes related to all geriatric syndromes and potential complications such as avoiding restraint use, initiating urinary catheter removal	Focus on improving nursing care of all geriatric syndromes Prepares staff nurses to take active part in geriatric care management including coordinating or facilitating other geriatric models of care	Program implementation by NICHE Coordinator (usually a geriatric nurse specialist) Geriatric Resources Nurses (staff nurses with additional training) implement protocols Depending on availability, other clinicians (geriatrician, hospitalist, social worker, etc.) work as interdisciplinary team	Nurse-initiated protocols: Restraint and psychoactive drug reduction Functional mobility Fall/injury prevention Pressure ulcer assessment/treatment Prevention of UTI – early catheter removal Delirium assessment/treatment Organizational strategies including measurement schema, performance improvement techniques, and management tools to promote

(continued)

Table 4 (continued)

Model type	*Clinical outcome focus*[a]	*Unique features*	*Program/team coordination*	*Interventions*[b]
				implementation of above protocols
HELP	Delirium prevention and early management	Requires use of volunteers	Elder Life Nurse Specialist or Elder Life Specialists coordinates interdisciplinary team (geriatrician, recreation therapy, physical therapy, etc.) and trained volunteers	Delirium risk factor protocols: Mental orientation Therapeutic activities Early mobilization Vision and hearing adaptations Hydration and feeding assistance Sleep enhancement
APN transitional care model	Reducing complications specific during the transition from hospital to home	Requires advanced practice nurse coordinator to follow patient in hospital and following discharge	Advanced practice nurse (nurse practitioner or clinical nurse specialist)	Protocols to assess/ intervene with: Medication discrepancies and inappropriate medication usage Case management and APN surveillance across settings
The care transitions intervention	Reducing complications specific during the transition from hospital to home, such as prevent post hospital medication discrepancies, increase likelihood of patient/ caregiver detection of worsening condition	Requires nurse transitions coach to follow patient in hospital and following discharge	Transition coach (nurse or advanced practice nurse) empowers patient and caregiver	Personal health record includes data elements essential to promote productive patient-provider encounters across settings Discharge preparation checklist to facilitate patient's knowledge of discharge instructions Medication discrepancy tool used by transition coach to identify medication issues

[a]All programs are meant to address geriatric syndromes and potential complications; however, for the purpose of this review, these syndromes and potential complications are more narrowly defined to six of the most common complications for older surgical patients
[b]Interventions are guided by the use of standardized assessment tools [4]

function and their ability to participate in complex medical decisions. This is particularly important when evaluating patients with cognitive impairment or dementia.

Please refer to the paper of Deschodt et al. that addresses the impact of geriatric consultation teams on clinical outcomes in acute hospitals and the work of Sennour et al., which describes the development and implementation of a proactive geriatric consultation model in collaboration with hospitalists [24, 25].

The following clinical vignette demonstrates the approach of the geriatric consult service in the acute care setting.

A 75 year old man had a coronary artery bypass graft (CABG) at a large community teaching hospital. His postoperative course was complicated by acute kidney injury, severe anemia, respiratory failure and delirium. His nurse described the patient as delusional, intermittently impulsive and restless. The patient was pulling his arterial line, chest tubes and catheters. He required pharmacologic intervention and physical restraints to address difficult behaviors. The geriatric consult service was formally consulted four days after his surgery. His geriatric syndromes were identified as hyperactive delirium, cognitive impairment in the setting of delirium, functional impairment, malnutrition, dysphagia, pain and sleep disorder. His multidisciplinary care team engaged a pharmacist, who reviewed the details of how the patient had taken medications prior to coming to the hospital. The patient's family reported that he was prescribed alprazolam. The patient was taking up to 3 to 4 pills of this medication a day for "anxiety." It was determined that the patient's delirium was multifactorial and the patient started on scheduled Lorazepam for benzodiazepine withdrawal. Restlessness and anxiety improved. The patient was more cooperative with nursing cares and medical treatments. He was slowly weaned off of his benzodiazepines and transitioned to a selective serotonin reuptake inhibitor. The geriatric consult service worked with the team to provide a detailed initial assessment and a daily monitoring of the plan of care.

Key elements to remember in this particular case include: the early identification of the patient's geriatric syndromes, the multidisciplinary team approach, and the timely communication with other medical/surgical disciplines to create a personalized and comprehensive plan of care.

The Community Aging in Place: Advancing Better Living for Elders (CAPABLE)

Another innovative model of care that addresses the unique needs of vulnerable community-dwelling older adults is the CAPABLE project. This model of care is based in the home-setting but demonstrates important concepts relevant to the care of vulnerable older adults. When older adults are discharged from the acute care setting, often, functional limitations and home environment are not taken into consideration when addressing transitions of care. Ignoring functional impairment and home environment in vulnerable older adults can have important repercussions in patient's quality of life and health care costs.

CAPABLE is a patient-directed, team-based intervention compromising of an occupational therapist, a registered nurse, and *a handyman*. The occupational therapist identifies problematic functional deficits and evaluates difficulties, safety concerns, and environmental barriers. The registered nurse, further, addresses pain issues, depression, and medication management. She/he communicates with the primary care provider, and helps to define functional goals. The handyman determines what equipment or home modifications are necessary to support patient's functional goals. The therapist and the nurse collaborate with other clinicians to discuss their challenging cases. The main goal of this model of care is to decrease hospitalization and nursing home admissions. The program focuses on community dwelling older adults with functional limitations who are eligible to Medicare and Medicaid. Older patients enrolled in this intervention have improved ability to perform their self-cares [26]. The novel aspect of this model is engaging a handy man with the health professionals to address the patient's needs in their home. Putting it all together, the hospital-based geriatric consult service could integrate the CAPABLE intervention to improve care for vulnerable community-dwelling older adults.

Acute Care for the Elders (ACE) Units

An ACE unit is an evidence model of care that focuses on improving the care of hospitalized older adults. The core components of the ACE Unit model of care are: (1) patient centered, (2) nurse-driven geriatric care process, (3) medical care review with an emphasis on preventing iatrogenic events, (4) early care transition planning, and (5) a prepared environment promoting safe mobility and cognitive stimulation. The main goal of the ACE unit is to prevent hospital-associated disability. The interdisciplinary team is an essential component of the ACE units**.** The members of the team include a geriatrician medical director, clinical nurse specialist, nurse manager, bedside nurses, social worker as well as other disciplines such as pharmacy, occupational and physical therapy, nutrition, dietitian, and chaplain. The interdisciplinary team emphasize on maintaining functional mobility, preventing and managing geriatric syndromes, and coordinating early care transitions. The interdisciplinary team led by geriatricians facilitates care coordination and thus identifies modifiable risk factors for geriatric syndromes to promote timely referrals to other disciplines or specialists.

Palmer and colleagues (1994) designed the first ACE unit at the University Hospitals of Cleveland [27]. A randomized controlled trial of Acute Care for Elders in an academic medical center reported improved functional status (ADL or activities of daily living, instrumental ADLs and ambulation) at the discharge of patients hospitalized in the ACE unit compared to those on other units. Fewer patients from the ACE group were discharged to nursing homes. These beneficial effects were achieved without increasing in-hospital or postdischarge costs. There were no significant differences in mortality, length of stay, readmission, or hospital costs between the two groups [28]. In another randomized trial conducted in a community hospital, patients were randomly assigned to either ACE care or a regular care unit. Positive outcomes of the ACE intervention were demonstrated in several processes of care including a reduction in restraint use, days to discharge planning, and use of high risk medications. They also found benefit in a composite outcome of ADL improvement and nursing home placement but not in discharge ADL levels alone. There was no significant reduction in length of stay, hospital costs, or mortality in the ACE unit subjects compared to the regular unit subjects [29].

In a 2012 published systemic review and meta-analysis for over 6800 hospitalized older adults, Fox et al. demonstrated that acute geriatric unit care based on all or part of the ACE Model improves patient and system level outcomes, including fewer fall risks, less delirium, less functional decline at discharge from baseline 2 weeks prehospital admission status, shorter LOS, fewer discharges to nursing home [30]. Data collection and following unit outcome measures is crucial to sustain the ACE unit and to maintain leadership and stakeholder support. Ongoing education of the interdisciplinary team will help to disseminate the ACE program to the rest of the hospital or across the health care system.

Nurses Improving the Care of Health System Elders (NICHE)

The NICHE program (www.nicheprogram.org) is a national program aimed at system improvement to achieve positive outcomes for hospitalized older adults. NICHE has two main goals: improving the quality of care to patients and improving nurse competence. This is accomplished by modifying the nurse practice environment with the infusion of geriatric-specific: (a) core values into the mission statement of the institution; (b) special equipment, supplies, and other resources; and (c) protocols and techniques that promote interdisciplinary collaboration [31]. NICHE includes several approaches, each of which facilitates transfusion of evidence-based geriatric best practices into hospital care. A geriatric nurse specialist as the NICHE Coordinator functions in both a primary care role (evaluating and managing patients directly) and in a leadership role (teaching and mentoring others and changing systems of care). Foundational to NICHE is the Geriatric Resource Nurse Model (GRN), which is an educational intervention model that prepares staff nurses as the clinical resource person on geriatric issues to other nurses on their unit. The GRN model provides staff nurses, via education and modeling by a NICHE coordinator, with specific content for improved knowledge of care management for geriatric syndromes. Clinical protocols and organizational strategies provide necessary tools to apply evidence-based practice. For example, in one NICHE orthopedic unit, GRNs received intensive education on the prevention and detection of delirium in a unit where the primary diagnoses were joint replacement and hip fracture repair. Utilizing a combination of standardized assessment of cognition and focused interventions to prevent post-op delirium, the unit realized a significant reduction in the incidence of delirium. Other NICHE hospitals have GRNs employ delirium-specific order sets.

In single site studies, NICHE hospitals demonstrate improved clinical outcomes, rate of compliance with geriatric institutional protocols; cost-related outcomes; and nurse knowledge [30]. A few studies using aggregate data from the NICHE Benchmarking Service have found that nurses who perceive that their hospital provides adequate geriatric-specific resources (continuing education, specialty services), promotes interdisciplinary collaboration, and fosters patient, family, and nurse involvement in treatment-related decision-making is associated with positive perception of quality geriatric care received by older patients [32–34].

NICHE also promotes a unit-based ACE model. The ACE model within NICHE emphasizes: (1) implementation of nurse-driven protocols, (2) geriatric training of all nursing staff, and (3) utilization of geriatric-specific units within a health system's overall geriatric care programming. Similar to other ACE studies, a NICHE-ACE unit in which the majority of the staff nurses were nationally certified in geriatric nursing reported lower fall and pressure ulcer rates, and lower length of stay when compared to overall hospital [35].

Since NICHE is a system-level approach it provides a structure for nurses to collaborate with other disciplines and to actively participate or coordinate other geriatric care models. For example, in hospitals with a geriatric department or consultation service, GRNs screen for appropriate referrals to these services and can effectively implement geriatric service recommendations with support from the NICHE coordinator. The models enhance NICHE program effectiveness by expanding the scope of geriatric programming within a health system.

The Hospital Elder Life Program (HELP)

The HELP program (http://www.hospitalelderlifeprogram.org/http://elderlife.med.yale.edu/public/public-main.php) targets the prevention and management of delirium, a common postoperative complication in older adults which increases the risk for prolonged length of stay, functional decline, institutional discharge, and 30-day readmission [6]. This multicomponent strategy includes the use of protocols that target delirium risk factors, addressing: mental orientation, therapeutic activities, early mobilization, vision and hearing adaptations, hydration and feeding assistance, and sleep enhancement. These protocols were tested in several well-designed clinical trials and demonstrated significant reduction in the incidence of new delirium. Further, among those who did develop delirium, these protocols are associated with a significant reduction of total number of episodes and days with delirium, functional decline, costs of hospital services, and reduction in use of long-term nursing home services [36, 37]. Moreover, HELP is useful for prevention of falls, one of the Medicare no-pay conditions [38] and has been shown to improve patient and family satisfaction, as well as nursing satisfaction [37, 39].

HELP employs geriatric specialists of various disciplines (geriatrician, geriatric nurse specialist, recreation therapy, and physical therapy) working together as an interdisciplinary team with trained volunteers. The program is coordinated by Elder Life Specialists, typically a nurse who has advanced geriatric nursing education and is responsible for implementing nursing-related assessments and tracking of delirium risk- factor protocol adherence. The latter depends on the involvement of well-trained and supervised volunteers in patient care interventions. The volunteers provide daily visits which focus on orienting communication, therapeutic activities, and assistance with mobilization, feeding and hydration, correction of vision and hearing deficits, and sleep hygiene [36].

Implementation in many hospitals has been adapted based on hospital resources. This has led to wide variations in adherence to the intervention protocol. Although higher levels of adherence have been associated with lower rates of delirium, these adapted protocols continue to provide positive results [40]. Recently, the HELP protocol set was expanded to include constipation and dehydration. Additionally, the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom enhanced the scope of the HELP program with three new protocols (hypoxia, infection, and pain) [41].

Transitional Care Models

Older adult patients with complex medical and social needs and their caregivers require assistance to effectively navigate the health care system, including recovery from surgery and return to premorbid health and living arrangements. There are numerous transitional care programs and the strength of the evidence to reduce post-discharge negative outcomes varies considerably. Two models that have demonstrated improved outcomes for older adults hospitalized for both medical and surgical interventions are the APN transitional care model and the Care Transitions model. More details can be found in ▶ Chap. 27, "Transitioning Care at Discharge."

The transitional care model (see http://www.transitionalcare.info/home) utilizes advanced practice nurses (APNs) whose primary responsibility is to optimize the health of high-risk, cognitively intact older adults with a variety of medical and surgical conditions during hospitalization and for designing and overseeing the plan for follow-up care following discharge. The APNs work collaboratively with the older adult, family caregiver, physician, and other health team members and are guided by evidence-based protocols. The same nurse implements this plan after discharge by providing traditional home care services and by phone availability 7 days a week.

The Care transitions coaching or Care Transitions Intervention (see http://www.caretransitions.org/index.asp) employs a nurse or "transitions coach" to encourage older patients and their family caregivers to assume more active roles during care transitions by facilitating self-management and direct communication between the patient/caregiver and primary care provider.

Surgical Specialty Models

Since recognition of comprehensive geriatric assessment enhances the recognition of older adults most likely to experience adverse events, independent of surgical prognostic indices [8], there has been proliferation of surgical programs consulting or integrating geriatrics. In some cases, a core geriatric interdisciplinary team screens patients for other related services such as palliative care, rehabilitative services, or pain management programs. Others have developed programs that integrate geriatrics within surgical specialties. Examples include orthopedics, cardiac surgery, oncology, and urology.

Orthogeriatric Models

The American College of Surgeons TQIP (Trauma Quality Improvement Program) Geriatric Trauma Management Guidelines (https://www.facs.org/quality-programs/trauma/tqip/best-practice) recommends specialized geriatric inpatient care including criteria for early geriatric consultation and geriatric expertise on the multidisciplinary trauma care team. During the last 25 years, orthopedic programs have emerged incorporating geriatrician input into hip surgery care. The expectation is that involvement of geriatricians in care management will avoid iatrogenic complications and streamline flow though in hospital care including early discharge that will improve survival, clinical, and cost outcomes [42].

There is, however, considerable variance in the way such orthogeriatrics programs are organized. These general models of practice include: (1) Routine geriatric consultation in which the geriatrician and/or geriatric interdisciplinary team consistently consults older patients admitted to an orthopedic hospital unit; (2) Geriatric unit, similar to an ACE unit, with the orthopedic surgeon providing consultation; and (3) Shared care or comanagement in which the responsibility for care of the older patient on an orthopedic unit is shared between the surgeon and the geriatrician [43]. In the last 10 years, comanagement has become the more utilized approach.

In addition to these different model types, the actual components of care that these orthogeriatric programs target also vary considerably [43]. For example, one program focuses on minimizing time to surgery and employment of standardized orders and protocols [44]. These programs have been shown to reduce delirium by over one-third, reduce severe delirium by over one-half, as well as decrease predicted length of stay, readmission rates, complication rates, and mortality [45]. Others have developed a geriatric trauma team that include a geriatrician and geriatric advanced practice nurse who evaluate older trauma patients and shared recommendations in weekly multidisciplinary rounds and performance improvement meetings of the trauma service. Most (91%) geriatric recommendations were followed and included: advanced care planning, disposition decisions to promote function, decreased inappropriate medications, and pain management [46].

The heterogeneity of the orthogeriatric programs (both the overall organization, personnel and the various assessments and interventions employed) makes it difficult to compare outcomes among these programs. A systematic review and meta-analysis of studies reporting outcomes associated with 18 orthogeriatric programs published between 1993 and 2012 [43]. Ten programs employed the routine geriatric consultation model of care and found significant decreases in long-term mortality, in-hospital mortality and time to surgery, compared to controls receiving traditional orthopedic oversight. It was not possible to report conclusions concerning the three geriatric unit studies due to low quality methodology and sample size. The five comanagement studies demonstrated shortened length of stay, compared to controls. Among the 18 studies, several varied clinical interventions were reported such as reduced post-op complications including decreased incidence of delirium and functional decline.

Since 2012, two other reviews of comanaged care have reported similar findings: reduction of short- and long-term mortality and in-hospital complication [42, 47]. Also two randomized control trials of orthogeriatric care have shown improved mobility at 4 months postsurgery compared to controls [48, 49].

The growing trend of orthogeriatric comanagement is consistent with US health care systems moving toward more integrated, multidisciplinary care. The studies to date demonstrate that consistent geriatric input embedded into the orthopedic service is ideal since “as needed” geriatric consultation is often too late to prevent common complications of older patients [42]. Reporting of a consistent set of outcomes is needed; the AO trauma network of Europe recommends that the following parameters should be collected at discharge: mortality, length of stay, time to surgery, complications (medical and surgical), and costs. At admission, quality of life, pain, satisfaction, function, falls, medication use, and place of residence should be collected [50]. Then, depending on the type of parameter, they as well as readmission rates should also be collected 30 days, 90 days, and 1-year post surgery.

Surgical Onco-Geriatrics

Cancer is considered mainly a disease of older adults, given that those over 65 years of age represent approximately 60% of cancer patients and account for 70% of annual cancer deaths. Additionally, the high complication rate, such as delirium, [51] with treatment has led to considerable attention of integrating geriatric assessment into standard oncology practice. A systematic review of nine systematic reviews reported that evaluations of functional status, comorbidity, and frailty are the most predictive of post-oncology surgery complications [52].

In response, oncology programs have either developed onco-geriatric consultation teams or have developed geriatric – oncology units, some of which are part of an existing ACE unit to address prevention or reduction of these complications [53–56]. These programs report that older oncology patients have more complex medical and social needs than adult oncology patients and thus require input from both perspectives.

Other Surgical Specialties

Both general surgery and other surgical specialties (urology, vascular surgery, cardiothoracic surgery, and neurosurgery) are developing geriatric comanagement programs. A VA hospital with these multiple comanagement surgical units reported higher rates of discharge back to the community [57]. A urology comanagement program utilizing a geriatrician-led unit rounds resulted in reduced inpatient stay by and total postoperative complications [58].

Conclusion

Although these models use different strategies, all share common goals of treatment. Each hospital or health system chooses a model based on the unique needs of that hospital's patient population, the resources available (geriatric specialists, bed capacity to support separate unit, volunteers, etc.) and especially senior administrator's commitment to geriatric programming. Since there is no direct reimbursement for many components of these models (interdisciplinary rounds, geriatric nurse specialist, volunteers, etc.), administrators seek external (grants, donor gifts) and internal funding (hospital foundation grants). Administrators are motivated by the model's alignment to the hospitals strategic plan (e.g., excellence in senior care), the institution's mission, patient/family satisfaction, relationship with the community, and costs savings by cost avoidance (i.e., reduction of complications). All of the models have demonstrated positive outcomes and each have been implemented in at least 50 hospitals; however, this still only represents a small proportion of American hospitals.

Each model was originally developed with government and/or foundation support. Future survival of these models may depend on advancing the unique contributions of each within an integrated model that will enhance the hospital experience of the older patient and/or integrating geriatrics within surgical subspecialties. Fulmer and Berman (2016) [59] of the John A. Hartford Foundation posit, "How do we move from a model at a time to a set of strategies that transform systems, drive improved health and cost outcomes, efficiently utilize available resources, deploy them strategically to those at greatest risk, and create the least amount of stress on the care delivery system?" The John A. Hartford Foundation has launched a new Age-Friendly Health Systems Initiative is launching with. Along with the Institute for Healthcare Improvement and the American Hospital Association, a \$3.19 million grant over 42 months will focus on initiating and evaluating a health systems-wide prototype model of care for older adults. The overall goal is that 20% of hospitals and health systems in the United States will be "age friendly" by 2020.

Another problem influencing geriatric model implementation is availability of geriatric clinicians. Since significant geriatric medicine input is needed for many of these models, they generally are limited to academic medical centers, which only represent a small proportion of US hospitals. All of these models require providers with knowledge of core concepts in geriatrics; however, there is a significant shortage of fellowship-trained geriatricians, geriatric psychiatrists, master's prepared geriatric nurse specialists, as well as other disciplines [60]. In addition to efforts to increase the training of geriatric specialists, several initiatives are underway that involve specialty organizations, medical schools, and resident training programs to integrate principles of geriatric care into curriculums and practice [61].

As more geriatrics is being integrated into undergraduate medical training and surgical resident training, knowledge of geriatric care principles, and collaboration with geriatric models will enhance outcomes of the older surgical patients. The Council of the Section for Surgical and Related Medical Specialties in the American Geriatrics Society program provides the Geriatrics Syllabus for Specialists; a useful guide (lectures, PowerPoint presentations, etc.) geared toward providing vital information for surgeons caring for older patients as well as faculty leadership training to promote geriatric training and research within their disciplines. The Special Resident toolkits are available for anesthesiology, general surgery, gynecology-urology, ophthalmology, and orthopedic surgery. The initiative also enables surgical professional certifying bodies and societies to build the capacity of their members to provide better care of older adults [62].

Financial and administrative barriers deter the implementation of geriatric models. Medicare payment system focuses on provider-specific reimbursement and thus limits payment for organizational redesign, multidisciplinary teams or nurse-coordinators. The new CMS financial incentives that will not reimburse for nosocomial "never" events such as pressure ulcers, catheter-associated infections, and fall-related injury, may eventually encourage the use of these models [9]. An IOM report recommended that "payers should promote and reward the dissemination of those models of care for older adults that have been shown to be effective and efficient" [60]. It is expected that these types of programs will increase in the next decade. In 2015, the John A. Harford Foundation awarded a $400,000 grant to the American Geriatric Society to develop a business strategy for implementing orthogeriatrics comanagement programs. This is expected to result in a business plan including marketing, training, outcome goals, and budget to facilitate sustainable programs.

Finally, most of the research documenting complications of the older patient are based on studies combining both medical and surgical patients, thus future research should address the risk factors of these complications specific to surgical patients. Further, with the exception of hip fracture and cardiac surgery, additional studies should also identify complications within specific types of surgical procedures. This may provide important data to tailor models to specific surgical populations.

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24 Nursing Issues in Older Adult Surgery Patients

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Abstract
Models of care addressing the unique needs of older hospitalized patients can be traced to the comprehensive geriatric assessment (CGA) programs first developed in the 1970s [1]. CGA programs screen older patients at high risk for geriatric-specific problems, assess for modifiable risk factors, and implement evidence-based strategies consistent with the patient's treatment goals. Over the last 30 years changes in the health-care system, coupled with the increasing older adult population, has led to development of several geriatric models of care across all health-care settings. In general, the goals of these geriatric models of care in the hospital focus on (1) prevention of complications that occur more commonly in older adults and (2) address hospital factors that contribute to complications. This chapter provides a brief overview of complications that are more frequently found in older patients, care delivery issues that are addressed by geriatric models of care and a description of the most commonly employed hospital models.

Complications of Older Hospitalized Patients

Although patients aged 65 and over represent about 13% of the US population, they account for 40% of those undergoing surgical procedures in American hospitals [2]. In addition to the high proportion of older patients, the most troublesome finding is that older patients also represent a higher complication rate for certain conditions which subsequently lead to higher health-care costs. Age may be viewed as a proxy for multiple chronic diseases. Postoperative complications that are known determinants of short and long-term survival following major surgery such as myocardial infarction and sepsis are associated with age due to the increased likelihood of co-morbidities such as cardiac disease [3].

Older adults are more likely to experience additional types of complications that, in addition to reducing survival, can result in loss of independence and lead to hospital readmission, increased usage of rehabilitation services, and new placement in a nursing home. Physical frailty and cognitive impairment [4–6] (either chronic dementia and/or delirium) can further compound an older person's vulnerability to complications during hospitalization [7, 8]. Frailty refers to "decreased reserves in multiple organ systems" [9] that is highly associated (after controlling for age, race, sex, and comorbid illness) with an increased risk for falls, cardiovascular disease, hypertension as well as reduced mobility, decreased functional status, institutionalization, and death (see Chap. 10, "Invited Commentary") [10, 11].

Persons with dementia are more prone to negative outcomes related to disease management and hospitalization. Older patients with dementia hospitalized for exacerbation of a chronic disease have significantly longer lengths of hospital stays (LOS) as compared to older patients without dementia. For example, the LOS of older patient with COPD is 121 days/1,000 persons as compared to older patients with both COPD and dementia, who have a LOS of 361 days/1,000 persons [12]. For those who develop delirium (for both those with and without an underlying chronic dementia) during hospitalization, increased LOS and higher hospital costs is well documented [13]. The complex challenges of those adult patients with cognitive impairment are often not adequately addressed. Table 1 provides examples of common behaviors of cognitively impaired persons that can lead to complications.

Although geriatric models of care can improve the overall outcomes and experiences of hospitalization, in general, these programs are designed to

Table 1 Behaviors of cognitively impaired patients contributing to high complication rate

Behaviors	Example	Potential complication
Inability to follow directions	Does not use call bell to ask for assistance and gets out of bed without needed assistance	Fall-related injury
Removal of treatments	Pulls out central lines	Hemorrhage Infection Physical restraints and associated complications
Not able to communicate needs	In pain but not able to verbally communicate this to nurse	Functional decline
Wandering	Leaves unit and exits hospital in gown	Hypothermia Other injuries Use of physical and chemical restraints that increase likelihood of delirium, falls, fall-related injury, nutritional problems
Misinterprets visual and auditory cues	Resists staff attempts to assist the patient to get out of bed which is perceived as an assault and then hits staff	Agitation-related injury Overuse of psychoactive medication that increase likelihood of delirium, falls, and fall-related injury
Decreases inhibition of inappropriate behaviors	Removes clothing and walk down hallway nude	Agitation-related injury Overuse of psychoactive medication that increases likelihood of delirium, falls, and fall-related injury

target those adverse events that occur more commonly in older patients. Table 2 provides a summary of these complications and the clinical and cost outcomes associated with these complications. These complications are often referred to as "geriatric syndromes" which refer to "clinical conditions in older persons that do not fit into discrete disease categories" [14].

A US congressional mandate instituted on August 1, 2007 significantly changed the Inpatient Prospective Payment System that the Centers for Medicare & Medicaid Services (CMS) use to reimburse hospitals [15–17]. As of October 2008, hospitals will no longer receive payment for eight hospital-acquired conditions; three of these eight are complications that are known to occur most frequently in older inpatients and have been found to be reduced when geriatric models of care are employed [18]. These three complications (fall-related injury, pressure ulcer, and catheter-associated urinary tract infection) are among the six adverse events or complications specifically associated with hospitalization of older adults. Although there are other geriatric syndromes (e.g., incontinence) and other potential complications associated with older inpatients (e.g., sleep deprivation, inadequate pain management, dehydration, adverse drug effects), many of these syndromes and complications are either risk factors or outcomes of the following.

Functional Decline

Functional decline refers to the loss of the ability to perform basic activities of daily living (ADL). A systematic review of 30 studies examining correlates of functional decline found that between 15 and 76% of hospitalized elders experience diminished performance in at least one ADL at discharge [19]. Of those with decline at discharge, only half will recover function at 3 months post-discharge, and, for many, this decline will result in permanent loss of independent living [20, 21]. Functional decline is considered a "profound marker of morbidity and mortality" [22, 23] resulting in longer lengths of stay, greater costs and increased rate of nursing home placement [24]. Among the ADLs, the ability to walk independently is considered the most critical in predicting health outcomes. Functional Mobility

Decline, defined as new walking dependence, is associated with poor posthospitalization outcomes such as discharge to a nursing home, continued impaired mobility and higher mortality rates [25]. The incidence of functional mobility decline occurs in 15–59% of hospitalized elders [26]. For older hip fracture patients, especially those with cognitive and affective disorders, there is a greater risk of functional decline and new nursing home placement [27, 28].

Table 2 Complications in the older surgical patient[a]

Complication	Hospital factors[b]	Clinical outcome	Cost implications
Functional decline	Immobility Bed rest without medical/ surgical indication Physical restraint Inappropriate medication prescribing New psychoactive drug use Obstacles in the hospital physical environment	Reduced/loss of independence in function (activities of daily living) Reduced/loss of ambulation Pain Increased rate of pressure ulcers, falls, fall-related injuries, and development of contractures	Longer length of stay (LOS) Increased rate of institutional or home-based rehabilitation Nursing home placement
Fall-related injury	Immobility Physical restraint Inappropriate medication prescribing New psychoactive drug use Obstacles in the hospital physical environment	Pain Fracture requiring surgical intervention Reduced/loss of independence in function (activities of daily living) Reduced/loss of ambulation	Medicare will not pay for treatment[c] Surgery Longer LOS Institutional or home-based rehabilitation Nursing home placement
Under/malnutrition	Immobility Inattention to oral care Lack of feeding assistance for those with physical or cognitive impairments	Reduced wound healing Discomfort due nasogastric tube placement Percutaneous enteral access procedures (gastrostomy) Delirium Physical restraint to prevent tube removal Aspiration Functional decline	Longer LOS Surgery Institutional or home-based enteral nutrition therapy
Pressure ulcer	Immobility Physical restraint Under/malnutrition Dehydration	Immobility Sleep deprivation Pain Sepsis Septicemia Surgical debridement Surgical techniques (direct closure, flaps, and skin grafting)	Medicare will not pay for treatment[b] Longer LOS Institutional or home-based skilled nursing treatment
Urinary tract infection (UTI: secondary to catheter use or CAUTI)	Emergency room placement without indication Incontinence treatment No postsurgical monitoring of catheter use	Immobility Pain Delirium Acute pyelonephritis Bacteremia Sepsis Prosthetic joint infection Higher risk for death	Medicare will not pay for treatment[b] Longer LOS Rehospitalization

(continued)

Table 2 (continued)

Complication	Hospital factors[b]	Clinical outcome	Cost implications
Delirium	Physical restraint Inappropriate medication prescribing New psychoactive drugs Urinary catheterization CAUTI Immobility Under/malnutrition Dehydration	Functional decline Persistent cognitive impairment Falls, injuries Undetected infection Sleep deprivation	Longer LOS Rehospitalization Nursing home placement Death

[a]Geriatric syndromes refer to "clinical conditions in older persons that do not fit into discrete disease categories." This may also include other conditions highly associated with aging such as frailty, sleep disorders, self-neglect. For the purpose of this review, these syndromes and potential complications are more narrowly defined

[b]Hospital factors. There is a myriad of patient and hospital factors that contribute to each complication, however, this list provides examples of those specific hospital practices that place the older adults at high risk and which are the focus of geriatric care model interventions

[c]As of October 2008, hospitals will no longer receive payment for 8 hospital-acquired conditions; 3 of these 8 indicated in the table are complications that are known to occur most frequently in older inpatients and have been found to be reduced when geriatric models of care are employed (fall-related injury, pressure ulcer, and catheter-associated urinary track infection)

Fall-Related Injury

Roughly 2–5% of older adults fall during hospitalization [29]. The number of falls per 1,000 patient days is highest in hospital units admitting mostly older adults such as geropsychiatry, rehabilitation, and geriatric medicine. Among hospitalized older adults, falls from bed account for approximately one-third of all falls. Almost one-third of all fall-related injuries occur among persons 85 years of age or older. Approximately 3–10% of falls happening in hospitals result in either serious or minor injuries [30]. Hip fractures, occurring in about 1–4% of hospital falls are particularly significant because older adults are more likely to suffer from a substantial decline in physical functioning and often require longer periods of active rehabilitation services as compared to younger persons [31].

Undernutrition/Malnutrition

Undernutrition and malnutrition are deficiency syndromes caused by inadequate intake or absorption of macronutrients. Malnutrition has long been associated with important adverse outcomes, such as increased morbidity and mortality and decreased quality of life. Weight loss and hypoalbuminemia are both strongly correlated with increased mortality in ill adults [32]. Body weight and body composition have important implications for physical functioning of older persons and the prevalence of malnutrition in older hospitalized patients has been estimated to be between 40 and 60% [33].

Pressure Ulcers

Pressure ulcers continue to present a major health problem for hospitalized adults with reported nosocomial incidence rates between 0.4 and 38% [34]. Pressure ulcers are highly correlated with age [35]. At least a fifth of pressure ulcers will progress to a more advanced stage of deterioration. Most ulcers develop in the sacrum and coccyx areas with rates higher in patients with mobility impairment. Pressure ulcers remain a major cause of morbidity and are associated with longer lengths of hospital stay. Nosocomial pressure ulcers and their progression in severity during hospitalization have been used as a quality care indicator [36].

Urinary Tract Infection

Approximately 4% of patients with urinary tract infection (UTIs) will develop bacteremia which is known to significantly increase in length of stay and is associated with higher mortality in older patients [37]. The major care-associated practice leading to UTI in older inpatients is the overuse of urinary catheters, defined as catheter use for longer than 2 days [38]. Catheter-associated urinary tract infection (CAUTI) is the most common nosocomial infection [39]. A study using a random sample of almost 36,000 Medicare patients undergoing major operations from 2,965 US hospitals reported that 86% had perioperative indwelling urinary catheters and among these 50% had catheters for longer than 2 days postoperatively. These patients' risk of developing a urinary tract infection was twice as likely compared to patients with catheterization [40]. Among another sample of approximately 39,000 Medicare patients undergoing major surgery who were discharged to a nursing home it was found that those patients discharged with catheters were at higher risk for rehospitalization for UTI and death within 30 days than patients who did not have catheters [41].

In addition to infection, catheter use is associated with immobility, delirium, and pain [42].

Delirium

Delirium, a transient state of cognitive impairment, may develop in both cognitively intact and impaired older adults. It is estimated that between 14 and 24% of older persons are admitted to the hospital with delirium, and an additional 6–56% of hospitalized elders will develop delirium during their hospitalization replace especially if they are admitted to an ICU [43]. Postoperative delirium is more likely to occur following hip fracture, cardiac, non-cardiac thoracic, aortic aneurysm, and abdominal surgery. Postoperative delirium is more likely in those deemed vulnerable. Patient vulnerability including presence of previous brain pathology, decreased ability to manage change, impaired sensory function, multiple co-morbidities and changes in pharmacodynamic responses to medications, are all suggested possible causes for delirium. In surgical patients both preoperative (use of narcotic analgesics, history of alcohol abuse and depression) and perioperative (greater intraoperative blood loss, more postoperative transfusions, postoperative hematocrit less than 30%, and severe postoperative pain) risk factors have been identified for delirium postoperatively [44]. Additionally, hospital practices that lead to iatrogenic events including use of physical restraints, malnutrition, more than three medications and urinary catheterization are also significantly associated with delirium [45]. There are no significant differences in incidence of postoperative delirium following general vs. epidural anesthesia.

Despite high incidence, most delirium goes undetected [46, 47] thus contributing to many negative consequences. Delirium is associated with poor hospital outcomes such as higher mortality rates, increased length of hospital stay, increased intensity of nursing care, greater health-care costs as well as increased risk of several adverse outcomes after discharge, including functional decline, persistent cognitive impairment, rehospitalization, and nursing home placement [48].

The occurrence of each of these complications leads to interventions that can often prolong the hospital stay. Following hospital discharge, they frequently contribute to death, institutionalization as well as disproportionately high rehospitalization rates, high emergency department usage, and increased need for rehabilitation therapy services. As illustrated in Table 2, the *interrelationships* among these various complications during hospitalization is obvious and also well documented [12]. The data supporting the importance of prevention, early detection, and treatment of these complications in older surgical patients is described in the ACOVE (Assessing Care of Vulnerable Elders) report, Quality Indicators for Hospitalization and Surgery in Vulnerable Elders [49].

Although patient characteristics, especially multiple co-morbidities, frailty, and cognitive impairment, may increase vulnerability of older inpatient to negative consequences, the hospital environment plays an independent and significant role in determining staff practice and subsequent patient outcomes such as iatrogenic complications. This has led to the development of geriatric models to address these hospital-based or institutional factors that are likely to contribute to complications among older patients. Effective resolution of these negative consequences is dependent on geriatric models that target both patient and environmental (institutional) risk factors.

Geriatric Care Model Objectives

Although geriatric models of care differ in their approach to prevent complications and address care delivery problems that can contribute to complications, all share a common set of general objectives. Although these objectives could be applied to any patient regardless of age, it is how geriatric care models apply these that are age-specific. Table 3 provides examples of processes and interventions to meet these six general objectives.

The six general objectives of geriatric care models are as follows.

Educate Health-Care Providers in Core Geriatric Principles

The complications most frequently encountered among older patients are often due to system-level problems. These include inadequate educational preparation of health-care providers to recognize age-specific factors that increase risk of complications. All geriatric care models require a coordinator or clinician with advanced geriatric education; however, the implementation of any model depends on direct care staff with the knowledge and competencies to deliver safe and evidence-based care to older patients. Thus, the coordinator or other geriatric clinician role includes teaching of other staff through rounds, journal clubs, conferences, and other internal institutional educational venues.

Target Risk Factors for Complications

Given the disproportion of certain complications or geriatric syndromes among hospitalized older adults, the clinical focus of all geriatric models is prevention via risk factor reduction and early detection of these problems. Some models may focus on a particular syndrome; however, the interrelationship of these complications and their shared risk factors often result in a reduction of the other geriatric syndromes. Targeting risk factors requires standardized assessment tools known to be valid and reliable for older adults. See the Hartford Institute's Try This and How to Try This series for examples of assessment instruments (http://www.hartfordign.org/trythis). Implementation of geriatric care models often include institutionalizing these practices such as incorporating these tools in the medical record as well as hospital policies, procedures, and protocols.

Incorporate Patient (Family) Choices and Treatment Goals

All health-care decisions should be guided by the patient's choices. Choices range from decisions about activity level and medication use to more complex issues including advance directives.

Decisions regarding life-sustaining treatment are often influenced by quality of life considerations balanced by the potential length of life. For family members acting in the best interests of patients who can no longer participate in decision-making, this can be a complicated dilemma. Life-sustaining treatments are often employed with very old patients who die in the course of hospitalization although most prefer comfort care. Geriatric models are meant to address this lack of congruence by supporting efforts to provide care that is more consistent with patients' preferences [50]. For this reason, many geriatric models work collaboratively or in conjunction with palliative care programs.

Employ Evidence-Based Interventions

Given that most physicians, nurses, and other health providers have received minimal content in their training regarding geriatrics, it is not surprising that there is a higher complication rate for older

Table 3 Geriatric care models: objectives, processes and interventions

Objective	Examples of processes	Examples of interventions
Educate health-care providers in core geriatric principles	Resident training includes required geriatric rotation *or* mandatory geriatric rotation for residents Institutional continuing education includes geriatric-specific training *or* Geriatric-specific interdisciplinary continuing education programs Geriatric specialist responsible for geriatric training initiatives	Hospital intranet includes geriatric programming Journal club includes geriatric journals and/or articles focusing on geriatric outcomes Medical, surgical, nursing, and interdisciplinary rounds includes geriatric case studies
Target risk factors for complications	Policies, protocols, and documentation system includes assessment tools and practices that identify older adults at risk for complications Assessment tools prompt providers to consult geriatric specialists for evaluation of high-risk problems Geriatric specialist provides individual evaluation of risk factors	Electronic medical record (EMR) provides alerts for medications prescribed that are known to increase fall risk EMR prompts providers to document daily cognitive testing results Hospital policy for daily cognitive assessment of at-risk patients Cognitive assessment indicates delirium that leads to geriatric specialist consultation
Incorporate patient (family) choices and treatment goals	Policies and protocols support and documentation system includes forms that elicit patient choices as well as family involvement in care Geriatric nurses are prepared to coordinate an interdisciplinary evaluation and promote development of *informed* patient/family treatment goals and plan of care Palliative care is consulted and provides informed choices to patients/families in situations of life- threatening illness	Admission history includes evaluation of patient's preferences for postdischarge rehabilitation Unlimited visiting hours and bedside recliners encourage family participation in recovery Patient and family preferences for type and degree of family involvement is documented Patient with Alzheimer's disease who is unable to verbally indicate needs is evaluated by palliative care specialist for pain evaluation/treatment
Employ evidence-based interventions	Policies and protocols integrate geriatric specific implications Education and training for all clinicians include core geriatric content	Hospital protocol for urinary catheter removal within 2 days postsurgery Unit-based mobility program Physical environment reduces injury risk for nonambulatory patients with dementia such as low-height beds and bedside mats
Promote interdisciplinary communication	Medical record facilitates patient information across disciplines Processes in place to encourage face-to-face interaction among disciplines Unit-based and hospital-wide committee includes geriatric specialist representation	Interdisciplinary team rounds held bi-weekly Programmatic initiatives include all applicable disciplines, e.g., physical and occupational therapy in unit-based mobility program Co-manage patients across specialties such as geriatric oncology Collaborate with other programs such as palliative care in providing symptom management
Emphasize discharge planning or transitional care	Documentation system provides comprehensive hospital course information to primary care provider and other postdischarge providers (home care, nursing home, etc.) as well as elicits pertinent information *from* other providers	Patient and caregiver receive comprehensive documentation of hospital treatment, changes in treatment plan, and postdischarge instructions Understanding of instructions is evaluated before discharge Phone follow-up postdischarge to evaluate patient condition and needs

hospitalized patients. Advances in geriatric science, similar to other research-based approaches, are not readily employed in hospital care. Problems with polypharmacy, inappropriate medications (e.g., overuse of psychoactive), overuse of restraints, inadequate detection of delirium, depression, and undermanagement of pain are some of the many hospital factors that can contribute to poor outcomes. Thus, geriatric models promote the use of standardized evidence-based protocols.

Promote Interdisciplinary Communication

Since geriatric syndromes are not just medical problems but represent a complex interaction of medical, functional, psychological, and social issues, other disciplines such as nursing, pharmacy, social work, physical and occupational therapy are needed. Geriatric care models all include interdisciplinary teams, i.e., an approach that facilitates communication among disciplines.

Emphasize Discharge Planning (or Transitional Care)

Many older patients will require rehabilitation or skilled nursing services following hospitalization. Almost a quarter of older hospital patients are discharged to another institution such as a rehabilitation hospital or nursing home and more than 10% are discharged with home care [51]. Older adults are more likely to experience problems associated with discharge planning that can lead to delays in discharge and greater use of emergency service use and hospital readmission. Hospital readmission for older patients is most likely associated with medical errors in medication continuity [52, 53], diagnostic workup, or test follow-up [54]. These poor outcomes are attributed to a lack of coordination among health-care providers that can result in unresolved medical issues [55] and deficient preparation of patients and their caregivers to carry out discharge instructions [56]. One study found wide variations among providers in discharge planning effectiveness; the providers cited their lack of knowledge and experience when not making appropriate home-care referrals [57]. Thus, geriatric models not only focus on the inpatient experience but also the post-hospital care environment and the care transition following hospital discharge. Two of the six models consider the care transition a primary focus of their programs.

Geriatric Models

There are several types of geriatric models that are currently employed in hospitals throughout the USA. In addition to incorporating the original tenets central to comprehensive geriatric assessment (screen for those at high risk for geriatric-specific problems, assess for modifiable risk factors, and implement strategies consistent with the patients' treatment goals), all strive to deliver quality care for older adults in a cost-effective manner. Comprehensive geriatric assessment assumes that the systematic evaluation of a frail older person by a multidisciplinary health-care team will uncover actual or potential health problems. The considerable advances in geriatric health-care science over the last 30 years can then be applied to treating or preventing these conditions and thus result in better health outcomes.

Although the specific mode of intervening may differ among the models, they all address both common health problems and care delivery issues. The geriatric model may consider all geriatric syndromes or target specific ones such as delirium or functional decline. Similarly, the geriatric model may be employed as a hospital-wide approach, unit-based intervention, or focus on specific processes of hospitalization such as admission screening or discharge planning. Regardless of the structure of the geriatric model, all facilitate the general objectives listed in Table 3. Table 4 provides a summary of the clinical foci, unique features, coordination, and interventions for each of the six most commonly employed geriatric models of care.

Table 4 Core components of six geriatric care models

Model type	Clinical outcome focus[a]	Unique features	Program/team coordination	Interventions[b]
Geriatric Consultation	Primary focus can vary depending on composition of consult team & may be specific to a surgical specialty or procedure	Employed by primary provider request	Individual consultant (geriatrician, gero-psychiatrist or geriatric nurse specialist) *or* Interdisciplinary team that is coordinated by geriatric medicine or psychiatry fellow, geriatric nurse specialist or an administrative director	Comprehensive geriatric assessment: medical, psychiatric, functional, and social Recommends interventions based on consultant discipline (medicine, psychiatry, or team that includes nurses, social workers, and others) Primary provider chooses which recommendation to employ
Acute Care for the Elderly (ACE)	Functional decline	Dedicated unit with explicit admission criteria Requires interdisciplinary team Redesign of physical environment to accommodate physical and cognitive needs	Unit directed and/or team coordinated by geriatrician, geriatric nurse specialist, administrator or co-managed by clinician-manager	Physical environment to promote patient mobility, orientation and staff observation Interdisciplinary rounds facilitate care coordination and thus: Identify modifiable risk factors for geriatric syndromes and complications Prevent avoidable discharge delay Promote timely referrals to disciplines or specialists
NICHE: GRN/ACE	Nursing processes related to all geriatric syndromes and potential complications such as avoiding restraint use, initiating urinary catheter removal	Focus on improving nursing care of all geriatric syndromes Prepares staff nurses to take active part in geriatric care management including coordinating or facilitating other geriatric models of care	Program implementation by NICHE Coordinator (usually a geriatric nurse specialist) Geriatric Resources Nurses (staff nurses with additional training) implement protocols Depending on availability, other clinicians (geriatrician, hospitalist, social worker, etc.) work as interdisciplinary team	Nurse-initiated protocols: Restraint and psychoactive drug reduction Functional mobility Fall/injury prevention Pressure ulcer assessment/treatment Prevention of UTI – early catheter removal Delirium assessment/treatment Organizational strategies including measurement schema, performance improvement techniques, and management tools to promote implementation of above protocols

(continued)

Table 4 (continued)

Model type	Clinical outcome focus[a]	Unique features	Program/team coordination	Interventions[b]
HELP	Delirium prevention and early management	Requires use of volunteers	Elder Life Nurse Specialist or Elder Life Specialists coordinates interdisciplinary team (geriatrician, recreation therapy, physical therapy, etc.) and trained volunteers	Delirium risk factor protocols: Mental orientation Therapeutic activities Early mobilization Vision and hearing adaptations Hydration and feeding assistance Sleep enhancement
APN Transitional Care Model	Reducing complications specific during the transition from hospital to home	Requires advanced practice nurse coordinator to follow patient in hospital and following discharge	Advanced Practice Nurse (nurse practitioner or clinical nurse specialist)	Protocols to assess/ intervene with: Medication discrepancies and inappropriate medication usage Case management and APN surveillance across settings
The Care Transitions Intervention	Reducing complications specific during the transition from hospital to home, such as preventing posthospital medication discrepancies, increase likehhood of patient/ caregiver detection of worsening condition	Requires nurse transitions coach to follow patient in hospital and following discharge	Transition Coach (nurse or advanced practice nurse) empowers patient and caregiver	Personal Health Record includes data elements essential to promote productive patient–provider encounters across settings Discharge Preparation Checklist to facilitate patient's knowledge of discharge instructions Medication Discrepancy Tool used by transition coach to identify medication issues

[a]All programs are meant to address geriatric syndromes and potential complications. Geriatric syndromes refer to "clinical conditions in older persons that do not fit into discrete disease categories." This may also include other conditions highly associated with aging such as frailty, sleep disorders, self-neglect. For the purpose of this review, these syndromes and potential complications are more narrowly defined to 6 of the most common complications

[b]Interventions are guided by the use of standardized assessment tools known to be valid and reliable for older adults. See the Hartford Institute's Try This and How to Try This series for examples of assessment instruments (http://www.hartfordign.org/trythis)

Geriatric Consultation Service

Geriatric Consultation Service provides a geriatrician, a gero-psychiatrist, a geriatric clinical nurse specialist or an interdisciplinary team of geriatric health-care providers to conduct a comprehensive geriatric assessment or evaluate a specific condition (delirium), symptom (patient dislodges or removes treatment), or situation (adequacy of family support for discharge back to community setting). The consultation may be requested by another primary service for an individual patient or may be initiated by a hospital policy for all patients that are screened at high risk for geriatric-related complications or are admitted from a homebound program or a nursing home [58].

Outside of academic medical centers, few hospitals have geriatric departments that can provide geriatricians or a geriatric consultation team. Although geriatric nurse specialists may be more prevalent in hospitals than geriatricians, many function without the benefit of a geriatric team or a geriatrician. Similar to geriatricians, it is difficult to evaluate their effectiveness when their practice is limited to a consultative role in which recommendations may not be followed or institutional resources are not adequately available for staff to implement [59].

Acute Care for the Elderly Units

Acute Care for the Elderly (ACE) Units are discrete geriatric care-focused units. Originally developed in the 1970s within Veterans Administration Hospitals, Geriatric Evaluation and Management (GEM) Units were meant to provide comprehensive geriatric assessment delivered by a multidisciplinary team with a focus on the rehabilitative needs of older patients. Multidisciplinary team rounds and patient-centered team conferences are considered the hallmarks of care. The core team includes a geriatrician, clinical nurse specialist, social worker as well as specialists from other disciplines providing consultation: occupational and physical therapy, nutrition, pharmacy, audiology, and psychology. GEM units usually have been redesigned to facilitate care of the older patient, which, in contrast to geriatric consultation services, have direct control over the implementation of team recommendations. Research conducted in the 1980s and 1990s have documented significant reductions in functional decline and suboptimal medication use as well as return to home postdischarge and, more recently, decreased rate of nursing home placement [60] among hospitalized veterans on GEMUs compared to general medical units.

Beginning in the 1990s, Acute Care of Elders (ACE) Units have been implemented in non-VA hospitals although they generally focus on more acutely ill patients than GEM units. These units utilize staff with geriatric expertise working collaboratively in an interdisciplinary team (fostered by care processes such as team rounds and family conferences) in a physical environment with adaptations to addresses age- related changes (e.g., flooring to reduce glare and low-height beds to reduce fall-related injury), promote orientation (clocks and calendars) and facilitate staff observation (e.g., alarmed exit doors, windows inserted in walls and communal space for meals). The interdisciplinary team (led by geriatricians and/or geriatric nurse specialists) aims to facilitate care coordination and thus identify modifiable risk factors for geriatric syndromes and complications, prevent avoidable discharge delay, and promote timely referrals to disciplines/specialist.

Palmer et al. designed the first ACE unit at the University Hospitals of Cleveland [61]. A randomized controlled trial of Acute Care for Elders in an academic medical center reported improved functional status (ADL or activities of daily living, instrumental ADLs and ambulation) at discharge of patients hospitalized on the ACE unit compared to those on other units. Fewer patients from the ACE group were discharged to nursing homes. These beneficial effects were achieved without increasing in-hospital or postdischarge costs. There were no significant differences in mortality, length of stay, readmission, or hospital costs between the two groups [62]. In another randomized trial conducted in a community hospital, patients were randomly assigned to either ACE care or a regular care unit. Positive outcomes of the ACE intervention was demonstrated in several processes of care including a reduction in restraint use, days to discharge planning and use of high-risk medications. They also found benefit in a composite outcome of ADL improvement and nursing home placement but not in discharge ADL levels alone. There was no significant reduction in length of stay, hospital costs, or mortality in the ACE unit subjects compared to the regular unit subjects [63]. These savings are recognized in integrated health-care delivery systems such as the VA, Kaiser, and PACE (Program of All Inclusive Care of the Elderly); however, our current "silo-based" reimbursement system to individual hospitals does not provide incentives for postdischarge reductions in health services usage [64].

Since one unit cannot provide care for all older patients within a hospital, many hospitals use this unit for patients at highest risk for age-related complications. The unit is an excellent environment for training of all disciplines. ACE staff may also provide consultation throughout the hospital to export ACE principles throughout the health system.

Nurses Improving the Care of Health System Elders

Nurses Improving the Care of Health System Elders (NICHE; http://www.nicheprogram.org) is a national program aimed at system improvement to achieve positive outcomes for hospitalized older adults. NICHE has two main goals: improving the quality of care to patients and improving nurse competence. This is accomplished by "modifying the nurse practice environment with the infusion of geriatric-specific: (a) core values into the mission statement of the institution; (b) special equipment, supplies, and other resources; and (c) protocols and techniques that promote interdisciplinary collaboration." [65] NICHE includes several approaches, each of which facilitates transfusion of evidence-based geriatric best practices into hospital care. A geriatric nurse specialist as the NICHE Coordinator functions in both a "primary care" role (evaluating and managing patients directly) and in a leadership role (teaching and mentoring others and changing systems of care)." [66] Foundational to NICHE is the Geriatric Resource Nurse Model (GRN) which is an educational intervention model that prepares staff nurses as the clinical resource person on geriatric issues to other nurses on their unit. The GRN model provides staff nurses, via education and modeling by a NICHE coordinator, with specific content for improved knowledge of care management for geriatric syndromes. Clinical protocols and organizational strategies provide necessary tools to apply evidence-based practice. For example, in one NICHE orthopedic unit, GRNs received intensive education on the prevention and detection of delirium in a unit where the primary diagnoses were joint replacement and hip fracture repair. Utilizing a combination of standardized assessment of cognition and focused interventions to prevent post-op delirium, the unit realized a significant reduction in the incidence of delirium. Other systemic interventions utilized by the GRNs include a revised nursing database and delirium-specific order sets [67]. An evaluation of responses of 9,802 direct-care registered nurses from 75 acute care hospitals participating in NICHE found that a positive geriatric nurse practice environment was associated with positive geriatric care delivery. The independent contribution of all three aspects of the geriatric nurse practice environment (resource availability, institutional values, and capacity for collaboration) influences care delivery for hospitalized older adult patients. The study findings demonstrate that a nurse practice environment that provides adequate geriatric-specific resources (continuing education, education, specialty services), promotes interdisciplinary collaboration, and fosters patient, family, and nurse involvement in treatment-related decision-making is associated with quality geriatric care [64]. In single site studies, NICHE hospitals demonstrate improved clinical outcomes, rate of compliance with geriatric institutional protocols; cost-related outcomes; and nurse knowledge. In a study of eight hospitals, nurses reported higher quality of geriatric care following NICHE implementation [68].

NICHE also promotes a unit-based ACE model. The ACE model within NICHE emphasizes: (1) implementation of nurse-driven protocols, (2) geriatric training of all nursing staff, and (3) utilization of geriatric-specific units within a health system's overall geriatric care programming. Similar to other ACE studies, a NICHE-ACE unit in which the majority of the staff nurses were nationally certified in geriatric nursing reported lower fall and pressure ulcer rates, and lower length of stay when compared to overall hospital [69].

Since NICHE is a system-level approach it provides a structure for nurses to collaborate with other disciplines and to actively participate or coordinate other geriatric care models. For example, in hospitals with a geriatric department or consultation service, GRNs screen for appropriate referrals to these services and can effectively implement geriatric service recommendations with support from the NICHE coordinator. The models enhance NICHE program effectiveness by expanding the scope of geriatric programming within a health system.

The Hospital Elder Life Program

The Hospital Elder Life Program (HELP; http://elderlife.med.yale.edu/public/public-main.php) is a program designed to implement protocols that target six delirium risk factors: mental orientation, therapeutic activities, early mobilization, vision and hearing adaptations, hydration and feeding assistance, and sleep enhancement. These protocols were tested in several well-designed clinical trials and demonstrated significant reduction in the incidence of new delirium. Further, among those who did develop delirium, these protocols are associated with a significant reduction of total number of episodes and days with delirium, functional decline, costs of hospital services, and reduction in use of long-term nursing home services [70, 71].

HELP employs geriatric specialists of various disciplines (geriatrician, geriatric nurse specialist, recreation therapy, and physical therapy) working together as an interdisciplinary team with trained volunteers. The program is coordinated by Elder Life Specialists, typically an Elder Life Nurse Specialist who has advanced geriatric nursing education and is responsible for implementing nursing-related assessments and tracking of delirium risk factor protocol adherence. The latter depends on the involvement of well-trained and supervised volunteers in patient-care interventions [72]. The research-tested protocol was made available to hospitals in 2000. Implementation in many hospitals has been adapted based on hospital resources. This has led to wide variations in adherence to the intervention protocol. Although higher levels of adherence have been associated with lower rates of delirium, these adapted protocols continue to provide positive results [73].

Transitional Care Models

An American Geriatric Society Position Statement defines transitional care as a set of actions designed to ensure the coordination and continuity of health care as patients transfer between different locations or different levels of care within the same location [74]. Older adult patients with complex medical and social needs and their caregivers require assistance to effectively navigate the health-care system, including recovery from surgery and return to pre-morbid health and living arrangements. Two models have emerged that have demonstrated improved outcomes for older adults hospitalized for both medical and surgical interventions.

APN transitional care model utilizes advanced practice nurses (APNs) whose primary responsibility is to optimize the health of high-risk, cognitively intact older adults with a variety of medical and surgical conditions during hospitalization and for designing and overseeing the plan for follow-up care following discharge [75]. The APN work collaboratively with the older adult, family caregiver, physician, and other health team members and are guided by evidence-based protocols. The same nurse implements this plan after discharge by providing traditional home-care services and by phone availability 7 days a week. Three federally funded, randomized, controlled trials consistently demonstrated that this model of care improves older adults' satisfaction, reduces rehospitalizations, and decreases health-care costs [76–78].

Care transitions coaching or *care transitions intervention* (see http://www.caretransitions.org/index.asp) employs a nurse or "transitions coach" to encourage older patients and their family caregivers to assume more active roles during care transitions by facilitating self-management and direct communication between the patient/caregiver and primary care provider. The four content areas or "pillars" of the patient/caregiver intervention are as follows: (1) medication self-management, (2) a patient-centered record, (3) primary care and specialist follow-up, and (4) knowledge of "red flags" warning symptom or sign indicative of a worsening condition

[79]. The Personal Health Record includes data elements essential to promote productive patient–provider encounters across settings such as an active health problem list; medications and allergies; a list of warning symptoms or signs that correspond to the patient's chronic illnesses; a checklist of activities that need to take place before and following discharge. This record is maintained by the patient and caregiver with assistance from the transition coach. The 4-week intervention begins in the hospital and continues through home visits and/or phone follow-up after discharge.

Several studies, including a randomized, controlled trial, found that patients who received this intervention had lower all-cause rehospitalization rates 30 and 90 days after discharge compared with control patients. Intervention patients also had lower rehospitalization rates for the same condition that they were admitted for in the index hospitalization at 90 and at 180 days than controls. Mean hospital costs were approximately $500 less for patients in the intervention group compared with controls [80].

New Specialty Models

In some hospitals, multiple geriatric models are employed. For example, a hospital may begin with NICHE. The NICHE coordinator, a geriatric nurse specialist, will then become an Elder Life Specialist to implement HELP hospital wide or within a discrete ACE unit. Often the core geriatric interdisciplinary team of any geriatric program screens patients for other related services such as palliative care, rehabilitative services, or pain management programs. Some have developed dual-function units such as merging an ACE unit with a palliative care unit [66]. Others have developed programs that merge geriatrics with other specialties. Examples include hip fracture, trauma, and oncology.

The American Academy of Orthopedic Surgeons recommends coordination of care and communication by providers as important aspects of quality care for hip fracture patients [81]. In response, several hospital programs that incorporate geriatric co-management of hip fracture patients have been developed. The expectation is that involvement of geriatricians in care management will avoid iatrogenic problems. For example, one program focuses on minimizing time to surgery and employment of standardized orders and protocols [82]. These programs have been shown to reduce delirium by over one-third, reduce severe delirium by over one-half, decrease predicted length of stay, readmission rates, complication rates, and mortality [83]. Others have developed a geriatric trauma team that include a geriatrician and geriatric advanced practice nurse who evaluate older trauma patients and share recommendations in weekly multidisciplinary rounds and performance improvement meetings of the trauma service. Most (91%) geriatric recommendations were followed and included: advanced care planning, disposition decisions to promote function, decreased inappropriate medications, and pain management [84].

Similarly, oncology programs have either developed geriatric – oncology consultation team or have developed geriatric – oncology units, some of which are part of an existing ACE unit [85, 86]. These programs report that older oncology patients have more complex medical and social needs than adult oncology patients and thus require input from both perspectives [87].

Conclusion

Although these models use different strategies, all share common goals of treatment. Each hospital or health system chooses a model based on the unique needs of that hospital's patient population, the resources available (geriatric specialists, bed capacity to support separate unit, volunteers, etc.) and especially senior administrator's commitment to geriatric programming. Since there is no direct reimbursement for many components of these models (interdisciplinary rounds, geriatric nurse specialist, volunteers, etc.) administrators seek external (grants, donor gifts) and internal funding (hospital foundation grants). They are motivated by the model's alignment to the hospitals strategic plan (e.g., excellence in senior care), the institution's mission, patient/family satisfaction, relationship with the community, and costs savings (i.e., reduction of complications). All of the models have demonstrated positive outcomes and each have been implemented in at least 50 hospitals; however, this still only represents a small proportion of American hospitals. Each model was originally developed with government and/or foundation support. Future survival of these models may depend on advancing the unique contributions of each within an integrated model that will enhance the hospital experience of the older patient.

Another problem influencing geriatric model implementation is availability of geriatric clinicians. Since significant geriatric medicine input is needed for many of these models, they generally are limited to academic medical centers, which only represent a small proportion of US hospitals. All of these models require providers with knowledge of core concepts in geriatrics; however, there is a significant shortage of fellowship-trained geriatricians, geriatric psychiatrists, master's prepared geriatric nurse specialists, as well as other disciplines [88]. In addition to efforts to increase the training of geriatric specialists, several initiatives are underway that involve specialty organizations, medical schools [89], and resident training programs [90, 91] to integrate principles of geriatric care into curriculums and practice. As more geriatrics is being integrated into undergraduate medical training and surgical resident training, knowledge of geriatric care principles and collaboration with geriatric models will enhance outcomes of the older surgical patients. The Council of the Section for Surgical and Related Medical Specialties in the American Geriatrics Society program provides the Geriatrics Syllabus for Specialists; a useful guide (lectures, PowerPoint presentations, etc.) geared toward providing vital information for surgeons caring for older patients as well as faculty leadership training to promote geriatric training and research within their disciplines. The initiative also enables surgical professional certifying bodies and societies to build the capacity of their members to provide better care of older adults [92].

Financial and administrative barriers deter the implementation of geriatric models. Medicare payment system focuses on provider-specific reimbursement and thus limits payment for organizational redesign, multidisciplinary teams or nurse-coordinators. The new CMS financial incentives that will not reimburse for nosocomial "never" events such as pressure ulcers, catheter-associated infections, and fall-related injury, may eventually encourage the use of these models [15]. A recent IOM report recommended that "payers should promote and reward the dissemination of those models of care for older adults that have been shown to be effective and efficient." [87] Incentives suggested included elimination of Medicare's co-payment disparity for mental health and enhanced payments for services under these models.

Finally, most of the research documenting complications of the older patient are based on studies combining both medical and surgical patients, thus future research should address the risk factors of these complications specific to surgical patients. Further, with the exception of hip fracture and cardiac surgery, additional studies should also identify complications within specific types of surgical procedures. This may provide important data to tailor models to specific surgical populations.

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Intensive Care in Older Adult Surgery Patients

25

Teresa S. Jones and Thomas Robinson

Contents

Abstract

Elderly patients account for the majority of inpatient and ICU admissions. Although mortality is higher compared to younger patients, older patients who survive their ICU stay can have an excellent quality of life and functional

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status. With age come physiologic changes in the body that can alter treatment in an acute setting. In this chapter, we review the changes and treatment options for the most frequently encountered ICU complications.

Keywords
Intensive care · Delirium · Shock · Acute kidney injury

Introduction

Patients >65 years old now account for up to 50% of intensive care unit (ICU) admissions and up to 60% of all ICU days [1–4]. In addition to medical advances that have prolonged life expectancy, there is now improved understanding of the different physiology that develops as patients age. Refusal of ICU admission is common in some countries, but the data now shows that elderly patients have a greater survival benefit from ICU admission compared to younger patients [5]. A geriatric patient's admission to the ICU requires a commitment of resources; however, it also represents a life-saving intervention now for the majority of medical and surgical patients.

Outcomes

Mortality has traditionally been the primary outcome used to assess health care delivery. Mortality among geriatric patients after hospital discharge remains high. In a study of medical and surgical patients ≥70 years, 1-year survival was 56% in patients age <85 years and 27% in those ≥85 years, rates markedly lower than in a matched population (93%) [6]. Age remains an independent variable in many prognostic scoring systems such as Acute Physiology and Chronic Health Evaluation (APACHE) II, APACHE III, and the Simplified Acute Physiology Score (SAPS) II. However, the impact of age on mortality weakens as the severity of the acute illness or physiologic derangement increases in both surgical and medical patients [7–10]. In addition to severity of their acute illness, preexisting conditions in older patients, particularly signs of frailty, are associated with poor prognosis [11, 12]. In one study, patients >75 years of age who had functional limitations were six times more likely to die in the hospital than those aged 50–64 years without limitations. Among patients without functional limitations, there was no difference in mortality between the youngest and oldest group [13, 14].

While overall mortality is high, the evidence demonstrates a clear benefit for geriatric patients who survive their ICU admission. In the largest single-center outcome study of geriatric patients who survive ICU admission, Kaarlola and coinvestigators evaluated 883 elderly ICU survivors and 1827 controls [15]. They found that cumulative 3-year mortality was higher among the older patients (57% vs. 40% in the control group). Most (66%) elderly nonsurvivors died within 1 month of ICU discharge. However, 97% of the geriatric survivors lived at home. Of those patients, 88% described their present state of health as good or satisfactory. In fact, 66% found it similar or better than 12 month prior, and 48% found it similar or better than before ICU admission. Additional prospective cohort studies have shown that patients who survive their acute intensive hospitalization can have excellent function in their activities of daily living (ADL) [16]. Therefore, despite the high overall mortality, we believe that older patients can benefit from an ICU admission. In the rest of this chapter, the goal will be to examine common ICU-related problems as they relate to geriatric patients: delirium, respiratory failure, shock, acute kidney injury, and malnutrition.

Delirium

Evaluation

Delirium is an acute state of confusion that develops over a short period and fluctuates over time. It is often the result of underlying organic derangements, such as infection, medical illness, and drug use or withdrawal. Delirium can be distinguished from dementia by its acute onset and fluctuating course.

The assessment of acute changes in cognition is difficult in the ICU setting due to the severity of underlying disease and the frequent loss of verbal communication due to mechanical ventilation. One tool for assessment of delirium in the ICU, which was adapted from the Confusion Assessment Method (CAM), is the CAM-ICU [17]. It has been validated in several studies as being both highly sensitive and specific for delirium [17, 18]. Using CAM-ICU, delirium is diagnosed in two steps. First, a standardized sedation scale, such as the Richmond Agitation-Sedation Scale [19], is used to determine the level of consciousness. Any patient not determined to be comatose is then assessed for four features of delirium: (1) acute onset of mental status changes or a fluctuating course, (2) inattention, (3) disorganized thinking, and (4) an altered level of consciousness. A diagnosis of delirium is made with the presence of both features (1) and (2) in addition to either feature (3) or (4) [18].

There is little doubt that as the elderly population ages, the prevalence and burden of delirium in the ICU will grow. Milbrandt and colleagues studied patient charges in 275 consecutive, mechanically ventilated ICU patients and found the presence of delirium to be associated with 39% increased ICU cost (95% CI, 12–72%) and 31% higher hospital cost (95% CI, 1–70%) [20]. In surgical patients, development of delirium increased ICU and overall hospital stay, cost, rate of postdischarge institutionalization, and mortality at 30 day and 6 months [21]. Prevention and treatment of delirium is critical not only to hospital survival but also long-term outcomes for elderly patients.

Prevention

The risk factors for delirium are divided into host factors, which are present on admission to the ICU, and precipitating factors, which occur during the course of illness. In a recent study of elderly patients admitted to the ICU, the rates of delirium were found to be >70% during their hospitalization, and patients with dementia had a 40% higher overall rate of delirium during hospitalization than those without dementia [22]. Other factors present on admission most commonly associated with the development of delirium are age greater than 65, poor vision, severe illness, and presence of infection [23]. It is difficult to modify these preadmission factors; therefore, it is the precipitating factors that develop during a hospitalization that are potentially modifiable and therefore the target of prophylactic and therapeutic intervention [24, 25].

The use of sedative and analgesic medications deserves special attention. Pain control is a critical issue in management of elderly patients and nearly all patients in the ICU receive these medications. Elderly patients are more sensitive to the effects of benzodiazepines and opioids due to both a decrease in the number of receptors and a decrease in affinity of receptors for neurotransmitters [26]. Cardiac output and hepatic and renal outflow all decrease with age, and overall decrease in lean body mass and total body water and increase in fat causes redistribution of drugs and interfere with appropriate metabolism and clearance [27]. These changes should motivate a multimodal strategy for pain management and sedation to prevent delirium.

To prevent or minimize the impact on mental status, choice and dosing of medications should be decided carefully. Benzodiazepines and anticholinergics have been consistently linked to delirium in the elderly [28]. Pisani and coworkers recently published data showing that use of a benzodiazepine or an opioid was associated with increased delirium duration, especially the first episode (relative risk of 1.64 with a 95% confidence interval of 1.27–2.10) [29]. Meperidine is consistently linked to the development of delirium, especially in the aged [30–32]. Trials of newer sedation agents have shown some promise. In a 2007 trial by Pandharipande et al., the use of dexmedetomidine (an alpha 2 agonist) was compared to lorazepam in mechanically ventilated patients. The use of dexmedetomidine was associated with more delirium-free days than lorazepam [33]. In a 2016 trial that randomized patients 65 years and older to dexmedetomidine vs. placebo, low dose dexmedetomidine significantly decreased the occurrence of postoperative delirium [34]. Choice of sedation may be limited due to cost as well as hemodynamic effects. With any medication choice, daily interruption of sedation and the use of intermittent as opposed to continuous dosing are two methods used to minimize the impact on mental status and the ability to assess for delirium [35].

The data regarding the use of opioids is less clear. A study by Ouimet and coworkers demonstrated higher daily use of opioids in ICU patients without delirium [36]. Similarly, in a study of hip fracture patients, Morrison and coauthors found that patients treated liberally with opioid analgesics were less likely to develop delirium than those who received less analgesia [37]. These findings point to the need for careful use of these agents with attention to providing adequate pain relief while avoiding oversedation. In general, narcotics are associated with more frequent respiratory disturbances following surgery and the use of nonnarcotic analgesics should be implemented if possible [38]. Nonsteroidal pain relief is useful but in practice, many elderly patients have absolute or relative contraindication to their use due to increased GI bleed risks with ventilation [39]. Regional techniques including epidurals or paravertebral blocks should be considered, but in the ICU setting, coagulopathy, respiratory depression, and hemodynamic effects can also limit their use [40].

Delirium prevention can reduce the incidence of delirium up to 30–40%. The American Geriatric Society currently recommends multicomponent interventions to prevent delirium in the postoperative patients including: cognitive reorientation, sleep enhancement, early mobility, adaptations for visual and hearing impairment, nutrition and fluid repletion, pain management, appropriate medication usage, adequate oxygenation, and prevention of constipation [41]. These measures should be monitored by a multidisciplinary team for adherence.

Treatment

Once delirium is diagnosed, treatment must be implemented. The first step is to rule out an underlying organic source. Altered mental status may indicate infection, metabolic and electrolyte abnormalities, or medication exposures; all risk factors for delerium must be addressed prior to intervention. If all critical illness-related factors are ruled out, nonpharmacologic approaches should be implemented first that are similar to those recommended in the AGS preventative guidelines. After the use of nonpharmacologic strategies, consideration should be given to the use of pharmacologic agents to manage the symptoms of delirium. Currently, the Society of Critical Care Medicine recommends haloperidol as the drug of choice for treatment of delirium in the ICU [42]. This recommendation holds true for the geriatric patients [43]. Using intermittent intravenous injection, a 2-mg dose, is recommended. Repeated doses are administered if symptoms are not controlled, doubling the previously administered dose every 15–20 min until agitation resolves. Once controlled, scheduled doses are given every 4–6 h and then tapered over several days. Side effects of haloperidol include QT interval prolongation, extrapyramidal symptoms, and neuroleptic malignant syndrome. Routine EKG monitoring is suggested to detect any QT prolongation [42]. Atypical antipsychotics, such as risperidone quetiapine, and olanzapine may also have a role in the management of delirium but the data is not yet conclusive [44]. Dexmedatomidine has also been used as a rescue medication when patients are refractory to Haldol with good effect [45].

Respiratory Failure

Changes in Pulmonary Function Associated with Aging

The aging process affects every aspect of respiratory physiology and oxygen transport with important consequences for the geriatric patients with critical illness [46]. Age-related changes include decrease in vital capacity, forced expiratory volume in 1 s, arterial oxygen tension, and maximal oxygen consumption. Ventilation is impaired due to blunted responses to both hypoxia and hypercarbia. Aspiration risk is high due to decreased airway sensitivity, impaired mucocilliary transport, and decreased cough strength. All of these changes make pulmonary complications very common in elderly patients, even following elective surgical procedures [38, 47–49].

Management

In the nonintubated patient, aggressive early management is critical to prevent need for mechanical ventilation. Pain management should be initiated early and in a preventative fashion. This allows elderly patients to mobilize as soon as possible. Even just assuming an upright position can increase functional residual capacity and lessen the closure of small airways caused by the supine position. It has been demonstrated that oxygen consumption following thoracotomy is lower in the seated rather than the supine position, suggesting that the work of breathing may be lessened when a patient is upright [50]. Lung recruitment maneuvers including incentive spirometry (IS) can complement patient mobility and pain management. Ideally, patient should start with IS every 6 h. If patients are unable to attain volumes of at least 8–10 ml/kg ideal body weight on IS, then noninvasive lung expansion therapy should be considered.

Techniques of mechanical ventilation and weaning do not differ in the elderly, but they may require a longer period of support, given the impairments imposed by age, comorbidities, and acute illness. Parameters used to predict successful weaning from mechanical ventilation in younger patients may also be less reliable in the elderly [51]. The ARDSnet investigators examined age as a factor affecting outcome from acute lung injury and acute respiratory distress syndrome [52]. They found that although patients >70 years of age were able to breathe spontaneously for 2 h without ventilator assistance, which was a common similar time point to younger patients, the older patients had higher reintubation rates, longer ICU and hospital stays, and lower survival rates at 28 days. Caution should be exercised when liberating elderly patients from mechanical ventilation even if they achieve weaning parameters.

Shock

Changes in the Cardiovascular System Associated with Aging

Structural and functional changes occur with the heart and peripheral vasculature that can seriously alter the management of shock in an elderly patient. Compliance of the peripheral vasculature decreases, which leads to an increase in afterload. To compensate, patients develop left ventricular hypertrophy and decreased diastolic compliance. This decrease in compliance results in a nearly 50% reduction in early diastolic filling, making elderly patients more reliant on atrial contraction for ventricular filling. Cardiac output is then more reliant on preload, making older patients more sensitive to hypovolemia and atrial arrhythmias. In addition to structural changes to the heart, the presence of coronary artery disease should always be suspected in the setting of hypotension. The Framingham Heart Study found that myocardial infarction was silent or unrecognized in over 40% of patients aged 75–84% [53].

Evaluation

Shock is best defined as a state of inadequate tissue perfusion. In the uncompensated state, it is easily recognized by tachycardia, oliguria, and hypotension. The initial monitoring of the critically ill patients should include close attention to the physical exam, vital signs, and urine output. These parameters, and more importantly their change over time, are the most useful in determining response to resuscitative efforts, but they also can fail to detect ongoing tissue hypoperfusion and hypoxia [54]. Even after hypotension has been corrected and urine output restored, a state of "compensated shock" may remain. Hypoxia forces tissue to utilize anaerobic pathways, resulting in lactic acid production and large amounts of hydrogen ions. Base deficit and lactate levels are frequently used to assess both the initial state of shock and monitor the effects of ongoing resuscitation. Clearly, no single end point is applicable to every scenario, and it is important to repeatedly examine patients to determine success or inadequacy of resuscitation.

The optimal way to monitor resuscitation is still debated. Central venous pressure (CVP) can be continuously monitored off of a central venous catheter. Changes in CVP can be used to assess response to fluid challenges or diagnose severe hypovolemia, but it is known that CVP correlates poorly with changes in cardiac output [55]. Monitoring resuscitation with pulmonary artery catheters (PAC) is also no longer stand practice since there has been no prospective evidence that supports their use. In a large meta-analysis, Shah et al. evaluated 13 randomized clinical trials and concluded that in critically ill patients, the use of PACs neither increased mortality or hospital days nor did it confer benefits. One of the reasons no benefit is seen may be the lack of any clear guidelines for treatment based on data collected from a PAC [56]. Regardless, an important indication for a PAC is the differentiation between distributive vs. cardiogenic shock; however, that differentiation can also be made with echocardiography, if available.

Mixed central venous oxygen saturation (SCVO2) and blood lactate levels may be a useful adjunct in determining the adequacy of oxygen delivery and resuscitation. A value of >70% is considered to be normal for ScVO2. Lower values are consistent with flow-dependent delivery of oxygen, and a variety of strategies have been published using SCVO2 as an end point for resuscitation. An early goal-directed resuscitation strategy aimed at achieving an SCVO2 of 70% in patients presented to the emergency department in septic shock resulted in a significant decrease in mortality (46.5% in the control group vs. 30.5% in the treatment group) [57]. Of interest to this chapter, the mean age in the treatment group was 67.1 years (±17.4 SD). To obtain true mixed central venous oxygen saturation, a PAC catheter must be used, but central venous oxygen saturation (ScVO2) can be used as a surrogate, with the understanding that ScvO2 may be slightly less than the true SvO2 [58]. Lactate has been similarly shown to accurately risk stratify patients, and lactate clearance has been associated with improved survival [59]. In a RCT comparing the lactate clearance vs. ScVO2 was goals for resuscitation; there was no significant difference in hospital mortality when patients were treated for either [60].

Newer monitoring devices include pulse contour analysis, which calculates stroke volume from analysis of arterial pressure or oximeter waveforms. While less invasive, these devices have significant limitations on reliability based on patient parameters and should be used with caution at this time.

Management

Resuscitation with crystalloid, blood, and the administration of vasopressors are all methods to improve tissue oxygen delivery. Guidelines for the optimal use of these techniques are varied, and each approach is not without complications. Early restoration of circulating blood volume with blood products and crystalloid is crucial, especially in the elderly who are preload dependent to maintain ventricular filling and cardiac output. In the early phase of resuscitation, fluids are probably superior to vasopressors for the maintenance of blood pressure [61]. Care, however, must be taken to avoid excessive amounts of crystalloid as this has been linked to cardiac and pulmonary complications, coagulopathy, and acid–base disturbances [62]. Transfusion of blood to restore adequate oxygen carrying capacity is vital in cases of frank anemia, but exact triggers for transfusion in the elderly are still debated. The Hebert study suggests a transfusion threshold value of <7 g/dl of hemoglobin, and this recommendation has been widely adopted. This study, however, excluded patients with chronic anemia, ischemic heart disease, or any patient in whom the attending physician was unwilling to tolerate a transfusion trigger of <7 g/dl [63]. In elderly patients with acute myocardial infarction, a lower 30-day mortality was associated with blood transfusion for hematocrit values <30% [64]. Other studies have documented increased myocardial ischemia when intraoperative or postoperative hematocrit fell below 28% [65, 66]. Given the high incidence of ischemic cardiac disease – often silent in the elderly – care should be taken in setting a "one-size-fits-all" transfusion trigger in the geriatric population.

Once effective volume has been restored, inotropes and vasopressors may be required to augment oxygen delivery. In elderly patients, the response to b-agonists declines, with subsequent reduction in the inotropic, chronotropic, and vasodilatory effects of these medications. With these changes, nonadrenergic effects may be more pronounced. With the geriatric patient, inotropic support may be required in atypical clinical settings such as septic shock. In cases of severe sepsis, norepinephrine is advocated as the initial vasopressors recommended in the Surviving Sepsis Guidelines, with a target mean arterial pressure of 65 mmHg [67]. However, Viellard-Baron and coauthors found a high incidence of global left ventricular hypokinesia, defined as an ejection fraction of <45%, in a mixed group of patients presenting with septic shock (mean age 65 years). Hypokinesia was often present on initial evaluation, and further cases were unmasked after 24–48 h of therapy with norepinephrine, bringing the total incidence to about 60% [68]. This hypokinesia can be counteracted by the addition of inotropic agents such as dobutamine [67]. Finally, the stiffened aorta should also be taken into account, and the addition of afterload reducing agents may be useful for refractory cases [69].

In summary, the clinician caring for the elderly patient with shock must walk a fine line, using both fluids and inotropes, while paying close attention to changes in their clinical status. Frequent adjustments will be required as the clinical situation evolves.

Acute Kidney Injury

Changes in the Renal System Associated with Aging

Changes in renal function related to advancing age are significant in the management of critical illness. There are predictable declines in the glomerular filtration rate (GFR) and creatinine clearance. These declines, while significant, have little impact on the measured serum creatinine level, as there is a parallel reduction in the amount of creatinine produced due to overall decrease in lean muscle mass.

With aging, homeostatic mechanisms become less capable of dealing with the fluid losses, acid–base disturbances, and electrolyte abnormalities. Insensible losses are increased through surgery, wounds, and mechanical ventilation. The aging kidney is less able to concentrate urine and compensate for these losses. In addition, the normal thirst mechanism is often impaired in the geriatric patient. The net result is an increased propensity for hypovolemia, which can be particularly harmful in the elderly who rely on preload to maintain cardiac function. Poor bicarbonate elimination also hampers renal compensation in acid–base disturbances. Compounding this problem is the diminished capacity of the kidney to excrete acute salt and water loads, which can manifest as pulmonary insufficiency secondary to acute volume overload. The key factors to successful management include meticulous attention to detail, frequent laboratory and physical assessment, and appropriate fluid administration to avoid any large or rapid changes in volume status, electrolytes, or acid–base loads.

Evaluation

The incidence of acute kidney injury (AKI) increases with age and is 3.5 times more prevalent in those >70 years of age [70]. The 2012 Kidney Disease: improving Global Outcomes Clinical Practice Guidelines for Acute Kidney injury defined AKI as one or more of three criteria: a rise in creatinine of at least 0.3 mg/dl over a 48 h period; an increase of ≥1.5 times of the baseline creatinine value within the seven previous days; urine volume ≤0.5 ml/kg per hour for 6 h [71]. The causes of AKI are no different in geriatric patients as compared younger ICU patients, but age itself remains a major risk factor for the development of AKI in the ICU [72]. This may be due to the increased incidence of diabetes, hypertension, and underlying chronic kidney diseases in the elderly population.

The etiology of AKI is usually divided into three categories: prerenal, intrinsic, and postrenal. Prerenal causes include fluid losses, decreased intake, diuretic treatment, and reduced effective circulating blood volume secondary to impaired cardiac output, systemic vasodilatation, and renal artery stenosis. The elderly are especially vulnerable to prerenal AKI due to impaired autoregulation and high risk of hypovolemia. Intrinsic causes include ischemia, sepsis, and nephrotoxins, otherwise known as acute tubular necrosis (ATN) and can account for up to 76% of cases of AKI in the ICU [73]. Postrenal causes in older patients usually are due to mechanical blockages due to malignancy.

The diagnostic approach to AKI should include a history and examination. A review of medications should focus on potential sources of kidney injury such as NSAIDs, intravenous contrast, diuretics, and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. Laboratory examination should include serum creatinine, urinalysis, urine electrolytes, urine creatinine, and osmolarity. These values can be used to determine the glomerular filtration rate and the fractional excretion of sodium. As a diagnostic tool, fractional excretion of sodium is often confounded by diuretics in the elderly. In that cause, fractional excretion of urea may be more accurate to distinguish between prerenal and intrinsic causes. Urine osmolarity, when <300 mOsm/kg, is indicative of intrinsic renal failure.

Clinical Management

Management of AKI should first involve the treatment of life-threatening complications, such as electrolyte abnormalities, pulmonary edema, and metabolic acidosis. Second, all nephrotoxic agents should be discontinued. Finally, fluid and hemodynamic status should be optimized.

Although still employed, medications to prevent AKI have not demonstrated a long-term benefit. Renal-dose dopamine and continuous fenoldopam have not shown to prevent need for renal replacement therapy or improve mortality [74, 75]. Furosemide may improve urine output, but it has no influence on return of renal function or survival, thus its utilization should be limited to maintaining fluid balance [76]. Mannitol has also been shown to have no efficacy in renal protection [76].

Outcomes: Renal Replacement Therapy

Renal replacement therapy (RRT) is required in approximately 85% of patients with oliguric renal failure and about 30% with nonoliguric renal failure [77]. Like tracheotomy, the initiation of RRT in the elderly is a significant decision point in the care of the elderly patient and should be approached with deliberation. Multiple recent studies have examined prognosis and outcomes following RRT during the course of critical illness. In a meta-analysis by Bagshaw, the mortality of ATN treated with RRT was reported at 46–74%. In studies confined to the critically ill, mortality was nearly 60% at 90 days. In the same analysis, quality of life was addressed, and studies consistently demonstrated lower global quality of life scores. However, survivors generally rated their quality of life acceptable [78].

In addition to survival, return of renal function, defined as freedom from RRT, is another important outcome measure. Schmitt and coworkers undertook a meta-analysis addressing recovery of kidney function after AKI in the elderly. They reported that 31.3% of the elderly did not recover function compared to 26% in younger patients (pooled RR, 1.28, 95% CI, 1.06–1.55). An interesting finding in their review was that the relative risk of nonrecovery was only slightly increased in the elderly when continuous RRT was used; however, this did not achieve statistical significance [79]. A multidisciplinary approach to this decision may help determine if RRT is in line with patient's goals of care, particularly after hospital discharge.

Nutrition

Body composition changes over the course of aging. Lean muscle mass is reduced up to 40% by the age of 80 with simultaneous increase in body fat. There is a corresponding decrease in muscle strength and decrease in resting energy expenditure by up to 15% [69]. As a result of this loss of muscle mass, the elderly patient may rapidly develop protein–energy malnutrition in the setting of acute illness and surgery. Malnutrition is reported in more than half of geriatric patients at the time of hospital admission, a proportion that is even high among patients who come from nursing homes [80]. On the other hand, obesity is not associated with an increase in mortality in the ICU, but is associated with increases in the duration of mechanical ventilation and ICU length of stay [81].

Ideally, nutritional support should be initiated within 24 h of admission to the ICU. An audit of feeding practices by Taylor found that in patients greater than 64 years of age prolonged starvation (>5 days) resulted in higher mortality than those without nutrition 0–5 days, which was not found in younger patients. This suggested a greater susceptibility to starvation in the elderly [82]. We routinely initiate "trickle feeds" as soon as vasopressor doses have stabilized and lactate levels are decreasing. Our preferred method of nutrition is the enteral route, with the choice of tube and position (gastric or postpyloric) determined by the clinical scenario. The use of early enteral nutrition in surgical patients has demonstrated reduced infection rates. No increase in the incidence of anastomotic failure has been documented, and there is a trend toward reduced mortality [83]. Deficiencies in micronutrients are common, and supplementation should be routine. It is important to be aware that caloric requirements are reduced in the elderly; overfeeding results in excess CO_2 production, mandating higher minute ventilation and should be avoided. Overfeeding will not decrease the amount of lean tissue loss, can increase fat synthesis, aggravated hyperglycemia, and can delay weaning from mechanical ventilation [84].

Parenteral nutrition (PN) should also be considered in malnourished older patients. PN can support improvement in function status, albeit at the lower margin than in younger patients [85]. Complications occur at the same rate as younger patients, but overall mortality is higher in older adults who received PN vs. younger. This rate is potentially due to underlying disease and prognosis. Parenteral nutrition should be considered a medical treatment, and its use should be balanced against a realistic change of improvement in condition [86].

Impaired glucose tolerance increases with aging, and nearly 40% of the US population over age 60 has either type 2 diabetes or impaired glucose tolerance. The mechanism of impaired glucose tolerance is a lifelong decline in insulin secretion by B-cells at a rate of 0.7% per year. No specific change in insulin sensitivity, as previously thought, has been identified [87]. Early evidence suggested that strict glycemic control may be beneficial for patients in the ICU with a decrease in mortality, especially when employed for more than 3 days [88, 89]. These initial findings generated controversy and concern over the risk of hypoglycemic events that occur during insulin therapy. The NICE-SUGAR study was undertaken to determine the best target for glycemic control in critical illness. In a study of over 6000 ICU patients, subjects were randomized to intensive control or conventional control of blood sugar. The incidence of hypoglycemia was significantly greater in the intensive-control group (6.8% vs. 0.5%, $p < 0.001$). Mortality in this study was greater in the intensive control group as well (27.5% vs. 24.9%, $p = 0.02$). The authors concluded that a blood glucose target of 180 mg/dl or less resulted in lower mortality than did a target of 81–108 mg/dl [90].

Caring for Dying Patients

Caring for dying patients is a natural part of working in the ICU, even more so with geriatric patients. A more complete discussion of palliative care and end-of-life decision-making is presented in ▶ Chap. 17, "Traumatic Injury in Older Adults." However, this is such an integral part of caring for the geriatric ICU patient that it bears some repetition. Cook and coworkers writing for the Canadian Critical Care Trials Group prospectively followed 851 patients with a mean age of 61.2 years who were receiving mechanical ventilation. Of these patients, 166 (19.5%) had mechanical ventilation withdrawn. Rather than age or the severity of the illness and organ dysfunction, the three strongest determinants of withdrawal of ventilation in critically ill patients were the physician's perception that the patient preferred not to use life support (hazard ratio, 4.19), the physician's prediction that the patient's likelihood of survival in the ICU was less than 10% (hazard ratio, 3.49), and a high likelihood of poor cognitive function (hazard ratio, 2.51) [91]. Surprisingly, Cook and coauthors did not find a significant relationship between withdrawal of ventilation and age, previous functional status, severity of illness, or severity of organ dysfunction. It should be concerning to all of us rendering care for elderly patients that the strongest determinate of withdrawal from mechanical ventilation was physicians' perception of patients' wishes. Unfortunately, we know that patients' wishes regarding ICU admission or initiation of ventilation are frequently unknown at the time of ICU admission [92]. In addition, these wishes may not correspond with the family members' understanding their advance directives [93]. Finally, patients' assessments of their quality of life does not necessarily correlate with their wishes regarding life-sustaining therapy.

Knowing these potential conflicts, it is essential upon admission to the ICU to assess the patient's goals of care, either with the patient or the family. When we feel that further critical care is unlikely to achieve a quality of life that would be acceptable to the patient – as previously defined in our discussions with patients when available or families and surrogates if not – we involve our palliative care colleagues early to help give families a better perspective on expectations after an ICU admission. Often, these decision points occur with acute events, such as need for reintubation, initiation of RRT, need for surgery, etc. The vast majority of families do not want to assume responsibility for a decision that they perceive as leading to the death of their patient, when in reality, it is often that the patient's disease process dictates the outcome. The decision surrogates are faced with is not whether death will occur, but how that death will happen. Occasionally, we are unable to reach a clear consensus with the family or surrogate decision makers. In these situations, we continue supportive therapy – usually with limitations about escalation – and reconvene the discussion in the near future. End-of-life discussions are almost never concluded in a single setting and generally mature over time as the disease process and the patient's physiologic response becomes clear to both physician and family.

Through experience, we have found that establishing consensus, providing open communication, and focusing on goals of therapy are effective tools in our daily practice. Involving other specialties, particularly palliative care, can give families the information they need to make an informed decision.

Conclusion

Critical care of elderly patients both compares and contrasts with that of younger patients. It is different in that age has multifarious effects on all organ systems, and these age-related changes influence the way elderly patients respond to their critical illness and to treatment. It is similar in that the principles, procedures, techniques, and devices used to support organ system insufficiency or failure are the same and that with a comprehensive approach to care and close attention to detail many can survive their critical illness and resume a valued and enjoyable life.

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Age, Frailty, and Impaired Wound Healing

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Abstract

Chronic wounds in older individuals are among the most devastating and difficult to treat age-related ailments and are strongly intertwined with a sense of self-worth and quality of life. As the population ages, it is increasingly clear that there is a subset of older adults that is disproportionately vulnerable to developing chronic wounds and is at especially high risk for iatrogenic complications with wound care interventions. In these frail older individuals, wounds are usually

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caused by decline in more than one domain of function, in contrast to younger individuals. New or difficult to treat wounds in older individuals can therefore be a sign of medical illness and like other geriatric syndromes should trigger a comprehensive evaluation. The aim of this chapter is to review the approach to older adults with wounds including comprehensive risk and functional assessment, identification of red flags, medications, special considerations for management of wounds in frailty, the role of palliative care and wound rehabilitation programs, counseling, and compensatory strategies.

Keywords
Frailty · Chronic wounds · Exudate · Odor management · Pain control · Medication debridement · Pressure ulcer · Neuropathic foot ulcer · Wound palliation · Wound finances

Key Facts

- 8.5 percent of people worldwide (617 million) are over the age of 65 with projections that it will rise to 17 percent of the world's population by 2050.
- Aging is associated with thinning of the epidermis, degeneration of collagen, fracture of the dermal layer, and atrophy of subcutaneous fat.
- The incidence of venous leg ulcers is 3–4 times higher, and of pressure ulcer is 5–7 times higher in persons older than 80 years compared with persons aged 65–70 years.
- Care for chronic wounds in older adults costs about $10 billion annually.

Introduction

Wound healing is a complex process that can be derailed by multiple factors including obesity, diabetes, smoking, vascular disease, infection, renal failure, and malnutrition. The current incidence of chronic nonhealing cutaneous wounds is estimated at 5–7 million in the United States, with total annual wound care expenditures exceeding $25 billion [1]. We are now entering a "perfect storm" in which there is rapid expansion of the population over 65 years of age, combined with an exponential increase in diabetes and obesity worldwide. The fastest growing segment of this population, those over 85 years of age, is also the cohort with the highest incidence of chronic wounds, particularly venous leg ulcers and pressure ulcers [2–4]. Meanwhile, older adults have significantly higher rates of surgical procedures, with increased potential for wound complications [5]. The full impact of caring for chronic wounds includes direct costs (wound care supplies, hospital and nursing costs), indirect costs (lost wages for patient or unpaid caregivers), and intangible costs (pain and suffering). Thus, in addition to the effect on morbidity and mortality, we can expect that chronic wounds in the elderly will account for a disproportionate share of our nation's healthcare expenditures.

Despite universal age-related changes in skin which include thinning of the epidermis, degeneration of collagen, fracture of the dermal layer, and atrophy of subcutaneous fat [6], it is becoming increasingly clear that the development of chronic wounds and the trajectory of rate of wound healing or the development of iatrogenic complications cannot be solely defined or constrained by chronological age or presence of comorbidities [7]. Data suggest that there is a subset of older individuals at significantly higher risk for adverse health outcomes, including falls, hospitalization, institutionalization, and mortality [8, 9]. Identification and risk stratification of these individuals by the wound care team is of critical importance in order to provide quality and cost-effective treatment and to avoid adverse outcomes that are associated with some wound treatment modalities. Optimizing care for the frail older individual with wounds requires a systematic multidimensional approach, focusing on somatic, functional, psychological, and social features [10].

Key Basic Pathophysiologic Changes in Chronic Wounds

- Oxidative damage
- Impaired cell proliferation
- Protein modification
- Impaired bioenergetics
- Dysregulated inflammation
- Catabolic/anabolic hormonal imbalance

Pathophysiology of Chronic Wounds in the Aging and the Frail

There is no uncertainty that cellular damage is a unifying feature shared between younger and older individual with wounds. Reduced ability to respond to this cellular damage by increasing repair and maintain homeostasis is what sets apart frail older adults from young and robust older individuals. In such frail older adults, *homeostenosis* (decreased ability to maintain homeostasis in times of acute stress) explains the lack of ability of these older adults to meet the increased demand imposed on them by the wound (great challenge and low reserve) [11]. Several basic pathophysiologic factors contribute to this homeostenosis including the continuous demand on aging cells to respond to oxidative damage, chronic inflammation burden, hormonal imbalance between catabolic and anabolic hormones, oxidative stress damage, and mitochondrial exhaustion limiting the ability of the "frail cells" to respond to challenge precipitated by the newly developing wound.

It is also widely accepted that the healthy octagenarian with a traumatic or surgical wound normally heals at a slower rate than a healthy young adult. This effect of "pure aging" is clinically apparent by age 60 and becomes statistically significant at age 70 [12]. However, because wound healing is a complex, highly orchestrated process, disruption of even a single aspect of that process can delay healing [13]. The development of chronic wounds is multifactorial and depends upon both intrinsic and extrinsic factors. The four principle aging processes are changes in body composition, energy imbalance, homeostatic disequilibrium, and neurodegeneration. These "intrinsic" factors can have a major effect on wound healing. Specifically, alteration of the skin architecture with loss of elasticity, thinning of the dermis, and reduced capacity of keratinocytes to proliferate and migrate make the skin vulnerable to even minor trauma. A recent study using an ex-vivo model demonstrated that application of a compressive load to ischemic aged skin resulted in subepidermal separation and altered orientation of the collagen fibers similar to that seen in patients with pressure ulcers [14]. Other changes in body composition include an increase in fat mass (FM) and decline in fat-free mass (FFM). Healthy, weight stable men and women, between the ages of 68 and 78, lose approximately 1% of FFM per year. This loss of lean muscle translates to a threefold loss of strength and is a primary predictor of disability [15]. Age-induced dysregulation of energy intake and utilization is brought about through a combination of reduced perception of hunger, early satiety, changes in the hormonal mediators associated with energy balance, and reduced energy expenditure [16]. The net effect in terms of weight gain or loss depends on a number of factors, including the overall health of the individual. However, all aspects of wound healing increase protein and energy requirements. In an older adult who is already at high risk for malnutrition, the presence of a wound can tip the balance toward involuntary weight loss, development of sarcopenia, impaired immunity, and increased risk of infection [17]. Sarcopenia, reduced functional ability, and malnutrition, combined with the inability of aged skin to distribute a pressure load substantially increase the vulnerability of older adults to developing pressure ulcers.

Alterations in the homeostatic balance include increased pro-inflammatory markers, decreased antioxidants, decreased anabolic hormones, and increased catabolic hormones and insulin resistance. All of these factors contribute to impaired wound healing and affect the skin's ability to function as an immune organ. Finally, neurodegeneration combined with impaired cognition, gait imbalance, and slow reaction times contributes to immobility and decreased ability for self-care [18].

Management of Chronic Wounds in Frail Older Adults

A holistic, multidisciplinary approach is critical aspect of geriatrics wound care management and recognizes that every individual may be different, extending beyond the physical manifestations of disease to consider personal circumstances and emphasizes that "it is more important to know the patient that has the wound than to know the wound that has the patient" (paraphrase of original quote by Sir William Osler).

Key goals of a comprehensive successful geriatrics wound care management include risk factor assessment, functional status determination, prognostication, promoting a healing environment, medication and wound debridement, dressing, antimicrobial use, and setting priorities for wounds that won't heal.

Key Risk Factors

- Advanced age
- Frailty and postoperative immobility
- Low or high body weight
- Incontinence
- Nerve damage
- Altered mental status
- Sedative drugs
- Vascular insufficiency
- Malnutrition
- Dehydration

Risk Factors and Red Flags

While intrinsic factors clearly increase the risk for developing wounds, the most vulnerable patients are those with multiple concurrent illnesses. Data from the US Wound Registry indicate that patients in outpatient wound centers have an average of six comorbid conditions, including a high prevalence of patients with renal failure, peripheral vascular disease, diabetes, and malnutrition [19]. Multimorbidity, defined by the National Quality Forum as "two or more chronic conditions that collectively have an adverse effect on health status, function, or quality of life," is known to be associated with an increased risk of death and disability. The complexity of these wound care patients is made evident by considering that only 14% of Medicare beneficiaries have six or more chronic conditions [20].

Obesity, defined as body mass index greater than 30, is a major public health problem that is not included in the indices of multimorbidity. The incidence of obesity in the United States increased dramatically between 1980 and 2008, doubling for adults and tripling for children· [21]. Although not often thought of as being a problem of aging, the startling reality is that more than one third of adults over the age of 65 are obese. What is concerning is that between 1990 and 2010 there has been a linear increase in the prevalence of obesity in older men. Thus, the prevalence of obesity has increased from 31.6% to 41.5% among men aged 65–74, while the prevalence among men 75 and older has increased from 17.7% to 26.5%· [22]. This alarming trend comes at great cost, with a health burden that includes an increased risk of diabetes, cardiovascular disease, osteoarthritis, stroke, and cancer, all comorbidities that impact wound healing [23]. Furthermore, obesity increases the risk of some of the most difficult wound healing problems: lymphedema and venous insufficiency [24, 25]. Presenting with chronically erythematous, edematous, and weepy legs, these patients are often admitted to the hospital for treatment of "cellulitis" and account for approximately 50% of visits to outpatient wound centers. Because bilateral lower extremity erythema and edema is more likely to be related to an exacerbation of congestive heart failure than acute infection, treatment requires a multidisciplinary approach, particularly in older adults who are at high risk for complications from repetitive antibiotic administration, fluid overload, and progressive disability. Older adults who are obese are also at risk for sarcopenia as fat replaces muscle mass. Intake of a calorically dense diet with increased carbohydrates and fat at the expense of protein, vitamins, and minerals, paradoxically puts obese individuals at high risk for malnutrition. Involuntary weight loss occurs disproportionately in older obese individuals and is associated with high mortality [16].

Diabetes is one of the most common comorbidities among people presenting to wound clinics. As our population lives longer and grows heavier, the prevalence of type 2 diabetes is steadily increasing. Current estimates are that over one quarter of individuals over the age of 65 are diabetic (*National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States*, 2014). Although the risk of type 2 diabetes is increased by obesity, both insulin resistance and reduced pancreatic islet cell function are age-related changes that can result in diabetes in older adults of normal weight [26]. Diabetes accelerates the normal rate of aging in a wide variety of physiological processes. Diabetes management is more complex in the older adult with multiple comorbidities, impaired nutrition, polypharmacy, and functional disabilities. The combination of peripheral neuropathy and peripheral vascular disease greatly increases the risk of wound healing complications, foot ulcers, and lower extremity amputations in the elderly patient with diabetes. Coexisting visual impairment and impaired cognitive function may lead to delayed presentation with greater severity and more difficult management. The good news is that the rate of hospital admissions for diabetics with lower extremity amputation and ulcers declined between 1988 and 2007. Although the discharge rate in 2007 for lower extremity conditions (peripheral arterial disease, ulcer/inflammation/infection, and neuropathy) as the first-listed diagnosis among diabetics aged 75 years or older was 21.6%, the rate has been steadily declining (http//:www.cdc.gov). The rate of nontraumatic lower extremity amputation in diabetics has steadily declined since 1996, particularly for those over 75 (dropping from 19.4% in 1996 to 3.7% in 2009). One interpretation is that outpatient care is improving, preventing the necessity of hospital admission.

Measurement Tools

- Activities of Daily Living
- Frailty Calculator
- Mini-Cog or MMSE
- Geriatrics Depression Scale
- Braden Scale to determine risk of future pressure sores

Functional and Cognitive Status Determination and Frailty Assessment

Frailty is considered to be highly prevalent with increasing age; it is estimated that 10–15% of older adults over the age of 65 are frail. The prevalence of frailty rises up to 25–50% of individuals older than 85. Frailty is a clinical state of weakness and susceptibility to stress arising from low physiological reserve across neuromuscular, metabolic, and immune systems. This low reserve increases an individual's vulnerability for adverse health outcomes.

As mentioned above, wounds and different wound care modalities including debridement and grafting are significant stressors that may further lower the physiological reserve; therefore, frailty has a clinical significance for older patients with wounds where potential exists to alter treatment options and adjust expectations (patient's and provider's) for cure [9].

Key Facts

- Frailty is a biologic syndrome of decreased reserve and resistance to stressors.
- Frailty is strongly linked to adverse outcomes after surgical interventions.
- Frailty index can serve as powerful predictor of outcomes.

Although studies of the association between frailty and wound intervention outcomes are lacking, some clues may be gleaned from prior work demonstrating worse surgical outcomes in frail patients, including mortality, delirium, and delayed discharge after elective general, thoracic, and cardiac surgery. Some early preliminary reports indicate that initial wound size is significantly correlated with frailty status [27]. Furthermore, it has been suggested that frail older adults with wounds experience more pain and have higher incidence of depression compared to age matched nonfrail older adults with wounds [27].

Diagnostically, it is difficult to discern frailty status based on lab tests. Evidence suggest that frail older adults with wounds will have similar erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), ankle-brachial index (ABI), and hemoglobinA1cC values as nonfrail older adults with wounds [27]. In geriatrics, the frailty index is widely used to determine frailty status and the score is used to prognosticate outcomes, provide a personalized approach to medical care, and enhance the patient's quality of life. The value of the frailty index has been proven in geriatric medicine and is being increasingly used in some surgical subspecialties [8].

Prognostication: Does This Wound Have the Potential to Heal in a Normal Time Frame?

Determining whether a wound has the potential to heal in a "normal" time frame is largely dependent on the underlying etiology, medical comorbidities, and duration and size of the wound [28–30]. Aside from those living with spinal cord injury, pressure injuries tend to occur in frail older adults. Venous leg ulcers may be accompanied by decompensated heart failure or immobility. Neuropathic foot ulcers can occur even in wheelchair users due to poorly fitting shoes or a malpositioned foot pedal. Concomitant ischemic changes secondary to a long duration of diabetes mellitus may impede wound healing even further.

Several retrospective cohort pressure injury studies suggest that many Stage 2 pressure injuries will close, even amongst frail long-term care patients [31–33]. It is important to note that these studies are heterogeneous both with regards to time followed (3–6 months) and location. The studies combined outcomes from coccyx, ischium, sacrum, and heels. Heel pressure injuries are more complex in that they have little subcutaneous tissue and may be complicated by inadequate arterial supply leading to lower tissue tolerance to pressure. Full thickness (unstageable and Stage 3 or higher) pressure injuries will take weeks to months to heal in those patients who can receive adequate nutrition, offloading, and local wound care. For those patients with an advanced illness, healing may not be the goal because there may not be enough time to heal the pressure injury prior to the patient's death [34].

Wound size and wound age are important prognostic signs for venous ulcer healing with standard compression therapy. A sophisticated cohort study that used modeling prognostic algorithms on 20,000 patients found a cut point with venous leg ulcers that were 10cm^2 and present for greater than 1 year. Those less than these parameters had a 70% chance of healing in 6 months, while those greater than these parameters had a 30% chance of healing in 12 months [29]. Likewise if there is early healing with standard compression therapy, then usually there will be closure within 3 months. A venous leg ulcer that is not showing evidence of healing in 6 weeks with standard compression therapy should raise the index of suspicion for an incorrect diagnosis, including the possibility of malignant transformation and warrants biopsy. Multiple punch biopsies that include skin at the wound edge may be required to achieve a correct diagnosis.

Neuropathic foot ulcers also have prognostic data for wound healing based on size and duration. A similar cohort study with modeling prognostic algorithms from 20,000 patients determined that those wounds greater than 2cm^2 that were present for greater than 2 months and showed evidence of osteomyelitis or abscess had a less than 25% chance of healing in 5 months. For those ulcers that show early healing by 1 month, a 53% reduction in size by 3 months is expected. This data was extracted from patients who were not treated with total contact casting, a therapy that has become a game-changer in healing these wounds [35]. However, because of the technical expertise and time involved and patient factors, real-world medicine has found that total contact casting is not often used despite its efficacy [36].

Promoting a Healing Environment

Nutritional Support

The nutritional impact of healing a chronic wound should not be underestimated. Caloric needs decrease with age, as does lean muscle mass and metabolic rate. Older adults frequently suffer from protein calorie malnutrition – 5% in community living adults and as high as 60% in those living in long-term care [37]. The protein requirement of patients with chronic wounds increases significantly. A patient can lose 12–25 grams of protein a day from a highly exudative wound [38]. Patients living with advanced illness will have difficulty with appetite, nausea, and swallowing function. Forcing them to eat can cause further suffering. While enteral supplementation can promote wound healing, feeding tubes are not recommended for patients with advanced dementia and pressure ulcers. Cohort studies have suggested that these patients are actually less likely to heal than those without feeding tubes and have an increased risk of pressure ulcer development [39]. Instead the provider should focus on the patient's goals of care – what foods do they like and can they be enriched in calories and protein? Several small meals through the day and focusing on oral care to reduce pain and improve taste may also be strategies to improve nutrition (Langemo 2010 NPUAP paper). Consulting a dietitian to calculate caloric, protein, and vitamin/mineral needs may be helpful in generating creative ideas to improve the nutrition.

Risk Factor Modification

Wounds are less likely to heal when the underlying cause cannot be reversed. Patients with complex contractures in the setting of advanced dementia may not be able to offload a pressure ulcer regardless of the repositioning. Nutritional deficiencies in that setting are also quite challenging. Sedentary patients whose legs are constantly in a dependent position and who cannot or will not wear compression wraps or garments are unlikely to heal their venous leg ulcers. Patients with neuropathic foot ulcers who are unable to offload their foot because of extenuating circumstances at home or work are also unlikely to heal. And for all of these wounds, if arterial insufficiency remains after the patient has received maximal revascularization or if there are no options for revascularization, then it is unlikely that the wound will heal. It is important to obtain a thorough social and functional history of the patient – inquiring about support at home, access to high quality/high protein foods, sleep habits, daily activities, ability to perform self-care, including wound care, and any depressive symptoms that may be occurring [40].

Physical Rehabilitation

Despite the low potential for some chronic wounds to heal, it is still important to keep the patient engaged and active to reduce functional decline. Especially those patients with arterial and venous disease, they will benefit from a walking program. Determining what the patient is already doing at baseline – maybe it is walking around the apartment – can help the provider motivate the patient to set goals for more walking in and around their home. Collaborating with physical and occupational therapy professionals is key to setting a self-care program that will minimize functional decline.

Medication Debridement

Almost 90% of older adults over the age of 75 are on chronic medications, a third of which are on three or more medications. On average, nursing home patients are on 7–8 medications. Some medications prescribed for older adults may indirectly (e.g., decreased alertness, falls, or impaired nutrition) or directly (interfere with coagulation, inflammation, matrix remodeling, or tissue perfusion) contribute to impaired wound healing. Medications should be regularly reviewed and discontinued if risk outweighs benefit. Special attention should be given to immunosuppressants, corticosteroids, NSAIDS, and anticoagulants as they have been shown to have the strongest effects on impairing wound healing. These and other medications that are commonly used in older population that may also contribute to slower wound healing are listed in Table 1 [41–44].

Table 1 Potentially high risk medication in older adults with wounds

Class	Common drug name	Mechanism	Wound specific effects	Recommendation
Anticoagulants	Warfarin, heparin, low molecular weight heparin	Inhibit coagulation cascade intrinsic and extrinsic pathways	Prevents fibrin deposition and impairs clotting, and resultant hematoma formation has been shown to cause mechanical disruption and may increase wound infection	Home safety check for clutter and risk fall, falls risk assessment
Antiplatelet drugs	Aspirin, nonsteroidal anti-inflammatory drugs, ticlopidine, dipyridamole	Inhibit platelet aggregation Inhibit arachidonic acid pathway	Affects wound hemostasis Interrupts inflammatory phase of wound healing and impairs epithelialization	Review indication and stop if possible, reduce dose/frequency if unable to stop
Cardiovascular drugs	Ramipril, lisinopril, captopril, irbesartan, candesartan Hydralazine, bendroflumethiazide, bumetanide, indapamide, furosemide, amiloride, spironolactone, metolazone Beta-blockers – doxazosin, alfuzosin, terazosin, tamsulosin	Bradycardia, hypotension, orthostatic hypotension, syncope	Both abnormal electrolyte states, especially in combination with epinephrine use and a diseased heart, can predispose the patient to poor wound blood flow. Some of the drugs in this category have anti-inflammatory effects that can impair/delay wound healing	Check laying and standing BP, review indication, and use alternative if possible
Gout medications	Colchicine, allopurinol, pegloticase	Inhibition of microtubule formation	Decrease cytokine release/ formation, decrease granulocyte migration, decrease blood supply from vasoconstriction, decrease fibroblast activity, interrupted excellular transport of, procollagen, increase collagenase synthesis	Review indication, stop if possible

(continued)

Table 1 (continued)

Class	Common drug name	Mechanism	Wound specific effects	Recommendation
Steroids		Inhibition of gene expression	Decrease inflammatory mediators, decrease platelet adhesion, decrease WBC recruitment and phagocytosis, decrease tissue formation, decrease tissue remodeling	Review indication, stop if possible, consider Vit A supplementation Of all the systemic corticosteroids, cortisone acetate is the least harmful in this regard. Doses less than the equivalent of 10 mg/day of prednisolone may have little effect on wound healing
Sedatives and hypnotics	Short- and intermediate-acting: alprazolam, estazolam, lorazepam, oxazepam, temazepam, triazolam Long-acting: chlorazepate, chlordiazepoxide, chlordiazepoxideamitriptyline, clidinium-chlordiazepoxide, clonazepam, diazepam, flurazepam, quazepam	Older adults have increased sensitivity to this class causing orthostatic hypotension, sedation, lightheadedness, slow reactions, impaired balance, and confusion	Alter alertness, difficulty meeting nutritional goals, may impair wound blood flow. Oversedation may lead to patient not repositioning self during sleep in bed or chair, making offloading more challenging	Avoid use Stop if possible Long-term use will need slow, supervised withdraw
Antipsychotics, first- (conventional) and second- (atypical) generation, tertiary TCAs, alone or in combination	Chlorpromazine, haloperidol, lithium,promazine, trifluoperazine, quetiapine, alanzapine, risperidone	Highly anticholinergic, sedating, and cause orthostatic hypotension; the safety profile of low-dose doxepin (≤6 mg/day) is comparable to that of placebo, slow reflexes, and Parkinsonian symptoms	Alter alertness, difficulty meeting nutritional goals	Avoid use for behavioral problems of dementia unless nonpharmacologic options have failed and patient is threat to self or others. Review indication and stop if possible Consider reducing dose
Antidepressants	Amitriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine, nortriptyline, paroxetine, protriptyline, trimipramine	Highly anticholinergic, sedating, and cause orthostatic hypotension; falls, drowsiness, blurred vision, constipation, urinary retention	Alter alertness, difficulty meeting nutritional goals	Avoid use. Review indication and stop if possible Consider reducing dose

(continued)

Table 1 (continued)

Class	Common drug name	Mechanism	Wound specific effects	Recommendation
Analgesics	Codeine, pentazocine, tramadol, morphine, oxycodone, meperidine	Drowsiness, confusion, hallucinations, orthostatic hypotension, apathy	Directly stimulate the sensation of nausea and delay gastric emptying; this can compromise the patient's ability to maintain oral fluids and diet	Review indication and stop if possible Consider reducing dose
Anti-epileptics	Amobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, secobarbital, pregabalin, carbamazepine, phenytoin, primidone, sodium valproate, gabapentin, lamotrigine, topiramate, levatiracetam	Unsteadiness and ataxia if levels high Phenytoin – permanent cerebral damage and unsteadiness in long-term use	Animal studies suggest poor wound healing	Review indication and stop if possible Consider reducing dose

A Different Focus on the Wound That Will Not Heal

After a patient has been informed that the wound most likely will not heal, they must be reassured that there are other areas on which to focus for wound care. Goals such as control of pain, exudate, odor, and bleeding are all important to the patient and can improve their quality of life. Much of the research with regards to palliative wound management has focused on pressure ulcers at the end of life. We have extrapolated that information to apply to all chronic wounds.

Pain Management

Pain associated with chronic wounds can be debilitating and a significant source of stress, further impairing the healing process [45]. The pain may be episodic – occurring with dressing changes or debridement, or it may be constant. Distinguishing in what situations and how often the pain occurs is important for management. Patients with a serious advanced illness, in whom repositioning may be painful, or patients with constantly painful wounds should receive premedication with nonsteroidal inflammatory medications or opiates 30 min prior to dressing changes and possibly afterwards as well. For those patients with pain due to dressing changes, determine whether it is the tape or the product removal that causes pain. Simply using skin adhesive remover can greatly relieve tape removal pain. Consider changing the wound product if it is sticking to the wound and causing pain, and choose a product with longer wear time so as to reduce the frequency of dressing changes. Periwound skin can become very irritated with dressing changes and there are skin preparations that can reduce tape trauma. Consider "window paning" a wound with a hydrocolloid – tape the dressing to the hydrocolloid and only change the hydrocolloid once a week to reduce periwound trauma. With regards to the dressings themselves, wet to dry dressings are not the standard of care. To be done properly they must be applied four times per day and are known to indiscriminately mechanically debride upon removal. Wet to dry dressings do not facilitate achieving moisture or bacterial balance, are very painful, and have no place in chronic wound care. Pain can be alleviated by applying liquid lidocaine 4% (moistened in fluffed gauze) or in a topical gel to the open wound for 5–10 min prior to conservative sharp debridement or if the patient states there is pain with dressing removal. Distraction techniques such as music, position changes, and guided imagery may be helpful. Lastly, always inform the patient that they are in control and can request a time out during a debridement or dressing change [34, 45].

Discharge and Exudate Management

Wound exudate can denude the surrounding skin and cause further pain and frustration. Thus it is important to assess the amount of exudate and adjust the dressing regimen accordingly (Table 2). One way to do this is to train the clinical staff or patient to put the soiled dressings on a separate surface so that you can assess amount and appearance of the exudate. Ask the patient and/or caregiver when it was last changed and assess the outside of the dressing for strikethrough (drainage that is visible from the outside). When considering dressings for exudate management, be mindful of

Table 2 Dressing options arranged by wound characteristics

Wound characteristic	Dressing category	Action	Common examples	Limitations/indications
Dry, shallow	Films	Moisture retentive, semi-occlusive. Keeps bacteria out, moisture in	Tegaderm® Opsite®	Cannot use on infected or draining wounds, may irritate skin
Dry, shallow	Impregnated gauze	Nonadherent, provides moist environment	Xeroform® Adaptic® Aquaphor®	Requires secondary dressing
Dry, shallow	Nonadherent gauze	Nonadherent, breathable	Telfa®	Adhesive and nonadhesive
Dry, shallow	Nonimpregnated, nonadherent	Prevents dressing adherence	Wound veil® Mepitel®	No active ingredients
Dry, minimal depth	Hydrogel	Polymer with high water content. Maintains moist environment, enhances autolysis	Normlgel® Carrasyn V® Solosite®	Viscosity varies
Low exudate, granulating	Hydrocolloid	Sheet dressing, promotes autolysis, may protect periwound skin	DuoDerm® Comfeel® Replicare® Restore®	May macerate or produce strong odor
Moderate drainage, shallow to deep	Alginate, derived from seaweed	Sheets and ropes, may have gelling properties, absorbs drainage while maintaining moist environment. May combine with honey or silver	Algisite® Kaltostat® Sorbsan® Curasorb® Melgisorb	May harden into “brick.” May create pressure if used for packing, requires semipermeable secondary dressing. It is bioabsorbable (OK to leave particles behind in the wound)
Moderate to high drainage, shallow to deep	Hydrofiber, synthetic from carboxymethyl-cellulose	Sheets and ropes, vertical wicking, ropes will not fall apart, absorbs and gels in the wound. May combine with silver	Aquacel® Drawtex®	Not bioabsorbable
Moderate to high drainage, shallow to deep	Polyurethane foam	Absorbent, wicking. May have silicone backing and border, sheets or cavity filling	Allevyn®, Mepilex® Cutimed®	May have gentle border for fragile skin; may combine with silver (expensive)
Moderate to high drainage	Composite	Attributes of alginate or hydrofiber combined with foam	Allevyn Life®	Expensive
High odor	Charcoal	Odor absorbent	Actisorb® Carboflex® Carbonex®	Activated charcoal binds bacteria but is not bactericidal. May be combined with silver

how to protect the wound edge. Skin preparations or barrier creams with zinc may be effective. Highly absorbent dressings that wick away moisture such as alginates, hydrofibers, or foams will increase wear time and protect periwound skin. There is a wide variety of dressings available, many of which are designed for fragile skin. In general, brand names are less important than matching the category of dressing with the wound characteristics.

For highly exudative leg wounds, consider using an incontinence undergarment (rather than a baby diaper). The incontinence undergarment is cost effective, super absorbent, and often does not have skin irritating deodorizers and perfumes that baby diapers may contain. Negative pressure wound therapy (NPWT) can be helpful for exudate management and to facilitate wound contraction. Hospice agencies will not pay for the treatment because CMS reimbursement mandates that the wound show evidence of closure. This is unfortunate for those patients living with serious advanced illness as NPWT can be very effective at controlling drainage and minimizing the frequency of dressing frequency changes, further reducing the need for painful repositioning [28, 34]. Data regarding the cost efficacy of NPWT compared to standard dressings, including personnel time combined with quality of life measures may be helpful in convincing payors to make exceptions for patients who require a palliative approach.

Odor Control

Wound odor primarily occurs due to heavy bacterial burden (anaerobes) and sometimes due to the wound product. Ask the patient and/or caregiver whether they notice wound odor. Determine whether you can smell odor – outside of the clinic room, only in the clinic room, in close proximity to the wound, or only with dressing removal. Remove the dressings and thoroughly cleanse the wound before reassessing. Hydrocolloid dressings tend to cause odor, and the patient and/or caregiver should be warned in advance so as to not confuse the odor with infection. Conservative sharp debridement to reduce the amount of necrotic tissue will aid in odor management. Short-term use of antiseptics for cleansing, such as 0.125 or 0.25% Dakin's solution or hypochlorous acid, can also reduce odor. Using these solutions longer than 2 weeks should be avoided. Topical metronidazole with each dressing change has been used for odor control. Crushed tablets are more cost effective than creams or ointments. Composite dressings that contain silver, cadexomer iodine, or honey and an absorbent component will further reduce the bacterial burden, thereby reducing odor. Patients and caregivers might find charcoal dressings, kitty litter under the bed, coffee grounds in the room, or other external deodorizers helpful [28, 34].

Hemostasis

Bleeding can be very frightening to the patient and to the caregiver. Bleeding in chronic wounds typically occurs due to high bacterial burden or a traumatic dressing. This can be alleviated simply by changing dressing types to reduce the bacterial burden or adding a nonadherent component such as an impregnated gauze, wound veil, or silicone dressing to prevent trauma to the wound bed during dressing changes. Bleeding occurs briskly in malignant wounds, as they tend to be hypervascular. Patients and/or caregivers should be given an action plan if brisk bleeding should occur. There are highly expensive hemostatic dressings on the market, but these can be used on an as-needed basis to prevent an emergency room visit before the Hospice nurse can arrive to advise changes in the wound treatment plan. Dark towels, which mask the appearance of bleeding, can be used to hold pressure and may further reduce anxiety. Cold compresses can promote vasoconstriction, but may be uncomfortable for the patient.

Quick Tips

- Code all procedures including HCPCS codes
- Take pictures and measurements
- Document wound requirements
- Make sure that products ordered meet the definition of durable medical equipment, prosthetics, orthotics, and supplies
- Promptly sign and date your wound notes

Financing Wound Care

In 1965 the US government enacted federal legislations to provide health insurance for the old, disabled, and poor. Today Medicare and Medicaid programs cover most healthcare expenditures for adults age 65 and older including physician office visits, home visits, early post-acute care through Medicare part B as well as a specific and more comprehensive Medicare part C coverage, and prescription drug coverage (Medicare part D).

In the wound healing field, Medicare covers 80% of the costs but requires clear and detailed documentation of wound dimensions and including supplies that are deemed medically necessary for treatment. Promptly dated and signed wound notes are essential to avoid reimbursement decline [46]. In general Medicare covers the following broad categories:

I. **Dressings:** under Medicare part B, almost all surgical dressings are covered for wound patients. Deductible and copayment should be considered when ordering these dressings.
II. **Compression stockings:** limited to venous or lymphedema wounds that are open and measurable. Ordering the compression garment when the wound is still open but near closure will help prevent wound recurrence and meet insurance requirements.
III. **Home nursing and wound care:** including home nursing to change dressing, clean wounds, and topical or systemic application of medications. This coverage is included with Medicare part A**.**
IV. **Out-patient care:** essential to this coverage that clinicians carefully document with each visit wound size, depth and if drainage is required.

Clinical Vignette

The Impact of Frailty on Stage 4 Pressure Ulcer Healing

The following scenario describes two patients who presented with very similar pressure ulcers. Both are wheelchair bound. Patient #1 is 71 years old with a 26 year history of multiple sclerosis. She has multiple chronic diseases including chronic obstructive pulmonary disease and has had multiple admissions for respiratory insufficiency. She was admitted to the hospital with pneumonia and was noted to have an unstageable right ischial pressure ulcer. There are four specialists involved in her care including infectious disease, nephrology, pulmonology, and palliative care. Her home medication regimen included seven medications, not including the antibiotics prescribed in the hospital. The right ischial pressure ulcer developed at home prior to admission. Her albumin was 2.5, prealbumin 26. Patient #2 is an 82-year-old paraplegic of 50 years duration after a motor vehicle crash. She has no other medical problems. She has a primary care physician and has no specialists involved in her care. She takes analgesics for chronic back pain. Admission albumin and prealbumin were 3.0 and 31, respectively. She also was admitted with pneumonia and noted to have a preexisting right ischial pressure ulcer that was unstageable at the time of consultation.

Based on the number of medications, the number of specialists, and the number of prior falls or hospitalizations, patient #1 meets criteria for frailty while patient #2 does not (Fig. 1).

This side-by-side comparison illustrates the complexity of caring for a frail older adult with multiple comorbid illnesses and a Stage 4 ischial pressure ulcer complicated by osteomyelitis. Both patients require intravenous antibiotics based on intraoperative bone cultures if available. Both patients require exudate management with appropriate moisture retentive dressings. Both patients require vigilant periwound skin care and offloading to improve tissue perfusion and prevent progression of pressure injury. Both patients require an involved caregiver who can help manage fecal and urinary incontinence. Both patients require nutritional supplementation.

In this scenario, the frail older adult required three times as long to reach the same level of healing as the nonfrail older adult.

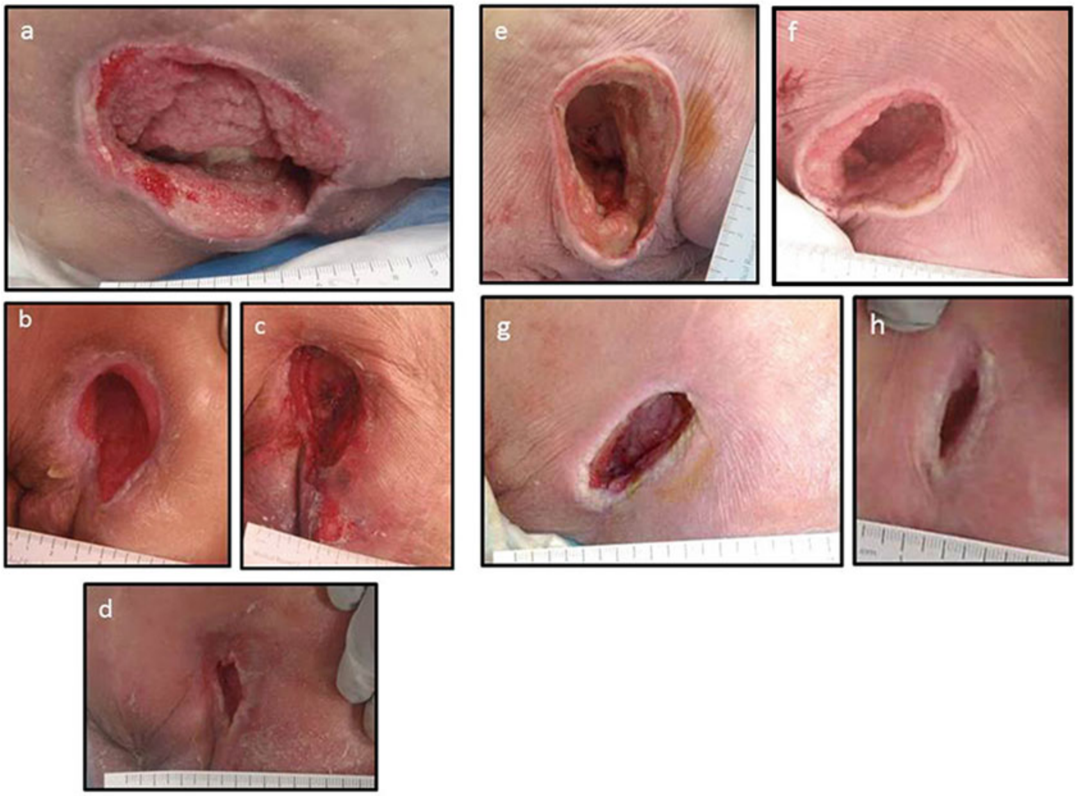

Fig. 1 Impact of frailty on healing in older adults with stage 4 pressure ulcer. (**a**) Patient #1 is a 71-year-old with multiple chronic illnesses who underwent operative debridement. After debridement the wound measured 6.5 × 5.5 cm, 3.6 cm deep. The patient was treated with intravenous antibiotics for osteomyelitis based on intraoperative bone culture. (**b**) 5 months after debridement and treatment with negative pressure wound therapy the wound is 5.5 × 3 cm, 1 cm deep. (**c**) There was marked improvement until admission for respiratory insufficiency. Upright posture is required for respiratory toilet and the wound waxes and wanes depending upon respiratory status. 11 months after debridement the wound measured 7 × 2 cm, 1.5 cm deep. (**d**) Negative pressure wound therapy is continued with the occlusive drape protecting the wound from fecal contamination. Time out of bed to chair is about 3 h per day and respiratory complications have been minimal. 18 months after debridement the wound measures 3 × 1cm, 0.5 cm deep (**e**) Patient #2 is an 82-year-old paraplegic with minimal past medical history who underwent operative debridement. After debridement the wound measured 6 × 5 cm, 3 cm deep. The patient was treated with intravenous antibiotics for osteomyelitis based on bone culture. (**f**) 2 months after debridement the wound measures 5.5 × 4.3 cm, 2 cm deep. Negative pressure wound therapy was discontinued because of difficulty maintaining a seal when getting out of bed to the chair. (**g**) 3 months after debridement the wound measures 4.5 × 1.7 cm, 1.5 cm deep. (**h**) 7 months after debridement the wound measures 2 × 0.5 cm, 0.5 cm deep and has minimal drainage

Conclusion: Putting It All Together

From the foregoing discussion it should be clear that care of the patient with chronic wounds requires a multidisciplinary approach and that this is even more critical in older adults. Many of these wounds require specialty care that is beyond the scope of what the primary care physician can provide. Specialized wound centers have been developed to facilitate healing of the most difficult wounds and need to be prepared to manage the complexities of the frail and older patient. Additionally, providers trained in geriatrics and palliative care are often involved in the care of these complicated patients to assist with symptom management, goals of care clarification, and to prevent functional decline, polypharmacy and to maximize quality of life. The goal of the comprehensive wound center is to promote wound healing through evidence-based protocols. An early and aggressive approach to wound closure reduces cost, improves quality of life, and prevents re-admission to the hospital. The wound care clinician will assist with the diagnosis, provide appropriate debridement to remove necrotic tissue and prescribe treatments that move the wound toward bacterial balance and promote healing.

However, older adults have additional special needs that merit multidisciplinary care and comprehensive assessment. According to the US

Table 3 Treatment modifications for older adults

Wound type	Offloading	Edema control	Moisture management
Pressure ulcer	Use friction reducing devices (FRDs) for transfers to reduce friction/shear on frail skin. Do not use heel offloading boots if the patient gets out of bed without assistance – increased risk of falls	N/A	Avoid use of foley catheters for sacral/coccyx/ischial pressure ulcers – increase risk of delirium Avoid wearing plastic incontinence garments at night that might trap moisture. Better to have highly absorbent pad under patient
Venous leg ulcer	Ask about positioning in bed, as pressure from bed or recliner on leg wound can retard wound healing	Assuming adequate arterial supply (ABI >0.8) start low compression wrapping (two layer) and increase weekly to four layer if patient tolerates Gradient compression wrap, nonelastic better than compression stockings. Indications are obesity, fragile skin, limited mobility or grip strength, limb shape not conducive to traditional stockings. Medicare will only pay when there is an active ulcer Consider intermittent pneumatic compression pumps if patient unable to don any stockings. May have to prove failure of compression stockings first Avoid long-stretch elastic wrap (e.g., ACE) as this will tourniquet and cause further skin injury Avoid thromboembolic deterrent stockings (TEDS) for edema control – they cause pedal edema as the strongest amount of compression is at the calf Consider PT consult for walking program to further reduce edema	For patients with highly exudative wounds not easily managed with wound products, consider use of incontinence undergarment. Avoid use of baby diapers/sanitary napkins (have perfumes)

(continued)

Table 3 (continued)

Wound type	Offloading	Edema control	Moisture management
Neuropathic foot ulcer	Total contact cast, CROW, forefoot offloading shoe, or knee scooter. These devices may not be a consideration if patient is at risk for falls. Older adults may not have sufficient shoulder strength for crutches Consider wheelchair, but with caution of coccyx/ischial pressure ulcer prevention. Need exercise plan to avoid deconditioning (hand pedal bike)	Address edema in patients with neuropathic foot ulcers – neuropathy affects the lymphatic system and can cause swelling that will impair wound healing	Wet wounds Foams Cadexomer iodine Hydrofiber Alginate Dry wounds Hydrogel Hydrocolloid (but can macerate skin)
Arterial ulcer	Consider vascular lambs-wool lined boot for offloading, protection, and warmth	Leg elevation Consider PT consult for walking program to increase arterial collateral flow and reduce edema. Challenging if patient is to remain nonweight bearing	Goal is to keep clean and dry until after revascularization (if an option). Can consider antiseptics (betadine) in this case

Census Bureau, 20% of people over age 65 have some chronic disability with 8% having significant cognitive impairment and 30% having difficulty with mobility. More than 40% of individuals over the age of 85 living in the community have difficulty performing activities of daily living and one in six report cognitive limitations (Rising demand for long-term services and supports for elderly people, 2013. www.cbo.gov/publications/4240. Retrieved August 18, 2015). Further assistance in activities of daily living may be required for patients who have been told to stay off of their neuropathic foot ulcer or limit time in the chair to promote pressure ulcer healing. Some older adults with wounds require more emphasis on palliation with control of symptoms and avoidance of infectious complications. Interestingly, more than 50% of wounds treated with a palliative approach ultimately heal [28]. Wound specialists have an in-depth knowledge of and access to advanced wound care modalities that promote healing, reduce odor, and increase comfort. The multidisciplinary approach emphasizes optimization of medical management, nutrition, mobility, pressure reduction, and perfusion while exploring barriers to care. Furthermore, best practice, evidence-based wound healing modalities such as diabetic foot offloading and compression wrapping need to be modified for the elderly patient with gait disturbances, risk of falls, or congestive heart failure (Table 3).

Other barriers for the older adult may include financial stress and lack of social support. The patient and caregiver may feel overwhelmed with tracking what treatments have worked best and what have caused problems. Getting to frequent appointments with a wound care provider can also be burdensome. An outpatient clinic setting can give a caregiver a break from dressing changes for a few weeks, but increases the burden of appointments. Skilled home health services can be a blessing; unfortunately, the patient may be discharged if the wound is not progressing. The provider will need to advocate for the patient, stating that the wound will make very slow progress due to underlying conditions. Teamwork is critical to facilitate care across the continuum and requires coordination with the family, with home health services and with the primary care physician. The $5 billion global market for "advanced wound management" is expected to triple in the next 10 years. Our nation's older adults will receive a disproportionate share of this advanced care. With a concerted interdisciplinary approach with the patient at the center of the algorithm, we can anticipate improved outcomes and better utilization of limited resources.

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Part IV

Outcomes and Transitions of Care

Transitioning Care at Discharge

27

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Contents

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Abstract

The vast majority of older patients undergoing surgical procedures are medically complex with multiple chronic medical conditions, which poses significant challenges during transitions of care. Older patients frequently require specialized care coordination as they transition between surgical and nonsurgical healthcare providers located in different care settings following surgery. Transitional care at the time of hospital discharge is a critical period to ensure that appropriate information is exchanged between inpatient and outpatient healthcare providers and ensure that patients receiving appropriate follow-up care and the best outcomes. There are several different types of interventions that can be carried out before and after patients leave the hospital after surgery to achieve these goals. In this chapter, we will review the challenges facing older patients during transitions of care after surgery and the spectrum of evidence-based interventions available to healthcare providers for improving transitional care. Applying these strategies can significantly improve the quality of care and outcomes for older patients undergoing major surgery.

Keywords

Care transitions · Surgery · Discharge planning · Care coordination · Post-discharge · Multimorbidity · Geriatric

Introduction

It is estimated that over eight million inpatients surgical procedures are performed annually in US hospitals across all surgical specialties [1]. Nearly half of these surgical procedures are performed in adults aged 65 years and older [2]. The vast majority of older surgical patients meet criteria for multimorbidity with two or more chronic medical conditions such as cardiovascular, pulmonary, or renal disease. Moreover, at least 20% of older patients have five or more chronic conditions and take >6 prescribed medications that require close medical surveillance [3]. Older patients with multimorbidity are considered *medically complex* and require extra steps to ensure that their care is highly coordinated during transitions of care.

Transitional care has been broadly defined as the set of actions taken to ensure that patients have coordination and continuity of healthcare as they transition between different care settings, healthcare providers, and/or different levels of care within a given healthcare setting [4]. This involves the deliberate organization of patient care activities and sharing information among all providers concerned with delivering care to an individual patient across transitions of care [5, 6]. This can be particularly challenging for medically complex older patients undergoing major surgical procedures. Care is often incomplete or fragmented given that patients frequently transition from the primary care provider who knows them well to surgical specialists whom are not familiar with a patient's chronic care plan [7]. Differences in organizational practices, clinical preferences, as well as cultural differences between surgical and nonsurgical healthcare providers all may contribute to poor communication and/or fragmented care coordination during transitions.

Poor coordination of care during transitions is estimated to effect the quality of care and outcomes in over a quarter of discharged patients [8]. Specifically, the failure of providers to communicate effectively and share a "mental model" of clinical goals has been identified as the primary root cause in 85% of adverse events that occur in the outpatient setting after patients have left the hospital [9]. These gaps in care coordination lead to a significantly higher risk for older patients to experience a medical error or adverse event and require hospital readmission [9]. Moreover, when post-discharge complications occur in older patients and they require readmission, the lack of care continuity with healthcare providers who performed their surgery has been associated with a 25% higher risk for mortality [10, 11]. These different types of breakdowns in care coordination also lead to increased costs of care [12].

As such, it is well recognized that care coordination needs to be optimized for older patients at the time of hospital discharge to achieve the best clinical outcomes. The Joint Commission, the Centers for Medicare and Medicaid (CMS), and the Institute of Medicine (IOM) have all identified care coordination during transitions of care as one of the keys to improving the effectiveness and safety of our US healthcare system [13]. Furthermore, transition care programs for vulnerable patients were incentivized by passage of the Patient Protection and Affordable Care Act of 2010 [14]. This has resulted in the development of multiple strategies to improve care coordination during transitions between outpatient and inpatient settings for older patients with multiple chronic disease conditions [15]. But while multiple strategies have been proposed to improve care coordination for medically complex older patients during transitions of care, it is unclear what strategies are most effective for patients following surgery.

In this chapter, we will review factors that place older patients at risk for fragmented care during transitions following surgery and the different transitional care strategies that have been developed to prevent adverse events and improve patient outcomes. Transitional care interventions have been found to be most effective among people older than 60 years of age, although most have not been designed to be specific for surgical patients [16]. It is critical to understand what strategies can be applied to surgical patients at different stages during an episode of surgical care, including pre-admission, during the surgical hospitalization, and post-discharge (Fig. 1). We will discuss specific interventions that can be used for improving care coordination (1) before patients leave the hospital (pre-discharge), (2) after patients leave the hospital (post-discharge), and (3) across the care continuum to bridge the transition between inpatient and outpatient care. The success of transitional care for many older adults relies upon applying multiple interventions, and many strategies involve bundling separate components in different combinations. It is hoped that this overview of transitional care interventions will help surgical providers and health systems guide implementation of strategies that can improve the quality of care and outcomes for older patients following major surgery.

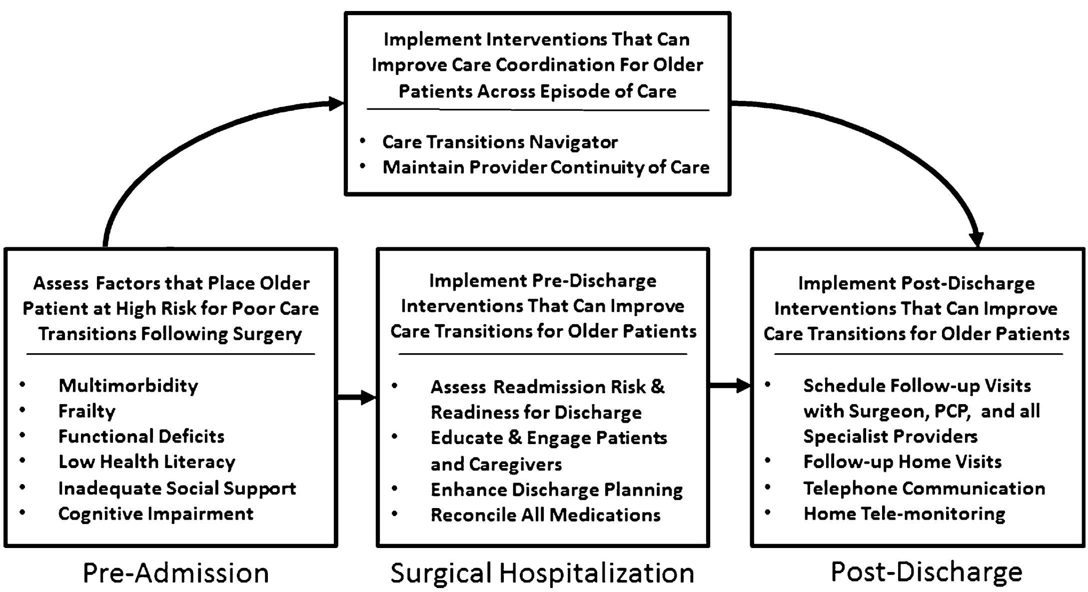

Fig. 1 Conceptual model of transitional care strategies during episode of surgical for older patients. Various interventions to improve surgical care transitions can be applied before admission, during hospitalization, and following discharge

Patients at Risk for Poor Care Transitions Following Surgery

There are multiple factors that place older patients at risk for fragmented care and poor outcomes during care transitions following surgery. This includes a spectrum of variables related to chronic medical conditions, socioeconomic status, as well as factors that are specific to their surgical procedure and postoperative care. Moreover, many older patients have components of frailty such as functional or cognitive deficits that limit their ability to respond to surgery. It is important to recognize these different types of risk factors for poor care transitions and the assessment tools that can be used to identify them before and after surgery (Table 1). Identifying risk in older patients can help providers target additional interventions during the discharge planning process to prevent unplanned readmissions.

Table 1 Risk factors for poor care transitions following surgery

Variable	Examples of available assessment tools
Multimorbidity	• Predicting Emergency Admissions Over the Next Year (PEONY) • Q-Admissions Risk Calculator • Gagne Index • Multimorbidity (MM) Index • National Surgical Quality Improvement Program (NSQIP) risk calculator • Charlson Comorbidity Index
Frailty	• Fried (Hopkins) Frailty Score • Comprehensive Geriatric Assessment • Risk Analysis Index (RAI) • Modified Frailty Index (mFI) • Vascular Quality Initiative Frailty Index (VQI-FI) • Clinical Frailty Scale (CFS) • Frail Non-Disabled (FiND) Instrument • Tilburg Frailty Indicator • SHARE Frailty Index
Functional deficits	• Hospital Admission Risk Profile (HARP) • Katz Index of Independence in Activities of Daily Living • Lawton Instrumental Activities of Daily Living (IADL) Scale • Activity Measure for Post-Acute Care (AM-PAC)
Low health literacy	• Short Assessment of Health Literacy (SAHL) • Rapid Estimate of Adult Literacy in Medicine (REALM) • Test of Functional Health Literacy in Adults (S-TOFHLA) • BRIEF Health Literacy Screening Tool (BRIEF)
Inadequate social support	• The Social Provisions Scale (SPS) • Perceived Social Support Scale (PSSS) • Social Support Questionnaire (SSQ) • Multidimensional Scale of Perceived Social Support (MSPSS)
Cognitive impairment	• Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) • General Practitioner Assessment of Cognition (GPCOG) • Memory Impairment Screen (MIS) • Mini-Cog Assessment • Mini-Mental State Examination (MMSE)

Multimorbidity

Comorbid medical conditions are one of the central factors that place older surgical patients at risk for difficult care transitions. Up to 90% of older patients meet diagnostic criteria for *multimorbidity* with co-occurrence of two or more chronic diseases [17]. And approximately a quarter of patients over 65 years old have five or more long-term health conditions that require more than six or more prescribed medications on a daily basis [3]. Patients with multimorbidity become increasingly difficult to manage when they transition across care settings, particularly when being referred to surgical specialists for evaluation and operative management. This results in large part from the inefficient exchange of complex health information between primary care and surgical providers and inability to share a mental model of how care should be coordinated. Furthermore, primary care providers do not always have a clear sense of what their role should be in the immediate post-discharge care of patients following surgery.

There are a variety of tools available to assess the degree of multimorbidity and corresponding degree of risk in older patients undergoing surgery. Table 1 shows a sample of the different risk calculators that have been developed and validated in medical and surgical populations using patient comorbidity data. They are available to predict risk for short-term outcomes such as unplanned readmission or need for post-acute care settings, as well as long-term outcomes and mortality. Moreover, many of these tools can be adapted and automated within EHR systems or found on publicly available websites to provide healthcare providers risk data at the point of care.

Most comorbidity risk assessment tools are not specific to surgical outcomes with the exception of the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) risk calculator. This tool is available online (http://www.riskcalculator.facs.org/) and can be used to assess a patient's risk for a number of different outcomes based on their specific surgical procedure and 19 different comorbidity variables. Another risk tool able to be calibrated for surgical populations is the Charlson Comorbidity Index, which can be used to predict an individual's mortality risk from a list of 30 different categories of comorbidities. However, this risk index is most commonly used for comorbidity adjustment in surgical databases and not typically used for prospective risk assessment.

Frailty

An older patient's degree of frailty is another measure that can be used by surgical providers to estimate risk for poor outcomes during transitions of care after surgery. Frailty is a multidimensional syndrome independent of age that is defined as a patient's loss of physiologic resilience to stress. As frail patients have a limited ability to respond to a major stress such as surgery, it is not surprising that frailty measures also correlate with postoperative morbidity and mortality [18].

Frailty can be measured in older patients undergoing surgery using several different approaches, broadly classified as *phenotypic frailty models* and the *accumulated deficits model (ADM) of frailty*. Phenotypic models focus on recognition of somatic or physical characteristics that are associated with frailty. The Fried or Hopkins Frailty Score is one of the most widely recognized phenotypic models of frailty, which measures five domains: unintentional weight loss, self-reported exhaustion, weakness as measured by grip strength, slow walking speed, and low physical activity [19]. The Fried Frailty Score has been validated for predicting postoperative outcomes among a variety of different surgical populations [20]. Other phenotypic methods used to assess frailty include measurement of nutritional status (e.g., serum albumin), triceps skinfold thickness, and sarcopenia. In particular, it has been suggested that computed tomography (CT) measurements of psoas muscle size can be used to quantify sarcopenia and serve as a preoperative measure of frailty [21].

The other main approach that can be used by healthcare providers to assess frailty is the ADM. This assessment tool originated from the Canadian Study of Health and Aging and probes 70 different items within physical, medical, cognitive, and functional domains as part of a Comprehensive Geriatric Assessment (CGA). While the CGA has been deemed too time-consuming to undertake in routine surgical practice, truncated versions of this model have been developed for surgical patients [20]. This includes the Clinical Frailty Scale, which is a simplified assessment tool using schematics to represent progressive degrees of frailty based on the ADM. Other models based on the ADM include the modified frailty index (mFI) and the Vascular Quality Initiative Frailty Index (VQI-FI). These last two frailty indices utilize data that is routinely collected as part of surgical quality improvement registries such as NSQIP or the Vascular Quality Initiative (VQI) and have been used to estimated risk associated with 30-day and 1-year mortality outcomes following different general and vascular surgery procedures.

Functional Deficits

Beyond assessing comorbidity data, other specific risk factors can be used to identify older patients who are at risk for having difficult care transitions following surgery. One significant factor to recognize and measure is whether older patients have any *functional deficits*. This is defined as any limitation or impairment in physical ability that results in lack of mobility or inability to independently complete their activities of daily living. Functional deficits directly impact a patient's ability to care for themselves after surgery and place patients at a greater risk for adverse postoperative events such as falls in the outpatient setting. Recent studies have shown that functionally dependent surgical patients have a significantly increased risk of discharge to post-acute care facilities, irrespective of whether postoperative complications occurred [22]. Loss of independence during the postoperative period is also associated with an increased risk for readmission and death following hospital discharge [23].

There are a wide range of tools that can be used to screen for functional deficits and risk for loss of independence in older patients before and after surgery (Table 1). Standardized tools that can be applied in the preoperative setting include the Hospital Assessment Risk Profile, the Katz Index of Independence in Activities of Daily Living, or the Lawton Instrumental Activities of Daily Living (IADL) Scale. In particular, these instruments are useful for assessing whether an older patient can perform daily tasks necessary to live independently in the community after surgery. The information provided from functional assessment tools can also provide objective data to assist with targeting individualized patient needs following discharge including in-home services such as meal preparation, nursing care, homemaker services, personal care, or continuous supervision.

During the postoperative period, it is important to re-evaluate older patients' functional status and assess needs for post-discharge care. Tools such as the Activity Measure for Post-Acute Care (AM-PAC) are useful for assessing activity limitations in older patients across post-acute care settings. In particular, the AM-PAC "6-Clicks" Basic Mobility Short Form is a simple measure used by physical therapists (PT) to assess mobility in the inpatient setting and can be used to predict when patients might benefit from further PT services in the outpatient setting [24].

Low Health Literacy

Low health literacy is found in up to a third of the US adult population and places older patients at risk for adverse events during transitions of surgical care [25]. Health literacy is defined as the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions. This includes specific skills needed by patients to navigate the healthcare system and allow clear communication with their healthcare providers. Older surgical patients in particular need to be able to access information and resources that are specific to their surgical condition following discharge. Adverse events may occur when patients don't understand their medications, discharge instructions, or warning signs following hospital discharge after surgery.

There are a wide variety of instruments available to healthcare providers for assessing health literacy in older patients undergoing surgery (Table 1). This includes tools that have been designed to objectively test an individual's health literacy or alternatively rely upon the elicitation of self-reported abilities [25]. Using the objective measurement approach, patient abilities are assessed by solving tasks dealing with print literacy, numeracy, or oral literacy. In comparison, the self-report approach is characterized by how a patient perceives their ability to interpret medical terminology in multiple domains. Many health literacy tools have been designed to be administered for non-English-speaking adults, and some can be administered in as little as 2 min. These can be quickly administered during the preoperative or postoperative period and can help surgical providers *personalize* an older patient's transition of care after surgery.

Inadequate Social Support

Many older adults undergoing surgery are found to have an inadequate social support network, which increases their risk for poor transitions of care. Social support is both the perception and actuality that patients have assistance or resources provided from other people, which may include caregivers, family, friends, neighbors, or other members within their community. The supportive resources provided by these individuals can be categorized by the form of aid provided and includes instrumental, informational, and emotional support [26]. Instrumental support refers to the availability of people who can provide functional aid in completing daily tasks, such as making meals or providing transportation if needed. Informational support refers to the availability of people who can provide information or advice needed to solve problems that arise. And emotional support refers to the availability of people to listen to a patient's problems and provide empathy, caring, and understanding. All of these forms of social support can influence a patient's ability to thrive during transitions of care following surgery.

There are multiple tools available for surgical providers to assess a patient's perception of their social support network (Table 1). While these instruments contain different questions, they are all designed to assess components of instrumental, informational, and emotional social support domains. Most of these questionnaires can be administered rapidly within the preoperative or postoperative periods and used to determine how much support older patients can count on from people around them following hospital discharge. They can also be used to help patients and healthcare providers identify specific individuals who can provide assistance with their post-discharge care plan. This is particularly important when older patients have outpatient wound care or physical therapy needs following surgery.

Cognitive Impairment

Cognitive impairment may be present at varying degrees in a high percentage of older patients undergoing surgery and influence their ability to transition successfully after surgery. This is defined as impairment of mental processes that limit a patient's acquisition of information and knowledge and influences how they understand and interact with their environment. Mild cognitive impairment is estimated to be present in up to 40% of patients older than 65 years of age who present for surgery, whereas dementia is found in up to 7% of patients [27]. Older surgical patients with cognitive impairment at baseline are also at high risk for postoperative delirium and postoperative cognitive dysfunction (POCD) [28]. POCD is typically a short-term decline in cognitive function, especially in memory and executive functions, which may last from a few days to a few weeks after surgery. The symptoms vary from mild memory loss to an inability to concentrate or process information.

Any type of impairment in cognitive function during care transitions places older patient at risk for poor outcomes after discharge. Surgeons caring for older patients should be aware of the various tools available to screen for cognitive impairment (Table 1). Most of these tools need 10 min or less to administer and can be performed by a mental health consultant working with the surgical team. While the evaluation of baseline cognitive function is not part of routine preoperative evaluation, nevertheless it is important to identify older patients who should undergo screening. Cognitive screening tools can help risk stratify patients who would benefit from close surveillance and interventions to support care transitions. Moreover, these measurements may help guide decision-making and customize both surgical treatments and post-discharge plans for older patients.

Interventions to Improve Care Transitions Before Hospital Discharge

Assessment of Readmission Risk and Readiness for Discharge

Roughly 20% of older patients who undergo major surgery will be readmitted to the hospital within 30 days after discharge [29]. The various risk factors defined above all place older patients at risk for poor care transitions and adverse events after discharge, which often require the need for readmission. As such, it is important to systematically assess a patient's readiness for discharge and identify risk factors for readmission before discharge so that the hospital team can work to begin to mitigate those risks while surgical patients are still inpatients. Assessing how well an older patient is prepared for discharge and their risk for readmission can also help clinicians identify older patients who might benefit from more intensive post-discharge care.

While assessment tools defined in Table 1 can be used to evaluate individual risk factors, they are not specific to calculating an older patient's risk for readmission. However, several clinician friendly readmission risk assessment tools have been developed and validated to meet this need (Table 2). The Length of stay, Acuity, Comorbidity, and Emergency department use (LACE) index is one of the most well-known tools and calculates risk for readmission based on an algorithm that combines a patient's length of stay, acuity of admission, comorbidities, and ER visits within the prior 6 months [30]. This model was derived using medical and surgical patients of all ages and has moderate discriminative ability to predict unplanned readmissions. Another risk index for predicting 30-day potentially avoidable readmissions among patients hospitalized for medical conditions of all ages is the HOSPITAL score [31]. This score is calculated using eight different patient risk factors and has a slightly greater discriminatory power to predict readmissions, but at the cost of needing to collect more variables. The Pra instrument is an eight-item questionnaire that can be used to screen older adults readiness for discharge and assess risk for readmissions and need for post-discharge outpatient healthcare services [32]. While this tool requires survey administration and has lower predictive power, nevertheless it is designed specifically for older patients. Finally, the TCM discharge screening and BOOST 8P tools define different risk factors that providers can use to categorize older adults at high risk for adverse events during transitions of care at the time discharge. Readmission risk is calculated by the severity of these risk factors and can be used to stratify patients prior to leaving the hospital [33].

The ACS-NSQIP risk calculator previously mentioned can also be used to estimate 30-day readmission likelihood using both patient and procedure-level data. This nomogram calculates readmission risk based on five patient-level variables and five procedure-related variables and has moderate discriminative power to predict unplanned readmission [34]. Using this tool, early 30-day readmission following both general and vascular surgery procedures has been found to be strongly associated with postoperative complications [35–37].

Education and Engagement of Patients and Their Caregivers

A central component of most care transitions interventions is a focus on education and engagement of patient and their caregivers. Many studies have shown that patients who are better educated and engaged about their health condition are more likely to participate in preventative and healthy behaviors, self-manage their health condition, have better healthcare experiences, and achieve better clinical outcomes [38]. It is recognized that patient and their caregivers or families must actively participate in informed decision-making and receive appropriate education prior to hospital discharge for self-care management. This includes recognition and understanding of important health issues, medications, as well as early identification and response to potential problems to prevent decline in health condition. Developing a patient-centered care plan individualized to specific post-discharge needs is a core part of several care transitions interventions. Furthermore, patients and caregivers need to be aware of resources that are available to them in the post-discharge outpatient setting.

In order for education and engagement practices to be effective during transitions of surgical care, they need to be patient-centered and tailored to the risk profile of the individual patient. For example, an older patient with low health literacy or who doesn't speak English will need resources that are specific to their level of comprehension and delivered in a language they can read. It is recommended that providers use "teach-back" methods to have patients recite what they have

Table 2 Readmission risk assessment tools

Risk assessment tool	Variables assessed using tool	Patient population and ages	Discriminatory or predictive power
LACE	Length of stay Acuity of admission (i.e., inpatient or outpatient) Comorbidities ER visits within previous 6 months	Surgical and medical; all age ranges	c-statistic – 0.70
HOSPITAL	Hemoglobin level Oncology (i.e., discharged from oncology service) Sodium level Procedure Index admission type No. of admissions in the past year Length of stay	Medical; all age ranges	c-statistic – 0.72
Probability of repeated readmission (Pra) instrument	Survey questions In general, how would you say your health is? In the previous 12 months, have you stayed overnight as a patient in a hospital and how many times? In the previous 12 months, how many times did you visit a physician or clinic? In the previous 12 months, did you have diabetes? Have you ever had coronary heart disease, angina pectoris, a myocardial infarction, or a heart attack? What is your sex? Is there a friend, relative, or neighbor who would take care of you for a few days, if necessary? What is your date of birth?	Medical; patients >65 years	AUC – 0.64
TCM hospital discharge screening criteria	Being age 80 or older Moderate to severe functional deficits More active coexisting health conditions Six or more prescribed medications Two or more hospitalizations in the past 6 months or hospitalization in the past 30 days Inadequate support system Low health literacy Documented history of nonadherence to the therapeutic regimen Cognitive impairment such as diagnosis of dementia or positive screening assessment using standardized tools	Surgical and medical; all age ranges	N/A
BOOST 8Ps	Problem medications (e.g., warfarin, insulin, etc.) Psychological (e.g., depression) Principal diagnosis (e.g., cancer, stroke, etc.) Polypharmacy (>5 medications) Poor health literacy (i.e., inability to teach back) Patient support (i.e., absence of caregiver) Prior hospitalization (nonelective, prior 6 months) Palliative care (progressive serious illness)	Surgical and medical; all age ranges	N/A
ACS-NSQIP risk calculator	Patient variables ASA class Steroid use Dialysis dependence Diabetes Cancer Procedure variables Wound class Operative time Urgent surgery Inpatient procedure Discharge destination	Surgical patients; all age ranges	c-statistic – 0.70

LACE, Length of stay, Acuity, Comorbidity, and Emergency department use; AUC, area under the receiver operating curve; ER, emergency room; ASA, American Society of Anesthesiologists; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; N/A, not available learned and confirm what has been explained to them. Moreover, it is recommended that patients and caregivers have access to high-quality educational resources specific to their surgical condition using a combination of different mediums or delivery formats. This includes print materials, Internet websites, videos, communication with other patients with similar health conditions, or resources that facilitate direct communication with healthcare providers. And at least one care transitions intervention advocates for the use of computerized bedside education systems consisting of a virtual nurse as the most effective way to engage and educate patients about their post-discharge self-care plan [39]. While these various types of computerized technology can help facilitate information delivery, it is important to ensure that older patients are comfortable with using them.

For older patients who have undergone major surgery, education and engagement activities typically need to be customized to their specific postoperative care plan. First, almost all surgical patients will have specific education needs related to the care of their incisions and surgical wounds. It is critical to provide surgical patients and their caregiver's in-depth instructions regarding specific wound care and/or dressing changes, as well as education on early identification and response to problems such as surgical site infections. This may come in different combination of print and visual media. Second, surgical patients are commonly prescribed new medications during the surgical encounter, including those for pain control or to help manage a complication. Patients and caregivers require detailed education pertaining to any new medications, including side effects and plans for dose titration. In cases where medications are intended to be taken long term, communication with the patient's primary care provider is needed to ensure they are continued and at the correct dose. Finally, it is equally important for patients to be educated and engaged in their care plan when receiving post-discharge care from a home care nurse or post-acute care provider. Many times patients serve as a key intermediary to ensure that health information is accurately communicated between inpatient and outpatient healthcare providers.

Enhanced Discharge Planning

Enhanced discharge planning is one of the most common strategies undertaken to improve transitional care at the time of hospital discharge and reduce readmissions. This includes strategies designed to *enhance* the organization of routine discharge planning, as well as efforts to make it more patient-centered. This intervention is generally undertaken by a nurse care coordinator or case manager and includes the development of a personalized or patient-centered care plan for each patient who is leaving the hospital. The patient-centered care plan considers their hospital course in the overall setting of comorbidities, functional status, cognitive status, health literacy, and social support. Enhanced discharge planning also intends to ensure that patients leave the hospital at an appropriate time in their care and that the coordination of post-discharge care is well-organized, including scheduling of follow-up appointments with specialists and outpatient providers.

There has been moderate strength evidence showing that enhanced discharge planning is effective at reducing hospital readmissions for older adults. A total of 30 different randomized controlled trials (RCTs) have been undertaken so far to evaluate enhanced discharge planning, including 21 studies that focused on older patients and 5 studies that recruited surgical patients. A recent Cochrane meta-analysis of these RCTs demonstrated that enhanced discharge planning reduced hospital length of stay by 27% and readmission rates by 13% (RR: 0.87, 95% CI: 0.79–0.97) relative to control groups [40]. Coordinated discharge efforts were also associated with increased satisfaction for patients and healthcare professionals in six different studies. The greatest improvements associated with this intervention were in participants' perception of the discharge process, continuity of care, and nonfinancial access to medical care.

Enhanced discharge planning strategies are very applicable to most older patients who undergo major surgery. The preponderance of older surgical patients has multimorbidity and other risk factors that place them at risk for poor care transitions following discharge and require more detailed discharge planning. Implementing enhanced discharge planning can help improve the efficiency and quality of care coordination for surgical patients during their transition from inpatient to outpatient care, without a significant investment to the healthcare system. In particular, the development of an individualized discharge plan can significantly help facilitate transitions to the post-discharge setting by providing information to patients about their surgical condition and establishing a post-discharge care plan that includes follow-up responsibilities for both surgical and nonsurgical providers.

Medication Management and Reconciliation

Another core component of care transitions interventions are specific efforts directed at optimizing medication management and reconciliation across different care settings. Most of these interventions are led by pharmacists and include strategies to ensure that patients are on the appropriate medication at the correct dose or frequency and do not have duplicated prescriptions when they transition to outpatient care settings, including home and post-acute care facilities. Nearly a quarter of the adult population over 65 years of age takes more than five different medications and are at high risk of experiencing such as medical errors or other adverse drug events (ADEs) during transitions of care [3]. ADEs occur most frequently following hospital discharge among older adults taking multiple medications, particularly when new drugs are started or chronic medications are stopped during their acute hospitalization. Reconciliation efforts may help to prevent ADEs by systematically comparing patient medication records across the different care settings and ensuring they are concordant with physician orders in both inpatient and outpatient settings.

The effect of pharmacist-led medication reconciliation strategies on patient outcomes during transitions of care has been well-studied. A total of five different RCTs and multiple observational cohort studies have been completed to date that have examined the effects of medication reconciliation at the time of hospital discharge on patient outcomes. When this pre-discharge intervention is combined with post-discharge follow-up efforts to ensure that outpatient medications are reconciled, there is solid evidence underscoring its effectiveness. A recent meta-analysis of eight RCTS found that medication reconciliation reduced drug event-related hospital revisits by 67% (RR 0.33; 95% CI 0.20–0.53), ED visits by 28% (RR 0.72; 95% CI 0.57–0.92), and 30-day readmissions by 23% (HR: 0.81; 95% CI: 0.70–0.95) when compared to control groups [41]. This evidence highlights the effectiveness of medication reconciliation for improving patient outcomes and post-discharge hospital utilization.

Medication reconciliation during surgical care transitions is particularly important for older patients with multimorbidity who have undergone major surgical procedures. There is a high likelihood that one or more chronic medications in these patients have been either stopped or had dosages altered during the postoperative period. This is a routine practice for high-risk medications, such as those used for anticoagulation (e.g., warfarin), diabetes (e.g., metformin), or heart failure (e.g., furosemide). However, some other types of chronic medications may also need to be held following surgery due to hemodynamic instability or as a result of varying degrees of organ failure during the perioperative period. In addition, many older surgical patients also require the addition of new medications during the postoperative period such as a narcotic for pain management. Furthermore, some surgical patients will require new medications to treat a postoperative complication such as anticoagulation for postoperative deep venous thrombus or an antibiotic to treat a surgical site infection. It is important to ensure that all medications for chronic and acute conditions are managed appropriately during the post-discharge period after surgery.

Interventions to Improve Care Transitions Following Hospital Discharge

Scheduled Early Follow-Up Visits with Healthcare Providers

One of the most common and important strategies employed to improve care transitions at discharge for older patients is directed at scheduling early follow-up visits with their healthcare providers and then making sure patients arrive at these appointments. This includes follow-up visits with members of their primary care medical home as well any specialty providers such as surgeons that cared for them during the recent hospitalization. The early follow-up visit is an opportunity for the patient and caregiver to be examined by their healthcare provider and have any outstanding questions clarified. This may include obtaining additional education or resources to supplement their outpatient care. From the perspective of the healthcare providers, this visit allows them to assess changes in health status since discharge and review or make any changes the post-discharge care plan. For many older patients, this requires coordination with home health nurses, case managers, or post-acute care facilities. The follow-up visit is also another opportunity to use *teach-back* strategies to ensure that patients and caregivers comprehend their care plan and are aware of the warning signs or symptoms that indicate a worsening condition.

Early follow-up visits with primary care providers (PCPs) after hospital discharge have been associated with improved outcomes among older patients hospitalized for both high-risk medical and surgical conditions. In a recent large observational study, adults 65 years or older who received PCP follow-up within 7 days of hospitalization for heart failure complications had a significantly reduced rate of 30-day readmissions compared to patients with longer follow-up. Another prospective cohort study enrolling patients with multimorbidity found that individuals lacking PCP follow-up within 30 days after discharge for a medical condition were ten times more likely to be readmitted ($P < 0.05$). Finally, early follow-up with a PCP also was also found to be associated with a significantly lower risk of 30-day readmission among medically complex surgical patients undergoing thoracic aneurysm repair, particularly when a perioperative complication occurred (20% vs. 35%; $p < 0.001$). This finding was supported by risk-adjusted regional analyses, where PCP follow-up reduced the likelihood of 30-day readmission following thoracic aneurysm repair by over 31% (risk-adjusted OR: 0.68; 95% CI: 0.55–0.85; $P < 0.01$).

There are several potential benefits associated with having older patients' follow-up with their PCP in addition to their surgical team within a short time period following hospital discharge after undergoing a major surgical procedure. First, the majority of older patients undergoing major surgery have at least one or more chronic medical conditions, including chronic obstructive pulmonary disease (COPD), diabetes, stroke, renal insufficiency, and heart failure. These conditions are all independently associated with an increased risk of readmission and may be exacerbated by surgical stress during the postoperative period [42]. The patient's PCP is typically in the best position to evaluate and treat the patients if any health condition has deviated from baseline. Second, many older patients take one or more medications that need to be stopped or titrated during the postoperative period. The PCP is generally in charge of managing an older patient's medication regimen and is the best provider to titrate or make changes necessary for long-term drug maintenance. A clinic visit with a PCP during the 2-week period after surgery will facilitate this. Finally, early follow-up visits with both primary care and surgical providers after surgery can help detect many complications that occur in medically complex older patients at an early stage before their condition deteriorates. This is supported by a retrospective review by Saunders et al. who noted that in many cases, outpatient follow-up did not occur early enough in the postoperative period to treat complications before patients required hospital readmission [43].

Home Visits

A home visit by a healthcare provider following hospital discharge is a component of several transitional care strategies used for older high-risk patients. This type of intervention is designed to evaluate any signs of deterioration in clinical status since discharge, as well as an opportunity to re-engage and educate the patient within their home setting. This includes reinforcing medication adherence, wound care, or any aspect of their post-discharge care plan. As such, home visits are typically conducted within a short time period after discharge (i.e., 1 week) by providers who are familiar with the patient's recent hospital course. This visit may be conducted by different members of the healthcare team, including nurses, advanced practice clinicians (e.g., nurse practitioners or physician assistants), pharmacists, or a specialized care navigator.

While home visits are a component of many care transitions interventions, the effect of this intervention on clinical outcomes has not been consistent across groups of older patients with chronic medical disease. One RCT that evaluated the effect of a single nurse home visits on outcomes in patients with heart failure found a significant reduction in readmissions and lower rates of out-of-hospital mortality [44]. But, this finding was not consistently replicated when including other types of patients with medical conditions. At least one meta-analysis that including all general medicine patients who had received at least one home visit did not find a significant effect on readmission rate. However, another recent meta-analysis found that medical patients who received two or more post-discharge home visits had the lowest likelihood of readmission [45].

Among older high-risk surgical patients, home visits have shown promise as a means to reduce readmissions in a few studies. The "Follow Your Heart" study enrolled older patients who underwent cardiac surgery to receive two home visits within 10 days of hospital discharge by a cardiac nurse practitioner (NP) who was familiar with the patient's hospital course [46]. When compared to patients who received a home visit from a home health agency, this study found that cardiac surgery patients who were visited by the cardiac NP had a significant reduction in hospital readmissions (3.9% vs. 11.5%; $P < 0.05$). Another cohort study found that cardiac surgery patients who were visited by a physician assistant with cardiothoracic training on days 2 and 5 following discharge had a significant decrease in the rate of infection-related readmissions [47]. Together, these studies support the effectiveness of in-home visits by providers who know the patient and have specialized training to manage postoperative conditions. The authors of both studies similarly concluded that providers familiar with the postoperative care of cardiac surgery patients were less likely to send patients to the emergency department because of their ability to manage complications in the outpatient setting.

Follow-Up Telephone Communication

A common component of care transitions interventions after discharge is some form of telephone communication between the patient and healthcare providers. This includes follow-up phone calls by members of the healthcare team or patient-activated telephone hotlines that patients can contact on their own. Follow-up telephone calls to patients may be personalized or involve generalized call scripts that inquire about new symptoms patients might be having since discharge, plans for ambulatory follow-up, use of prescribed medications, and any warning signs for impending adverse events. During follow-up calls, patients are also usually provided information on resources to help support post-discharge care. Both follow-up telephone calls and telephone hotlines aim to identify and remedy possible gaps in care that may occur after hospital discharge, allowing patients to get their questions answered while giving providers an opportunity to reinforce key elements of the discharge instructions.

While follow-up telephone calls are among the most commonly used transitional care interventions used in practice, the evidence supporting their effectiveness as a solitary post-discharge intervention has been mixed. Among patients with chronic disease, recent systematic reviews have found inconclusive evidence that a single follow-up telephone calls by themselves are effective in reducing 30-day readmissions [48]. Similarly, the effectiveness of post-discharge telephone calls in surgical patients is unclear. A recent RCT known as the CONNECT trial randomized patients who underwent colorectal surgery to post-discharge telephone calls by a nurse provider, but found no significant difference in 30-day readmissions compared to patients who didn't receive the intervention [49]. However, another recent meta-analysis found that interventions involving multiple follow-up telephone calls during the post-discharge period had the lowest likelihood of readmission [45].

The variability in effectiveness of post-discharge telephone calls for older patients following surgery may depend on several factors. First, the ability to contact an older patient by phone during the post-discharge period can be variable. While telephone calls are made to a number provider by the patients, studies have shown that only a fraction of patients are able to actually answer a telephone call. It is important to have contact information for the patient or caregiver, but also other members of their social support environment such as family or neighbors. Second, there needs to be a mechanism for addressing any problems that are identified during a follow-up call in order to prevent a potential readmission. If the provider making the telephone call does not have the medical training to answer patient questions or triage clinical issues, the benefit of telephone follow-up may not be maximized. Finally, the results of systematic reviews suggest that follow-up calls need to be combined with other transitional care interventions in order to adequately impact clinical outcomes. This includes combing follow-up calls with home visits or early follow-up with their provider to reinforce the post-discharge plan.

Home Telemonitoring

Another emerging technology-driven strategy for care transitions is the incorporation of home telemedicine or telemonitoring into follow-up care after hospital discharge. Telemonitoring has been defined as the process of transmitting data concerning a patient's health status from home by a patient or their caregiver back to a healthcare provider or healthcare setting. This strategy encompasses the use of several different types of technologies to monitor a patient's health status from a distance, including video consultation; mobile phone; automated device-based, interactive voice response; and web-based telemonitoring. These strategies may include remote transfer of physiologic data between patients and providers, such as vital signs, images to document a disease state, or confirmation of medication or treatment compliance. This strategy may also involve partnering with home health agencies to improve gaps during the discharge transition process [50].

Telemonitoring has shown promise as a transitional care strategy for older patients with different types of chronic disease conditions. Multiple studies have shown an effect between different telemonitoring interventions and significant reductions in mortality, readmissions, and healthcare utilization for older patients with chronic conditions including heart failure, COPD, and asthma [51]. Telemonitoring has also been shown to improve patient-reported quality of life and satisfaction with care [52]. In particular, the benefit of these interventions has been correlated with increased knowledge of self-care behaviors that prevent complications in the outpatient setting.

While telemonitoring strategies have not been specifically studied in older surgical patients, nevertheless they can also be expected to benefit from these types of interventions during transitions following hospital discharge. Telemonitoring is well suited for older surgical patients who live far from the hospital and have specialized postoperative care needs such as wound care. For example, the ability to remotely monitor surgical wounds for healing and or development of surgical site infections (SSI) can help decrease the need to see a patient back in clinic. There have been several smartphone applications developed over the past couple of years that allow patients or home health nurses to take a wound photograph and transmit it through secure web-based platforms to healthcare providers. This exchange of wound images allows providers to remotely assess for evidence of SSI or wound breakdown and determine if an in-person visit is needed, many times saving the patient an obligatory visit back to the hospital.

Interventions to Improve Care Transitions Across Episode of Care

Maintaining Continuity of Provider Care

Maintaining continuity of provider care is an important part of care coordination and a strategy for improving transitions across episodes of care for older patients. The ideal concept of *continuity* is having a patient's healthcare managed by a single provider who knows every aspect of their medical and surgical history and is responsible for coordinating all aspects of chronic health maintenance. This type of strategy helps establish and maintain strong patient-provider relationships and minimizes the potential for gaps in information exchange when patients are cared for by multiple providers in a health system.

Although the ideal notion of a single provider is not feasible in most modern healthcare systems, particularly for patients with multimorbidity, there are still models of care continuity that can be applied to older patients. For example, hospitals with integrated post-hospital care delivery where patients are seen by their same primary care or specialist provider have been shown to reduce readmissions for patients with acute and chronic medical conditions, such as pneumonia, urinary tract infections, heart failure, and COPD [53]. Moreover, continuity of care has been reported to reduce complications and reduce overall healthcare costs for patients with chronic diseases [54]. This benefit is maintained when patients are cared for by teams within the same healthcare setting, regardless of whether the same providers are involved with every episode of care.

There is accumulating evidence showing that continuity of care is also critical for the management of older patients during the post-discharge period following surgery [10, 11]. Specifically, older patients who experience a postoperative complication following surgery and then return to the same index hospital for management have significantly improved outcomes when compared to patients who are readmitted to different hospitals. A recent study by Brooke et al. showed that returning to the index hospital where surgery occurred was associated with a 26% lower odds of 90-day mortality (OR: 0.74; 95% CI: 0.66–0.83) [10]. Moreover, this study found that the decrease in mortality risk was greatest for patients readmitted for surgical versus medical complications, and there was a dose-dependent reduction in mortality when patients were managed by the same surgical providers who performed their initial operation. These data support the importance of continuity in surgical care at both the hospital and provider level and suggest that maintaining continuity of care following surgery can be used as a metric of care quality.

Care Transitions Navigators

One of the major issues facing older patients undergoing surgery is how to navigate the complexity of the healthcare system during care transitions before and after their operation. Care transitions navigators are individuals whose specific job is to assist patients in this capacity, as well as provide continuity across the episode of care. This role is a central component of several different care transitions programs and typically involves a healthcare professional with some form of advanced training in nursing or social work. Care navigators function as another set of "eyes and ears" for patients or caregivers to bridge the gap between inpatient and outpatient care. This includes helping them understand their care plan, new medications, follow-up appointments, or the myriad of questions that pop up as they transition back to their primary care team. The navigator also helps the patient coordinate any needed outpatient care, including pending labs and imaging studies, and following up with patients' primary care providers to relay updated problem lists and treatment plans. They also work closely with discharge planners and case managers in addressing the essential aspects of care coordination before, during, and after the time of hospital discharge.

Care navigation has been shown to be an effective transitional care strategy for improving outcomes among patients with various medical and surgical conditions. A recent meta-analysis of 25 different RCTs found that patients assigned to care navigators were significantly more likely to access health resources and adhere to follow-up treatment plans when compared to usual care [55]. Many of these studies found that care navigators were most effective among older female patients and those from disadvantaged socio-demographic backgrounds. Furthermore, care navigation was found to be associated with a significant improvement in patients' overall satisfaction with their care delivery.

Care navigators are well-suited to assist older patients undergoing different types of major surgery and provide assistance with care transitions extending across the entire episode of surgical care (Fig. 1). Starting during the pre-admission period, navigators can help patients and caregivers prepare for surgery and the recovery period, which often is a new or foreign experience. Through the coordination of care with primary care and surgical teams as well as helping patients obtain educational resources, navigators can smooth the transition from outpatient to inpatient care. This may include helping patients develop a patient-centered care plan that outlines their personal goals and expectations of surgical care. During the postoperative period, navigators continue to be a source of education to the patient and their family and work with different care teams to ensure that the patient-centered care plan is reinforced. This includes helping with discharge planning and then ensuring that the care plan is understood and maintained by outpatient providers. Care navigators are another resource to ensure that older patients have continuity of care into the post-discharge period.

Bundled Care Models for Transitional Care

There have been multiple transitional care models developed over the past several decades seeking to maximize patient benefit through bundling different combinations of the care intervention described above (Tables 3 and 4). While the data supporting the effectiveness of single interventions isolated to either the pre- or post-discharge settings, bundled care models for transitional care have been rigorously tested in well-designed clinical trials and found to improve care coordination at the time of discharge and reduce hospital readmission. Moreover, a common element of these care transitions strategies is that they have all been designed to promote patient-centered care by using techniques to engaging patients and their caregivers across care settings.

Transitional Care Model

The Transitional Care Model (TCM) is a multidisciplinary approach to transitional care championed by Mary Naylor and colleagues at the University of Pennsylvania [3, 56]. This model is designed as a comprehensive approach to transitional care at the time of hospital discharge for medically complex older adults and includes different types of strategies as shown in Table 3. This includes a major emphasis on engaging patients and their caregivers in the self-care of their health issues and the early identification and response to potential problems to prevent decline in health status. In addition, the TCM assigns patients to nurse-trained *transitional care navigators*, who provide continuity of healthcare to the

Table 3 Evidence-based care transitions strategies using multiple components

Care transitions models	Components	Key findings from clinical trials
Transitional Care Model (TCM)	1. Use of advanced knowledge and skills by a transitional care nurse (TCN) to deliver and coordinate care 2. Comprehensive, holistic assessment of each older adult's priority needs, goals, preferences 3. Collaboration with older adults, family, caregivers, and team members in implementation of a streamlined, evidenced-based plan of care 4. Regular home visits by the TCN with available, ongoing telephone support through an average of 2 months 5. Continuity of healthcare between hospital, post-acute, and primary care clinicians facilitated by the TCN accompanying patients to visits to prevent or follow-up on an acute illness care management 6. Active engagement of patients and family caregivers with a focus on meeting their goals 7. Emphasis on patients' early identification and response to healthcare risks and symptoms to achieve *longer-term* positive outcomes and avoid adverse and untoward events that lead to acute care service use 8. Multidisciplinary approach that includes the patient, family caregivers, and health-care providers as members of a team 9. Strong collaboration and communication between older adults, family caregivers, and healthcare team members across episodes of acute care 10. Ongoing investment in optimizing transitional care via performance monitoring and improvement	Naylor et al. *JAMA* 1999: Older patients with multimorbidity randomized to receive TCM at discharge were less likely than control group patients to be readmitted once within 6 months (20.3% vs. 37.1%; $P < 0.001$) or have multiple readmissions (6.2% vs. 14.5%; $P = 0.01$). The TCM intervention group had fewer hospital days per patient (1.53 vs. 4.09 days; $P < 0.001$), and after 6 months, total Medicare reimbursements for health services were significantly lower about in the intervention group (\$0.6 million vs. \$1.2; $P < 0.001$) Naylor et al. *J Am Geriatr Soc*. 2004: Older patients with heart failure randomized to receive TCM at discharge have significantly longer time to readmission ($P < 0.05$) as well as fewer readmissions ($P < 0.05$) and lower mean total costs (\$7636 vs. \$12,481, $P < 0.01$) within 52 weeks after intervention
Care Transitions Intervention (CTI)	Four pillars of transitional care and transitions coach 1. Medication self-management 2. Dynamic patient-centered record 3. Scheduled follow-up with PCP and specialist providers 4. Patient education and knowledge of "red flags" and how to respond 5. Transitions coach* *Patients work with a nurse-trained transitions coach to help navigate the pre- and post-discharge process. This includes providing continuity across care settings and ensuring that their needs are met irrespective of the type of care settings. The transitions coach also conducts one home visit and at least three follow-up phone calls	Coleman et al. *Arch Intern Med.* 2006: Older patients with multimorbidity randomized to receive the CTI had a significant reduction in readmission rates at 30 days (8.3% vs. 11.9%; $P < 0.05$) and 90 days (16.7% vs. 22.5%; $P < 0.05$) when compared to usual care. Patients receiving the CTI also had significantly lower readmission rates for the same condition that precipitated the index hospitalization at 90 days (5.3% vs. 9.8%; <0.05) and at 180 days (8.6% vs. 13.9%; $P < 0.05$) than controls. Finally, the mean hospital costs were lower for intervention patients (\$2058) vs. controls (\$2546) at 180 days (log-transformed $P < 0.05$)

(continued)

Table 3 (continued)

Care transitions models	Components	Key findings from clinical trials
Project Re-Engineered Discharge (RED)	1. Ascertain need for and obtain language assistance 2. Make appointments for follow-up medical appointments and post-discharge tests/labs 3. Plan for the follow-up of results from lab tests or studies that are pending at discharge 4. Organize post-discharge outpatient services and medical equipment 5. Identify the correct medicines and a plan for the patient to obtain and take them 6. Reconcile the discharge plan with national guidelines 7. Teach a written discharge plan the patient can understand 8. Educate the patient about his or her diagnosis 9. Assess the degree of the patient's understanding of the discharge plan 10. Review with the patient what to do if a problem arises 11. Expedite transmission of the discharge summary to clinicians accepting care of the patient 12. Provide telephone reinforcement of the discharge plan	Jack et al. *Ann Intern Med*. 2009: Older patients on medical service at single institution randomized to receive RED intervention had a lower 30-day rate of hospital utilization including ED visits and readmissions (31% vs. 45%; $P < 0.01$) than patients receiving usual care
Project Better Outcomes by Optimizing Safe Transitions (BOOST)	BOOST toolkit includes 1. 8P risk assessment 2. General Assessment of Preparedness (GAP) for discharge 3. Written discharge instructions 4. PASS 5. DPET (Discharge Patient Education Tool) 6. Teach-back 7. Follow-up telephone calls 8. Scheduled follow-up appointments 9. Inter-professional rounds 10. Post-acute care transitions 11. Medication reconciliation	Hansen et al. *J Hosp Med*. 2013: A pre-post study was conducted within 11 different hospital units consisting of both medical and surgical patients before and after implementation of the BOOST toolkit. Among hospital units that implemented BOOST, the 30-day readmission rate was significantly lower (12.7% vs. 14.7%; $P = 0.01$) when compared to site-matched control units

Table 4 Components of bundled transitional care strategies

	Intervention used in bundled care transitions model			
Intervention	TCM	RED	TCI	BOOST
Assessment of patient risk and readiness for discharge	X	X	X	X
Education and engagement of patients and caregivers	X	X	X	X
Enhanced discharge planning	X	X	X	X
Medication management and reconciliation	X	X	X	X
Scheduled early follow-up with providers		X	X	X
Post-discharge home visits	X		X	
Follow-up telephone communication		X	X	X
Maintaining continuity of provider care	X		X	X
Care transitions navigator	X		X	

patient between hospital and post-acute care settings. This role includes accompanying patients and caregivers to follow-up visits with primary care providers and specialists for a total of 2 months after discharge. Care navigators are also available to provide ongoing telephone support to patients during this post-discharge time period.

The TCM has been evaluated in several large multi-site RCTS among a mixture of different medical and surgical patient populations [3, 56, 57]. These studies all enrolled patients 65 years and older with different types of chronic health conditions who were admitted for both medical and surgical reasons. Among patients randomized to the TCM intervention, there was a significantly less likely to be readmitted within 6–12 months after hospital discharge and less likely to have multiple readmissions within this time period (Table 3). These studies also found that Medicare reimbursements and mean costs were significantly lower in the patient cohorts receiving TCM versus usual care.

Care Transitions Intervention

The Care Transitions Intervention (CTI) is a model championed by Eric Coleman at the University of Colorado and is one of the most widely recognized evidence-based bundled care transitions strategies [58]. The CTI model recognizes that care coordination is often fragmented during transitions of care, and patients and their caregivers are often the only common thread across different care settings. As such, this model focuses on providing patients and their families different support tools discussed in this chapter, which help self-management of their conditions after discharge from the acute care setting (Table 4).

The CTI is a 4-week intervention focused on the *four pillars* or conceptual domains of transitional care in addition to a care transitions navigator, which have all been discussed previously in this chapter. As shown in Table 3, these domains are (1) assistance with medication self-management, (2) utilization of a patient-centered record that is maintained by the patient to facilitate cross care setting information exchange, (3) patient empowerment to schedule timely follow-up visits with their primary and specialty care physicians, and (4) patient education of red flags to include signs that their health condition is worsening. In addition, each patient within the CTI is assigned a nurse-trained care navigator known as a *Transitions Coach*. This person visits the patient in the hospital as well as their home and conducts frequent follow-up phone calls to help the patient navigate the pre- and post-discharge process. This includes coaching patients and caregivers on ways to take a more active role in their post-discharge care.

The CTI model was shown to have a significant impact on reducing readmissions in a large single-center RCT among adults 65 years or older admitted with chronic medical conditions [58]. Among patients randomized to the CTI strategy, there was a significantly lower rate of readmission at 30 days and at 90 days when compared to control subjects with usual care (Table 3). Patients who received the intervention also had a significantly lower rate of readmission at 90 days and 180 days following discharge than control patients for the same condition that precipitated the index hospitalization controls. Finally, this study also found that mean hospital costs were lower for older patients receiving the CTI versus controls at 180 days following discharge.

Project RED

Project Re-Engineered Discharge (RED) is a bundled model focused on enhancing the transitional care at the time of discharge, which has been championed by Brian Jack and colleagues at Boston University [39]. This approach is unique in that it advocates for a *virtual patient advocate* discharge approach using computer-generated patient instructions, in addition to a nurse discharge advocate who focuses on enhanced discharge planning.

There are 12 separate components of the RED intervention that are focused at the time of hospital discharge at shown in Table 3. This includes bundled interventions such as routine risk assessment, scheduling follow-up appointments, medication reconciliation, development of a patient-centered discharge care plan (with education and teach back principals), identification of warning signs, and communication with the outpatient providers including follow-up telephone calls. The implementation of RED also includes components that can be customized for older adults, which includes an assessment of health literacy and tools to make it appropriate for sociodemographic diverse patient populations.

The bundled approach used in Project RED has been shown to be an effective strategy for improving care transitions and patient outcomes in a single-center RCT [39]. Older patients hospitalized for medical conditions randomized to receive the RED intervention were found to have a significantly lower 30-day rate of hospital utilization including ED visits and readmissions than patients receiving usual care (Table 3). In addition, patient receiving the RED intervention could identify their index discharge diagnosis, and PCP name more often than control patients. Finally, the total costs associated with post-discharge care among patients receiving RED were substantially lower than control patients, which underscored its overall effectiveness.

Project BOOST

Project Better Outcomes for Older Adults through Safe Transitions (BOOST) is a care transitions program that was developed by the Society of Hospital Medicine to target the discharge process from hospital to home. This program consists of multiple evidence-based interventions reviewed in the chapter that help optimize the safety of care transitions (Table 4). BOOST has bundled these different interventions shown in Table 3 into a *toolkit* for healthcare providers, with individual components addressing multiple aspects of hospital discharge and follow-up process. In particular, this model is focused on improving patient satisfaction with the discharge process, improving the flow of information between hospital and outpatient healthcare providers, and identifying patients at high risk for readmission and mitigates the risk for readmissions before discharge. This includes the use of teach-back methods to increase patient and caregiver learning. The BOOST program is also focused on providing healthcare systems the necessary support to implement these bundled care transitions interventions within their own clinical settings.

While the BOOST program was designed as a quality improvement initiative, its effectiveness in clinical practice has been supported by a recent clinical implementation study [59]. A pre-post assessment was conducted within medical and surgical units at 11 different community and academic hospitals before and after implementation of the BOOST toolkit. Among hospital units that implemented at least two of the BOOST care transitions tools, the 30-day and 1-year readmission rate was found to be significantly lower when compared to site-matched control units (Table 3). However, there was no difference in hospital length of stay between BOOST and control units. While this study was not randomized, nevertheless the data supports comprehensive care coordination as an effective real-world strategy for optimizing outcomes in older adults.

Conclusion

Older patients undergoing major surgical procedures are exposed to many different factors that place them at risk for fragmented care during transitions of care after surgery. Improving care coordination at the time of discharge for these patients is essential to achieving optimal outcomes, including the prevention of avoidable readmissions and improving patient satisfaction with care. The various care transitions interventions discussed in this chapter are different types of strategies to help accomplish this goal. Successful care transitions interventions are more likely to be “bundled” together, address multiple components of the discharge process, and span different care settings. While many interventions have not been specifically designed for older surgical patients, they are nevertheless well-suited for this vulnerable patient population. It is critical for surgical providers to understand and apply appropriate evidence-based transitional care strategies in order to achieve high quality of care and outcomes for their older patients who undergo major surgical procedures.

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28 Postoperative Recovery and Rehabilitation

Simon Bergman and Laura M. Drudi

Contents

Abstract

Surgical recovery is a concept which has traditionally been poorly defined and poorly measured. The expectations of elderly patients with regards to their postoperative outcomes, including what they consider a success, may be very different when compared to the expectations of their younger counterparts or of their surgeons. In this chapter, the authors review the impact of surgery on a patient's functional status, on how they report their symptoms, and how they perceive their health and their quality of life. Important risk factors for a prolonged recovery, such as complications, malnutrition, and frailty, are described. Finally, strategies for optimizing recovery are discussed, starting with the preoperative period (comprehensive geriatric assessment, pre-habilitation), followed with hospitalization (enhanced recovery pathways, multidisciplinary intervention

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teams and programs), and finally with rehabilitation in the postoperative period.

Clinical Vignette

The surgery was a success, but. . .

Mrs. K is an 87-year-old woman who undergoes a laparoscopic anterior resection for sigmoid colon carcinoma. The surgery is uneventful, and she does quite well postoperatively "for someone her age." Her urinary catheter is kept in for 2 days because of a low urine output, which eventually resolves following several fluid boluses. During this time, she has become confused and uncooperative, most likely due to some degree of delirium. Consequently, she does not start ambulating until the fourth postoperative day when she is helped out of bed by a physiotherapist. She is eventually discharged home 8 days after surgery. She returns to the emergency department 4 days after discharge, when her niece reports that the patient has fallen, has difficulty feeding herself, and is generally too weak to manage on her own. The patient is readmitted until a bed is available in a specialized nursing care facility, where she "recovers" for 3 weeks, before returning home. Six months later, during a visit to her family doctor, the patient reports that she is still too weak to go to the shopping mall, to attend her usual weekly card games, or to travel to visit her family and friends.

Introduction

The satirical phrase "The surgery was successful, but the patient died" could well be rephrased to "The surgery was successful, but the patient was transferred to a specialized nursing care facility, became dependent, and never fully returned to his or her previous way of living." There is no doubt that, regardless of age, when discussing the success of a surgical procedure, traditional outcomes such as complications, length of stay, and mortality are now complemented by what some might call patient-centered or patient-reported outcomes, such as quality of life, functional status, and return to professional or social activities, to name a few. It is increasingly clear that these types of outcomes, which have a medium- to long-term impact, are of particular importance to elderly patients, a patient population that generally has very different goals and expectations when it comes to surgical recovery.

In the vignette above, the surgeon may have been quite satisfied with an uneventful surgery, with seemingly good oncological outcomes, and a patient discharged home in a very acceptable time frame. The patient, on the other hand, may have seen things in quite a different light. This is well illustrated by a study by Terri Fried et al. in which over 226 elderly patients with a severe medical illness (cancer, chronic heart failure, or chronic obstructive pulmonary disease) were asked how likely they would be to undergo a life-saving procedure if this procedure resulted in cognitive or functional impairment. As the risk of dependency increased, fewer patients chose the procedure. In fact, if the outcome was survival associated with functional impairment, 74% of patients chose death. As many as 89% of patients refused the life-saving procedure when the outcome was survival with severe cognitive impairment [1]. In a study of elderly patients considering orthopedic surgery, a list of all potential concerns was established in semi-structured patient interviews. 155 out of 164 concerns (70%) had to do with anticipating postoperative quality of life (mainly with respect to perceived threats to physical and social well-being) and their capacity to cope with surgery and the postoperative recovery. Perhaps not surprisingly, only a little over 50% of these concerns were addressed with the surgeon [2]. Considering the fact that 80% of studies in gastrointestinal surgery only report morbidity and mortality [3], it seems clear that there remains a significant disconnect between traditional surgical goals and the treatment preferences and expectations of functional preservation that are valued by elderly patients [4].

Understanding what can be expected after surgery following hospitalization is important to the surgeon when he or she counsels the patients regarding perioperative outcomes. For patients and their caregivers, only with a true understanding of recovery is it possible to make a judgment on how the benefits of the procedure measure up to the risks. It allows them to align their expectations with realistic goals and to plan accordingly. A better understanding of recovery may be useful information for the surgeon or primary care physician in understanding when a patient has fallen off the normal recovery curve and at what point that deviation from normal may indicate the need for further investigations. In addition, from a professional development or physician-centered point of view, surgeons would likely benefit from recognizing and integrating the importance of longer-term functional outcomes in the context of personal practice audits, of measuring intervention effectiveness, or even in comparing new procedures or approaches. Finally, notwithstanding the impact on the patient and on the caregivers, loss of independence after surgery is independently associated with healthcare costs [5].

In general, surgeons understand recovery to be the period of time following surgery during which patients return to or exceed their preoperative state. But because it is such a complex, multimodal concept that can be measured and interpreted in many different ways, there does not exist a uniformly accepted definition. Perhaps the best definition of recovery is that suggested by the surgical pioneer, Dr. Francis Moore, who, in 1958, wrote that recovery was "the interlocking physical, chemical, metabolic, and psychological factor commencing with the injury, and terminating only when the individual has returned to normal physical well-being, social, and economic usefulness, and psychological habitus." [6]

The outcomes used to describe recovery can be categorized using a pre-defined framework, the Wilson-Cleary model [7], which captures the elements of Moore's definition. It establishes a relationship between clinical interventions, biological and physiological impairment, and the resulting effects on four health status domains: symptom status, functional status, general health perception, and quality of life [8, 9]. This model underlines the shift in modern therapeutic goals from improving physiological impairment and survival to improving patient function and well-being [10, 11].

Table 1 Definition of health status domains and validated measures of recovery

Functional status: ***Ability to perform physical or cognitive tasks***
Katz index [12]
Abbreviated mental test [13]
Mini- Mental Status Exam [14]
Short physical performance battery [15]
Handgrip strength and gait speed [16]
Symptoms status: ***Perception of an abnormal feeling in the patient's body***
Visual analogue pain scale [17, 18]
Verbal descriptive pain scale [18]
General health perceptions: ***Subjective assessment of how patients view their overall health***
Geriatric Depression Scale [19]
Quality of life: ***Defined by Emerson as the "satisfaction of an individual's values, goals, and needs through the actualization of their abilities or lifestyle"*** [20]
Short Form 36 [21]

Definitions of the health domains and examples of measures of recovery which have been validated for use in elderly patients are found in Table 1. The following discussion focuses on the general outcomes of surgical recovery, as opposed to procedure-specific outcomes, such as limb function after orthopedic surgery or exercise capacity after cardiac surgery, for example, which are outside the scope of this chapter.

Functional Status

The idea of a return to preoperative functional status is central to the majority of surgical recovery studies. It is of particular clinical importance, being one of the health domains, that takes longest to return to baseline [22]. Examples of outcomes assessing functional status include the ability to perform basic physical activities independently or to perform a cognitive task. In this patient population, the most commonly used clinical tools to assess physical function and dependency are the activities of daily living

Table 2 Activities of daily living and instrumental activities of daily living

Activities of daily living	Instrumental activities of daily living
Feeding	Using the telephone
Continence	Shopping
Transferring	Preparing food
Toileting	Housekeeping
Dressing	Doing laundry
Bathing	Using transportation
	Handling medication
	Handling finances

(ADL) and instrumental activities of daily living (IADL), which are described in Table 2. Although some authors have shown that elderly patients can recover completely at 3 months following surgery [23], this seems to be the exception rather than the rule. In the general elderly surgical population, there is a persistent impairment in ADL in less than 10% of patients at 6 months [22, 24]. However, in the more vulnerable geriatric patients, such as those above the age of 80, there is 58% dependency in an equivalent time frame [25]. Similarly, a population-based study by Finlayson et al. of 6822 nursing home patients undergoing colon surgery for cancer demonstrated functional decline in 42% of patients at 3 months, 28% at 6 months, and 24% at 12 months [26]. Furthermore, there is considerable dependency in IADL noted in 19% of geriatric patients at 6 months following major abdominal surgery [22]. In elderly critically ill patients, most of which had undergone surgery, at a median follow-up of 21 months, 13% had increased their dependency, and an additional 4% had become completely dependent [27]. When using objective physical performance measures, such as timed walk, functional reach, and hand grip strength, as many as 58% of patients had not return to baseline after 6 months [22]. Such studies raise the important question of whether, in patients who have not yet returned to baseline at 6 months, 12 months, or 24 months, recovery is still actively progressing or whether it has reached a plateau and permanent disability has led to a new baseline state.

From a cognitive standpoint, there is a significant incidence of postoperative delirium, which varies between 5% and 40%, depending on the type of surgery. By definition, this is usually transient in nature and limited to the hospitalization period [28, 29]. In general, based on older studies, it was thought that approximately 8–10% of patients undergoing non-cardiac surgery suffered from cognitive dysfunction, detectable as early as 3–6 months after surgery and possibly persisting for several years [30, 31]. Postoperative cognitive dysfunction has been poorly defined and its etiology is unclear. It may simply represent a preexisting chronic state uncovered by the acute stress of surgery. More recent studies have reported an improvement in MMSE scores at 3–6 months, when compared to preoperative values, possibly related to the overall improvement in patients' medical status following surgery [22]. The data on this important topic are too conflictual and vague to effectively synthesize in order to properly counsel patients with regards to long-term cognitive risk. In general terms, it seems fair to say that, for the vast majority of patients, cognitive functional status seems to be preserved following surgery.

Symptoms Status

Symptoms are usually reported by the patient, and protracted symptoms represent the expression of the patient's underlying ill-being. These symptoms may include the perception of heightened pain, fatigue, or nausea. Generally, unless complications occur, resolution of pain or nausea following surgery will occur within days to weeks, sometimes even during hospitalization. The symptom which seems to persist for weeks or months is a patient's fatigue, even following relatively minor procedures. In several studies of elderly patients undergoing colorectal surgery, fatigue persisted for at least 1 month [23, 32, 33].

General Health Perception

The subjective perception of fatigue, pain, and depressive symptoms have been found to be important factors to acknowledge in elderly patients undergoing surgery. In a study by Zalon et al., it was found that patients perceived to be 33% recovered at 1 month and 92% at 3 months [34]. They found that depression, along with symptoms of pain and fatigue, also improved, but persisted past 3 months. These symptoms contributed significantly to the patients' perception of their own health.

Quality of Life

Quality of life is highly correlated with the health domains describe above, with the addition of the concept of patient satisfaction. Although it seems intuitive that surgery would have an undeniable impact on quality of life, it seems to be minimal, usually with a mild attenuation in the first several weeks after surgery and a return to baseline within 3–6 months [24, 35]. This may be more related to the physical component of the quality of life construct, as the mental component does not seem to be affected negatively by surgery or by critical illness [27, 35]. In fact, some studies have shown that the mental component score of the Short Form 36 quality of life questionnaire may sometimes even surpass baseline scores [36, 37], which is a phenomenon that has also been described in a younger patient population. It is postulated that perhaps, beyond the physical manifestations of the recovery process, the satisfaction of having gone through the procedure, having survived, returned home and begun a life free of the morbidity that prompted the surgery, is enough to improve the patient's overall condition.

For any given outcome, a patient can be imagined to progress along the hypothesized recovery trajectory developed by Feldman et al. [10] and reproduced in Fig. 1. The patient starts at their baseline or preoperative state. When surgery occurs, the surgical trauma and resultant hospitalization begin the deterioration phase, in which the curve of the outcome in question slopes down. This usually takes place during hospitalization. Eventually, usually as the patient returns home and starts reintegrating their pre-procedural life, the rehabilitation phase begins. This can last anywhere between a few weeks and several months. As suggested by Moore, recovery ends when the patient has returned or exceeded their preoperative state [6]. In this figure, the dotted line represents the minimum level of functioning. Protracted recovery can occur when the baseline curve starts at a lower level than expected or is oriented downwards as might be the case in someone who becomes sedentary because of progressive leg pain while awaiting vascular surgery. Conversely, a patient on a pre-habilitation program may benefit from an upward baseline curve. Similarly, the deterioration curve may be steeper than expected in a patient who is not well mobilized after surgery. That same curve would be made less steep if a patient was recruited to an enhanced recovery pathway. Finally, the rehabilitation curve may be modified negatively by a patient with chronic pain after surgery

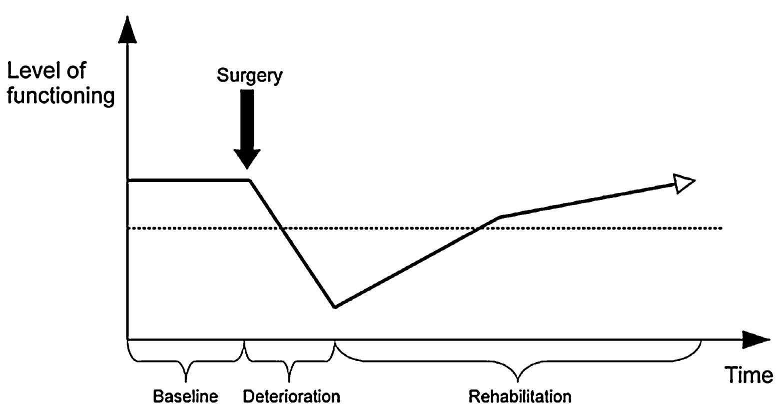

Fig. 1 The hypothesized trajectory of recovery [10]

or positively if undergoing rehabilitation after discharge. Some of the more important risk factors for protracted recovery as well as the strategies to optimize recovery are discussed below.

Risk Factors for Protracted Recovery

Postoperative complications have consistently been shown to be predictors of a slower recovery [26, 38]. This was described by Tahiri et al. who reported that the greater number and severity of complications increased the time to recovery in elderly patients undergoing abdominal surgery. Using the short physical performance battery, an objective measure of functional capacity, the deterioration curve was deeper for those with complications as compared to those without. 58% and 74% of patients who did not suffer postoperative complications had recovered at 1 and 6 months, respectively, compared to 34% and 58% of patients who had experienced complications [39]. In patients above the age of 80 undergoing colorectal procedures, one study found that elective surgeries were associated with a return to premorbid functional status in 83% of patients, whereas this number was as low in 53% of patients undergoing emergency colorectal surgery. This difference was mainly attributable to the higher number of complications in the emergency group. Finally, in a multivariate analysis, the development of postoperative complications was associated with an odd ratio of 24.5 of not returning to premorbid function, far surpassing in importance every other factor included in the analysis [40].

Malnutrition has been shown to be related to poorer traditional outcomes, but there is also good data to suggest that it has a significant impact on recovery of longer-term functional outcomes. This is of particular importance in elderly patients who are at greater risk of malnutrition [41]. Six months after major abdominal surgery, increased dependency in daily activities was seen in 80% of malnourished patients as opposed to 30% of those who were well nourished. [25] In a study of elderly hip fracture patients, Goisser et al. measured the daily oral intake of patients during postoperative hospitalization. Regardless of their preoperative functional status, patients who ate smaller amounts had significantly lower ADL scores up to 6 months after surgery, and a greater percentage of them had long-term mobility loss [42]. Bastow et al. demonstrated the potential impact of preoperative tube feeding in a randomized controlled of 744 women with femoral neck fractures, stratified in 3 groups according to the level of nutrition: well nourished, thin, and very thin. Independent mobility was achieved at postoperative days 10, 12, and 23 days, respectively, and postoperative tube feeding in the thin and very thin patients reduced the time to full recovery to 10 and 16 days, respectively [43]. Despite these data and although nutritional screening is recommended for all hospitalized, medical or surgical, and elderly patients, there is still debate as to whether or not early optimization with parenteral or enteral nutrition improves postoperative recovery [44].

Frailty is a multidimensional syndrome that reflects a state of decreased physiologic reserves and vulnerability to stressors [45]. Currently available risk scores capture only a snapshot of a patient's health status at the time of the preoperative evaluation, which is heavily focused on comorbidities [46, 47]. They fail to capture the multitude of subclinical impairments that progressively accumulate with age and that ultimately determine the patient's physiologic reserve, which will be called upon at the time of major stress, such as the perioperative period [48]. These subclinical impairments may be responsible for the heterogeneity that is seen in older patients and may be better measured by the clinical frailty phenotype: slowness, weakness, weight loss, low physical activity, exhaustion, cognitive impairment, and mood disturbance [49, 50]. However, frailty may also be characterized by an accumulation of deficits that can encompass diverse signs, symptoms, comorbidities, as well as disabilities [51–53]. In a prospective study of almost 600 elderly patients undergoing elective surgery, Makary et al. demonstrated that frail patients were significantly more likely to have a prolonged hospital stay, more complications, and more often be discharged to skilled or assisted living facilities [54], findings corroborated by others [55]. Although these studies do not make a direct link between frailty and recovery, the higher incidence of complications and subsequent functional decline observed in this group serve as satisfying evidence that recovery is indeed impaired in frail individuals.

When the impact of poor baseline functional status is studied on its own, the data are more convincing and provide validation to the concept of pre-habilitation, which is discussed in the next section. Low preoperative physical function independently predicts slower recovery of ADL and IADL scores [22]. Finlayson et al. reported that in elderly patients undergoing surgery for colon cancer, preoperative functional decline was one of the most important predictors of postoperative functional decline [26]. A population-based study by Oresanya et al. paints a grim picture of the impact of baseline function. In a particularly functionally dependent population of over 10,000 nursing home patients with extensive vascular disease, 64% of patients experienced functional decline 1 year following lower extremity revascularization. At that time, among those that were ambulatory prior to surgery, 63% had become non-ambulatory or suffered a fatal event. Among those that were non-ambulatory at baseline, 89% had remained non-ambulatory or died. [56]

Strategies for Optimizing Recovery

Preoperative Care

Comprehensive Geriatric Assessment

The comprehensive geriatric assessment (CGA) is "a multidisciplinary diagnostic and treatment process that identifies medical, psychosocial, and functional capabilities of older adults to develop a coordinated plan to maximize overall health with aging." [57] In surgery, such a tool is useful for risk stratification, for preoperative optimization of modifiable risk factors, for informed decision-making, and for planning postoperative strategies and treatments to minimize age-specific complications. The domains that are evaluated by the CGA are summarized in Table 3 [58].

Table 3 Comprehensive geriatric assessment domains and tests [58]

Domain	Tests
Functional status	ADL and IADL Objective performance tests
Socioeconomic status	Income and housing Social support Transport
Comorbidities	Cumulative Index Rating Scale Revised Cardiac Risk Index
Cognitive Function	Mild cognitive impairment or dementia Depression and anxiety Risk of delirium
Nutritional Status	Mini nutritional assessment Nutritional global assessment Recent weight loss
Polypharmacy	Medication reconciliation
Geriatric syndromes	Frailty Incontinence Pressure ulcers Falls

There are few studies comparing CGA to regular care and even fewer looking at the long- to medium-term impact of this type of intervention. A recent systematic review by Partridge et al. showed that the use of the CGA in older persons scheduled to undergo elective surgery was associated with reductions in the number of cancelled surgeries and in length of hospital stay, with one study demonstrating fewer postoperative complications [59]. Despite there being no direct evidence of the CGA improving recovery, intuitively, identifying the factors that affect recovery, such as poor functional status, for example, and potentially modifying them to minimize their impact and avoiding complications, is a reasonable strategy to entertain in selected individuals.

Pre-habilitation

In the last decade, preoperative exercise therapy, or "pre-habilitation," has been investigated across several surgical fields, including general surgery, colorectal surgery, hepatobiliary surgery, orthopedic surgery, thoracic surgery, and gynecological surgery [60–71]. The goal is to maintain or possibly enhance the physical functioning and capacity of an individual to withstand the physiological stressors associated with a surgical intervention, thereby improving the baseline segment of the recovery trajectory [72]. A randomized controlled trial comparing pre-habilitation to rehabilitation in patients undergoing colorectal surgery showed that a greater percentage of patients in the pre-habilitation group had recovered to their baseline exercise capacity levels at 8 weeks (84% vs. 62%) [64]. Similarly, pre-habilitation programs for elderly patients undergoing colorectal surgery were reported to be associated with better postoperative performances on the 6-min walk test when compared to controls [66]. Although there remains many questions with respect to patient selection, exercise program design, and overall compliance and effectiveness, pre-habilitation seems to be a very promising strategy for optimization of recovery.

Hospitalization

Enhanced Recovery Pathways

Enhanced recovery pathways are multimodal evidence-based protocols, which span the entirety of the surgical experience, from preoperative patient preparation and nutrition, to intraoperative fluid and pain management, to early postoperative feeding and mobilization. Significant benefits have been demonstrated when enhanced recovery pathways are successfully implemented, such as shorter length of stay and fewer complications [73–76]. Many believe that these strategies are becoming the gold standard of care in many areas of abdominal surgery [77], although there has been uptake in other surgical disciplines as well. Contrary to what the term enhanced recovery would suggest, the great majority of the literature on the topic is quite limited when it comes to demonstrating or even studying the impact of these pathways on mid- to long-term outcomes or patient-centered outcomes, such as return to preoperative functional status [11, 78]. Nevertheless, a small number of studies in patients of all ages would suggest that enhanced recovery pathways are associated with improved quality of life and a quicker return to baseline function [79–81].

It seems intuitive that elderly patients, with their greater vulnerability to surgical stressors and decreased physiologic reserve, would have more to gain from the improved quality of surgical care that comes with these pathways [82]. In the context of enhanced recovery pathways, an early landmark study published in 1995 had demonstrated that enhanced recovery pathways provided effective postoperative pain relief, thus enabling earlier mobilization, reducing length of stay, and avoiding functional impairment in elderly surgical patients [83]. Following this, though, very little has been reported with regard to the impact on enhanced recovery pathways on functional recovery in this population. The few studies that exist are limited to short-term, traditional outcomes, such as length of stay and morbidity [84].

Multidisciplinary Intervention Team

The goal of multidisciplinary intervention teams is to ensure that care is delivered according to best known practices across a variety of complementary fields, in particular geriatrics, nursing, social work, physiotherapy, and occupational therapy. The key to the success of such teams is having (i) a shared, as opposed to competing vision; (ii) coordinated planning of interventions; (iii) effective communication; (iv) the ability of all team members to understand the purpose of the other members; and (v) proper completion and follow-through of tasks [85]. Unfortunately, most models of geriatric care that broadly implemented comprehensive groups of best practice processes did so in medical, rather than surgical patient populations. In fact, in a recent systematic review of geriatric co-management systems for in-hospital patients, only one high-level surgical study was included. There were conflicting results with respect to functional status improvement, with some studies showing mainly short-term improvement over standard care, while others showed no difference at all. [86] Several successful surgical programs are discussed below.

Hospital Elder Life Program (HELP)

The Hospital Elder Life Program consists of systematically putting into practice key processes to mitigate the effects of hospitalization in elderly patients, specifically functional decline, nutritional depletion, and delirium. Initially developed for a medical population, Chen et al. studied its impact on elderly patients undergoing a variety of abdominal surgical procedures. A single nurse carried out mobilization and rehabilitation, oral care and dietary education, and cognitive stimulation following surgery. The authors found that in the control group, 68% of patients who were pre-frail had transitioned to frailty, whereas in the HELP group, only 18% became frail, with another 18% actually becoming non-frail. Overall, at discharge, 19% of HELP group patients were frail as compared to 65% in the control group. This difference did not persist at 3 months, at which point 17–23% of patients were considered frail. [87] This intervention also reduces the rate of delirium from 15% to 7% and reduces length of hospital stay by 2 days [88]. The CareWell in Hospital program, based on HELP, reported more modest results in their mostly surgical patient population, in part because of the very variable adherence to the large number of processes that had been implemented during the study period [89].

Proactive Care of Older People Undergoing Surgery (POPS)

The POPS team consists of a geriatrician, a geriatric nurse, a physiotherapist, an occupational therapist, and a social worker. Eligible patients benefit from supervised care throughout the preoperative, hospitalization, and postoperative phases. This includes a CGA, planning of discharge needs; education on recovery, including counselling on physical activity, nutrition, and pain management; in-hospital assistance to the surgical team with mobilization; and prevention of population-specific complications, followed by postoperative ambulatory visits to address any outstanding or residual medical problems. POPS was studied in various surgical disciplines. In orthopedic surgery, the program demonstrated better pain control, less short-term dependency, and a shorter length of stay [90]. In elderly patients undergoing elective abdominal aortic aneurysm repair or limb revascularization, even when only the preoperative arm of the POPS program was implemented, a randomized clinical trial demonstrated a shorter length of stay, less delirium, and less dependency at discharge [91]. Finally, in urology, although reductions in length of stay and complications were observed, the impact on functional status was not examined. [92]

Acute Care for Elders (ACE)

ACE units have been studied almost exclusively in medical patients. Results have shown successful prevention of functional decline, reduced length of hospital stay, and reduced rates of delirium. A small pilot study in a surgical patient population admitted to a specific unit, where surgical and geriatric nurses carried out all interventions, showed only a modest improvement in ADLs when comparing the Katz score before surgery and at the time of discharge, as well as no documented falls and very minimal use of restraints [93].

Geriatric Surgery Service (GSS)

Tan et al. reported the benefits of a "dedicated collaborative transdisciplinary geriatric surgery service," which was involved in all aspects of the pre- and postoperative care of elderly surgical patients. This group consisted of a surgeon, a nurse clinician, an anesthetist, a geriatrician, a cardiologist, a physiotherapist, a dietician, a social worker, a pharmacist, and a "befriender" (an individual who would provide cognitive stimulation or "food for the soul" by conversing with the patient). 85% of elderly colorectal surgery patients in this program recovered to their baseline ADL level as early as 6 weeks [94, 95]. When pre-habilitation was added to the GSS, 100%

of patients (of which 26% were frail) had recovered to their preoperative functional levels by 6 weeks [96].

Post Hospital Care

Rehabilitation

Elderly patients are predisposed to a state of decreased physiologic reserves and stressor vulnerability [45]. The decreased physiologic reserves seen in geriatric patients are believed to be a result of predisposing molecular and disease-related triggers, compounded by the socioeconomic environment, immobilization, malnutrition, and numerous comorbidities, which in turn lead to multiple physiologic impairments. The impaired physiologic systems are centered around the dysregulation of the immune, hormonal, and endocrine systems, resulting in an upregulation of inflammatory cytokines and insulin resistance [97, 98]. This dysregulation leads to a catabolic milieu, which consequently results in a progressive decline in muscle mass and strength known as sarcopenia [99]. As skeletal muscle is the principal reservoir for amino acids [100], a decline in muscle mass impedes the body's capability to mobilize amino acids that are needed for protein synthesis [101], which are needed during periods of stress to promote immune function, wound healing, and acute phase reactants. The end result is a perpetual catabolic cycle that results in deconditioning, prolonged recovery, perioperative morbidity, and mortality [102, 103]. On the other hand, exercise has been shown to improve skeletal muscle blood flow, pulmonary gas exchange, and cardiopulmonary fitness and tolerance and have an upregulating effect on hundreds of genes that play a role in tissue maintenance and homeostasis [104, 105]. Counteracting the state of decreased physiologic reserve forms the rationale for surgical rehabilitation.

The goals of rehabilitation in the geriatric population are to (a) maintain and improve fitness, (b) assist and accelerate recovery, (c) improve range of motion, and (d) reduce pain after surgery. The rehabilitation process can be divided into several stages [106].

1. *Initial assessment*: An assessment focused mainly on physical function can be performed by a physiotherapist, or alternatively, information may be derived from a more global assessment performed by a geriatrician. This may be done prior to surgery by identifying the existing disabilities or after surgery by analyzing the physical impact that surgery has had on the patient (i.e., how far below baseline they now are).
2. *Planning*: In collaboration with the patient, goals of care are set, taking into account several facets, which may include, but are not limited to, physical disability. These facets include a positive goal (e.g., the ability to attend a future family event), a social goal (the ability to continue living independently at home), a functional goal (completing IADL without assistance), and a health-related goal (survival).
3. *Treatment*: Exercise-based interventions or therapies are implemented to reduce disability following surgery. Treatment is usually different for the deterioration (or hospitalization) and the rehabilitation (or at home) phases of recovery. In the former, the primary goal is to bring the patient from a state of physical dependency to one of physical autonomy, wherein the patient is able to leave the hospital safely. Traditionally, this was achieved somewhat passively through the use of incentive spirometry devices and breathing exercises to prevent cardiopulmonary complications. This has now progressed to a more proactive focus on early mobilization, facilitated by enhanced recovery pathways (early feeding, pain control, avoidance of tubes and drains, etc.). In this phase, rehabilitation protocols may be supervised by physiotherapists, nurses, or physicians. The goal of treatment in the rehabilitation phase (following discharge) becomes return to baseline physical function, or, if this is not deemed possible, return to a function which would allow the patient the greatest autonomy and quality of life possible. This is usually achieved through gradual

endurance and muscle building programs. These are less often supervised and may involve outpatient physiotherapy or personal training services, either in the home or at the gym. There exist several postoperative rehabilitation protocols that are tailored to the patient and specific surgery being performed, but there is little consensus on which are most effective at helping patients return to their preoperative state. Table 4 summarizes the Oxford University Hospitals rehabilitation program [107]. This structured program can be carried out throughout hospitalization and then at home, following discharge, does not require any special equipment or expertise, and is low-cost.

4. *Re-evaluation*: The effectiveness of the interventions is evaluated in the context of the goals which were established at the onset of the process. If needed, the program is modified to reorient the therapy toward the desired outcomes.
5. *Management of disability*: If permanent disability ensues, additional care and

Table 4 Oxford University Hospitals postoperative rehabilitation program [107]

A. Immediately postop
Breathing exercises (3–6 deep breaths and then rest. Repeat these exercises 3–4 times an hour) 1. While sitting upright, relax your shoulders and upper chest 2. Take a slow, deep breath in to fill your lungs as fully as you can 3. Hold this breath for 3 s 4. Breathe out slowly through your mouth
Sitting out of bed The nursing and physiotherapy staff will help you sit out of bed either on the first morning after your operation or on the same day. They will continue to help you until you are able to do this yourself. You should sit out of bed twice a day, at first for 1 h and then gradually increasing the time each day
Walking The nursing or physiotherapy staff will help you until you can walk safely on your own. Once you can do so, you will be responsible for walking regularly and increasing the distance that you can go. You should aim to walk once every hour if able. You may also be taken to try climbing stairs with nursing or physiotherapy staff or alone when comfortable
Exercises *1. Ankles*: Bend and stretch your ankles up and down firmly and quickly. Repeat 10 times *2. Knees*: Tighten your thigh by pushing the back of your knee down against the bed. Hold for 5 s. Repeat 5 times with each leg. Then, pull your toes/foot up, tighten your thigh muscle, and lift and straighten one leg. Hold for 5 s and slowly relax. Repeat 5 times with each leg *3. Buttocks*: Tighten your buttocks regularly to relieve pressure from your bottom *4. Abdomen*: Lie flat with back on bed, lying your head on a pillow and your knees bent and flat on bed. Gently place your hands on lower tummy or hips. Breathe in through your nose, and as you breathe out, gently pull your tummy down toward your spine. Feel muscles tighten. Hold for a count of 3 and then relax. Breathe in and out normally. Do 5 times, 3 times a day *5. Pelvis*: Lie flat with back on bed, lying your head on a pillow and your knees bent and flat on bed. Place your hands in the hollow of your back. Tighten your tummy, flatten your lower back onto your hands, and tilt your bottom up and back toward your chest. Breath normally and hold for 3 s and release gently. Do 5 times, 3 times a day *6. Knee Rolling*: Lie flat with back on bed, lying your head on a pillow and your knees bent and flat on bed. Tighten your tummy and gently lower both knees to one side as far as possible. Bring them back to the middle and relax. Repeat to the other side. Do 5 times, 3 times a day.
B. At home
Weeks 1–3: After being at home for a few days, you can build strength and stamina by having a short walk each day. Start with 5–10 min and gradually try to add to your distance each day. It is safe for you to go up and down stairs from the day you go home. By the second week, you can start to carry out light chores, such as cooking, wiping, and dusting. Increase your walking time and distance each week
Weeks 4–6: You can gradually do more household jobs such as ironing and cooking. Break tasks
down into smaller parts and ask other people to help. Aim to be walking between 30 and 45 min by 6 weeks. You must still avoid heaving lifting and standing for long periods of time
Weeks 6–12: You can begin more strenuous tasking such as vacuuming so that by week 12 you are back to normal

interventions may be needed to alleviate and reduce the consequences of the disability. Occupational therapists have expertise in person-environment interactions within the home and work environment and may provide recommendations for the integration of assistive technologies and environmental modifications. Assistive technology may include bathroom or self-care aids, prosthetics, or mobility aids, such as canes, crutches, walkers, or wheelchairs. Environmental modifications use methods to minimize the effects of one's environment in exacerbating disability and promote ease of access. Finally, social workers may be useful in introducing coping strategies for patients, family, and caregivers to address the psychosocial issues that may arise secondary to the disability.

In surgery, the benefits of postoperative rehabilitation are evident in specific fields, mainly cardiac and orthopedic surgery, in which it has been shown to improve physical function, to reduce pulmonary complications, to decrease length of stay, and to lower hospitalization costs [108–111]. Furthermore, postoperative physiotherapy has reduced postoperative pulmonary complications and reduced length of stay in hospital in other heterogeneous cohorts of hospitalized patients [112, 113]. Following hospitalization, postoperative rehabilitation may be delivered in a variety of facilities, including the home, outpatient physiotherapy services, and inpatient rehabilitation services. The optimal setting will depend on the individual needs of the patient and the resources available in their milieu, but it would seem that inpatient rehabilitation services may be superior in improving functional independence when compared to skilled nursing facilities delivering physiotherapy services [114, 115].

Evidence-based practices for postoperative rehabilitation in abdominal surgery are sparse. Houborg et al. showed that postoperative physical training had no effect on physical function in patients undergoing colorectal surgery; however, the study may not have been adequately powered for this endpoint. [23] The benefits of enhanced recovery programs and the focus on encouraging early mobilization and exercise-based physiotherapy are increasingly recognized and integrated into practice; however, it is unclear what the contribution of the exercise therapy is to the overall benefit seen in programs with several other simultaneous interventions. Given the paucity of evidence, it is difficult to make any strong recommendations, although most would agree that early mobilization following surgery, whether assisted or not, is important and should be carried out in most patients. In-hospital rehabilitation programs may have some value in achieving this goal, although this is a resource which may not be available in all centers and certainly not always at the intensity needed to make an impact. Although data is lacking on whether post-hospitalization rehabilitation centers improve recovery, they may nevertheless be useful in providing a bridge between the ward and the home, during which function can be optimized, and the support can be provided to the patients who would otherwise not have access to it at home.

Conclusion

Surgical recovery in the elderly is poorly defined and poorly studied. It seems to revolve mainly around the return to preoperative functional status, although other domains are sparingly reported, including cognition, fatigue, and quality of life. Depending on the measure that is used, recovery may take up to 6 months, and sometimes longer, in a significant number of elderly individuals. Major risk factors for prolonged recovery include frailty, or at least a poor baseline functional status, malnutrition, and the occurrence of surgical complications. To optimize recovery, several strategies have shown success. The preoperative identification of higher-risk individuals using the CGA may help better address modifiable patient characteristics, leading to fewer complications and a quicker return to functional independence. Pre-habilitation protocols are in their infancy, but show promise in improving preoperative functional status in order to better withstand the stressors of surgery. Several postoperative strategies, such as enhanced recovery pathways and multidisciplinary programs, share a common goal: to minimize the functional deterioration that is characteristic of hospitalization following surgery, by improving the adherence to best-practice processes, thereby promoting early mobilization and independence. Finally, following discharge, rehabilitation programs, which come in all shapes and sizes, should intuitively promote a faster return to the preoperative state, although the data are lacking. Overall, the fields of recovery and rehabilitation in elderly surgical patients suffer from a lack of knowledge. As the population continues to age, it is crucial to recognize the relevance of the surgical experience which occurs after discharge and to actively include elderly patients in surgical trials addressing the issues discussed in this chapter.

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Available Government and Community Resources for the Care of Older Adults

29

Hadley K. Wesson

Contents

Abstract

In 2005, there were 37 million people who were aged 65 years or older in America, making up 12% of the population. By 2030, this is estimated to nearly double to 70 million. The fact that the elderly will make up more than 20% of the American population has inevitable implications to our health care system. We, as surgeons, receive little, if any, formal education regarding resources available to assist in our care of the elderly. This chapter outlines the availability and use of government resources, including Medicare and Medicaid, as well as community resources and providers as a context for their successful utilization.

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Introduction

In 2005, there were 37 million aged 65 years or older in America, making up 12% of the population. By 2030, this is estimated to nearly double to 70 million or 20% of the population [1]. This increase in the elderly population has inevitable implications to our healthcare system that we begin to feel now. Advanced age is associated with an increase in chronic health conditions, healthcare needs, and medical expenses. As surgeons, we receive little, if any, formal education regarding resources available to assist in our care of our older patients.

Treating the older adult patient, whether in an outpatient or emergent setting, includes important components if longitudinal success in care is to be achieved. It is not only necessary to know how to medically and surgically tailor treatment towards the older adult, but also to understand the context in which these patients live. This chapter outlines the availability and use of government resources, including Medicare and Medicaid, as well as

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community resources, while aiming to provide a context for their successful utilization. It is also important that we recognize the limitations of these programs and how we as surgeons can and must advocate for our patients.

Government Resources: Medicare and Medicaid

Medicare is the federal health insurance program for people 65 years old and older. Medicare was created in 1965 and expanded in 1972 to include people younger than 65 years old with permanent disabilities. Medicare currently serves 59 million Americans with a budget of $672.1 billion or 15% of the total federal spending [1, 2].

People 65 years and older can enroll in Medicare if they or their spouse are eligible for Social Security payments and paid payroll taxes for 10 years or more. Medicare covers basic health services including hospital stays, physician services, and prescription drugs. It is organized into four parts: Part A, Part B, Part C, and Part D.

Part A covers inpatient hospital stays, skilled nursing facility stays, some home health visits, and hospice. It is subject to a deductible which in 2018 was $1,340. In addition, beneficiaries must pay a coinsurance for extended inpatient hospital stays [1].

Part B covers physician visits, outpatient services, preventative services, and some home health visits. In 2018, there was a $183 deductible and a 20% coinsurance for most benefits [1]. Exceptions are preventative services and wellness visits to which there is neither a deductible nor a coinsurance payment.

Part C, also known as Medicare Advantage, allows beneficiaries to enroll in private health plans that contract Medicare to receive all Part A and Part B benefits and typically Part D benefits. In 2017, approximately 33% of Medicare beneficiaries were covered through Medicare Advantage [3]. The number of plans available to beneficiaries however varies by county: in 2018, beneficiaries living in 206 counties throughout the United States were able to choose from more than 30 different plans offered by six firms. In contrast, in 44 counties, beneficiaries only had one option to choose from [3].

Part D covers outpatient prescription medications using private health insurance plans to offset drug costs after a beneficiary's deducible is met. It also offers catastrophic coverage for very high drug costs. Part D has a coverage gap, often referred to as the "doughnut hole." What this means for the beneficiary is that in 2018, they would enter the doughnut hole after they paid $3,750 in drug costs for that year. Once in the doughnut hole, beneficiaries have to pay 35% for brand-name medications and 44% for generics. They continue to pay this until their out-of-pocket costs reach $5,000. After they reach this limit, they will be out of the doughnut hole and pay no more than 5% for their drug costs for the reminder of the year [1]. Under the Affordable Care Act, the coverage gap will close by 2019, when enrollees will pay 25% of the cost of their prescription drugs.

Medicare has relatively high deductibles and co-payments under Parts A and B. To help Medicare recipients with these costs, there are different types of supplemental coverage, including employer-sponsored retiree health plans, Medigap policies, and Medicaid. Approximately 19% of Medicare beneficiaries however remain without any supplemental coverage [1].

Supplemental health insurance coverage through employer-sponsored retiree health plans was once very common. Yet over the last four decades, employer-sponsored plans have decreased from 66% of Medicare beneficiaries in 1988 to 25% in 2017 as many employers have stopped offering this as an option to employees [1]. While this trend does not appear to have affected health outcomes, it is estimated that retirees' out-of-pocket healthcare costs increased [4]. In the highest 40% of out-of-pocket Medicare spenders, beneficiaries without an employer-sponsored plan spend on average 22% more than those enrolled in an plan [5].

Medigap, or Medicare Supplement Insurance, is supplemental coverage sold by private insurance companies to help cover the cost of Medicare

Part A and B deductibles, co-payments, and coinsurance. Approximately 23% of Medicare recipients have Medigap [1].

Medicaid is the federal program that provides health and long-term care to low-income people. It is a supplement to Medicare for approximately 11 million Americans or 22% of Medicare recipients. To be eligible for Medicaid, beneficiaries must have low incomes, limited assets, and a limited ability to work due to advanced age or a disability. Low income is defined as $733 per month per individual or $1,100 per month per couple which is approximately 75% of the federal poverty level [6]. Assets are limited to $2,000 per individual or $3,000 per couple [6]. To assist low-income Medicare recipients with the out-of-pocket costs of Medicare, state Medicaid programs must offer three Medicare savings programs: Qualified Medicare Beneficiaries, Specified Low-Income Medicare Beneficiaries, and Qualified Individuals.

Eligible Qualified Medicare Beneficiaries are Medicare recipients with incomes up to 100% of the federal poverty level. Once a recipient is enrolled in the program, Medicaid pays their premiums and coinsurance directly to Medicare. Specified Low-Income Medicare Beneficiaries have higher incomes from 100% to 120% of the federal poverty level and receive financial aid for Medicare premiums only [6]. Qualified individuals are those individuals who have incomes up to 135% of the federal poverty level and pay their Medicare Part B premiums through an expansion of the Specified Low-Income Medicare Beneficiaries program passed by Congress in 1997. However, there is a limited amount of funds allocated to each state by Congress each year for this plan. Once the state has spent that amount, beneficiaries who would have qualified for the Qualified Individual program do not receive financial assistance [6].

It is estimated that approximately one in three people over the age of 65 years will require nursing home or long-term care at some point in their life [7]. The average annual cost of nursing home care in 2016 was $82,000, or approximately three times the average annual income of older Americans [7]. Long-term care is not covered under Medicare but rather Medicaid. As such, 44 states allow Medicare recipients who need long-term nursing home care to qualify for Medicaid if they have incomes less than 300% of the Supplement Security Income level, or roughly 219% of the federal poverty level or $2,199 per month per individual [6]. In 2015, Medicaid paid $55 billion for long-term care covering 60% of the 1.4 million Americans living in nursing homes, making Medicaid the country's primary payer for long-term care [6, 7].

Community Resources

Key resources for older adults living in their communities are made available through the Older Americans Act. Passed by President Johnson in 1965 as part of his "Great Society" initiative, the Older Americans Act supports programs to help the older adults live independently in their communities for as long as possible [8]. It falls under the mandate of the Administration for Community Living within the Department of Health and Human Services.

A range of programs are available to eligible seniors through the Older Americans Act such as home health aids, nutritional programs, transportation, counseling, and legal aid. For example, through the Administration for Community Living, states can provide one, two or three meals a day five to seven times per week, of which each meal is required to provide at least one-third of the recommended dietary allowances [9]. A note of caution, however: the availability of these resources is state dependent and highly variable. A list of resources available by state is available through the Eldercare Directory (https://www.eldercaredirectory.org/state-resources.htm) [9]. Also note that receiving these resources does not correlate with improvements in health. In fact, the opposite has been shown: a recent retrospective review of over 2,000 adults found that those receiving Older Americans Act meals had poorer health and functional disabilities compared to adults who did not receive such benefits [10].

Two-thirds of Medicare beneficiaries have two or more chronic conditions. Fourteen percent have more than five chronic conditions which accounts for 55% of total Medicare spending and 63% of post-acute care, such as nursing homes [11]. Studies show income is related to chronic conditions and that older Americans who live in disadvantaged neighborhoods are more likely to have functional limitations [12, 13].

Medicare beneficiaries on average have two primary care physicians and five specialists [14]. In addition to offering community health programs, efforts are underway by the Institute of Medicine to develop care coordination programs for Medicare recipients. Ideally these programs would assess gaps in healthcare and develop individualized plans to collaborate with medical and community health providers [15]. Such programs have the potential to greatly contribute to current community resources.

There is some debate within the literature as to how surgeons can contribute to this concept of care coordination. One proposal is to identify high-cost patients in the preoperative setting, the so-called hot spotting, and develop preoperative cost reduction strategies such as prehabilition programs and readmission prevention initiatives [16]. This concept is currently in a trial phase but could prove to be a cost-effective approach in the future.

In its current state, the government spends more on Medicare than it accrues, and estimates predict that Medicare's funds will be depleted by 2030 [17]. Proposals to cut Medicare and Medicaid spending are ever present and hotly debated, especially within the political realm. It is however a "Catch 22": reductions in federal financing would limit the supply of Medicare and Medicaid services, while the demand will increase as America's baby boomers continue to age in an era aptly described as a "Silver Tsunami" [18].

Conclusion

Surgeons must be aware of these constraints and the out-of-pocket costs their older adult patients face despite coverage from federal insurance plans and available community resources. This adds a complexity to the practice of medicine in America. Not only must we as healthcare providers strive to provide excellence in care, but we much do so in a cost-effective manner, recognizing the investigations we order, medications we prescribe, and surgeries we perform are all at a cost borne ultimately by our patients.

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Outcomes of Surgery in Older Adults

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Contents

Abstract

Older individuals represent a growing proportion of patients undergoing surgery. The outcomes of elderly patients are worse across a broad range of complication types, highlighting the importance of efforts to improve and maintain quality of care. Special consideration needs to be given to risk stratification and preoperative optimization in order to provide appropriate patient-centric care. Postoperative cognitive decline, loss of independence, and advanced directives are all areas where providers need to focus on the specific needs of this vulnerable population. This chapter reviews existing data supporting an approach that focuses on the elderly patient and surveys evidence-based methods to optimize care.

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Introduction

Between 2012 and 2050, the US population aged 65 years and older is projected to nearly double, from about 42 million to more than 80 million individuals [1]. This unprecedented change in the demographics of the US population will significantly alter the landscape of surgical care and require increasing attention to the outcomes of surgery in older adults. Differences in physiology, metabolism, comorbidity, frailty, social support, and cognition can all affect the response of older adults to the stress of surgery. Thus, the clinical outcomes of operations and the strategies to optimize surgical care may differ for older adults.

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Table 1 Ten most commonly performed inpatient operations in the United States (2012)

ICD 9 codes	Procedure description	# Performed	% in 65+ yo
81.54–81.55	Total knee replacement	613,290	56.5%
81.51–81.53	Hip replacement (partial, total, revision)	391,265	62.0%
51.21–51.24	Cholecystectomy	335,130	30.7%
47.01	Laparoscopic appendectomy	182,325	8.1%
45.71–45.83, 17.31–17.39	Colon resection	144,115	50.7%
8102	Other cervical fusion of the anterior column (anterior technique)	128,665	21.8%
6849	Other and unspecified total abdominal hysterectomy	119,585	10.9%
7935	Open reduction of fracture with internal fixation (femur)	117,570	73.8%
8107	Lumbar and lumbosacral fusion of the posterior column (posterior)	107,350	41.8%
7936	Open reduction of fracture with internal fixation (tibia and fibula)	105,335	27.7%
	TOTAL	2,244,631	43.7%

In general, older individuals use medical and surgical services at substantially higher rates than younger individuals. According to data from the US census, individuals over the age of 65 comprised approximately 14% of the US population in 2012 (Table 1) [1]. Yet, they account for [2]:

– 31% of cholecystectomies
– 49% of colon resections
– 62% of total hip replacements
– 57% of total knee replacements
– 53% of hospitalizations
– 67% of hospital days of care

Of the top ten most commonly performed inpatient operations in the United States, 4 are performed more often in patients 65 years old or older (Table 1).

The incidence of numerous operations increases with age, such that for many procedures, individuals in their eighth or ninth decade of life have the highest frequency of surgery, as shown in Fig. 1. As a result, the majority of major inpatient operations involve older adults.

Likewise, outpatient surgical procedures are also much more common in older individuals. The following graph (Fig. 2) examines rates of seven of the most frequently performed outpatient procedures based on data from the state of Florida. Two procedures – myringotomy tubes and tonsillectomy/adenoidectomy – are performed more commonly in younger patients and less so in older individuals. For the remaining 5 procedures, the age range with the highest rates of surgery is individuals aged 60 years and older. This is particularly true for cataract operations, which could not be included in the figure below for reasons of scale. The annual rate of cataract surgery among individuals aged 70–79 is 74 per 1,000 population, greater than the other 7 procedures combined.

In addition to generating an increased number of surgical procedures, older adults are more likely to require greater care and increased resource utilization around surgery. After major inpatient surgery, older patients have longer postoperative hospital length of stay and higher rates of readmission [3]. They are also significantly more likely to require postoperative inpatient skilled nursing care and prolonged utilization of health services. After major cancer surgery, for example, 24–44% of octogenarians used extended care facilities after hospital discharge [4], as do half of patients over 80 who undergo coronary artery bypass grafting [5]. Prolonged functional recovery is common in older adult surgical patients, with objective measures of disability often persisting as much as 6 months after major

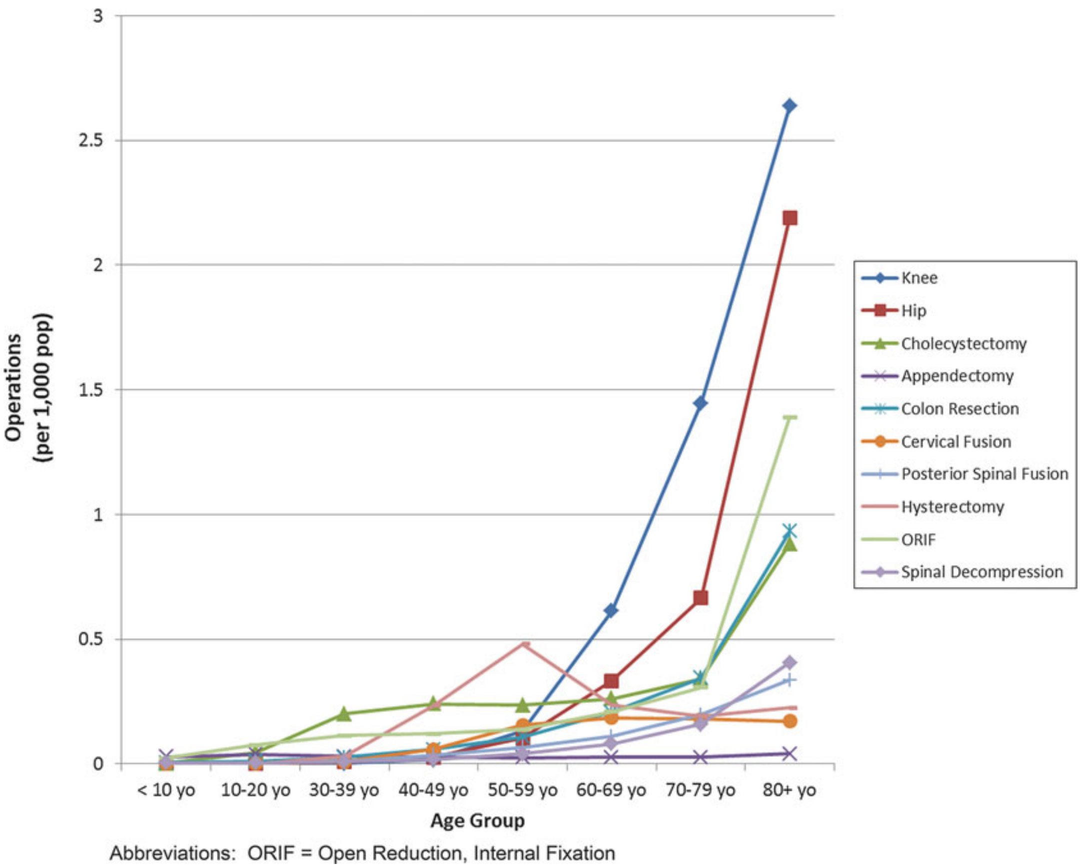

Fig. 1 Incidence rates for top 10 inpatient operations, by age group [2]. (Abbreviations: *ORIF* open reduction, internal fixation)

abdominal surgery [6]. During their hospitalization, older patients require greater medical services as well. In a recent analysis of Medicare claims data, Kuo et al. found a more than fivefold increase in the proportion of surgical admissions that involved care from a medical hospitalist [7].

Despite the increased care burden required by older surgical patients, there is a trend toward increasingly performing operations that were historically considered too risky to undertake in elderly patients [8–10]. The bias against aggressive surgical treatment for patients considered empirically "too old" appears to be diminishing, and the rates at which elderly individuals are undergoing several types of major surgical procedures are increasing [11]. These trends, as well as the demographic shift toward an increasingly older US population, will demand attention to research on clinical outcomes in elderly patients [12]. This chapter will address the evidence base informing our current understanding of the measurement of surgical outcomes in older adults.

Surgical Outcomes in the Elderly Population

Even after all other factors are considered, older/elderly patients incur a higher risk of complications after major operations. The challenge is to quantitatively consider this greater level of risk with the proposed benefit of a specific surgical intervention in a specific patient.

A large study by Hamel et al. used the National Surgical Quality Improvement Program (NSQIP) to evaluate 26,648 patients aged

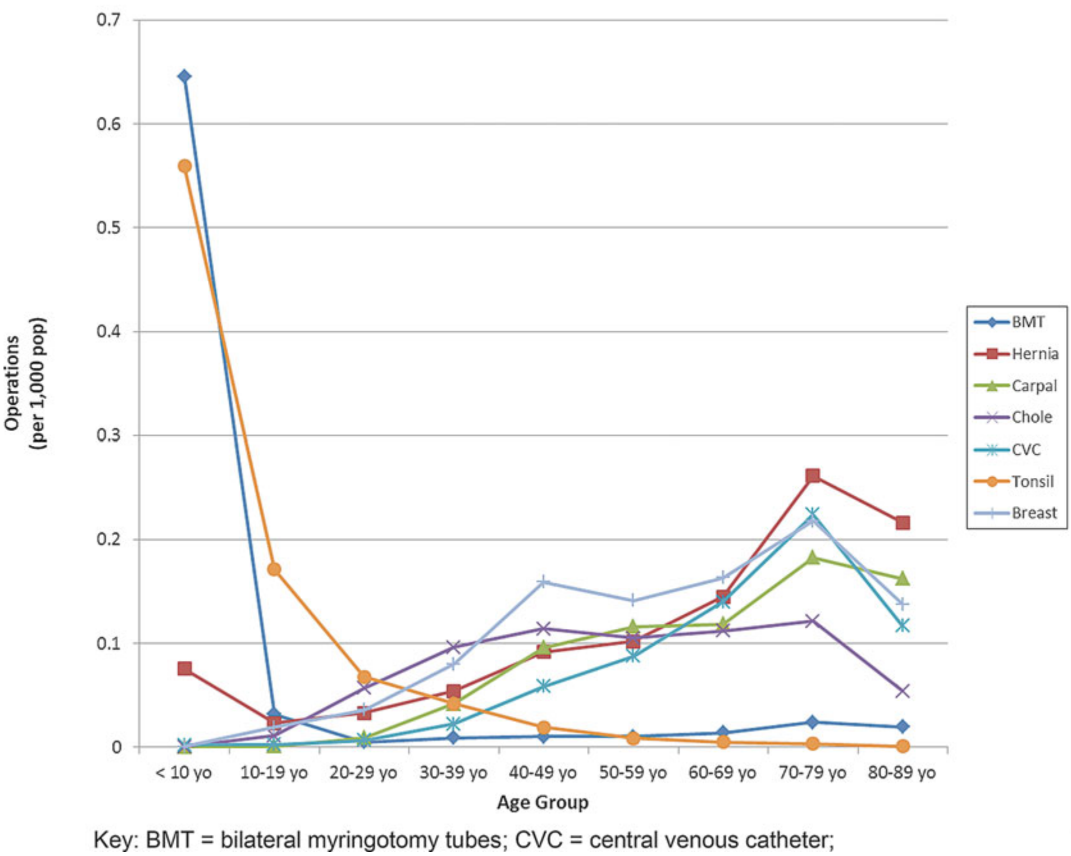

Fig. 2 Incidence rates for top 10 inpatient operations, by age group. (Key: *BMT* bilateral myringotomy tubes, *CVC* central venous catheter)

80 years or older undergoing major noncardiac surgery [13]. Patients >80 years of age had higher all-cause mortality rates than younger patients (8% vs. 3%, $P < 0.001$). Furthermore, of the patients >80 years, 20% had one or more of 21 identified potential postoperative complications (i.e., pneumonia, myocardial infarction). Postoperative complications are also distinct drivers of postoperative mortality. Of those with postoperative complications, a 30-day postoperative mortality was higher than for patients who did not have a postoperative complication (26% vs. 4%, $P < 0.001$). Interestingly, they also found that for patients >80 years, after adjusting for 33 baseline variables, there was a 5% increase in 30-day mortality risk for each year over the age of 80 (i.e., a 90-year-old has a 50% greater risk of 30-day mortality than an 80-year old). As might be expected, patients >80 had a higher 30-day mortality risk when undergoing emergent versus elective surgery (adjusted odds ratio 1.7) [13].

This study demonstrates that elderly patients have worse outcomes after surgery than younger patients, which is important to communicate when discussing expected outcomes after elective or emergent surgery.

Optimizing Surgical Outcomes for Elderly Patients: Best Practice Guidelines

With the goal of improving quality of care and optimizing the preoperative period for geriatric surgery patients, the ACS-NSQIP and American

Geriatric Society (AGS) collaborated to create best practice guidelines [14]. An expert panel was assembled to perform a systematic review of the literature and establish evidence-based recommendations for improving the preoperative assessment of geriatric patients (summarized in Table 2).

Special Considerations

Optimization of outcomes also includes understanding the concept of frailty, prehabilitation, postoperative cognitive decline, and how DNR orders may affect patients' postoperative course.

Assessment of Frailty

Preoperative assessments (e.g., American Society of Anesthesiologists (ASA) score) are commonly used to predict postoperative outcomes. However, these traditional scores account for organ function rather than physiologic reserve. Frailty is an emerging concept that takes an important step forward in conceptualizing and measuring physiologic reserve. Unfortunately, there is no gold standard for diagnosing frailty. Age and comorbidity alone do not define frailty since there is a spectrum of active versus debilitated elderly at each age. For now, frailty is defined as a syndrome characterized by a loss of biologic reserve causing increased vulnerability to minor stressors and risk for adverse outcomes, including disability, hospitalization, and death [15, 16].

Due to a relatively vague definition, multiple frailty assessment tools have been developed and validated for the identification of frail patients. Most tools have been developed around the conceptualization of physical frailty rather than cognitive assessment. The most commonly cited frailty screening tool is the physical frailty phenotype which defines frailty as meeting three or more of the following: weight loss of more the 5% of body weight in the last year, exhaustion, weakness, slow walking speed, or decreased physical activity [17]. A simpler, faster tool is the FRAIL scale that defines frailty if patients answer having three or more of the following: fatigue, resistance, ambulation, illnesses, and loss of weight [18, 19].

Makary et al. prospectively measured frailty in 594 patients age 65 years or older undergoing elective surgery to determine if frailty predicts surgical complications and enhances current perioperative risk models [20]. Frailty was defined as a score based on age-associated decline in five domains: shrinking, weakness, exhaustion, low physical activity, and slowed walking speed. Their main finding was that frailty is an important predictor of postoperative complications, increased length of stay, and discharge to a skilled or assisted-living facility. The group also found that frailty had considerable predictive capability above and beyond the known indices of ASA score, Lee's revised cardiac risk index, and Eagle score, underscoring the importance of physiologic reserve in the elderly population undergoing surgery.

More recent studies have investigated the association of frailty with postoperative mortality. McIsaac et al. used a population-based retrospective cohort to examine 1-year all-cause mortality among 6,289 frail patients, as defined by the Johns Hopkins Adjusted Clinical Groups (ACG) frailty-defining indicator [21]. The authors found frailty to be associated with a significantly increased risk of 1-year mortality. This association was especially important in the early postoperative period and after joint arthroplasty. Another study by Mosquera et al. analyzed 232,352 patients by using the NSQIP database to determine if frailty was associated with adverse postoperative events including mortality [22]. The study found frailty to be significantly associated with postoperative complications, prolonged duration of stay, and 30-day mortality on multivariate analysis. Colectomy and esophagectomy showed the greatest mortality in severely frail patients at a rate of 9.36 and 8.2%, respectively.

Prehabilitation

Given the importance of frailty as a risk factor for complications, the potential of frailty as a target for preoperative optimization is clear. Any intervention to strengthen (diminish frailty) patients before surgery has intuitive appeal, either because (1) patients are better able to recover from surgery or (2) patients have improved outcomes (fewer

Table 2 Domains of preoperative assessment in elderly surgical patients

Area of preoperative assessment	Instrument	Additional evaluation	Relevance
Cognitive impairment and dementia	Mini-Cog	If evidence of cognitive impairment based on the Mini-Cog, consider further evaluation	Dementia is common and the prevalence increases with age
Decision-making capacity	Use 4 legally relevant criterion		Critical to determine patient's ability to provide informed consent
Depression	Patient Health Questionnaire-2	If answers YES to either question, then evaluate further	Depression is common in elderly and can be associated with higher analgesic use
Risk factors for postoperative delirium	Potential risk factors include cognitive or metabolic disorders, comorbidities, and functional impairment	Avoid medications such as benzodiazepines and antihistamines. Correct any modifiable risk factors such as sleep deprivation and immobilization due to urinary catheter	Postoperative delirium is associated with increased morbidity, mortality, length of stay, and need for institutionalization
Alcohol and substance abuse	Modified CAGE questionnaire	If yes to any question, consider perioperative withdrawal prophylaxis	Preoperative alcohol abuse and dependence are associated with increased rates of postoperative morbidity and mortality
Cardiac	ACC/AHA algorithm	Important to effectively communicate operative risk	Older patients are more vulnerable to perioperative cardiac events
Pulmonary	Identify patient-related and surgery-related risk factors	Consider preoperative strategies to reduce risk such as smoking cessation, optimization in uncontrolled COPD, or asthma	Pulmonary complications are common and predict long-term mortality in the elderly
Functional status	Assess ability to perform daily activities; deficits in vision, hearing, or swallowing; history of falls. Perform timed up and go test	Consider formal assessment of ADLs/IADLs and referral to physical therapy if abnormal timed up and go	Poor functional status is an independent predictor of mortality
Frailty	Criteria include shrinkage, weakness, exhaustion, low physical activity, and slowness		Frailty independently predicts higher rates of postoperative adverse events, increased length of stay, and higher likelihood of discharge to a skilled or assisted-living facility
Nutritional status	Screen using BMI, albumin, and unintentional weight loss	If any of these items are abnormal, perform full nutritional assessment	Poor nutritional status is associated with infectious and wound complications
Medication management	Review and document patients' complete medication list	Identify medications that should be started, continued, or stopped before surgery, adjust doses for renal function, monitor for polypharmacy	Polypharmacy is associated with poor medication compliance, increased adverse events, cognitive impairment, morbidity, and mortality

(continued)

Table 2 (continued)

Area of preoperative assessment	Instrument	Additional evaluation	Relevance
Patient counseling	Discuss advanced directive, treatment goals, postoperative course and potential complications, family/social support	If concern for poor family/ social support, consider preoperative referral to social worker	Patient expectations and preferences influence treatment preferences
Preoperative testing	Hemoglobin, renal function, and albumin for all geriatric surgery patients	Other labs, ECG, CXR, PFTs, and noninvasive cardiac tests are for selected geriatric surgery patients	Many studies have highlighted the low yield and high cost of routine preoperative screening

Abbreviations: *ACC/AHA* American College of Cardiology/the American Heart Association, *ADLs/IADLs* activities of daily living/instrumental activities of daily living, *BMI* body mass index, *CAGE* questionnaire for alcoholism, *COPD* chronic obstructive pulmonary disease, *CXR* chest X-ray, *ECG* electrocardiogram, *PFTs* pulmonary function tests

complications). This concept – "prehabilitation" – is an emerging focus of research, and several studies have examined the extent to which these types of interventions are associated with improved patient outcomes.

A recent systematic review found 5 studies including 353 patients who prospectively received prehabilitation before elective colorectal surgery [23]. Overall, this body of research suffered from small sample sizes, poor compliance with interventions, and heterogeneity of intervention. The accumulated findings were that the interventions were not effective in significantly reducing rates of complications or length of hospitalization. These findings were similar to those seen in a systematic review of the effect of prehabilitation in joint replacement surgery [24]. In an examination of 22 studies including 1492 patients, Wang et al. found only nominal improvements in pain and level of function but no impact on length of stay and costs.

These initial findings are discouraging, but it is worth observing that this field is still in a very early stage. Because there was no consensus among colorectal surgeons as to whether preoperative exercise was beneficial, a Delphi survey was performed across a group of colorectal surgeons in an attempt to form a consensus opinion on prehabilitation in the elderly colorectal cancer patients [25]. Twenty two statements were included, and more than 80% agreement was defined as consensus. After three rounds, it was agreed upon that exercise training should form part of the preoperative care and would be supported by surgeons and that suitable programs posing significant risk to patients were rejected. There was no agreement on the strength of the current literature. Future study will better inform the community of the efficacy of preoperative rehabilitation.

Postoperative Cognitive Decline

Elderly patients are at significant risk for developing short-term, long-term, or permanent decline in the level of cognitive function. This phenomenon was first recognized after cardiopulmonary bypass (CPB) but is now increasingly well recognized as a complication after any operation under general anesthesia. A recent review found the incidence of postoperative delirium to range from 10% to 65% and that up to 40% of these patients never return to their baseline level of function [26]. For surgeons, an understanding of the likelihood and severity of postoperative cognitive decline is important.

The likelihood of long-term or permanent cognitive decline is an important element of informed consent for patients undergoing elective surgery. This consideration is a challenging one for surgeons, patients, and surrogate decision-makers as it is inherently difficult to quantify. Despite this challenge, it is critical that all parties to the consent process be aware of the potential for short-term and long-term decline.

Preexisting Do Not Resuscitate (DNR) and Failure to Rescue

As the patient population ages, the number of patients with DNR orders undergoing surgery has risen, and the question has been raised whether or not a DNR order should affect surgical management. The presence of a DNR order as a surrogate marker of illness or impending death is not well documented in the surgical literature. Recently, Speicher et al. used the NSQIP database to evaluate DNR and non-DNR patients undergoing emergent surgical management of intestinal obstruction in order to understand the expected postoperative complication and mortality rate in patients with a DNR order [27]. The main finding was that a DNR order status was an independent predictor of postoperative mortality even after adjusting for comorbidities and overall complication rate.

An important question that remained unanswered by Spiecher's study was *why* the DNR order was an independent risk factor for mortality. A subsequent study by Scarborough et al. also used data from the NSQIP to evaluate 25,558 patients over the age of 65 undergoing emergency surgery for common general surgery procedures such as appendectomy, cholecystectomy, and colon resections [28]. Patients with a DNR order had a significantly higher postoperative mortality rate than non-DNR patients but not a significant difference in the incidence of major postoperative complications. Interestingly, among those patients who did sustain one or more complications, subsequent mortality (i.e., failure-to-rescue) was significantly higher in the DNR group than in the non-DNR group (57% vs. 41%) despite the fact that the two groups had no detectable difference in their physiological ability to withstand such complications. The group concluded that the likely reason for higher mortality in the patients with a DNR order was the failure to pursue aggressive postoperative management, also called a "failure-to-pursue rescue." While patients with DNR orders may initially consent to surgical intervention to fix their acute problem, they may be less inclined to continue to pursue aggressive treatment after surgery.

Specific Patient Populations

The Nursing Home Patient

Nursing home residents may be the most vulnerable of elderly patients. While most of the published studies suggest that major surgery can be performed safely in older adults, they do not include nursing home patients in their analyses. This cohort makes up 5% of patients 65 years and older, and it is estimated that more than one third of people over 70 years will spend some time in a nursing home before they die [29]. Thus, a significant proportion of the elderly will reside in or be exposed to a nursing home.

In 1992, Keating et al. published a retrospective chart review of skilled-care nursing home residents who underwent major surgery. Of the 74 patients included, serious complications occurred in 43%, which the authors reported to be comparable to unselected geriatric populations [30]. A later study in 1996 by Zenilman et al. did a prospective study of nursing home patients who underwent major abdominal and vascular operations [31]. Overall survival was similar for nursing home residents who did versus did not undergo these operations. The authors concluded that the patients' overall survival was not affected by the need for surgery or the operation performed, and, therefore, surgery was not futile in this patient population and should be performed if of benefit to the patient in terms of patient dignity and a relief of suffering.

More recently, Finlayson et al. evaluated 70,719 nursing home patients by using national Medicare claims and the nursing home Minimum Data Set (1999–2006) to identify nursing home residents undergoing surgery [32]. These patients were compared to noninstitutionalized Medicare enrollees aged 65 years and older undergoing the same procedures. Operative mortality among nursing home residents was substantially higher than among noninstitutionalized Medicare enrollees for all procedures ($P < 0.001$), and invasive operations were more among common nursing home residents than controls ($P < 0.0001$). Through this well-designed study, the authors were therefore able to conclude that nursing home residents experienced substantially higher rates of mortality after major surgery even after correcting for age and comorbidities.

This population-based study, while limited by the use of administrative data, did raise some important points regarding the optimal management of surgical diseases in nursing home residents. For conditions that are truly life threatening, over half of nursing home residents over 85 years survived. Thus, surgery may not be futile for these patients who will die without surgery. However, for nonlife-threatening surgical diseases, less invasive treatment strategies such as antibiotics for appendicitis or percutaneous cholecystotomy tube for cholecystitis may be preferred in this population rather than undergoing elective surgery. Patients and their families should be appropriately counseled that surgery in this cohort results in much higher mortality regardless of age.

Elderly Patients with Dementia

Dementia is one of the most common cerebral disorders in older adults and is significantly associated with advancing age. The incidence of dementia rises rapidly at older age, from 5% of those 71–79 to greater than 37% of individuals over 90 years of age [33], and these patients are particularly vulnerable in the postoperative period for complications and worsening cognitive decline [34, 35].

Special attention is needed for older surgical patients with dementia, as perioperative complications, including acute renal failure, sepsis, stroke, and urinary tract infection, are far more common than in similar aged controls [36]. Further, functional recovery may be impaired in these patients. For example, lower extremity joint replacement among patients with Alzheimer's disease is associated with prolonged hospitalization and more frequent need for revision, even in the absence of perioperative complications [37]. Surgery for rectal cancer in patients with dementia incurs increased risk of postoperative incontinence [38]. It is also patients with preoperative dementia who are at greatest risk of long-term cognitive decline after surgery [26]. Unfortunately, alterations in anesthetic approaches have not altered perioperative outcomes for patients with dementia, as the incidence of perioperative complications and delirium is no different with the use of general versus regional anesthesia [39].

Both short- and long-term mortality rates after surgery are also significantly higher among older patients with dementia [40]. For example, death after hip fracture repair among nonagenarians was doubled among those with dementia, with mortality rates of 6% at 90 days and 62% at 1 year after surgery [41]. Although these worse outcomes have been attributed by some to inability to complete rehabilitation, efforts to redesign postoperative rehabilitation approaches to meet the needs of patients with dementia have not consistently demonstrated benefit [42].

Postoperative Care

The Use of Enhanced Recovery Pathways in the Elderly

Over the last decade, enhanced recovery programs (ERPs) have redesigned the approach to perioperative care of surgery patients in some settings. The multidisciplinary set of interventions in the perioperative and postoperative phases was initially proposed by Professor Henrik Kehlet from Denmark and focused on noncardiac surgery [43]. Among the main interventions, restrictive intravenous fluid therapy, the use of laparoscopy in combination with appropriate anesthesia, early enteral feeding, and early postoperative mobilization seem to be the most important to the pathway's success. There is now extensive literature documenting that adherence to ERPs can minimize morbidity and mortality while decreasing hospital length of stay and overall cost [44–48].

In order to achieve these improved outcomes with enhanced recovery, there need to be implementation and compliance to multiple interventions. This can be difficult to achieve, especially in certain patient populations. Therefore, elderly patients have been excluded from ERPs in some institutions due to the perceived impediments of physical impairments or medical comorbidities [49]. However, recognizing that frail older patients may have the most to gain from efforts to improve and hasten postoperative recovery, it is important to know whether similar care principles should be adopted.

Recently, three studies have demonstrated successful introduction of ERPs for elderly patients with outcomes suggesting they are safe and feasible. Despite greater comorbidities, older patients experience equivalent adherence to enhanced recovery pathways, fewer complications, and shorter length of hospital stay with enhanced recovery, which may further improve outcomes in this patient population [50–52].

Prevention of Postoperative Complications in the Elderly

The ERAS movement has clearly identified ways in which perioperative care can be improved to minimize metabolic derangement and lower risk of complications. A best practice guideline was recently published by the American College of Surgeons in conjunction with the American Geriatrics Society – this guideline is a highly recommended resource for all surgeons [53]. Many of the domains that are highlighted in these guidelines are inherent in the emerging ERAS guidelines discussed earlier in this chapter. These interventions are sensible for all patients, but there may be a subset of interventions that is specific to the needs of elderly patients.

As mentioned earlier, elderly patients are at risk for postoperative cognitive decline. This decline can be mitigated with some level of effectiveness. Widely recognized risk factors for cognitive decline include CPB, hypoxemia, hypotension, metabolic stress, neurotoxic anesthesia, analgesics, sleep disruption, and fasting [54]. Intuitively, minimizing patient exposure to these risk factors is sensible, but not always possible due to clinical factors [26]. With some focused attention, sleep protection, increased daytime activity, and minimization of opioids can be achieved without undue burden.

Older patients may be at greater risk for issues related to mobility and independence. Highly frail patients need a constant level of vigilance to prevent the occurrence of pressure ulcers. Physical therapy and early mobilization are needed to prevent rapid loss of physical function that can lead to loss of the ability of patients to complete activities of daily living. An important aspect of preoperative counseling is a discussion regarding expectations of where the patient will stay/live after discharge and what the level of help (friends, family, healthcare professionals) will be available. If a postoperative transfer to a rehabilitation facility or skilled nursing facility is planned, then this discussion should be initiated preoperatively.

Conclusion

With the fastest-growing segment of the population aged ≥65 years, the number of operations performed on elderly patients is increasing. It is imperative that physicians understand surgical outcomes specific to the elderly, best practice guidelines for improving and optimizing care prior to undergoing surgery, as well as the impact of both frailty and DNR orders on postoperative outcomes. There are several other areas specific to the elderly that also warrant further investigation including avoiding inappropriate medication use, prehabilitation, accurate assessment of preoperative cognitive function, and prevention of postoperative delirium. Further work is needed to better understand this vulnerable population in order to provide high-quality care and optimize postoperative outcomes.

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Surgery in the Frail Elderly: Nursing Home Patients

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Emily Finlayson and Michael E. Zenilman

Contents

Abstract

Throughout our careers, each of us – the co-authors of this chapter and the editors of the textbook – have published about the role of general surgery in the nursing home population. The topic has retained its timeliness over the past 30 years, as the term “nursing home” evolved from a place of last resort for patients on their destination to death to a place where the frail, vulnerable elderly may go to for both short-term rehabilitation and long-term stay.

We will all encounter such high-risk patients in our practice. To aid the surgeon in assessing and caring for this group of people with very little reserve, in this chapter we review how to establish a consult service for academic and community-based nursing homes, and describe the types of surgical illnesses encountered. We then show data for 70,000 Medicare patients who underwent surgery in nursing homes using the powerful tool of population-based analysis. The studies

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delineate the type of patients and procedures we will face, the resource utilization, and expected outcomes. This information is critical to help manage the expectations for physicians, patients, and family members.

Introduction

As a result of medical advances, healthier life styles, and decreased health risk, the aging population of the United States and other Western societies will approach the limit of aging, or the life-span. A comparative study performed on life expectancy of 80-year-old persons in Western countries showed that American octogenarian men and women are expected to live 7.0 and 9.1 more years, respectively. In England, the survival of octogenarians was 6.2 and 8.1 years, respectively; in France 6.7 and 8.6 years, respectively; in Sweden 6.5 and 8.3 years, respectively; and in Japan, 6.5 and 8.9 years, respectively [1].

As the limit of life expectancy is reached, a significant percentage of elderly persons become debilitated and become increasingly dependent on others for care. We already known that at age 65 about 10–20% of persons become dependent on others for one or more basic activities of daily living (ADLs). This proportion has been shown to increase to 25% at age 75 and to 50% at age 85 [2]. It is predicted that the overall average life expectancy in the United States will increase to 83 by the year 2050 [3], and by 2030 there will be 8.8 million persons over the age of 85 [3].

Many of these patients will, no doubt, need chronic nursing care.

A population with increased disability must have care, which is typically undertaken in nursing homes. One study forecast that of the 2.2 million persons who turned 65 in 1990, 43% (900,000) will enter a nursing home before they die: 32% are expected to spend more than 3 months under such care, 24% more than 1 year, and 9% more than 5 years [4]. The implications for medical management of these patients is obvious, and there is a definite need for good surgical care, as delineated below.

Focusing Surgical Care on the Frail Elderly: Development of a Dedicated Consult Service for Nursing Home Patients

A number of studies have addressed the utility of focused medical care for frail elderly patients in the inpatient setting. The establishment of an aggressive medical geriatric assessment service for frail elderly populations has been shown to increase patient survival, quality of life, and ability to return to independence [5–7]. In these studies, rehabilitation, independence in self-care, detailed discharge planning, and avoidance of iatrogenic illness were stressed. The interventions resulted in 10% improvement in function on discharge (34% vs. 24%) and decreased need for long-term care (14% vs. 22%) [7].

One study, however, found no real benefit of focused geriatric assessment in the hospital [8], but in this study, the geriatrician was used only as a consultant, not the coordinator of care. There is little argument about the fact that the only person capable of dealing with the complicated elderly patient is one who coordinates the medical, social, rehabilitative, and surgical care.

Little has been reported about the surgical care of nursing home patients. There are a fair number of reports on the treatment and outcomes of care for decubiti [9–11] but little else. Most studies on this population have been limited to addressing risk factors for death and survival. As a result, little is known about the utility of aggressive surgical care for the hospitalized or nursing home frail elderly patient. Moreover, some surgeons are reluctant to deal with common surgical illnesses in nursing homes because the patients are usually chronically sick, there is a question about its utility, and some patients have active “do not resuscitate” (DNR) orders.

It is reasonable to assume that a service devoted to the surgical care of chronically ill elderly patients would have a positive impact on their survival and quality of life. Therefore a geriatric surgery consult service was developed at the Johns Hopkins Bayview Medical Center, whose goal was to improve surgical care of the frail elderly resident at home, in the hospital, and in the nursing home.

The consult service was established on August 1, 1991. The Johns Hopkins Bayview Medical Center campus had an active general surgery service and geriatric medicine service. The Geriatric Medicine Department has an active acute medical care facility in the hospital, and they control the Johns Hopkins Geriatric Center as well, a 240-bed chronic care facility/nursing home on campus for patients who require both simple and complex chronic nursing home care. The consult service therefore established a close association with the geriatric division, giving exclusive surgical care for the patients residing in this nursing home facility. Using this service, with subsequent expansion to care for patients in other nursing homes affiliated with the institution, the primary questions were.

1. What is the typical makeup of the patient population referred to this service?
2. What is the incidence and severity of specific general and vascular surgical problems in this patient population?
3. What are the risks of surgical intervention, specifically the complication and morbidity rates?

Patients needing elective surgical consultation were consecutively referred to this service. All patients evaluated and treated by the service were enrolled, along with specific demographic data, into a computer database. All patients were followed in a prospective manner until June 1, 1994. We subsequently reported the results elsewhere [12].

Altogether 153 patients were enrolled, and 117 of them required intervention. The admission diagnoses to the nursing home and reasons for the surgical consultation are shown in Table 1. While maintenance care (decubitus, stoma, and enteral tube care) made up a substantial percentage of referrals, common surgical diseases of the abdomen, breast, and vascular systems were routinely encountered (55%). The actuarial 18-month survival of all patients referred was 35% (Table 2).

A total of 117 patients underwent 168 surgical procedures. The distribution of cases is shown in

Table 1 Diagnoses for geriatric surgery consult service

Diagnosis	%
At admission	
Dementia	20.9
Stroke	19.4
ADL	14.2
Peripheral vascular disease	9.0
Infection	7.5
Abdominal	6.7
Cancer	6.7
Chronic renal failure	6.0
Coronary artery disease	4.5
Chronic obstructive pulmonary disease	3.7
Diabetes	1.5
Total	100
At consult	
Maintenance	32.5
Abdominal/rectal	27.7
PVD	16.0
Breast	10.6
Hernia	4.6
HD access	1.2
Total[a]	92.6

Source: Adapted from Zenilman et al. [18]
Maintenance, decubitus care, chronic intravenous lines, enterostomy, and enteral tubes
[a]Others included gynecologic problems, lymph node biopsy, trauma, posttransfusion hepatitis

Table 2 Operations in Nursing Home Patients

Procedure	No.	%
Abdominal		
Total biliary	11	6.5
Endoscopy/gastrostomy tube	12	7.1
Laparotomy	26	15.5
Total	56	29.1
Nonabdominal		
Débridement of decubitus	42	25.0
Amputations	22	13.1
Intravenous access	25	15.0
Breast	14	8.3
Hernia	5	3.0
Other	11	6.5
Total	119	70.9

Source: Adapted from Zenilman et al. [18]

Table 3 Goals of Medical and Surgical Care for Individuals with Limited Life-Expectancy

Maximize or maintain potential life-span
Maintain dignity of life, maximize self-esteem
Maximize independent function, minimize dependence
Relieve suffering, with particular attention to pain
Cure might not be possible; palliation and comfort are just as important

Table 3. In patients subjected to surgery, the 30-day mortality rate was 8.5% and complication rate 9.4%. Interestingly, the 30-day mortality of the 36 patients not undergoing any intervention was 11.4%; this translated into *absolutely no difference* in overall survival for patients who underwent surgery compared to those who did not.

Although those undergoing major abdominal and vascular procedures had a higher complication rate (17.6%) than those undergoing lesser procedures (6.3%, $p = 0.05$), there was no difference in 30-day mortality (9.8% vs. 6.3%, respectively) or 18-month actuarial survival (33% vs. 32%, respectively). Multivariate analysis of survival using the Cox regression model showed that survival was adversely affected by the presence of the comorbid conditions of coronary artery disease [relative risk (RR) 3.27, $p = 0.01$] and dementia (documented by a Mini-Mental Score less than 24) (RR 2.39, $p = 0.04$), and age greater than 70 (RR 2.03, $p = 0.06$). It is interesting that the significance value of age was low compared to that of the other variables. Although univariate analysis showed age to be significant, multivariate analysis put it right on the edge of significance when compared to the comorbid conditions of cardiac disease and dementia. Overall survival was unaffected by the need of surgery, the magnitude of the procedure performed, sex, number of comorbid conditions or medications, and whether a preoperative DNR order was present.

This study concluded that general surgical disease is routinely found in the geriatric population, and, therefore, proper surgical care by a general surgeon is necessary. It also showed that routine surgical procedures can be performed safely in residents of nursing homes. Unfortunately, the overall survival of residents of nursing homes referred for surgical intervention is poor, even worse than the published survival of patients in geriatric inpatient units, which is approximately 77.2% (1-year survival) [13].

Analysis of Data from the Geriatric Surgery Consult Service: Role of Dementia, Age, and Coronary Artery Disease in the Nursing Home Patient

In this population of patients, the relative risk of death was increased by the presence of cardiac disease and dementia (determined by a Mini-Mental Score less than 24). Age, as described above, only approached statistical significance. Studies have shown that the presence of dementia adversely affects survival rates of nursing home patients [14–16]. The reported survival of nursing home patients with dementia is 68% at 1 year, 55% at 2 years, and 28% at 3 years [16]. The diagnosis alone increases the relative risk of mortality in these patients by a factor of 2.7 [17, 18].

Dementia is prevalent among not only the nursing home patient [14, 16–19] but also the "healthy elderly." Skoog et al. [20] showed that in a cohort of 494 nonhospitalized or institutionalized subjects aged 85 and older the prevalence of dementia was 29.8%. The dementia was mild in 8.3%, moderate in 10.3%, and severe in 11.1%. Interestingly 43.5% of the dementia was Alzheimer's type, 46.9% was vascular (multiinfarct)-related, and 9.5% was due to other causes. As in our study and others, the presence of dementia was a risk factor for death: The 3-year mortality was 23.1% in normal persons, 42.2% in those with Alzheimer's dementia, and 66.7% in those with vascular dementia.

Dementia can be assessed rapidly by the Mini-Mental examination [14, 19]. Although in our study we used only the Mini-Mental Score obtained on admission to the nursing home, in the future it might be useful to obtain a score at the time of the surgical consult to see if it can be an accurate predictor of short-term survival.

Contrary to what others have shown, survival in our nursing home population was also not dependent on the absolute number of concomitant medical diseases. This result is in contrast to those of other studies, which showed that in the general hospitalized elderly patient co-morbid illness significantly increased the relative risk of death [14–16].

The absence of difference in survival in nursing home patients who required surgical intervention compared to those who did not is interesting. Although one might infer that surgery in this population had no effect on survival because most of the procedures performed were lifesaving (e.g., amputation for infected or gangrenous limbs, gallbladder removal for acute cholecystitis) or life-maintaining (e.g., long-term intravenous access for nutrition or antibiotics, wound débridement to prevent systemic infection, mastectomy for local control of breast cancer), surgery in these patients actually improved their chances and brought their survival curve back to the downward sloping baseline.

Case Examples

Three cases highlight the utility of a geriatric-oriented surgical service and the need for surgical leadership in this arena.

Case 1

We were consulted to evaluate a 92-year-old arthritic woman who had had symptomatic gallstones for more than a year. She was maintained on chronic antibiotics and pain medications after eating. Her only other medications were nonsteroidal antiinflammatory drugs (NSAIDs) for the arthritis. After evaluation by our service, elective removal of the gallbladder was recommended. It was performed laparoscopically without incident. Postoperatively, she remained intubated overnight but was discharged back to the nursing home on postoperative day 2. Almost immediately after discharge, she noted only minimal symptoms after eating, her appetite improved, and she gained weight. She expired from unrelated illness 3 months later. She, her family, her geriatrician, and the nurses caring for her thought that she was much more comfortable after removal of the inflamed gallbladder.

Prior to our evaluation, all thought she was too old and frail for even elective surgery. She was a good surgical candidate; furthermore, because of the significant complication of the biliary system that had developed from the gallstones, I believe she would have expired rapidly. This patient was clearly helped by seemingly aggressive, but appropriate, surgical management. The patient, her family, and her health care providers had to be educated about the benefit of elective surgery, as all were basically uninformed prior to the surgical consult. Her DNR order, in effect during her nursing home stay, was rescinded during her procedure and her short stay in the intensive care unit (ICU).

Case 2

We were consulted to evaluate a malfunctioning percutaneously placed gastrostomy in an 85-year-old man. An endoscopic photograph of the stomach showed that the tube had migrated out of the stomach and into the prefascial space. Under local anesthesia with intravenous sedation, the tube was removed, the stomach was identified, and a new gastrostomy was placed. This procedure was performed as an outpatient operation, and the feeding tube was used the next day.

Case 3

A 78-year-old woman was a nursing home resident for 8 months after emergency subtotal colectomy due to septic colitis complicated by respiratory and cardiac problems. After a remarkable but prolonged recovery, she began to tolerate oral food well. Over a 2-week period she developed right upper quadrant pain, nausea and vomiting, anorexia, and fevers. Her white blood cell (WBC) count was 15,000 cells/mm^3; alkaline phosphatase was 400 IU/L; and other liver function tests and amylase were normal. Ultrasonography revealed a large gallstone and normal common bile duct. To convert this urgent situation to an elective one, a percutaneous cholecystostomy tube was placed, 250 cc of pus was removed, and the patient was placed on intravenous antibiotics. The WBC count normalized, and a diet was started the next day. Cholangiography was performed through the cholecystostomy 3 days later due to persistently elevated alkaline phosphatase, and a stone was noted in the common bile duct. Endoscopic retrograde cholangiopancreatography was performed 3 days later, and the stone was removed successfully. The patient did well and underwent elective cholecystectomy 1 month later.

Comment

These three cases illustrate the need for surgical involvement in the care of nursing home patients. We must educate the patient, family, and even primary physician about the utility of an invasive procedure for palliation of the patient's illness. We also must coordinate the multidisciplinary care these patients frequently need.

Development of a Second Geriatric Surgery Consult Service: Decubitus Care

An issue raised by the aforementioned study [12] is that the nursing home studied was situated near a tertiary care center and hence may have had a different population of patients from the "community nursing home." Furthermore, it dealt with a multitude of surgical illnesses, and conclusions about individual types of illness cannot be drawn from such studies.

To evaluate factors determining survival in residents of community nursing homes suffering from a single disease, we retrospectively studied 105 patients consecutively referred for surgical débridement of decubiti in a nursing home in the Bronx, New York.[27] The mean (±SD) age of the patients was 75 ± 1.3 years, and 70% were women. Patients were followed for 10.9 ± 1.0 months. The 1- and 2-year actuarial survivals were 60% and 42.7%, respectively, somewhat higher than what we previously observed. This survival is similar to that of the general nursing home population. It is probable that persons with decubiti are not as ill as others who develop surgically treatable illness.

Univariate analysis showed that the patient's sex and the diagnosis of coronary artery disease had a statistically significant effect on survival, whereas the diagnosis of dementia appeared not to matter, neither dementia nor age factored into survival in this study. Interestingly, these two factors were identified as significant in the previous study. There were differences between the two studies. The first was a prospective analysis in a nursing home associated with a tertiary care center and dealt with all surgical problems. The second (present) study is retrospective, in a community nursing home, and dealt only with surgically managed decubitus ulcers.

Cox regression analysis revealed the relative risk of death for male patients was 2.56 ($p = 0.004$) and for patients with coronary artery disease, 2.2 ($p = 0.008$). We concluded that survival of nursing home patients referred for surgical intervention for decubiti is similar to that of the overall nursing home population. The presence of decubiti in these patients does not adversely affect outcome, and their treatment should be aggressive. Obviously, a dedicated decubitus service in this setting may even improve patient quality of life.

A Dedicated Surgical Service for Community Nursing Home: The Einstein College of Medicine Experience

A surgical consult service was established at Albert Einstein College of Medicine to serve patients residing in a community nursing home. These patients were prospectively studied and overall survival was analyzed as well as the effect of independent variables such as age, gender, presence of coronary artery disease, presence of dementia and location and severity of ulcer on survival [21].

There were 105 nursing home patients referred to the consult service, all for debridement of chronic decubitus ulcers. The mean age of this cohort was 75 +/− 1.3 year and 70% were female. These patients were followed from January 1995 to August 1997 for an mean +/− SEM of 10.9 +/−1.0 months (range 0–36 months). 34% suffered from coronary artery disease, 31% had diabetes, 21% respiratory disease, and 9% from renal disease. Most decubiti were debrided at the bedside in the nursing facility. 33% were extremity decubiti, 27% trunk, and 17% were on both the extremity and trunk, and 23% were not specified.

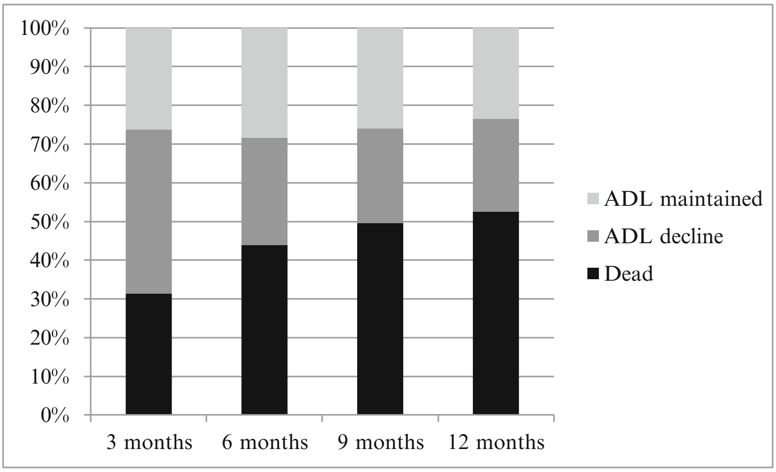

Fig. 1 Proportion of nursing home residents who experienced ADL decline, maintenance of ADL, and death after colon cancer surgery. (Source: Adapted from Finlayson et al. (ref))

Most procedures performed in this group were minor. We observed 1 and 2-year actuarial survival rates to be 60% and 42.7%, respectively. Multivariate analysis demonstrated that in this population, gender and the presence of coronary artery disease significantly affected overall survival, but older age, presence of dementia or comorbid illness did not.

Population-Based Outcomes After Major Surgery in Nursing Home Residents

In recent years, Medicare claims data and the Minimum Data Set for Nursing Homes, a national registry of nursing home residents, has been used to examine short- and long-term outcomes after major surgery in the nursing home population (refs). The Minimum Data Set for Nursing Homes is a standardized assessment administered quarterly for all residents of nursing homes participating in Medicare or Medicaid. It contains longitudinal information about medical, cognitive, and functional status [22–25].

In an analysis of over 70,000 nursing home residents who underwent surgery for common emergent abdominal operations (surgery for bleeding ulcer, cholecystectomy, appendectomy, and colectomy), operative mortality was two to threefold higher than among noninstitutionalized Medicare enrollees [23]. Furthermore, postoperative invasive life-sustaining interventions were significantly higher in the nursing home population than among noninstitutionalized Medicare enrollees – ranging from 18% versus 5%, respectively, after cholecystectomy to 55% versus 43%, respectively, after ulcer surgery.

Studies examining functional outcomes after surgery among nursing home residents have demonstrated that the majority of nursing home residents who undergo surgery experience substantial and sustained functional decline postoperatively [22, 24, 25]. Among residents who underwent colectomy for cancer, 53% were dead after 1 year and over half of 1-year survivors experienced functional decline [22] (Fig. 1). For residents who undergo lower extremity bypass, half die within a year of surgery [24]. At 1 year, 13% of the initial cohort was ambulatory and 18% had maintained or improved their baseline functional status – calling into question the efficacy of this procedure in the nursing home.

Hip fracture is mordid and not infrequent event in the nursing home population. Neuman et al. used the Minimun Data Set for Nursing Homes and Medicare Claims to examine functional outcomes after hip fracture in the United States Nursing Home Population [25]. They found that over a third of residents died and over half of residents had dies or experienced functional decline within 180 after fracture. Residents with multiple comorbidities and advanced cognitive impairment and those who did not undergo surgical correction of the fracture experienced the worst outcomes.

Conclusions

The population of nursing homes is going to increase over the next few decades, resulting from the increased population of elderly patients and the increased disability that accompanies the normal aging process. Common surgical illnesses are encountered in nursing home patients, and careful consideration is needed to guide the care of such patients. In this patient population, quality of life, patient dignity, and relief of suffering take often precedence over curative therapy and prolongation of life. Surgical decision-making must be informed by realistic prognostic information. The goals delineated in Table 3 should be followed to allow our elders dignity and comfort in their final days.

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Part V

Specific Specialties

Neurosurgery-Intracranial

32

Toral R. Patel and Joseph T. King Jr.

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Abstract

Neurologic illnesses are a leading cause of death and disability in the elderly population. Many of these diseases require surgical evaluation. The US Census Bureau estimates that by 2030, 52 million Americans will be over 70 years of age [1]. The presentation, management, and outcomes of neurosurgical emergencies can be quite different in the geriatric population. It is imperative that practitioners are aware of the unique challenges that exist when caring for geriatric patients with neurosurgical emergencies.

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Introduction

Neurologic illnesses are a leading cause of death and disability in the elderly population. Many of these diseases require surgical evaluation. The US Census Bureau estimates that by 2030, 52 million Americans will be over 70 years of age [1]. The presentation, management, and outcomes of neurosurgical emergencies can be quite different in the geriatric population. It is imperative that practitioners are aware of the unique challenges that exist when caring for geriatric patients with neurosurgical emergencies.

Traumatic Brain Injury

Recent studies report that approximately 1.1 million new cases of traumatic brain injury (TBI) are diagnosed and treated in US hospitals each year, approximately 450 cases per 100,000 people. Subgroup analyses demonstrate that the elderly have a significantly higher rate of TBI. In persons over 85 years of age, there were approximately 1,000 cases per 100,000 people [2, 3]. The majority of these injuries are caused by falls [4]. Multiple studies have demonstrated that despite similar injury severity, older patients have worse outcomes than younger patients [5, 6]. Morbidity and mortality from TBI start to increase in the fifth decade of life, but rise sharply after age 70 [7]. It is postulated that elderly patients have worse outcomes due to diminished cardiovascular reserve and fundamental differences in the aging central nervous system (CNS) and its response to injury [6, 7]. Because of this disparity, the literature suggests that age >70 years should be a criterion for full trauma team activation and that those patients should also be considered for transfer to a certified trauma center, regardless of the severity of the actual event [8, 9].

Extra-Axial Hematomas

Extra-axial hematomas are defind as hemorrhages within the intracranial space, but outside of the brain parenchyma. They occur almost exclusively in the setting of trauma and can be either acute or chronic in nature. Extra-axial hematomas that form under the dura mater are termed subdural hematomas (SDH), while those that form above the dura mater are termed epidural hematomas (EDH).

SDH may be caused by a variety of conditions, but they most commonly occur as a result of trauma. In the elderly population, SDHs occur in 46% of TBIs, while in younger patients, they occur in only 28% of TBIs [7]. This is thought to be due to the increased adherence of the dura mater to the inner surface of the elderly skull, which in concert with general cerebral atrophy, results in continuous stretching of the bridging veins that connect the cerebral cortex to the dural sinuses. With the added insult of a trauma, these stretched veins are easily injured, resulting in hemorrhage between the dura and brain, otherwise known as a SDH. The clinical manifestations of SDHs are the result of focal or diffuse pressure on the brain, or chemical irritation of the underlying cortex. Signs and symptoms include headache, nausea/vomiting, diplopia, altered mental status, pupillary dilatation, seizures, dysphasia, and hemiparesis/hemiplegia. Acute SDHs can become rapidly symptomatic as blood accumulates in the subdural space and presses on the underlying brain. Chronic SDHs can accrue over time as the result of multiple episodes of bleeding from repeated small traumas. Often times, they are larger than acute SDHs, however, their signs and symptoms are usually milder because the chronology of their development allows the brain to accommodate the mass effect. On CT scan, all SDHs appear as crescent-shaped extra-axial collections, which may cross suture lines but do not cross midline. Acute SDHs appear hyperdense to adjacent brain tissue on CT scan, while chronic SDHs are hypodense (Fig. 1a, b). Chronic SDHs may also have internal septations visible on the CT scan caused by the formation of membranes. Imaging appearance and symptoms are used to determine the need for surgical evacuation. Any symptomatic acute or chronic SDH needs to be evacuated promptly. In addition, acute SDHs >10 mm in maximal thickness or with >5 mm of midline shift are typically removed, regardless of symptoms [10]. The need for surgical

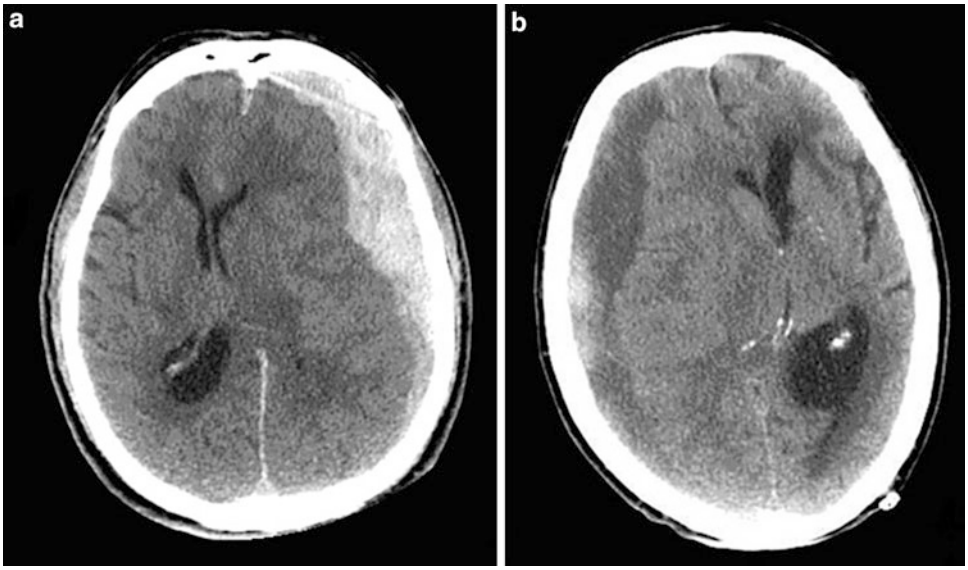

Fig. 1 Noncontrast axial head CTs demonstrate (**a**) acute subdural hematoma – a hyperdense crescent-shaped extra-axial collection and (**b**) chronic subdural hematoma – a hypodense crescent-shaped extra-axial collection. Both of these lesions are causing significant mass effect and resultant shift of midline brain structures

evacuation of large asymptomatic chronic SDHs is less clear. Operative intervention for an acute SDH usually requires a generous craniotomy, evacuation of the hematoma, and control of bleeding. Depending on the degree of underlying parenchymal injury and edema, expansion duroplasty and bone flap removal may be necessary to accommodate swelling of the underlying brain and minimize dangerous increases in intracranial pressure (ICP). Operative intervention for a chronic SDH usually involves burr holes and removal of chronic liquefied hematoma via suction and irrigation, often followed by the placement of temporary postoperative subdural drains. A special consideration in the elderly population is the degree of underlying cerebral atrophy. Because the atrophic brain is often unable to expand and fill the subdural space even after the mass effect has been removed, bridging veins remain under tension and at risk for future traumatic injury, and recurrent chronic SDHs often form. Occasionally, craniotomies are performed for chronic SDHs if there is concern for significant membrane formation and therefore inadequate drainage of the loculated subdural hematoma through one or two burr holes.

EDHs also occur as a result of trauma, but are much less common than SDHs, with an estimated incidence of 2.7–4.1% in TBI patients [10]. The increased adherence of the dura mater to the skull in the elderly serves to tamponade bleeding into the epidural space, thus EDHs are unusual in the geriatric population. When present, EDHs are often associated with skull fractures. Traditionally thought to be of primarily arterial origin, recent studies have indicated that EDHs from venous injuries are quite common as well [10]. Clinically, patients with significant EDHs present with focal and diffuse brain pressure findings similar to those with SDHs. Signs and symptoms include headache, nausea/vomiting, diplopia, altered mental status, pupillary dilatation, seizures, dysphasia, and hemiparesis/hemiplegia. Additionally, some patients present with the classic "lucid interval," an asymptomatic time period immediately following trauma before the onset of symptoms, attributed to the expansion of the hematoma as it slowly dissects between the skull and adherent dura, gradually increasing pressure on the underlying brain. On CT scan, EDHs appear as hyperdense biconvex extra-axial collections, which do not cross suture lines (Fig. 2a, b). Surgical evacuation of the

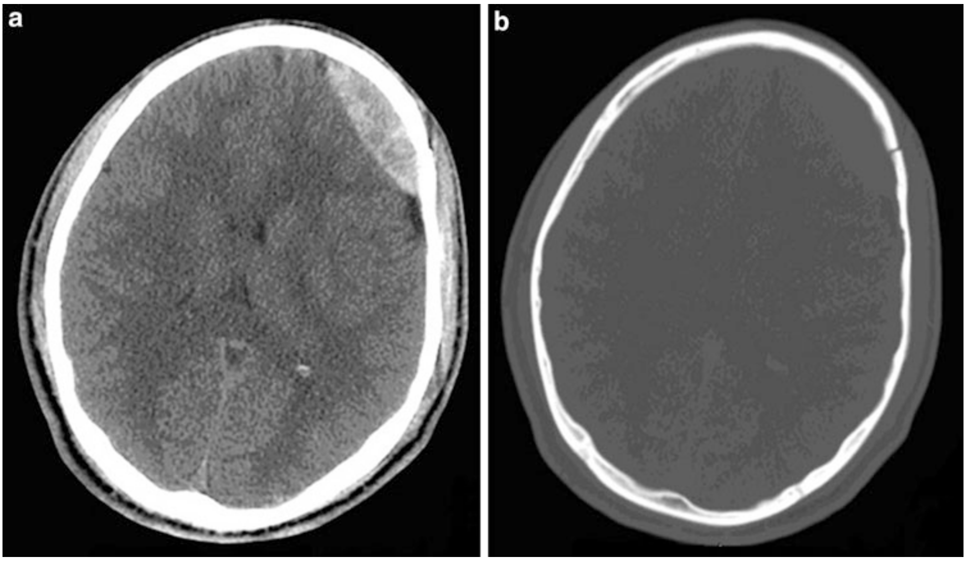

Fig. 2 Noncontrast axial head CTs demonstrate (**a**) acute epidural hematoma – a hyperdense biconvex extra-axial collection and (**b**) in the same patient, a minimally displaced left frontal skull fracture adjacent to the epidural hematoma, the likely cause of the vascular injury producing the hematoma

hematoma is indicated for symptomatic lesions. EDH evacuation usually requires a craniotomy, with or without expansion duroplasty and bone flap removal, based on the extent of the underlying parenchymal injury and edema.

Intracerebral/Subarachnoid Hemorrhage

In addition to extra-axial hematomas, patients with traumatic brain injuries often have intra-axial hemorrhages, either within the parenchyma of the brain or in the subarachnoid space. The management of traumatic intracerebral hemorrhages is similar to that of nontraumatic intracerebral hemorrhages. These lesions appear as hyperdense intra-axial collections on CT, which can vary in diameter from under a millimeter to several centimeters. Initial treatment should focus on blood pressure control, to prevent rebleeding, and management of ICPs. Frequent neurologic examinations should be performed to assess for acute decompensation and serial imaging studies should be performed to evaluate for rebleeding. In the event of elevated ICPs, medical management should be initiated, and in some cases, surgical decompression is required due to the degree of mass effect (Fig. 3) [10, 11].

Subarachnoid hemorrhages are also common sequelae of TBI. Although these hemorrhages seldom require surgical evacuation, they are often associated with seizures, altered mental status, and diffuse axonal injury, all of which can lead to significant morbidity and mortality. On CT, traumatic subarachnoid hemorrhages appear as layered, hyperdense lesions within the subarachnoid spaces, most commonly along the cortical surfaces. Patients with traumatic subarachnoid hemorrhages should be given prophylactic anticonvulsant medications for 7 days posttrauma [12]. Care should be taken in the administration of these medications to the elderly population, as they often have significant side effects including hypotension, cardiac arrhythmias, and confusion. Additionally, for those patients with traumatic subarachnoid hemorrhage and poor neurologic exam in the absence of a focal compressive lesion, placement of an ICP monitor is often required to measure ICPs, which require further management if elevated (Fig. 3) [10, 11].

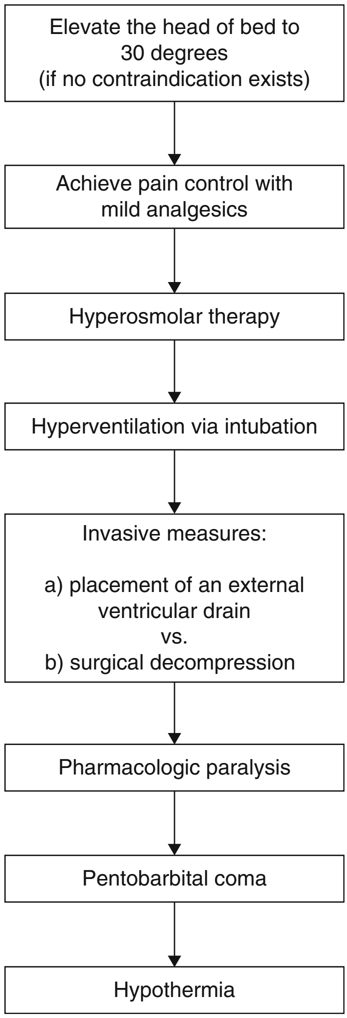

Fig. 3 General schematic for the management of elevated intracranial pressures

Fractures

The skull is a protective layer meant to absorb high-energy forces and to prevent direct intracranial parenchymal injury. In doing so, the skull is also placed at risk for fracture in the event of a significant trauma. Skull fractures can be loosely categorized into four groups: linear, depressed, skull base, and open, each of which has unique management strategies.

Linear fractures are the most common type of skull fracture and are usually the result of low-energy trauma over a large surface area. These fractures are nondisplaced, seldom require surgical intervention and are treated with observation and expectant management [13].

Depressed skull fractures are usually the result of high-energy trauma over a small surface area. Clinically, depressed skull fractures often manifest with seizures, due to an underlying cortical injury, or as an epidural hematoma, due to laceration of a meningeal artery adherent to the skull. Those fractures that are depressed below the inner table of the adjacent normal bone typically require surgical elevation [13].

Skull base fractures occur in the context of severe trauma and can manifest with a variety of neurologic symptoms [13]. Often, skull base fractures are associated with additional intracranial injuries due to the magnitude of the causative trauma. Most significantly, skull base fractures can cause vascular injuries, commonly to the internal carotid arteries, as well as cerebrospinal fluid (CSF) leaks [14–16]. Therefore, all patients with skull base fractures should undergo computerized tomographic angiography (CTA) to rule out vascular injury [14, 15]. Additionally, they should be monitored closely for the evidence of CSF otorrhea or rhinorrhea. Management of vascular injuries should be deferred to an experienced neurovascular team, which includes both neurosurgeons and neurointerventionalists. Management of CSF leaks includes initial conservative treatment with bed rest and head of bed elevation to reduce the hydrostatic pressure gradient and CSF flow across the dural defect, allowing for the body to seal the breach. If the CSF leak persists despite these conservative measures, CSF diversion using a lumbar drain and/or surgical repair are needed to eliminate the leak to prevent bacterial ingress and subsequent meningitis [16].

Open skull fractures are defined as those lesions with an overlying skin laceration, such that there is a communication between the external environment and the intracranial space. These lesions are at particularly high risk for infection [17]. Open skull fractures often demonstrate significant pneumocephalus on imaging due to the abnormal communication with the external environment. Open skull fractures may be classified as either clean or contaminated. All patients with open skull fractures should receive tetanus toxoid, and those with contaminated fractures should also receive prophylactic antibiotics [17]. In most cases, these injuries require operative exploration for wound cleansing, debridement, and closure [13, 17].

Penetrating Trauma

Penetrating brain injury (PBI) refers primarily to gunshot wounds to the head, although all foreign bodies that invade the cranial vault may be included in this group. The management of PBI has undergone fundamental changes since initial descriptions in the early twentieth century, which were based primarily on military injuries. The current literature includes accounts of both civilian and military experiences. The former contains mostly reports of low-velocity injuries and self-inflicted wounds, while the later includes a higher percentage of high-velocity and shrapnel injuries [18]. Regardless of injury etiology, studies of both groups have derived similar conclusions, and current management recommendations are based on Class III evidence from both civilian and military case series [18].

The primary goals in the treatment of PBIs are infection prevention and ICP management. World War I trauma surgeons advocated extensive exploration and debridement of PBIs, with removal of all foreign bodies and bone fragments to decrease the risk of infections and seizures. Subsequent military and civilian studies have indicated that extensive exploration and debridement of PBIs is unnecessary and leads to higher rates of morbidity and mortality [18, 19]. Modern studies have demonstrated that the primary cause of PBI-related infections is a persistent CSF leak [18–20]. As such, during the initial management of a PBI, care should be taken to achieve good local debridement, followed by a watertight dural and scalp closure. Extensive brain debridement should be avoided to prevent injury to normal tissues. Additionally, prophylactic anticonvulsant medications should be given to prevent seizures [18]. Surgical evacuation of large intracranial hematomas may be necessary to manage elevated ICPs, and earlier surgery is associated with better outcomes [18, 21]. Additionally, intraparenchymal or intraventricular ICP monitors are often needed to follow the response to treatment.

Increasing age is associated with poorer outcomes in patients with PBIs [22]. However, given that PBIs are relatively uncommon occurrences, and even more uncommon in the geriatric population, analyses of this association have been somewhat limited [22]. Of the studies which have examined the role of age in outcome from PBIs, two have demonstrated that increasing age is associated with higher mortality [21, 23]. It is likely that many of the same mechanisms which contribute to poor outcomes in the elderly from general TBIs play a role in PBIs.

Nontraumatic Vascular Lesions

Neurovascular lesions constitute a broad spectrum of pathologies, yet common to each of these disease processes is precipitous neurologic decline from disruption of vital bloodflow to brain tissue. Population studies indicate that neurovascular diseases are more prevalent among the elderly [24]. Moreover, the geriatric population appears to fare worse from neurovascular diseases than their younger counterparts [3]. This finding has significantly affected the treatment strategies for the elderly.

Aneurysms

The accepted prevalence of intracranial aneurysms is 5% of the total population, although the prevalence in autopsy series has ranged from 0.2% to 7.9% [25–27]. It is postulated that most intracranial aneurysms develop as a result of combined hypertension, atherosclerosis, cigarette smoking, and congenital predisposition [27]. Most commonly, these lesions develop in the intracranial anterior circulation arterial blood vessels – carotid, anterior cerebral, middle cerebral, anterior communicating, and posterior communicating arteries – although posterior circulation aneurysms of the vertebrobasilar and posterior cerebral arteries account for approximately 15% of all lesions [25]. Ruptured intracranial aneurysms are one of the most devastating and challenging neurosurgical emergencies.

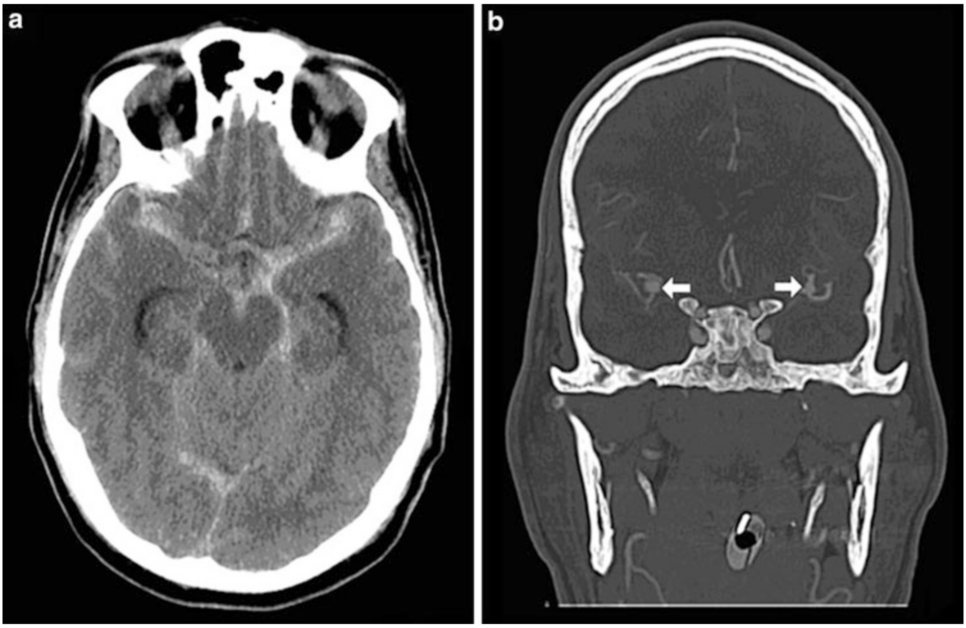

Fig. 4 (**a**) Noncontrast head CT demonstrates diffuse subarachnoid hemorrhage throughout the basal cisterns and bilateral Sylvian fissures, from a ruptured intracranial aneurysm and (**b**) contrast-enhanced cerebral CT angiogram reveals bilateral middle cerebral artery aneurysms (single arrows)

The majority of ruptured intracranial aneurysms cause sudden-onset of worst headache of life, focal neurologic deficits, and symptoms of increased ICPs (nausea, vomiting, headache, and decreased level of consciousness). Brain imaging shows acute subarachnoid hemorrhage (SAH), although intraventricular and intraparenchymal hemorrhages are not uncommon (Fig. 4a, b) [25]. The initial management of these patients focuses on the treatment of elevated ICPs and strict blood pressure control to prevent aneurysm rebleeding [28]. Additionally, the patient must be monitored closely for evidence of neurologic deterioration, which may be indicative of rebleeding, seizures, or hydrocephalus. Systolic blood pressures should be maintained <140 mmHg using short acting, titratable antihypertensive agents, such as labetalol, hydralazine, and nicardipine. However, hypotension must also be avoided as this may lower cerebral perfusion pressure and cause cerebral ischemia. Care should be taken to avoid antihypertensive agents which raise ICPs, such as nitroprusside. If there is clinical evidence for elevated ICPs, these should be treated as previously described (Fig. 3) [10, 11].

The incidence of aneurysmal SAH is 6–8 per 100,000 people in most western populations [25]. Approximately 10–15% of patients with aneurysmal SAH incur fatal brain damage and die before reaching medical care [25]. In the early survivors, the initial aneurysm bleeding stops; however, they have a 15–20% risk of rebleeding in the first 2 weeks post-SAH [28, 29]. The 30-day case fatality rate is approximately 50% [30, 31]. Following acute stabilization, decisions must be made regarding aneurysm repair to prevent future bleeding. Several studies regarding the timing of open surgical treatment have been published; however, no definitive conclusions have been drawn [32–34]. Following aneurysmal SAH, patients may develop cerebral vasospasm, during which blood vessels constrict and reduce blood flow to the brain, causing reversible neurologic deficits, stroke, or death. The prevalence of cerebral vasospasm is greatest between days 4 and 10 post-SAH, and patients who undergo aneurysm repair during this interval fare worse than those treated earlier or later [35]. The primary consideration in opting for early intervention within the first 96 h after aneurysm rupture is to repair the aneurysm and reduce the risk of rebleeding, an event that can cause stroke or death. Many patients are in poor medical and neurological condition after SAH, and may not be stable enough to tolerate aneurysm repair via open surgery or endovascular techniques. Later aneurysm treatment may allow for the improvement of medical and neurological issues, but exposes the patient to a greater risk of rebleeding from the unsecured aneurysm. Currently, the trend is toward early intervention for all patients with aneurysmal SAH, except for those in extremely poor neurological or medical condition.

Intracranial aneurysms may be treated with either open surgical or endovascular techniques [25]. Open surgical treatment involves craniotomy and placement of a small spring-loaded clip across the neck of the aneurysm, isolating the aneurysm from the parent blood vessel while maintaining vital blood flow to the brain. Endovascular treatment involves femoral artery catheterization and deposition of metal coils within the aneurysm, sealing it off from the parent blood vessel. In a randomized trail comparing endovascular treatment with open surgery for patients with aneurysms deemed treatable with either technique, there were 278 patients age 65 or older [36, 37]. Overall neither of the treatments produced better functional outcomes; however, subgroup analyses based on aneurysm location showed that open surgery was superior for middle cerebral artery (MCA) aneurysms and that endovascular treatment was better for internal carotid and posterior communicating artery aneurysms. The generalizability of these findings is limited, since many aneurysms are not equally treatable by open surgery or endovascular techniques. The durability of endovascular repairs has also been questioned [38, 39]. In current practice, the treatment plan is usually decided by a team of neurosurgeons and neurointerventionalists while considering patient condition, aneurysm location, and angioarchitecture. Despite treatment, only ~1/3 of those patients who survive their initial aneurysm rupture will regain a good functional status, while the remaining 2/3 will have significant deficits or die [25]. These outcomes are strongly associated with the patient's admission neurological exam [25, 40].

Historically, patients with aneurysmal SAH and advanced age (>70 years) have been deemed poor candidates for surgical or endovascular treatment [40–44], based on the worse neurological condition of older patients when compared with their younger counterparts [42]. Elderly patients were traditionally treated conservatively, with only medical management of their SAH symptoms. Not surprisingly, this led to very poor outcomes, with the vast majority (>75%) of elderly patients suffering severe morbidity and mortality [40, 43]. Evidence showing improved outcomes in elderly patients who receive surgical or endovascular treatment when compared with medical management [43] has spurred a recent trend toward offering geriatric patients with aneurysmal SAH definitive treatment for their aneurysm. However, it is clear that even with treatment, the geriatric population fares worse than their younger counterparts [42]. Using data from a multicenter randomized trial, it was found that with advancing age, patients have significantly worse admission neurological exams, thicker subarachnoid clots, and higher rates of intraventricular hemorrhage, hydrocephalus, and aneurysm rebleeding [42]. Additionally, older patients have higher incidences of preexisting medical comorbidities [42]. Interestingly, in this study, there were no age-related differences in time to presentation, timing of surgery, aneurysm size and location, or surgical complications. After controlling for the above factors, increasing age was still significantly associated with a poorer outcome [42]. This was thought to be related to the impaired ability of the aging brain to recover from acute stress, as well as the overall diminished cardiovascular reserve in older patients, which can lead to suboptimal cerebral perfusion [6, 42]. As endovascular technology evolves, it is likely that it will be used with increasing frequency in the elderly as a means to mitigate the risk of open surgery while still offering definitive therapy [41]. Regardless, it is clear that geriatric patients have better outcomes with definitive treatment than conservative treatment, although outcomes are worse than those in younger patients.

Vascular Malformations

CNS vascular malformations are congenital vascular lesions that fall into four categories: arteriovenous malformations (AVMs), capillary telangiectasias, venous angiomas, and cavernous malformations [25]. Of these, AVMs are most prone to hemorrhages requiring emergency neurosurgical care and will therefore be the focus of this discussion.

The prevalence of intracranial AVMs is not well known; hospital-based autopsy estimates range from 5 to 613 AVMs per 100,000 persons [45]. Anatomically, AVMs represent abnormal tangles of arteries and veins, with an absence of normal intervening capillary architecture, resulting in high-flow arterio-venous shunting [25, 45]. AVMs are congenital and occur throughout the CNS [45]. Although they may cause a variety of neurologic symptoms, the most common presentation is intracranial hemorrhage (ICH), which is a neurologic emergency (Fig. 5a–c) [25, 46].

The management of AVM-related ICHs begins with strict blood pressure control to prevent rebleeding. Subsequently, if there is evidence of increased ICPs, medical management should be initiated, as previously described (Fig. 3) [10, 11]. If significant mass effect and concern for herniation exists, surgical evacuation of AVM-related ICHs can be performed; however, the surgical approach is much different than that for typical ICHs and is beyond the scope of this discussion. If possible, it is preferable to stabilize the patient medically and treat the AVM in a nonacute setting. Treatment options include open surgical resection, radiosurgery, and endovascular embolization.

Most AVMs are diagnosed at an early age (~35 years), and patients who present with hemorrhage are even younger (~31 years) [45, 47]. Prospective data indicate that the patients at highest risk for future hemorrhages are those who have AVMs with deep locations, exclusively deep venous drainage, and a history of previous AVM-related ICH [48]. Additionally, the risk of future hemorrhages increases with age [48]. Given the rarity of this disease, there are no data on specific or different treatment strategies for the elderly population. However, it is likely elderly patients are more often treated with less invasive methods (i.e., radiosurgery and endovascular embolization) when possible, due to the perceived increased risks of open surgery with advanced age.

Stroke

Cerebrovascular accidents, or strokes, are a leading cause of morbidity and mortality, especially among the elderly [3]. Strokes can be either hemorrhagic or ischemic, both of which constitute

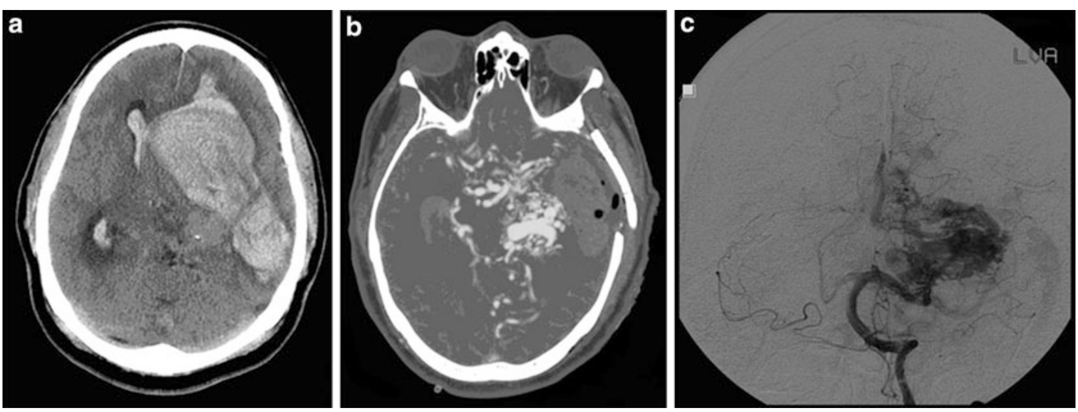

Fig. 5 (**a**) Noncontrast head CT demonstrates a large left fronto-temporo-parietal intracranial hemorrhage with associated intraventricular hemorrhage, mass effect, and midline shift, (**b**) contrast-enhanced cerebral CT angiogram reveals an underlying arterio-venous malformation, and (**c**) cerebral catheter angiogram confirms the presence of a large arterio-venous malformation

neurologic emergencies that may require surgical intervention.

Hemorrhagic strokes affect approximately 10–20 per 100,000 people each year [24, 49]. Although these events are less frequent than ischemic strokes, they have much higher rates of associated death and disability [3]. Specifically, the 1-year mortality rate following hemorrhagic stroke is approximately 62% [24]. The most common risk factor for hemorrhagic stroke is hypertension, which is the focus of this discussion [24]. Amyloid angiopathy is also a significant cause of hemorrhagic stroke and will be discussed in detail later in this chapter. Advancing age, male sex, and alcohol and tobacco use are known risk factors for hypertensive hemorrhagic stroke (HHS). Additionally, blacks have an incidence of HHS that is twice that of whites [24].

HHSs most commonly occur from the rupture of small intracranial perforator arteries in deep regions of the brain (e.g., basal ganglia and brainstem), although cortical and cerebellar hemorrhages occur as well (Fig. 6) [24, 25, 50]. The initial management of HHS patients focuses on strict blood pressure control and treatment of elevated ICPs (Fig. 3) [10, 11]. The INTERACT randomized controlled trial demonstrated that intensive blood pressure control reduces subsequent hematoma growth, although clinical outcome data are lacking [51]. The role of surgical evacuation in the treatment of HHS is controversial. A recent randomized controlled trial (STICH) evaluated the role of early surgical intervention in supratentorial ICHs and determined that there was no overall benefit from early surgery as compared to initial medical management [49]. Given the deep location of many of these hemorrhages and the need to traverse normal intervening brain to evacuate them, it is not surprising that there was no clear benefit with surgical intervention in this study. On the other hand, anecdotal evidence suggests that superficial supratentorial HHSs with significant mass effect may respond well to surgical decompression and therefore these patients should be evaluated on a case-by-case basis with the assistance of a neurosurgical team. Alternatively, HHSs in the cerebellum respond much more favorably to surgical evacuation. Cerebellar hemorrhages have a propensity for early hydrocephalus and brainstem compression [24]. Craniotomy and decompression is the definitive treatment for this process and studies have shown that those patients with large cerebellar hematomas (volume greater than 40 mL) have a clear benefit from surgical intervention [24, 52]. Of note, significant research has also been performed to ascertain the role of recombinant-activated factor VIIa (rFVIIa) in the treatment of acute ICHs, including HHSs. The final results of the phase 3 randomized controlled trial (FAST) demonstrated that although rFVIIa reduces the growth of the hematoma, it does not result in any significant improvements in survival or functional outcome, and therefore, the use of rFVIIa for acute ICHs has not become part of standard practice [53].

Fig. 6 Noncontrast head CT demonstrates an acute basal ganglia hemorrhage with mass effect and intraventricular extension

Ischemic strokes (IS) account for the vast majority of all strokes, with an incidence of 300–500 cases per 100,000 people each year [3]. In general, management of IS should be directed by a neurology team. On rare occasions, IS may require surgical intervention. The role of surgical intervention has been well examined in patients with a “malignant” MCA infarction, where swelling from the damaged brain can cause rapid neurological deterioration and 1-year mortality rates reach up to 80% [54–57]. Several randomized controlled trials (DESTINY, HAMLET, and DECIMAL) have been performed to evaluate the efficacy of early surgical decompression via hemicraniectomy and durotomy, to relieve the mass effect of the infracted and edematous brain [55–57]. The pooled analysis of these trials demonstrates a significant reduction in mortality; however, overall patient morbidity and functional outcomes remain unchanged despite surgical decompression [54]. It should be noted that these trials did not include patients greater than 60 years of age and therefore, surgical intervention in elderly patients should be considered on a case-by-case basis.

Amyloid Angiopathy

Cerebral amyloid angiopathy (CAA) is an important cause of nontraumatic ICH, comprising approximately 10% of all ICHs and 30% of all lobar ICHs [25, 58]. Moreover, this pathology has a predilection for the elderly population, making its review particularly germane to this discussion [25, 58]. CAA is characterized by the deposition of beta-amyloid, a fibrillar protein, in the media and adventitia of small- and medium-sized arteries [25, 58]. The exact prevalence of CAA is difficult to determine due to the lack of definitive histopathology in most cases; however, it is well known that the prevalence of CAA increases with age and it is rarely identified in those less than 55 years of age [58]. CAA has an equal predilection for both sexes. Approximately 1/3 of people greater than 60 years of age have evidence of CAA on autopsy, and in individuals over 90 years of age, the prevalence of CAA exceeds 60% [58]. Studies have also demonstrated that those individuals who possess the E2 and E4 alleles of the apolipoprotein E gene have a significantly increased risk of developing CAA [25, 58].

Although CAA can cause progressive dementia, transient ischemic attacks, seizures, and ischemic stroke, arguably the most concerning manifestation is ICH, caused by the rupture of amyloid-laden vasculature [25, 58]. These hemorrhages are most frequently lobar and can be multifocal [25, 58].

The management of ICHs due to CAA is not significantly different from the management of hypertensive ICHs. Most hemorrhages do not require surgical intervention; however, if significant mass effect and neurologic deficits exist, craniotomy for evacuation and decompression can be considered. Unlike cerebral aneurysms and AVMs, ICHs due to CAA do not require treatment of a discrete, underlying vascular abnormality. Although the vasculature is altered in patients with CAA, it does not require unique surgical maneuvers to control bleeding. In contrast with ICHs due to hypertension, CAA-associated ICHs are typically more superficial and therefore more amenable to surgical intervention [25, 58]. Although no specific pharmacotherapy exists for the treatment of CAA, there is ongoing research into the development of antiamyloid medications and vaccinations [58]. Additionally, as discussed above, the use of rFVIIa has not resulted in a significant clinical benefit in this patient population [53].

Adverse Drug Reactions

As the population ages, the use of antiplatelet and anticoagulant medications such as aspirin, clopidogrel, and warfarin, has increased dramatically. Protocols for managing patients with acute ischemic stroke using thrombolytic therapies, such as intravenous and intraarterial tissue plasminogen activator (tPA), have become more common [59]. Traditional guidelines recommend administration of tPA within 3 h of onset of stroke symptoms; however, many stroke centers now aim to administer tPA in an urgent fashion, within 60 min of onset of symptoms, for embolic stroke [59]. Given the potency of these medications, it is not surprising that some of their primary side effects include undesired bleeding, including ICHs [60, 61]. Patients who receive tPA and have early hypodensities on CT have significantly higher rates of ICH [62]. Patients who develop ICHs secondary to antiplatelet or anticoagulant therapies should have the offending medications discontinued immediately, followed by reversal of the platelet dysfunction and/or anticoagulation with the appropriate blood products and/or medications. The remainder of their management should follow that of other nontraumatic ICHs; strict blood pressure control should be employed and surgical decompression considered on a case-by-case basis for those patients with significant mass effect. In a study of surgical evacuation of ICH following administration of streptokinase for acute myocardial infarction, surgery was beneficial, although survival was dependent upon the time from the initiation of thrombolytic therapy to onset of stroke symptoms, initial Glasgow coma scale score, volume of ICH, and "baseline clinical characteristics" (defined as age, systolic blood pressure, Killip class, heart rate, infarct location, previous myocardial infarction, height, time to treatment, history of smoking, current smoking, diabetes, weight, history of coronary bypass surgery, type of thrombolytic agent, history of hypertension, and history of cerebrovascular disease) [63]. Importantly, all patients who are started on antiplatelet and anticoagulant medications should be counseled about the potential risk of ICH.

Sinus Thrombosis

Intracranial venous sinus thrombosis (VST) is a relatively rare condition that constitutes a neurologic emergency. There are several factors which predispose individuals to developing VSTs, including: a hypercoagulable state, dehydration, adjacent tumor or infection, pregnancy, vasculitis, systemic inflammatory disorders, and local trauma [25, 64]. Although most intracranial VSTs become evident through headache and other symptoms of increased ICPs, a significant portion of patients develop seizures, intracranial infarcts, ICHs, or focal motor deficits [25, 64]. VSTs cause venous outflow obstruction and subsequent parenchymal edema and infarction [25, 64]. The primary goal in the treatment of VSTs is the prevention of thrombus propagation while allowing for natural thrombolysis and recanalization of the affected vessel. This is achieved with anticoagulation and is typically managed by a neurology team [25, 64]. However, endovascular thrombolysis of the clot/affected vessel using pharmacologic and mechanical techniques is sometimes indicated, and in cases with large ICHs, surgical decompression and evacuation is occasionally performed [64]. As compared to intracranial arterial thromboses, VSTs have an overall better prognosis [64]. In the largest series to date of patients with VSTs, there was a 13% rate of death or dependence at 6 months after ictus [64]. Risk factors associated with poor outcome include advancing age, male sex, altered mental status on admission, deep cerebral venous system thrombosis, ICH, malignancy, and CNS infection [64].

Infection

Infections of the CNS are neurological emergencies, which must be treated in a timely fashion. Generally, CNS infections can be categorized by their location: meningeal, subdural, epidural, intraparenchymal, and intraventricular. Most CNS infections have bacterial, viral, or fungal etiologies; this discussion will focus on bacterial infections, as these most commonly require surgical intervention. Additionally, this discussion will be limited to intracranial CNS infections; a review of spinal CNS infections can be found in Chap. 87, "Benign and Malignant Tumors of the Brain".

Infections of the meninges, also known as meningitis, are the most common intracranial CNS infection [25]. Patients typically develop fever, headache, neck stiffness, photophobia, and malaise. Contrast-enhanced imaging studies often reveal diffuse meningeal enhancement, and CSF analysis demonstrates elevations in the nucleated white blood cell count. As meningitis is most often managed medically, without the need for surgical intervention, further discussion of its management is beyond the scope of this discussion.

Infections of the epidural space, also known as epidural abscesses (EA), comprise approximately 2% of intracranial CNS infections [65]. These infections present with fever, headache, neck stiffness, photophobia, periorbital swelling, scalp tenderness, ear pain, nausea, vomiting, and lethargy. Imaging studies reveal an extra-axial, biconvex lesion with peripheral enhancement. Imaging studies may also reveal evidence of underlying osteomyelitis, sinusitis, or mastoiditis. Cranial EAs typically occur via direct extension of an adjacent sinusitis, although they may also be the result of hematogeneous spread from infections located throughout the body. They most commonly occur in adolescent males, though all age groups may be affected [65]. Treatment of cranial EAs involves surgical evacuation, followed by prolonged antibiotic therapy. If the adjacent bone appears to be involved, it must also be debrided and/or removed [65]. The most commonly isolated organisms in cranial EAs are microaerophilic or hemolytic streptococci; however, staphylococci may also be involved in cases of postoperative or posttraumatic infections [65].

Subdural infections, also known as subdural empyemas (SE), occur in 12–25% of intracranial CNS infections [65]. These infections present similarly to cranial EAs; however, focal neurologic deficits are more common given the direct contact with the cortical surface [65, 66]. Imaging studies reveal extra-axial, crescent-shaped collections with peripheral enhancement. As with cranial EAs, there is often evidence of adjacent osteomyelitis, sinusitis, or mastoiditis. Intracranial SEs typically occur in the setting of sinusitis, via direct extension or hematogenous spread, but may also occur as a result of trauma or neurosurgical intervention [65, 66]. Treatment involves prompt surgical evacuation, followed by prolonged antibiotic therapy [65, 66]. The most commonly isolated organisms in intracranial SEs are aerobic and anaerobic streptococci species, as well as staphylococci species [65, 66].

Intraparenchymal intracranial CNS infections, also known as brain abscesses (BA), are occurring with increasing frequency as the prevalence of immunocompromised individuals rises [65]. These infections cause fevers, headache, meningismus, malaise, seizures, and focal neurologic deficits – and they most often have a rapid progression of symptoms. On contrasted imaging studies, BAs appear as intra-axial lesions with marked peripheral enhancement and restricted diffusion on MRI (Fig. 7a–c). They can occur in the setting of sinusitis and mastoiditis, but are also commonly the result of bacteremia in the setting of congenital heart defects, bacterial endocarditis, dental abscesses, pulmonary infections, and acute diverticulitis [65]. Treatment consists of abscess drainage, often with the use of intra-operative stereotactic navigation systems, followed by prolonged antibiotic therapy [65]. The most commonly isolated organisms include aerobic and anaerobic streptococci and bacteroides species, staphylococci species, and fungal organisms in the immunocompromised [65].

Intraventricular CNS infections are rare entities. They commonly cause signs and symptoms of obstructive hydrocephalus: headache, nausea, vomiting, lethargy, and coma [25, 65]. Most often, intraventricular infections are caused by parasites (i.e., neurocysticercosis) [25]. Imaging studies reveal an intraventricular mass with a variable enhancement pattern and evidence of obstructive hydrocephalus. Surgical management of these lesions is usually curative. Medical management using antihehninthics remains controversial and should be discussed with an infectious disease specialist [25]. Of note, bacterial ventriculitis may also develop in the setting of a prolonged intracranial bacterial infection. As with intraventricular parasitic infections, individuals with bacterial ventriculitis typically develop symptoms of hydrocephalus. Imaging studies reveal diffusely enhancing ventricular walls. Management includes CSF diversion for elevated ICPs and prolonged antibiotic therapy.

With the exception of meningitis, most CNS infections require neurosurgical intervention. Risks of prolonged, untreated CNS infections include VST, osteomyelitis, hydrocephalus, seizures, and catastrophic intraventricular BA rupture. Importantly, in the management and initial work- up of CNS infections, lumbar puncture is often considered. Although this can be performed safely in most patients with simple meningitis, for those patients with intracranial mass lesions,

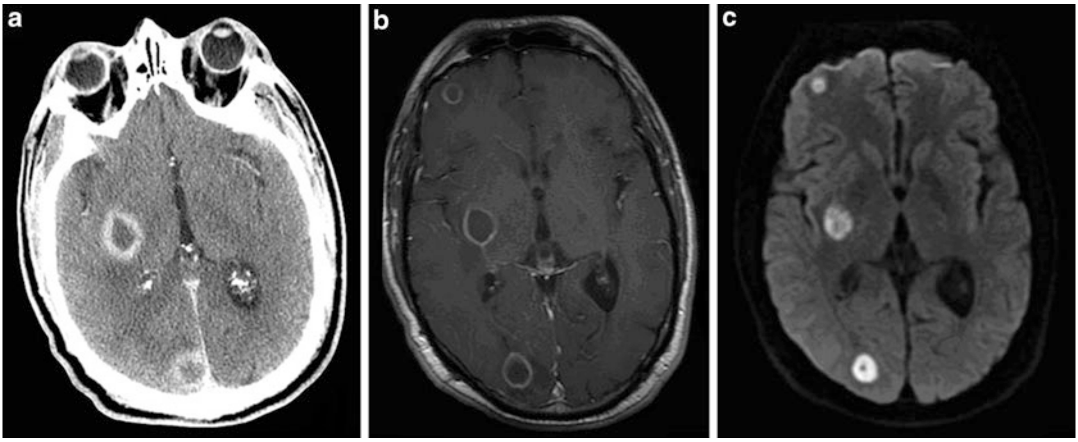

Fig. 7 (**a**) Contrast-enhanced head CT demonstrates multiple hypodense ring-enhancing lesions, (**b**) T1-weighted contrast-enhanced brain MRI demonstrates multiple hypodense ring-enhancing lesions with surrounding edema, and (**c**) diffusion-weighted brain MRI reveals restricted diffusion throughout the enhancing lesions, consistent with multiple brain abscesses

lumbar puncture should be deferred due to the risk of causing cerebral herniation [25]. Additionally, significant controversy exists regarding the use of steroids in the context of CNS infections [25]. This issue is best dealt with on a case-by-case basis, after careful review of the particular clinical scenario.

Most CNS infections tend to occur in the young; however, the elderly population deserves special consideration for several reasons. First, geriatric patients often have nonspecific signs and symptoms in the setting of infection [3, 67]. This increases the need for vigilant physical examination and CNS imaging studies in this population. Additionally, the elderly population has a relative immunosenescence, therefore, their clinical course and response to therapy may be worse than a younger counterpart with a similar illness [67]. Finally, the elderly tend to have more frequent and more severe adverse drug effects, especially from antibiotics, and this should be taken into account when choosing the appropriate drug regimen [67].

Peripheral Nerve Injury

Traumatic peripheral nerve injuries (PNIs) are relatively rare occurrences and are treated by a variety of specialists, including neurosurgeons, plastic surgeons, and orthopedic surgeons [68, 69]. Despite their rarity, PNIs can result in devastating functional loss and represent an important neurologic emergency. Clinically, they typically present in the setting of trauma with neurologic deficit confined to a single extremity [70]. PNIs often occur in tandem with bony fractures and peripheral vascular injuries [70]. Traumatic PNIs can be loosely categorized into three broad groups based on mechanism: stretch/avulsion injuries, lacerating injuries, and compressive injuries [71].

Stretch and avulsion injuries are the most common types of PNI [70, 71]. They are usually the result of motor vehicle accidents in which the torsional force of impact results in the movement of an extremity in one direction and the patient's trunk in another [70]. This results in a stretching of nerve roots, which, if severe enough, can cause complete nerve root avulsion from the spinal cord. Spinal imaging studies may reveal pseudomeningoceles indicative of dural nerve root sleeve disruption and adjacent soft tissue injury. Penetrating and lacerating PNIs typically occur as a result of gunshot and knife wounds. They are the second most common type of PNI and are often associated with injuries of adjacent vascular structures [70, 71]. These injuries are usually discovered on physical exam, as the external signs of trauma can be quite obvious. Compressive PNIs often occur as a result of local hematomas, soft tissue swelling, and bony hypertrophy. They cause indirect neural injury via external compression [71].

Operative interventions for PNIs vary widely based on the mechanism of injury, extent of neurologic deficit, presence of additional injuries, and surgeon preference [72, 73]. Surgical interventions may involve decompression, direct repair, removal of neuromas, and nerve grafting or transposition [72, 74]. Nearly all interventions employ the use of pre- and post-operative electromyography, and intraoperative nerve action potential and somatosensory evoked potential recordings [72]. Given the increased incidence of osteoporosis and bony fractures in the elderly, it is likely that they are at increased risk for PNIs in the setting of trauma. Therefore, since early identification of PNIs can maximize the potential for a functional recovery, it is imperative that elderly patients undergo complete neurologic examination as part of their trauma evaluation.

Tumors

Intracranial primary or metastatic tumors can cause medical emergencies via mass effect from tumor growth, edema in the surrounding brain, intratumoral hemorrhage, or seizures. Initial management should focus on the treatment of elevated ICP symptoms, blood pressure control, and seizure cessation. Further discussion of these lesions can be found in Chap. 87, "Benign and Malignant Tumors of the Brain".

Conclusions

Geriatric neurosurgical emergencies encompass a broad range of pathologies. Elderly patients have unique treatment challenges that must be accounted for by healthcare providers. The loss of cardiovascular reserve and the fundamental changes within the aging CNS appear to play a significant role in morbidity and mortality and should be carefully considered when treating and counseling geriatric patients with neurosurgical illnesses.

Case Study

History

An 82-year-old male, with multiple medical problems, seeks medical attention after the acute onset of worst headache of life. He also notes nausea, photophobia, and neck pain. He denies trauma, numbness, weakness, tingling, seizures, chest pain, and shortness of breath. A noncontrast head CT (Fig. 8a) is obtained and the patient is subsequently transferred to a tertiary care center. During transfer, the patient is noted to become progressively lethargic.

Past Medical History

1. Hypertension
2. Coronary artery disease
3. Chronic renal failure
4. Type II diabetes mellitus
5. Atrial fibrillation

Admission Neurologic Examination

Temp: 99.1 degrees Fahrenheit, HR: 70 beats per minute, BP: 160/70 mmHg, RR: 10 breaths per minute, O_2, Sat: 98% on 4 liters nasal cannula

Lethargic, nonverbal

Opens eyes to noxious stimuli

Pupils equally round and reactive to light, bilaterally

Moving all extremities symmetrically, not following commands

Localizes to noxious stimuli

Unable to assess sensory function

2+ deep tendon reflexes throughout

Toes downgoing, bilaterally

Relevant Admission Laboratory Values

Na: 138

Troponin-I: 0.40

WBC: 8.9 k

PLT: 228 k

INR: 2.8

(continued)

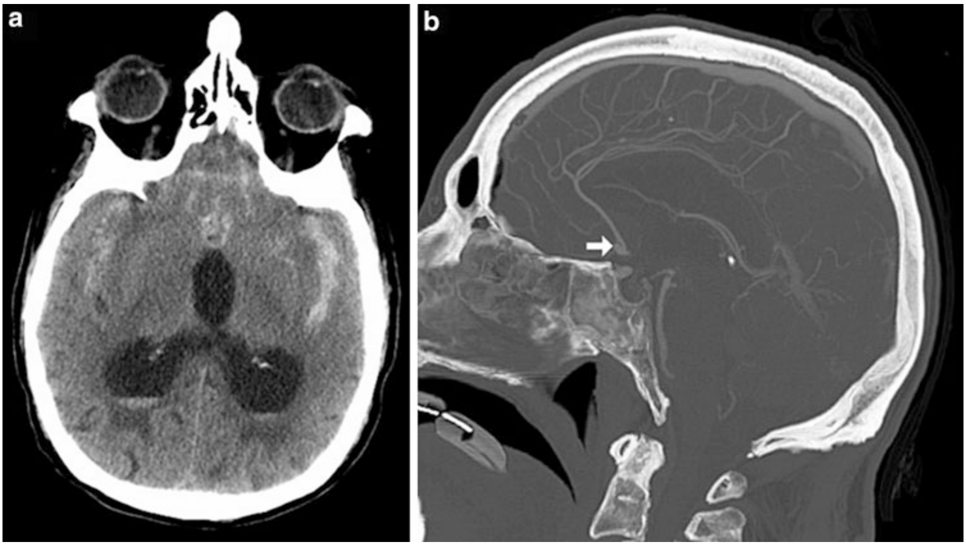

Fig. 8 (**a**) Noncontrast head CT demonstrates diffuse subarachnoid hemorrhage involving the bilateral Sylvian fissures as well as intraventricular hemorrhage and hydrocephalus and (**b**) contrast-enhanced cerebral CT angiogram reveals an anterior communicating artery aneurysm (single arrow)

Clinical Course

Upon arrival to the tertiary care center, the patient is intubated for airway protection. Subsequently, he is treated for hypertension and his systolic blood pressure is maintained below 140 mmHg. He is also given 1 g of IV phenytoin for seizure prophylaxis and 6 U of fresh frozen plasma to normalize coagulation. A cerebral CT angiogram is obtained (Fig. 8b), which demonstrates an anterior communicating artery aneurysm. The patient is transferred to the intensive care unit. His head of bed is elevated to 30°, he is sedated and hyperventilated, and a ventriculostomy catheter is placed to decompress hydrocephalus and manage elevated intracranial pressures. The patient's examination improves over the next 24 h; specifically, he begins to follow commands. An echocardiogram is obtained because of the abnormally elevated cardiac enzymes. The patient is found to have an ejection fraction of 35%. A family discussion is held regarding the risks and benefits of treatment and the decision is made to pursue endovascular therapy. The following day, the patient is taken to the angiography suite where he undergoes successful coil embolization of his intracranial aneurysm. Over the next 2 weeks, he is monitored carefully in the intensive care unit for evidence of vasospasm. His hydrocephalus resolves during this time and the ventriculostomy catheter is discontinued. His neurologic exam slowly improves, although his cognitive function appears somewhat diminished to his family members. He is extubated successfully. His ejection fraction also improves to 45% over this time period. He is later transferred to the floor and subsequently to a rehabilitation facility.

Discussion Questions

1. What are the most important initial measures that should be taken when caring for a patient with a ruptured intracranial aneurysm?

(continued)

2. What are the possible etiologies of the patient's change in mental status during transfer to the tertiary care facility?
3. What is the clinical and operative significance of the elevated cardiac enzymes on admission?
4. What is the current standard of care for treatment of ruptured intracranial aneurysms in the elderly?

Discussion Answers

1. The most important initial measures to be taken when caring for a patient with a ruptured intracranial aneurysm include: strict blood pressure control, administration of prophylactic anticonvulsant medications, and management of elevated intracranial pressures, if present.
2. Possible etiologies of the patient's change in mental status during transfer include: aneurysm rebleeding, hydrocephalus, and seizure.
3. Elevated cardiac enzymes in the setting of subarachnoid hemorrhage are associated with an increased risk of cardiogenic shock, pulmonary edema, and cerebral vasospasm. Elevated cardiac enzymes are also associated with higher rates of death and severe disability following aneurysmal subarachnoid hemorrhage. Therefore, when caring for patients with elevated cardiac enzymes, careful attention should be paid to optimizing their cardiopulmonary status. Moreover, in the setting of acutely elevated cardiac enzymes, it is often more judicious to treat patients with less invasive procedures (i.e., endovascular treatments) as opposed to maximally invasive procedures (i.e., open surgery), in order to minimize the degree of cardiac stress.
4. The current standard of care for treatment of ruptured intracranial aneurysms in the elderly is definitive surgical or endovascular repair in order to secure the aneurysm and prevent rebleeding. Aneurysm location, size, and configuration will often determine whether open surgery or endovascular techniques are the optimal approach to aneurysm repair. However, the patient's overall systemic health should be evaluated, and if significant comorbidities exist, strong consideration should be given to less invasive endovascular procedures, even if open surgery might provide a more definitive repair. Previously, elderly patients were treated with conservative, medical management without aneurysm repair. However, longterm studies have demonstrated that elderly patients have significantly better outcomes with definitive management and thus, this has become the standard of care. Nonetheless, elderly patients still fare worse than their younger counterparts, and as such, providers should have an open discourse with the patient and their family to discuss the potential need for longterm hospitalization, rehabilitation, and home care, so that treatment plans are made in accordance with the patient's wishes.

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33 Anatomic and Physiologic Changes in the Ears, Nose, and Throat

Ara A. Chalian and Karthik Rajasekaran

Contents

Abstract

Physiological and anatomical changes with age in the ears, nose, and throat have long been the subject of clinical interest; increasingly, they are the subject of basic and clinical investigations [1–6]. Nonetheless, the role of alterations in cells and tissues and distinctions among genetic, pathological, environmental, and interactive effects on cellular, tissue, and organ functions are still emerging [3, 7–12]. Currently, presbycusis, presbystasis,

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presbyosmia, presbylarynx, and presbyphonia are the terms used to denote the functionally and clinically apparent manifestations of aging changes in the ears, nose, and throat [1, 2, 13–15]. Presbyvertigo has also been proposed as a relevant term for matters of dizziness and falls in older adults though presbystasis is more commonly used [15, 16]. Notably, presbypharynx is, while being a parallel term to represent the manifestations of aging changes in the anatomy and physiology of the pharynx, not used in current literature. Instead, various uses of senescent swallowing and dysphagia predominate in the literature [17, 18].

Introduction

Research into conditions of the aging ears, nose, and throat offers a disparate and inconsistent body of evidence that connects aspects of the biology of aging, anatomy and histology, and functional changes. Related clinical literature has developed differentially, often relying on clinical observation and correlative science as well as treatment experience and case series reports. The magnitude of applicable science specific to the ears, nose, and throat varies by organ and senescent function. Similarly, the quality and quantity of translational science is inconsistent. Presbycusis is, for example, well studied with science that illuminates functional effects and clinical pearls [1, 19]. Conversely, presbyphonia and presbylarynx are only recently receiving significant attention in basic and clinical science [14]. Evenwith growing evidence ofmechanisms, processes, and effects, direct translation of this evidence to care of the older surgical patient remains limited. Application thus requires careful review and interpretation.

This chapter describes important known anatomical and physiological changes with aging in the ear, nose, and throat. Each organ is addressed separately with focus on relevant changes in organ anatomy and physiology, and the chapter highlights alterations in function that result in presbycusis, presbystasis, presbyosmia, presbylarynx and presbyphonia, and senescent oropharyngeal anatomy and physiology, respectively. The sections detailing functional conditions of aging conclude with a brief summary of clinical surgical considerations. The chapter concludes with a summary of highlights.

The Aging Ear

Auditory Anatomy and Physiology

Targeted review of the anatomy and physiology of the ear predicates understanding presbycusis and presbystasis and their impact on function and implications for surgical care [1, 2, 20]. This section reviews in sequence the anatomy of the ear and aspects of physiology relevant to understanding presbycusis and presbystasis.

External Ear

The external ear, from the pinna through ear canal to tympanic membrane, captures and intensifies sound in the 2–5 KHz range – frequencies in much of human speech – by acting as a resonator [13, 21] (see Fig. 1). These external structures change with advancing age. Importantly, cartilage collapses, resulting in somewhat deceptive appearance of larger ears for many elders. Further, the tympanic membrane and the ossicular chain in the middle ear stiffen, though the functional impact is minor. The conductive aspects of hearing promoted by these structures do not change appreciably with age [22] (see Fig. 2). Instead, concerns that are cosmetic and mildly distressing emerge, including larger pinna size, more apparent cerumen production, and growth of excessive hair in the pinna. Cerumen and hair growth often result in complaints of pruritus. While these matters may seem minor, they may influence acceptance and use of hearing aids as well as prove distressing to some older adults as they consider changes in appearance.

Middle Ear

Sound perception begins with vibration of the ossicular chain [23, 24] (see Figs. 2 and 3). The tympanic membrane and the ossicles (viz., malleus, incus, and stapes) are fairly resistant to aging

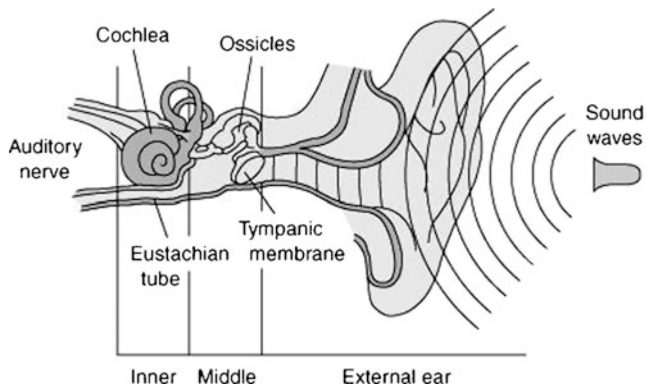


Fig. 1 The ear and its divisions. (Reprinted from Lalwani AK. Current diagnosis and treatment of otolaryngology, head and neck surgery, 2nd edn, with permission from McGraw Hill Companies)

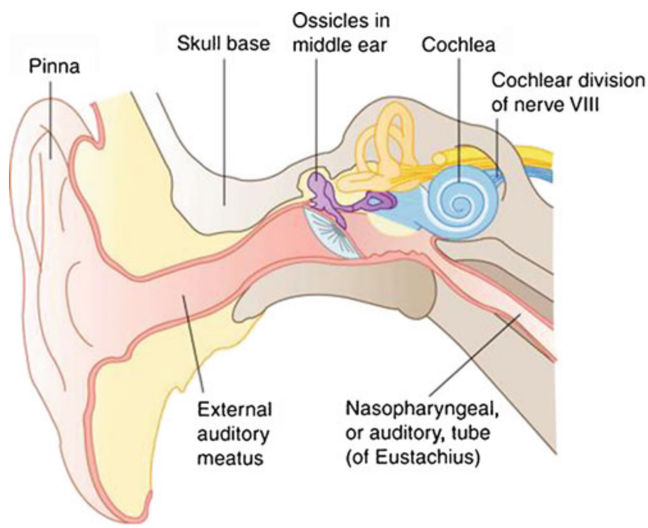


Fig. 2 The ear. (Reprinted from Waxman SG. Clinical neuroanatomy, 26th edn, with permission from McGraw Hill Companies)

changes unlike larger skeletal bones. Thus, age-related considerations and functional impact here are minor if they are present at all [23, 24].

Cochlea

The cochlea is the anterior portion of the inner ear, called the bony labyrinth, which also contains the vestibule and the semicircular canals [13] (see Fig. 4). This hollow bone contains the neuro-epithelium for auditory perception (cochlea) and balance perception (vestibule and semicircular canals) [16]. This section addresses aging changes in the cochlea and the resultant condition of presbycusis. Alterations in the vestibule and semicircular canals are discussed in a following section to explicate presbystasis as a separate condition of aging in the ear.

A membranous canal, known as the cochlear duct, wraps around a central bony core, the modiolus, for two and a half to two and three-quarters turns through which the auditory nerve fibers penetrate [22] (see Figs. 5 and 6). The cochlear duct is divided into three compartments: the scala tympani, scala media, and scala vestibule (see Fig. 7). The scala media has a fluid composition (endolymph) different from that of the other two compartments (perilymph) and contains the organ of Corti, which is the sensory organ of hearing [22] (see Fig. 5). The organ of Corti rests on the basilar membrane, which separates the scala media from the scala tympani (see Fig. 6). The organ of Corti contains afferent nerve endings (about 3,500 inner hair cells), afferent/efferent nerve endings (approximately 12,000

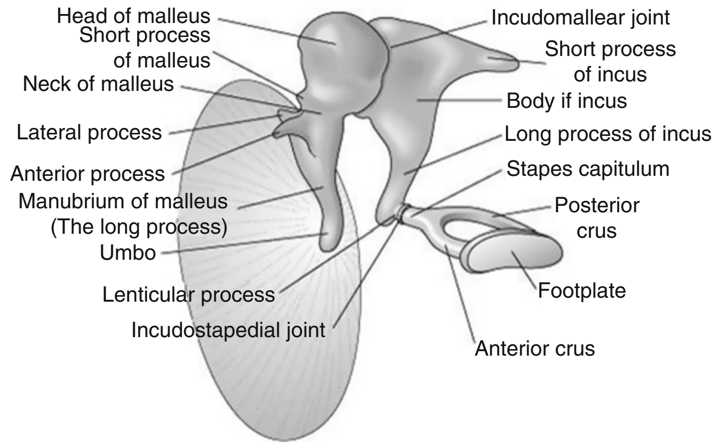


Fig. 3 The middle ear. (Reprinted from Lalwani AK. Current diagnosis and treatment of otolaryngology, head and neck surgery, 2nd edn, with permission from McGraw Hill Companies)

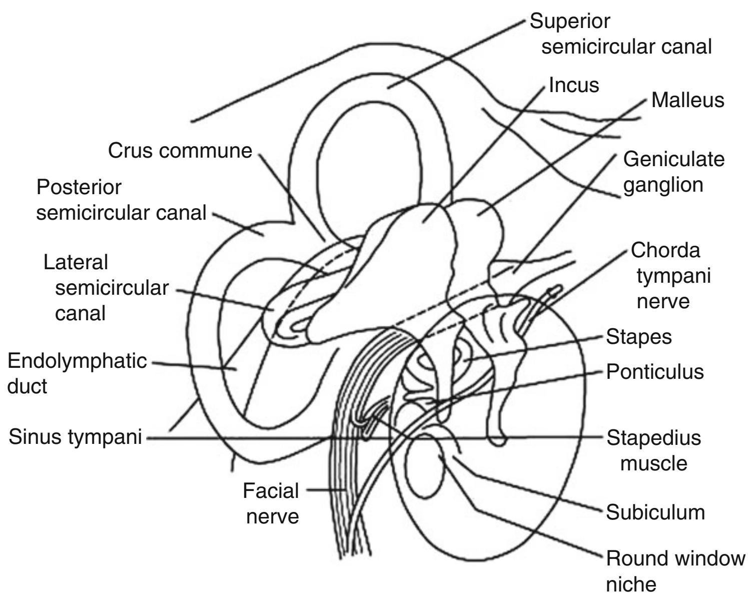


Fig. 4 The inner ear in relation to the middle ear structures. (Reprinted from Lalwani AK. Current diagnosis and treatment of otolaryngology, head and neck surgery, 2nd edn, with permission from McGraw Hill Companies)

outer hair cells), and a variety of other supporting cells. The hair cells communicate with the dendritic terminals of the bipolar cochlear neurons whose cell bodies are located within the modiolus. The hair cells serve as mechanoreceptors, converting the mechanical energy of basilar membrane displacement into an action potential to stimulate the ganglion cells. The cochlea's capacity to analyze periodicity, synchrony rate, phase, and spread of excitation of sound results in specific ganglion cell population stimulation and ultimately the perception of sound frequency patterns in the auditory cortex. The normal function of the cochlea occurs as sound energy in the form of vibrations reaches the oval window; the basilar membrane is set into motion and vibrates. The stereocilia of the hair cells on the basement membrane move and increase the permeability of the hair cell to potassium that depolarizes the hair cell (see Fig. 8).

A neurotransmitter is released by the hair cell onto the afferent ending of the cochlear nerve leading to a neurological signal [23]. Cochlear changes with advancing age result in presbycusis [13, 25]. Among the most significant alterations in anatomy and physiology include atrophy in the organ of Corti, vascular changes that affect the stria vascularis, and collapse of the cochlear duct [26,

Fig. 5 The semicircular canals. (Reprinted from Lalwani AK. Current diagnosis and treatment of otolaryngology, head and neck surgery, 2nd edn, with permission from McGraw Hill Companies)

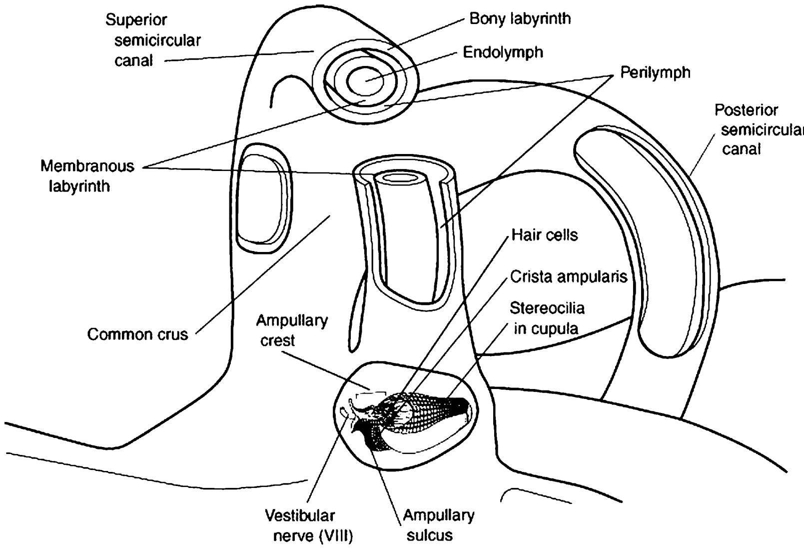


Fig. 6 The organ of corti. (Reprinted from Lalwani AK. Current diagnosis and treatment of otolaryngology, head and neck surgery, with permission from McGraw Hill Companies)

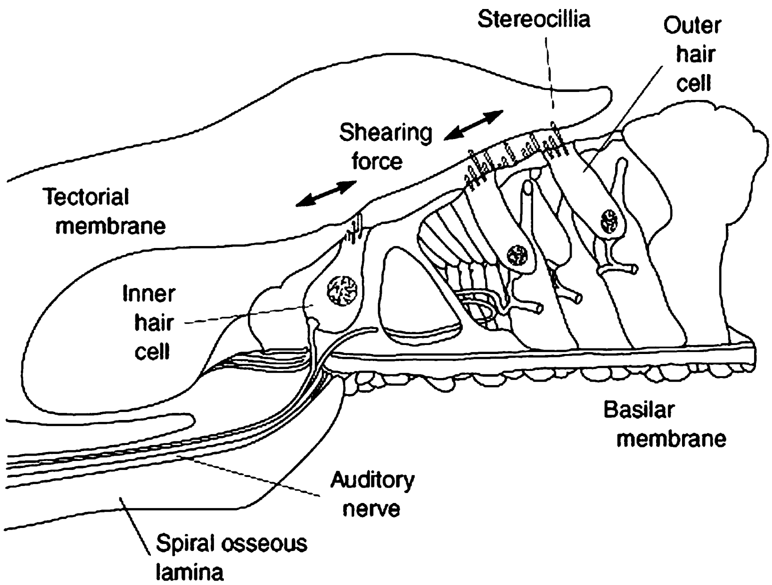
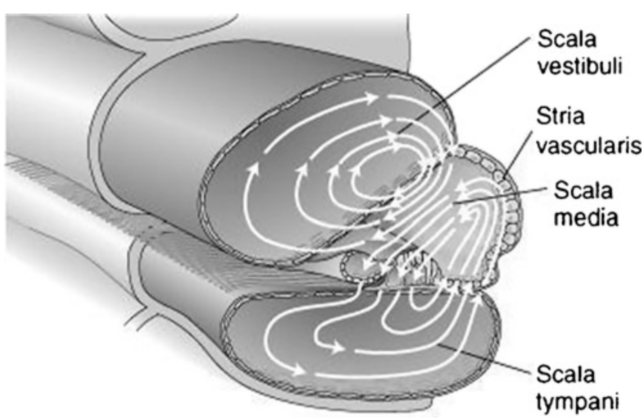


Fig. 7 The cochlea, cross-sectional view. (Reprinted from Lalwani AK. Current diagnosis and treatment of otolaryngology, head and neck surgery, with permission from McGraw Hill Companies)



27]. These changes lead to hair cell loss, neural fiber degeneration, and reduction in number of synapses at the base of the hair cells [25]. Accumulation of cochlear debris in the spiral bundles, abnormalities of the dendritic fibers and their sheaths in the osseous spiral lamina, and degenerative changes in the spiral ganglion cells and axons follow.

Auditory Nerve

The auditory nerve consists of about 30,000 afferent and 1,000 efferent bipolar neurons [22]. Ninety-five percent of the spiral ganglion is composed of myelinated (type 1) fibers that innervate only inner hair cells and nonmyelinated (type 2) fibers that innervate outer hair cells. The spiral ganglion is the densest at the mid and basal portions of the modiolus. The nerve fibers course in the nerve trunk in an orderly spatial arrangement (basal fibers located at the periphery and inferior portion of the nerve) through the temporal bone into the cerebellopontine angle into the pons to enter the cochlear nuclei [21].

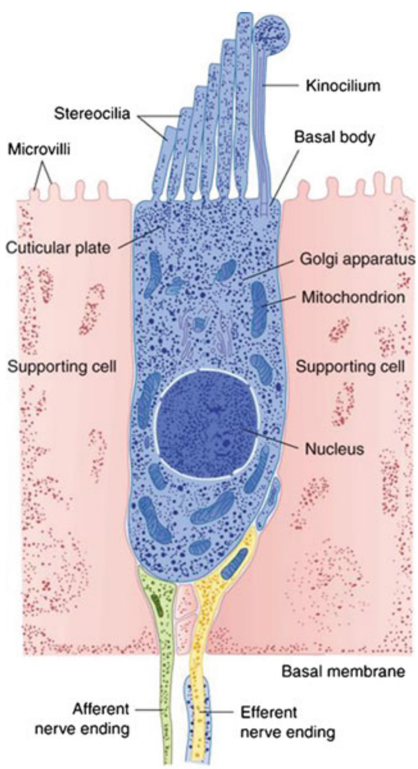


Fig. 8 A hair cell. (Reprinted from Waxman SG. Clinical neuroanatomy, 26th edn, with permission from McGraw Hill Companies)

Central Auditory Processing

Central auditory processing involves the cochlear nerve, the cochlear nuclei, and the auditory cerebral cortical regions [28]. Through this process, the neuronal signal is appreciated as sound and interpreted by the cognitive regions of the brain to recognize content [29]. The process is bilateral. Three morphologically distinct auditory nuclei are appreciated within the pons. Upon entering the pons, each fiber divides into an anterior branch, which terminates in the anterior part of the ventral cochlear nucleus, and a posterior branch, which again divides to terminate in the posterior part of the ventral cochlear nucleus and the dorsal cochlear nucleus.

Cells from these nuclei send axons in a complex pattern from the contralateral superior and accessory olive areas to the lateral lemniscus, the inferior colliculus, and through the medial geniculate body to the auditory cortex in the temporal lobe [21]. Aging results in decrease in neurons in the cochlear nuclei and auditory centers [29]. Neurons decrease in size as well, thus altering their physiology. Diseases and injuries that alter brain anatomy and physiology – such as cerebral atherosclerosis and stroke or mild cognitive impairment and dementia – may further alter central auditory processing [29]. Changes in central auditory processing account for complaints in hearing that exceed that anticipated by the audiogram [30]. These changes are manifest in limited auditory comprehension in noisy environments and in failure of simple amplification through hearing aids to remedy complaints of dysfunction [30]. The effects of normal brain aging on central auditory processing are a focus of dedicated current investigation [19, 31–33].

Auditory Function

Changes in auditory function resulting in hearing impairment associated with aging are termed presbycusis, a prevalent and disabling condition [13]. Presbycusis results largely from aging changes in the inner ear and is a form of sensorineural hearing loss. Subtypes, however, can be detected on audiogram though the differences are likely to be functionally undetectable. They are sensory, neural, strial, and cochlear conductive presbycuses [13]. Conductive hearing loss per se does not play a role in presbycusis. Early presbycusis affects high-frequency range, beyond the frequency characteristics of the human voice [13]. Thus, early alterations in function are often imperceptible to older adults. With advancing age, hearing loss encroaches on the speech frequencies. Impairment then becomes consequential in daily activities. Despite the expectation of presbycusis, hearing loss among older adults is often multifactorial. The contribution of central auditory processing changes, along with the influence of genetics and family history of congenital hearing loss, cumulative environmental damage through occupational or leisure exposure, and the use of ototoxic drugs should be considered [21, 34]. In fact, there are over 130 drugs and chemicals that have been reported to be potentially ototoxic [34]. Aminoglycosides and some chemotherapeutic agents are commonly identified as ototoxic medications. Additionally, other drug classes such as loop diuretics and beta-blockers may damage auditory function, albeit in a manner that may be reversible [21].

Clinical Implications

Presbycusis, while seemingly peripherally related to surgical care, has direct impact on all processes of care from decision-making through perioperative care to self-care after surgery. Gates and colleagues [35] suggest the simple screening question "Do you have a hearing problem now?" as the means to assess for impairment that results in disabling limitations in function. There are also screening tools that have been developed that provide a standardization of self-assessment for hearing screening of the elderly [36, 37]. In elective surgeries, opportunity to refer for otolaryngologic assessment and clinical audiometric testing should result in improved interdisciplinary care. Emergent surgical care, conversely, requires anticipation of problems that require compensation including decision-making, patient and family education, and postoperative care and the risk of reactions to the environment of care. Importantly, those older adults who wear hearing aids require additional support as their presbycusis may be inadequately corrected and central auditory processing problems unaddressed.

Vestibular Anatomy and Physiology

The vestibule is composed of three semicircular canals, the portions of the inner ear that are responsible for balance (see Fig. 5). The canals are posterior, superior, and horizontal, accounting for the dimensions in which the body is positioned in the physical environment of space [22]. The otolithic organs are the utricle and the saccule; they are structured to respond to linear acceleration of the body in space [21, 22]. The macula is the sensory portion of the utricle and the saccule. Type II hair cells are those that function in the vestibule (see Fig. 8). These cells are cylindrical with efferent and afferent synapses. Each type II hair cell contains approximately 50–100 stereocilia and 1 kinocilium. The kinocilium is located on one end of the hair cell, imparting anatomical polarization. Movement of the hair bundle toward the kinocilium causes an increase in the firing rate of the hair cell, while deflecting away causes a decrease in the firing rate. In the lateral semicircular canal, the kinocilium is located near the utricle [22, 26]. The opposite is true in the superior and posterior semicircular canals (see Fig. 5). Cilia extend from hair cells to touch the statoconial membrane. It has a gelatinous consistency with calcareous particles embedded in that gelatinous layer. The surrounding endolymph has a lower specific gravity, and hence when the body accelerates, the hair cells of the macula are triggered. The central section of the statoconial membrane is called the striola. In the utricle, the hair cells are toward the striola. In the saccule, they are oriented away from the striola, again accounting for spatial dimension and direction of movement.

The bipolar vestibular neurons create the inferior and superior vestibular neurons that merge when entering the brain stem [22, 26]. The vestibule is supplied by the labyrinthine artery.

The vestibular system senses linear and angular acceleration of the body. The semicircular canals sense angular acceleration, while the otoliths sense linear acceleration. This system also coordinates eye-head movement. The vestibulo-ocular reflex enables focus on an object (see Fig. 9). The vestibule-spinal reflex accounts for postural placement of the body. Together, these physiological functions contribute to a sense of the body in space [38]. Together with visual sensation and peripheral nervous system sensation in the feet, the vestibular reflexes create the complex sensory-perceptual system of proprioception [38]. Vestibular changes with age include alterations in the otoconia and in the hair cells [8, 15, 39, 40]. Atherosclerosis in the vascular supply and decline in the number of neurons in the vestibule further contribute to dysfunction and to altered vestibule-ocular and vestibule-spinal reflexes. Nevertheless, direct observation of the actual dysfunction is not possible given current assessment technology. Thus, clinical assessment relies on diagnosis by exclusion, employing means of inference including the caloric reflex test and other forms of electronystagmography [7, 15]. These tests attribute vestibular function through manipulation of the vestibulo-ocular and the vestibulo-spinal reflexes and may create acute discomfort for patients [41].

Vestibular Function

Presbystasis is the condition in which age-related changes in the vestibular system result in altered balance and symptoms of dizziness and vertigo [2, 15]. Vertigo and dizziness are common presenting complaints among older adults [7, 42, 43]. Nonetheless, presbystasis is a diagnosis of exclusion as vision and peripheral proprioception contribute to the sensation of dizziness and vertigo, which may culminate in a fall. Agrawal and colleagues [7] provide an elegant analysis of the prevalence of vestibular dysfunction among adults using a four-step test. The fourth step relies on standing on a foam-covered surface with an eye shield in place to isolate vestibular function. In their sample drawn of over 6,700 adults in the National Health and Nutrition Examination Survey, more than a third showed signs of vestibular dysfunction and could not remain standing without visual and proprioceptive cues. Prevalence was significantly associated with age. Almost half of those aged 60–69 and more than two-thirds of those aged 70–79, while the great majority of those over 80 years showed vestibular

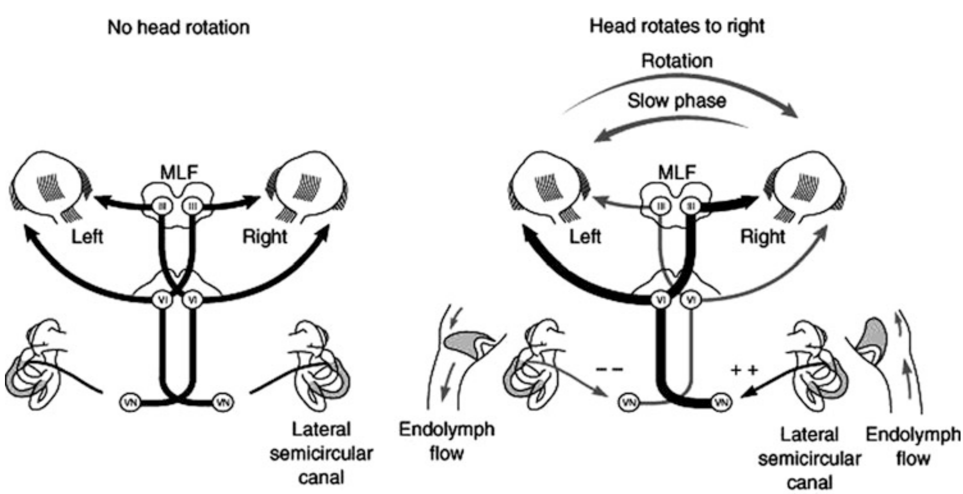


Fig. 9 The vestibulo–ocular reflex. (Reprinted from Lalwani AK. Current diagnosis and treatment of otolaryngology, head and neck surgery, with permission from McGraw Hill Companies)

dysfunction [7]. Thus, the functional state of dizziness is likely to be presbystasis among the very old. However, aligned conditions such as benign paroxysmal positional vertigo (BPPV) and Meniere's disease must not be excluded [42]. BPPV is, in particular, a competing diagnosis that may create great distress from the periodic nature of its presentation. The mechanism of BPPV is suspected to be otoconial debris – which results from aging changes – moving in the semicircular canals and creating hypersensitivity to bodily movement [42]. Despite aging-related elements, BPPV is considered a separate, narrower condition than the breadth denoted by presbystasis.

Clinical Implications

Presbystasis is extremely common and thus an important clinical consideration throughout the surgical trajectory [7, 16]. It creates risk of both minor and serious injuries as well as discomforting sensations throughout the process of surgical care. Individuals affected by presbystasis then carry a clinically important risk of falling at some time during surgical treatment. An estimated $10 to $20 billion dollar annual cost has been reported to be associated with fall-related injuries and a 20% mortality rate [16]. Individualized plans of care should include attention to preoperative condition and reconditioning efforts as possible, as well as modification of the hospital environment and promotion of visual and proprioceptive cues [44]. Aspects of surgical care, including pharmacotherapy such as anesthetics, analgesics, and diuretics, may interact with altered balance and promote the potential to fall. As with presbycusis, elective surgery affords the opportunity for screening through preoperative history and physical assessment to generate appropriate referrals to otolaryngology and physical therapy [44]. These referrals aim for specialized assessment and discrete diagnosis along with treatment designed to mitigate the effects of presbystasis and promote visual and proprioceptive cues with spectacles, well-fitting footwear, and similar interventions. In emergency surgery, efforts to modify the hospital environment, provide compensatory support and supervision, use visual and ambulation aids, and integrate rehabilitative interventions for overall physical condition as well as vestibular accommodation are paramount.

The Aging Nose

Anatomy and Physiology

The nasal vault lies behind the external structures of the nose, through which air passes during respiration [43]. Inspired air enters through the nares. The nasal septum divides the vault into two cavities, each of which contains three turbinates. Turbinates are rounded projections that extend the length of the cavity and labeled by position – superior, middle, and inferior. The space or valley below each turbinate is named for the turbinate above it. The paranasal sinuses drain into the meatuses. These sinuses, also labeled by location, are maxillary, frontal, ethmoid, and sphenoid. All the sinuses are lined with a specialized ciliated epithelium that secretes mucus and maintains mucosal flow with ciliary movement [45]. Together, the turbinates, mucus, and cilia insure humidification of inspired air and prevent gross and microscopic debris from entering the lower respiratory tract. The aging nose, like the external structures of the aging ear, is subject to cartilage collapse [43]. Few other changes in the nose are expressly linked to aging, though older adults may complain of more frequent rhinitis and sinusitis [46, 47]. Atrophic mucosa is a significant factor in these processes [45, 46]. The elderly may, as well, be more susceptible to nasal allergens and allergic rhinitis despite common clinical wisdom that allergen response declines with age [47].

The olfactory region is in the superior aspect of the nasal vault, a combination of olfactory and respiratory epithelial tissue [48, 49] (see Figs. 10 and 11). Olfactory epithelium is organized into pseudostratified columnar shape with four cell types constituting this epithelium (viz., ciliated olfactory receptor neurons, sustentacular cells, microvillar cells of unknown function, and basal

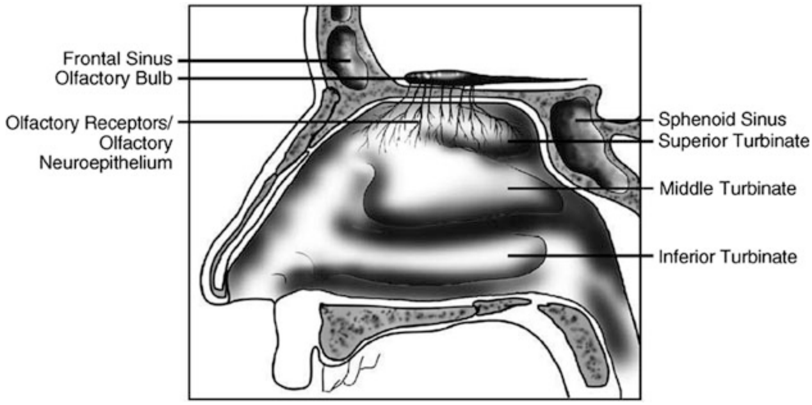


Fig. 10 Olfactory neuroepithelium – sagittal view. (Reprinted from Wrobel BB, Leopold DA (2004) Smell and taste disorders. Facial Plast Surg Clin North Am 12 (4):459–468, with permission from Elsevier)

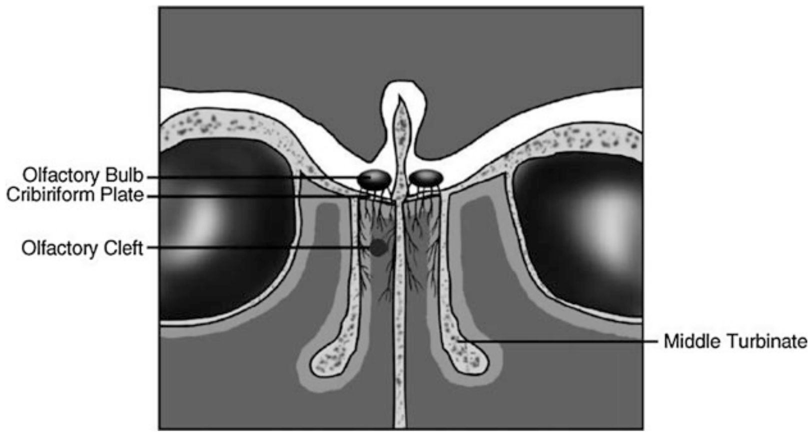


Fig. 11 Olfactory neuroepithelium – coronal view. (Reprinted from Wrobel BB, Leopold DA. Smell and taste disorders (2004) Facial Plast Surg Clin North Am 12(4):459–468, with permission from Elsevier)

cells). Basal cells are the stem cell population responsible for differentiating and replacing lost olfactory receptor neurons [48]. Olfactory respiratory neurons transmit the signal from the odorant molecules to the central nervous system. Early in life, there is a balance between neurogenesis and the lifespan of the olfactory respiratory neurons. With aging, this process of neurogenesis degenerates and is no longer one of equilibrium in terms of maintenance of the type of the epithelium [48, 49]. Additionally, there are increased patches of respiratory epithelium, representing a loss of the primary olfactory receptor neurons. The boundary between olfactory and respiratory epithelium becomes less well-defined with advancing age. Thus, age-related changes in olfactory function are multifactorial and encompass interactions among the composition of olfactory epithelium, decline in specialized cell populations, and decline in olfactory cilia [49].

Olfactory Function

Presbyosmia, loss of the sense of smell with aging, can significantly affect safety and quality of life [48]. Loss occurs on a continuum and is more correctly labeled by degree: anosmia (absent olfactory function), hyposmia (decline in olfactory function), and dysosmia (distorted olfactory function) [50]. Hyperosmia is less commonly noted in older adults. Well over half of adults aged 65–80 years of age have major olfactory disturbances [48, 49]. The potential implications of olfactory loss are significant and range from inability to perceive noxious odors that present threats to environmental or food safety to depression and anhedonia [48, 49]. Nonetheless, many patients are unaware of olfactory changes with age, will have no clinical response, and are unlikely to report changes to clinicians [48].

Clinical Implications

The aging nose presents few clinical ramifications for surgical treatment. Cartilage collapse in the very old may challenge the utility of nasal intubation (endotracheal and nasogastric) and should be considered by the anesthesiologist and the surgeon. Effects of presbyosmia in surgical treatment are also limited. Clearly, attention to patients' complaints with otolaryngologic and neurological referrals is critical. Abrupt or distinct anosmia, rather than being a manifestation of aging changes, may be a sign of Alzheimer's disease or Parkinson's disease, and, in mild cognitive impairment, olfactory decline may herald progression to dementia [51–53]. Additionally, given the intersections of the senses of smell and taste, presbyosmic patients may report disabling dysgeusia rather than altered olfaction specifically [54]. Further, these patients may be malnourished as a result of this complex of conditions with commensurate risk of immune dysfunction and impaired postoperative wound healing. Thus, preoperative assessment of nutritional status and referrals to an otolaryngologist and to a registered dietician optimize care of patients in elective surgery. The same consultations are warranted as soon as possible after emergent surgery if presbyosmia, dysgeusia, or consequent or multifactorial malnutrition is suspected. Patients who have respiratory allergies, including asthma and allergic rhinitis, may be candidates for allergen immunotherapy, which is the only disease-modifying treatment thus for patients with allergies [55].

The Aging Throat

Anatomy and Physiology

The anatomy of the larynx, the central anatomical component of the throat, comprises a cartilaginous skeleton, internal and external muscles, and a mucosal lining [56] (see Figs. 12 and 13). The larynx and pharynx sit below the nasopharynx and the oropharynx to form, with the oral cavity and the nasal structures, the upper aerodisgestive tract. The thyroid cartilage and the cricoid cartilage are visible anteriorly, with the cricoid forming the lower bound and the hyoid bone the upper bound of the organ (see Fig. 12). The two arytenoid cartilages are visible posterolaterally (see Fig. 12). These cartilaginous elements of the skeleton form two joints in the larynx. The cricoarytenoid joint is superior and the cricothyroid joint inferior at the posterior of the larynx. The vocal folds – or cords – attach to the arytenoids and form the glottis as their aperture (see Fig. 13). The cricothyroid muscles and the smaller vocalis muscle are responsible for tension and relaxation of the vocal folds. The posterior cricoarytenoid is the abductor of the vocal folds. The lateral cricoarytenoid, thyroarytenoid, and arytenoideus muscles adduct the vocal folds.

Branches of the inferior and superior thyroid arteries supply the larynx. Motor innervations arise from the cranial division of the accessory nerve, which travels with and therefore is clinically indistinguishable from the vagus nerve. The recurrent branch of the vagus nerve supplies almost all laryngeal muscles, save for the cricothyroid muscle that is innervated by the external laryngeal nerve. Sensory innervation is achieved through the internal laryngeal nerve above the vocal folds and the recurrent laryngeal nerve below them. These are branches of the vagus nerve that also supplies parasympathetic innervation.

The skeletal and muscular structures together create the form of the larynx [56]. In cross section, from the superior most aspect, the larynx begins with the aryepiglottic fold, the vestibule and the vestibular fold, the ventricle, the vocal fold, and the infraglottic cavity. The larynx is lined with mucosal tissue that maintains the humidity of inspired air during respiration and phonation, the central functions of the larynx. The mucosal lining also contributes to the pitch produced by the vibrating vocal folds when inspired air is drawn over them, creating phonation [56]. The epiglottis, which is critical to the laryngeal component in deglutition, sits behind the thyroid cartilage. The aryepiglotticus, thyroepiglotticus, and thyroarytenoid muscles close the larynx entirely, as during deglutition.

The pharynx begins behind the nasal structures, at the base of the skull, and extends to the cricoid

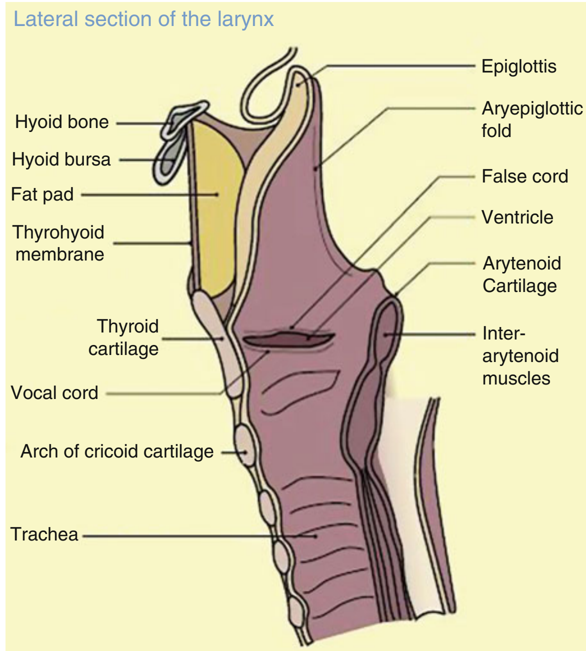


Fig. 12 The larynx – lateral view. (Reprinted from Marchant W (2005) Anatomy of the larynx, trachea and bronchi. Anaesth Intensive Care Med 6(8):253–255, with permission from Elsevier)

cartilage [57] (see Fig. 14). At this point, the pharynx becomes the cervical portion of the esophagus. Unlike the complex larynx, the pharynx is a muscular tube. The outer anatomy of the pharynx is composed of three circular, skeletal muscle constrictors – superior, middle, and inferior. The inner muscular layer of the pharynx is composed of the stylopharyngeus, palatopharyngeus, and salpingopharyngeus muscles. Together these muscles support the successive contraction necessary to move a food bolus to the esophagus. In addition, the inferior constrictor maintains tone to function as a sphincter to limit air entering the digestive tract. Like the larynx, most motor innervation is supplied by branches of the accessory nerve. The stylopharyngeus muscle is the sole exception as it is innervated for motor and sensory function by the glossopharyngeal nerve. The glossopharyngeal nerve is the sensory supply for the pharynx, while the parasympathetic supply arises from branches of the vagus nerve. The functions of the pharynx and larynx require neuromuscular coordination and feedback for functional respiration, phonation, and deglutition, including protection of the respiratory and digestive tracts [57, 58].

The oral cavity is delimited anteriorly by the oral labia [57] (see Fig. 15). The muscles that control the lips and thus the oral cavity aperture are levator labii superioris, depressor anguli oris, and risorius. The cavity is lined with mucosal epithelium that covers the buccal surfaces and the hard palate. The transition to the soft palate marks the transition to the pharynx. Several muscles form the palatal aponeurosis: tensor veli palatini, levator veli palatini, palatopharyngeus, uvulus, and palatoglossus. German and Palmer [57] note that these muscles coordinate to open or close the airway during swallowing and to contribute to deglutition itself by altering the shape of the pharynx. The oral tongue and 32 permanent teeth are contained within the oral cavity. The muscles of the oral tongue include the extrinsic muscles – genioglossus, hyoglossus, styloglossus, and palatoglossus – which are innervated by hypoglossal and the vagus or accessory nerves and the intrinsic fibers, vertical, transverse, and longitudinal, which are innervated by the hypoglossal nerve. The neuromuscular coordination of tongue movement is complex and involves the lingual nerve, branches of the glossopharyngeal nerve, and the internal laryngeal nerve in a minor capacity. The tongue, as well as aspects of adjacent structures like the soft palate, is covered with specialized papillae [58]. These papillae are found in fungiform, folliate, and vallate morphologies with a precise

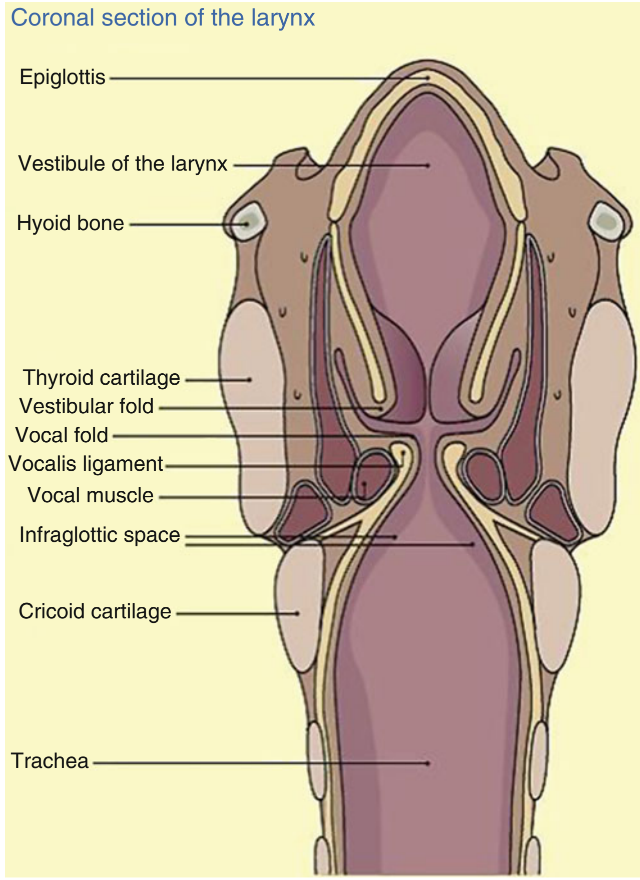


Fig. 13 The larynx – coronal view. (Reprinted from Marchant W (2005) Anatomy of the larynx, trachea and bronchi. Anaesth Intensive Care Med 6(8):253–255, with permission from Elsevier)

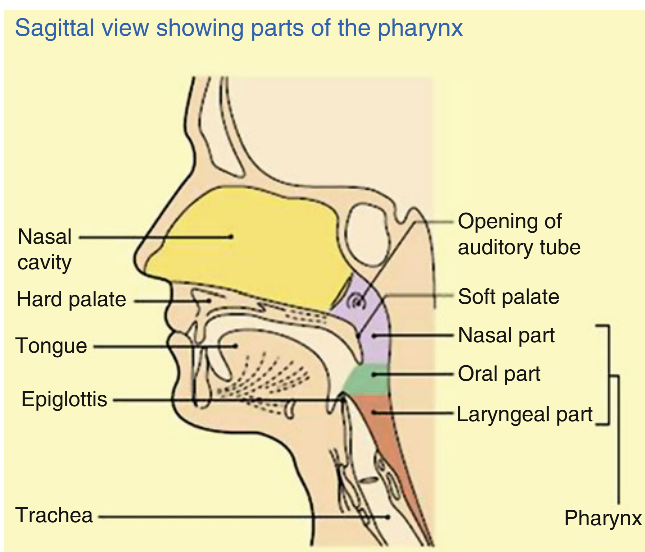


Fig. 14 The oropharynx and pharynx – sagittal view. (Reprinted from Craven J (2005) Anatomy of the naso- and oropharynx. Anaesth Intensive Care Med 6(7):217–218, with permission from Elsevier)

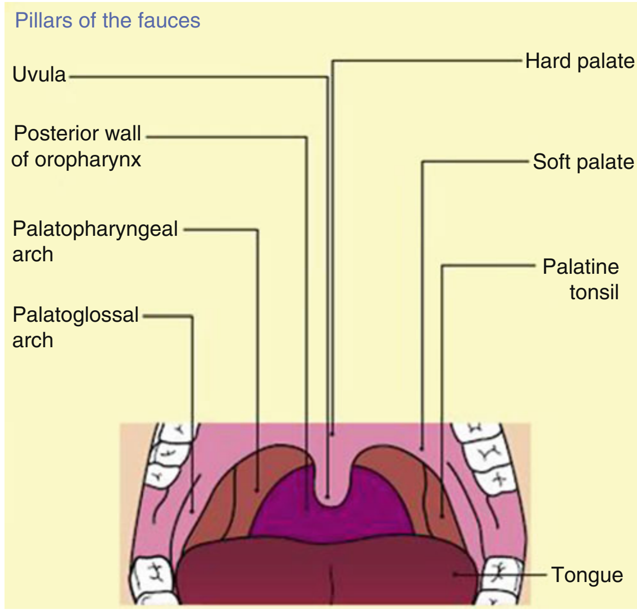


Fig. 15 The oral cavity. (Reprinted from Craven J (2005) Anatomy of the naso- and oropharynx. Anaesth Intensive Care Med 6(7):217–218, with permission from Elsevier)

distribution over the tongue, creating the peripheral taste anatomy [54, 58]. Taste sensation is innervated by a branch of the facial nerve, the glossopharyngeal nerve, and the internal laryngeal nerve [54]. The muscles of the oral floor form the inferior boundary of the oral cavity and include digastric, mylohyoid, and geniohyoid muscles. Dentition arises from the maxilla and mandible, elements of the oral skeleton. The functions of the oral cavity are supported by adjacent structures without which mastication and transit of food are not possible. These components of oral function are the salivary glands, including the parotid, submandibular, sublingual, and minor salivary glands; the nasal structures, most importantly the olfactory epithelium with its direct contribution to chemosensation; and the muscles of mastication, temporalis, masseter, medial pterygoid, and lateral pterygoid [57].

Aging Changes in Voice Function and Swallowing

Voice Function

Presbylarynx is the result of muscular atrophy and decreased elasticity in the muscular and skeletal components of the larynx [59, 60]. In fact, these changes begin early and are noted on examination as early as the fifth decade of life though functional effects are not noted by the individual potentially until the eighth or ninth decade of life if ever. Bowing of the vocal fold is the primary physical change. This bowing alters the aperture of the folds and results in incomplete closure causing a glottic gap. Other ligamentous and cartilaginous structures of the larynx are further altered with advancing age. The cartilaginous skeleton and joints ossify, and the joints may become arthritic and dysfunctional. Microscopically, fibroblasts in the lamina propria may senesce and lose elasticity [14]. The lamina propria becomes denser as it produces less hyaluronic acid and more collagen. These changes alter the vibratory characteristics of the vocal folds [14, 56]. The voice changes experienced by older adults with advancing age are termed presbyphonia [14, 56]. The alterations in the laryngeal skeleton and function of the vocal folds include poor projection, shorter duration of phonation, and vocal roughness or instability. Importantly, presbyphonia is a diagnosis of exclusion [56]. It is the least common cause of vocal disturbance among older adults, accounting for approximately ten percent of voice complaints. More commonly, in order of incidence, older adults will suffer benign polyps, malignant vocal cord lesions, vocal cord paralysis, or functional dysphonia [56]. Neurodegenerative conditions, such as Parkinson's disease, also frequently create significant vocal dysfunction [56].

Oropharyngeal Function

Oropharyngeal function in later life is less a matter of tissue senescence [57, 61, 62]. Dysfunction emerges more often as a product of "wear and tear" in the oral cavity with contributions of effects of local and systemic disease as well as treatment side effects of discrete functions like salivation [61]. Oropharyngeal dysphagia is a highly prevalent clinical condition, which affects up to 13% of patients aged 65 years and older and 51% of institutionalized older persons [63]. Taste sensation likely remains relatively robust in the absence of pathology or significant presbyosmia [54]. Notably, as many as a third of all older adults experience xerostomia [62]. Nevertheless, age-related changes in salivary production are often indistinguishable from primary salivary disease and the contributions of medications with antihistamininergic and anticholingeric effects. Percival [64] notes that microbial flora of the oral cavity remains stable with age, all other factors being equal. However, conditions like xerostomia; changes in dentition and oral hygiene; significant local disease, such as oral premalignant and malignant lesions; and systemic diseases including acute problems such as pneumonia and chronic concerns like Alzheimer's disease and Parkinson's disease may alter oral flora, salivary production, and functional capacity to perform hygiene [61–63]. As a result, oropharyngeal dysfunction among older adults is most often a complex and progressive cycle of direct and indirect functional changes [65]. Loss of muscle mass and function, a reduction of tissue elasticity, changes to the cervical spine, reduction of saliva production, impaired dental status, reduced oral and pharyngeal sensitivity, reduced olfactory and gustatory function, and decreased compensatory capacity of the aging brain increase the susceptibility to dysphagia [63]. Importantly, specific age-related alteration in taste is rarely noted, though Fukanaga and colleagues suggest that loss of taste perception may play a role in dysgeusia [66]. Dysgeusia is more likely the result of presbyosmia or the effects of disease or its treatment that impairs olfaction, tastes, or both or effects of contributory functions like salivation [62, 67]. Hall [67] notes that age-associated neuromuscular deconditioning or disease may result in oropharyngeal dyskinesia. There are resultant and often severe risks of dysphagia and aspiration, especially in stroke or with progressive neurodegenerative disease.

Clinical Implications

Presbylarynx and presbyphonia have circumscribed effects on surgical treatment. For patients who are distressed by presbyphonia, anxiety about being misunderstood or subjected to discrimination because of the "old" quality of their voices is likely real and thus a warranted concern. Attention to communication, discrete consideration of the basis for clinical decisions, and appropriate referrals to an otolaryngologist are important elements in addressing presbyphonia. Concerns about endotracheal intubation for surgery, given skeletal changes in the larynx, are probably theoretical and lack substantive evidence. However, rigidity in the cartilage and joints may offer some risk in the most affected elders, though the more clinical prominent issues of cervical spinal arthritis and kyphosis outweigh potential laryngeal rigidity. Skillful intubation with tacit recognition of laryngeal fragility is thus important in the absence of detailed and clinically relevant data. Nevertheless, post intubation voice changes may affect communication and comfort. Research into tissue engineering and electrical reanimation are some potential future options for treatment of presbyphonia [68]. Currently, a multidisciplinary approach offers the most complete improvement in the vocal quality of life.

Oropharyngeal dysfunction among older adults poses significant risk and threats to surgical treatment. Such dysfunction may arise from aging changes in the anatomy and physiology of swallowing, dental pathology, comorbid disease that affects neuromuscular coordination, or any combination of these factors [17, 65]. Side effects of intubation and anesthesia as well as postoperative healing, as it creates fatigue and saps functional reserves, may breach thresholds of functional compensation for dysphagia and aspiration. Elective surgery affords opportunity for integration of an interdisciplinary plan of care to assess and address for age-related and, more importantly, age-associated disease effects. Essential referrals include routine dental prophylaxis and treatment of dental caries and gingival disease that might affect tooth retention during the postoperative period as well as xerostomia; otolaryngologic and speech language assessment and intervention for diseases and dysfunction in deglutition, respiration, and phonation; and nutrition consultation and intervention to optimize visceral protein and overall nutritional status. These referrals are likely to be more successful given continuous collaboration with a particular patient's primary care provider. Comprehensive patient and family education further supports an effective plan of care and can be delivered by nurses on an outpatient basis before surgery, integrated into the inpatient care plan, and then reinforced during inpatient or outpatient rehabilitative postoperative follow-up. There is compelling evidence that active rehabilitation focusing on increasing strength of the head and neck improves swallowing in the elderly [17]. New treatments aiming at recovering the swallowing function are under research with promising results [69].

Conclusion

Aspects of aging anatomy and physiology in the ears, nose, and throat have manifold and often consequential implications for surgical treatment of older adults. In the ears, presbycusis affects communication that results in possible problems in decision-making and participation in perioperative care. Presbystasis is even more consequential as it is extremely common and results in significant risk of falls with the additive effects of anesthetics, analgesics, and diuretics, along with other postoperative interventions. Conversely, presbyosmia has little direct influence on surgical treatment save for implications of malnutrition when combined with the likelihood of dysgeusia and problems with food safety as a general concern. Presbyphonia conveys intermediate risk in surgical care for older adults. Older adults with noticeably affected voices may have difficulty in communication, both because of auditability and because of ageist discrimination for an "old" and infirm sounding voice. Finally, older adults with age-associated dental problems and acute or chronic disease that impinge upon neuromuscular coordination of the oropharynx are at significant risk for dysphagia and aspiration. The results of age-related functional changes in the anatomy and physiology of the ears, nose, and throat require thoughtfully integrated interdisciplinary surgical care. Knowledge of changes and functional implications is a rapidly evolving area of basic science and clinical investigation. Thus, surgeons can lead integration of a comprehensive plan of care that includes targeted referrals to specialists, preoperative preparation when possible, postoperative rehabilitation, and clear, consistent communication with patients, their family members, primary care providers, and other members of the interdisciplinary team. Modifications to the hospital environment that account for common sensory-perceptual and vocal changes, as well as ongoing patient and family education, further support successful care of the older surgical patient.

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Cardiac Surgery in the Older Adult

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Abstract

The aim of this chapter is to identify and discuss characteristics of older adults that affect pre-, peri-, and postoperative decisions in the setting of cardiac surgery. There are unique physiologic considerations in this population that affect many aspect of cardiac surgery, from medication dosing to postoperative healing. To guide care providers who are treating elderly cardiac surgery patients, this chapter identifies epidemiological characteristics of the older adult, particular considerations for preoperative assessment, postoperative complications in this population, and a brief discussion of less invasive alternatives to cardiac surgery in older adults. In order to do this effectively, this chapter is structured such that characteristics of the older adult are discussed early on in the chapter as a bridge to explain strategies to maximize preoperative reserve and mortality and morbidity predictors and quality of life considerations in the older adult. The chapter goes on to consider both general and older adult-specific postoperative complications. The final sections briefly examine nonsurgical options for coronary artery and valvular disease and cardiac mechanical support. The chapter concludes with a pragmatic deliberation on longer-term postoperative follow-up strategies.

List of Abbreviations

ACE Inhibitors	Angiotensin-Converting Enzyme Inhibitor
ARB	Angiotensin II Receptor Blockers
AVR	Aortic Valve Replacement
CABG	Coronary Artery Bypass Graft
CAM-ICU	Confusion assessment method for the intensive care unit
CCB	Calcium Channel Blockers
CT	Computerized tomography
DSWI	Deep sternal wound infections
ECG	Electrocardiogram
FTR	Failure to rescue
GFR	Glomerular filtration rate
HRQoL	Health-related quality of life
ICDSC	Intensive care delirium screening checklist
ITA	Internal thoracic artery
LVAD	Left ventricular assist device
MI	Myocardial infarction
MRI	Magnetic resonance imaging
NYHA	New York Heart Association
OPCAB	Off-pump coronary artery bypass
PCI	Percutaneous coronary intervention
RAAS	Renin angiotensin aldosterone system
STS	Society of Thoracic Surgery
TAVI/TAVR	transcatheter aortic valvular implantation/replacement
TBW	Total body water
TSH	Thyroid-stimulating hormone

Introduction

Ancient physicians believed the living heart to be sacred and untouchable. They also observed that wounds and injuries to the heart were nearly always fatal. Over the past century, the art and science of cardiac surgery has expanded exponentially in both the number of cases performed and the complexity and sophistication of the surgical procedures. It is estimated that over 800,000 cardiac surgery procedures are performed worldwide each year. In the past 20 years, however, the increasing burden of heart disease in an aging population has resulted in cardiac surgery being offered to older and more *frail* patients, often with multiple comorbidities [1, 2]. In the current era of cardiac surgery, more than half of procedures are being performed in patients aged 75 years and older [3]. By extension, it is expected that increasing numbers of frail, older adult individuals will be offered cardiac surgery [4, 5]. Indeed, previous studies have demonstrated that despite an overall improvement in functional outcomes in recent years, older patients typically experience higher rates of postoperative morbidity, mortality and prolonged hospital length of stay, loss of independence, as well as associated increased costs to the health-care system [6–9]. As a result, it is becoming critically important for the health-care system to improve awareness and develop strategies to improve clinical outcomes in the contemporary, high-risk patient population undergoing cardiac procedures.

The purpose of this chapter is to provide an overview of the key issues pertaining to the preoperative evaluation, perioperative care, and postoperative recovery of the older adult (and by extension their caregivers) undergoing cardiac surgery in the current era.

Characteristics of the Older Adult Undergoing Cardiac Surgery

It is anticipated that from 2010 to 2040, the number of individuals in the United States (US) age 65 or older will double as a result of the aging baby boomer demographic and increased life expectancy [10]. Although death due to heart disease has been declining steadily since 1980, heart disease continues to be the leading cause of mortality in North America and remains the most common cause of mortality in the older adult population [11, 12].

Since coronary artery disease disproportionately affects older adults, the anticipated increase in the population of older adults is expected to result in considerable disease burden [10]. An estimated 25% of adults over age 75 experience symptoms of cardiovascular disease [13]. In patients with severe symptomatic cardiac disease, surgical procedures are often prescribed as a first-line treatment strategy. Although older adults account for half of the cardiac surgeries performed in North America, up to 78% of the major complications and deaths occur in this cohort [14]. Even so, randomized and observational studies continue to demonstrate that older adult patients can receive significant benefits from cardiac surgery, including improvement symptoms, quality of life, prevention of cardiovascular events, and survival [15–19].

The older adult with coronary artery disease poses many unique challenges for health-care providers, including physiologic changes of aging, which can lead to preoperative, perioperative, and postoperative challenges. Compared to younger cohorts, the older adult may have more numerous and advanced comorbid disease, in addition to heart disease, that compounds a reduction in physiologic reserve. Additionally, older patients may have more advanced coronary artery disease at the time of referral for cardiac surgery compared to younger cohorts [14, 20].

Over time, despite the increasing risk or negative periprocedural outcomes in older adults, there have been consistent reductions in mortality among octogenarians undergoing cardiac surgery [20]. Risk factors associated with increased mortality after CABG in younger patient groups are different than risk factors in the older adult population. Such risk factors include renal dysfunction and sternal wound infection. Furthermore, assessment of cognitive function and baseline functional status is crucial to establish prior to cardiac surgery. These measures may help assess for the risk of postoperative delirium and may help guide the clinician to optimize postoperative functional trajectory. It is estimated that one-third of individuals over the age of 80 have some degree of cognitive dysfunction. These patients are at higher risk of experiencing postoperative delirium and possible further deterioration in cognition. In addition to a comprehensive cognitive assessment prior to surgical intervention, assessing for baseline functional status and physiologic reserve is also becoming increasingly important. The concept of frailty has been well described in geriatric medicine literature as a "biological state characterized by increased vulnerability and decreased resistance to physiological stresses" [13, 21–23]. While frailty is not synonymous with age, it is more prevalent among older adults, more common in women and in patients undergoing cardiac procedures [22]. It is recognized that frailty in older adults with cardiovascular disease is an important condition that may help identify operative risk in these patients [13]. Preoperative assessment, including cognitive and frailty assessment, will be discussed in more detail in this chapter.

Pharmacokinetics and Pharmacodynamics in the Older Adult Undergoing Cardiac Surgery

This section focuses on common physiologic changes of the aging individual that may impact cardiac medication administration decisions.

Age-Related Changes in Pharmacokinetics and Pharmacodynamics

Pharmacokinetics refers to the relationship between a drug dose and the concentrations of that drug in the systemic circulation due to patient factors, or simply, pharmacokinetics is how an individual's body affects a drug [22]. There are several physiologic changes that occur with normal aging that can result in suboptimal drug handing of administered medications. These include changes in absorption, distribution, metabolism, and elimination [24]. Medication absorption can be decreased in older adults due to decreased gastrointestinal motility, decreased gastrointestinal blood flow, and increased in gastric pH. Generally, this does not result in clinically relevant changes for most medications. Medication distribution refers to the relative proportion of medication in patient tissue [25]. Distribution may decrease in older adults for a variety of reasons. As individuals age, there is generally a decrease in lean body mass, an increase in adipose tissue, and decrease in total body water (TBW). These changes result in a decreased volume of distribution for hydrophilic drugs and increased volume of distribution for lipid soluble drugs [25]. Hepatic metabolism of many medications decreases with age for a variety of reasons. Decreased hepatic blood flow can result in less effective first-pass metabolism. Decreased hepatic mass can impair phase I metabolism of some medications [26]. Therefore, medications that rely on hepatic metabolism will have decreased drug clearance, and for a given medication dose, there may be a higher concentration of the circulating drug. In the older adult patient, this may increase the risk of drug toxicity depending on the medication administered.

One of the most significant pharmacokinetic changes associated with aging is decreased renal elimination of medications. This results from decreased renal blood flow and decreased glomerular filtration rate (GFR) that occur with age. In older adults, medication doses may need to be reduced for drugs with a large reliance on renal elimination.

Pharmacodynamics refers to the relationship between concentrations of a drug in the systemic system and the body's pharmacologic response. More simply, pharmacodynamics refers to how a medication acts on an individual's body. Pharmacodynamics may be affected by drug-receptor interactions and homeostatic regulation. For example, in older adults the sensitivity of the cardiovascular system to beta adrenergic agonist and antagonists is decreased, and the incidence of orthostatic episodes due to drugs that lower blood pressure increases [27]. With increasing age, the central nervous system becomes more susceptible to drugs that affect brain function, including opioids, antipsychotics, and benzodiazepines [27].

Cardiac Medications and Aging

Due to the effects of pharmacokinetics and pharmacodynamics associated with aging, there are some important considerations when using cardiac medications in this population. We will briefly discuss some of these considerations as they apply to the following commonly used drugs in cardiac surgery patients: beta blockers, angiotensin converting enzyme inhibitors and angiotensin receptor blockers, neprilysin inhibitors, calcium channel blockers, and digoxin.

Beta Blockers. Increased age is associated with decreased baroreceptor reflex response, drops in blood pressure, downregulated Beta (β)-adrenoceptors, and increase in orthostasis [28, 29]. Overall there is a decreased response to β-adrenoceptor agonists and decreased antihypertensive effect of β-adrenoceptor blockers, the latter of which may be related to decreased renal levels in older adults. There have been several theories to explain the decreased effects of β-blockers in older adults, including variations in β-receptor conformation and receptor down-regulation due to increased serum noradrenaline [28, 29]. Regardless of the mechanism, aging is associated with decreased response to β-blockers, making these agents less effective than others at decreased blood pressure in older adults [29].

Angiotensin-Converting Enzyme Inhibitors (ACE Inhibitors) and Angiotensin II Receptor Blockers (ARB). The relationship between aging and vascular responsiveness to angiotensin II is unclear, but data indicate that there is no difference in vascular resistance responsiveness to angiotensin II with aging [29, 30]. In general, with age the circulating renin-angiotensin-aldosterone system (RAAS) becomes less active, renin activity is decreased, and aldosterone concentrations are decreased. These effects may become amplified with RAAS stimulation due to salt restriction, volume depletion, or upright posture. Increases in renin and aldosterone secretion with these stimuli are expressed as a percentage in baseline values, so the increases are similar in young and older normotensive individuals, suggesting that the RAAS is able to maintain its ability to respond to stress with age [31]. There does not appear to be a significant change in drug effect between younger and older adults, and it is not recommended to adjust initial dosing of ACE inhibitor or ARB in the older adult population. There was an age-related difference with the reporting of adverse drug reactions of ACE inhibitors; younger adults tended to report headaches while older adults displayed light-headedness and orthostasis.

Neprilysin Inhibitors. Neprilysin inhibitor sacubitril/valsartan (trade name Entresto) was approved for use by the US Food and Drug Administration in 2015 for patients with chronic heart failure with reduced ejection fraction. It provides simultaneous neprilysin and angiotensin II receptor blockage, causing increased effect of natriuretic peptides, and resulting in diuretic, vasodilation, decreased sympathetic tone, and suppression of the RAAS [32]. Available data suggest that there are no clinically relevant pharmacokinetic differences observed in older adults (age greater than 65) or very old adults (age greater than 75) compared with the overall population [32, 33]. Dose adjustment based on age is not necessary [32].

Calcium Channel Blockers (CCB). Dihydropyridine calcium channel blockers selectively block L-type calcium channels in cardiac and vascular smooth muscle to decrease arterial pressure and systemic vascular resistance. Studies suggest that in treatment-naïve older adults, dihydropyridines initially have a greater effect on blood pressure, but after prolonged exposure, the sensitivity of older adult patients approximates that of younger patients [29]. The mechanisms for this are unclear but may include decreased hepatic clearance, age-related decrease in baroreceptor response, and potentially higher baseline blood pressure in older cohorts. Initial doses of dihydropyridines may have to be adjusted to account for increased sensitivity in treatment naïve older adult patients, but this sensitivity may be transient [29]. Examples of dihydropyridine CCBs include amlodipine, nifedipine, and felodipine. Nondihydropyridine calcium channel blockers bind to L-type calcium channels in cardiac and vascular channels at a different site than dihydropyridines. Compared to dihydropyridines, nondihydropyridines have a greater suppressive action on AV node conduction, a greater negative inotropic effect, and decreased vasodilation. Examples of non-dihydropyridine CCBs include verapamil and diltiazem, which both have increased volume of distribution in the older adult [28]. Older people tend to have a greater drop in blood pressure and heart rate with verapamil, which is suspected to be due to decreased drug clearance with age [29].

Digoxin. In the older adult, the effect of digoxin is altered due to decreased volume of distribution caused by increased adipose tissue and decrease in TBW. Clearance may also be decreased due to decreased GFR, resulting in accumulation of the drug. As a result, the loading dose of digoxin should be decreased by approximately 20% in this population [27]. Drug monitoring is recommended, particularly in patients with impaired renal function. Generally, the therapeutic range for serum digoxin concentration is 0.5–2 ng/mL. Toxic effects may occur with a digoxin level greater than 3 ng/mL but are usually not experienced when the concentration is 1.4 ng/mL or less. However, in patients over the age of 70, clinical evidence of digoxin toxicity may occur even when digoxin level is within the therapeutic range. Animal studies with digoxin have shown that with increasing age there is increased sensitivity to the cardiotoxic effects of digoxin, likely related to a reduction in the sarcolemmal content of the enzyme Na,K-adenosine triphosphatase, which reduces digitalis-induced pump inhibition required before the onset of toxicity [27, 30].

Amiodarone. Amiodarone is often used in the postoperative setting due to atrial fibrillation or ventricular tachycardia after cardiac surgery. It is a class III antiarrhythmic agent that prolongs the cardiac action potential duration and repolarization time and may have a protective antioxidant effect on cardiac myocytes against oxidative stress [34]. It affects heart rate and rhythm by increasing the refractory period of SA and AV nodes, as well as the ventricles, bundle of His, and Purkinje fibers. Like digoxin, the effect of amiodarone is affected by decreased volume of distribution in older patients, and doses of amiodarone may need to be adjusted because of this. Amiodarone is highly bound to plasma proteins. The drug is poorly absorbed from the gastrointestinal tract, has slow elimination, and is very lipophilic. Due to its large volume of distribution, amiodarone requires a loading dose [34]. Additionally, it is a potent inhibitor of cytochrome P-450, which results in drug-drug interactions that potentiate the effects of lidocaine, digoxin, procainamide, quinidine, warfarin, lithium, and phenytoin. Although older adult patients may be more likely to develop arrhythmias postoperatively that may be treated with amiodarone, the lipophilic distribution and long half-life of amiodarone (25–100 days) may also put older adults at higher risk of developing drug-related toxicity.

Amiodarone has significant cardiovascular and non-cardiovascular side effects that can lead to end organ toxicity. Cardiovascular side effects due to its antiarrhythmic properties include bradycardia, atrioventricular block, QT interval prolongation, and hypotension [34]. Non-cardiovascular side effects include pulmonary fibrosis, hypothyroidism, hyperthyroidism, corneal micro depositions, peripheral neuropathy, ataxia, fatigue, skin discoloration, photosensitivity, abnormal liver enzymes, and hepatitis [34]. Amiodarone exposure at low maintenance doses for periods of 12 months or longer is associated with higher odds of developing thyroid, skin, neurologic, optical, and bradycardic adverse events [35]. Older adults with structural heart abnormalities may be more predisposed to bradycardic effects of amiodarone, and hypothyroidism may be more common than in younger adults using amiodarone [35, 36]. Due to the long elimination half-life of amiodarone (25–100 days), drug interactions or side effects caused because of amiodarone may exist long after the cessation of the drug. Due to the potential for toxicity amiodarone, this agent has been listed in the 2012 American Geriatrics Society Beers Criteria list of medications that require careful consideration due to the risk of potential inappropriate use [37]. This and the potential impact to multiple organs systems, a thorough medication history looking for amiodarone use in the older adult patient is crucial in individuals who present with new systemic symptoms. Surveillance with chest x-ray and electrocardiogram (ECG) is recommended annually, and thyroid-stimulating hormone (TSH) and hepatocellular liver enzymes should be checked every 6 months.

Preoperative Assessment of the Older Adult Undergoing Cardiac Surgery

Frailty in the Cardiac Surgery Patient

Frailty is a syndrome characterized by decreased physiologic reserve and is defined by an increased vulnerability to stressors, including cardiac surgery (Fig. 1) [22, 38].

The term is often used to describe a vulnerable subset of individuals that are at an elevated risk for poor health outcomes, including falls, admission to long-term care facilities, and mortality [38]. Currently, a universally accepted definition of frailty does not exist (Fig. 2). One common assessment of frailty was validated by Fried and colleagues using data from 5317 community-dwelling men and women enrolled in the Cardiovascular Health Study [22]. Demographically, participants were 65 years of age and older, and frailty was defined by the presence of three or more of the following characteristics: (1) unintentional weight loss (i.e., 10 pounds in past year); (2) exhaustion (i.e., self-reported); (3) weakness (i.e., grip strength in lowest 20% for gender and body mass index); (4) slow walking speed (i.e., slowest 20% on time to walk 15 ft); and (5) low physical activity (i.e., lowest quintile of kilocalories expended per week). Although this is a widely accepted definition of frailty, many other standard assessments and models exist, including the *Canadian Study of Health and Aging* accumulation of deficits model, the *Clinical Frailty Scale*, and singular measures such as gait speed or grip strength [39–41].

Due to an aging demographic and advances in surgical procedures, older and increasingly frail patients are being referred for cardiac surgery. In fact, the proportion of patients aged 75 years and older undergoing surgical procedures has increased from 16% in 1990 to over 25% in recent estimates made in 2012 [42]. While the prevalence of frailty in the general population of older adults ranges from 14% to 24% (i.e., depending on the definition of frailty used) [43], the prevalence of frailty in patients with cardiovascular disease, or in those requiring cardiac surgery, is estimated to be as high as 54% [44, 45]. Chronological age has been demonstrated to be associated with poor outcomes after surgery [46–48]; however, emerging evidence has also demonstrated that frailty, as a marker of physiologic reserve, may be an equally important prognostic indicator of surgical success (Table 1) [5–7, 9, 42, 44, 49]. One of the first studies to demonstrate an association between frailty and adverse postoperative outcomes was conducted by Lee and colleagues, which evaluated frailty in 3826 patients

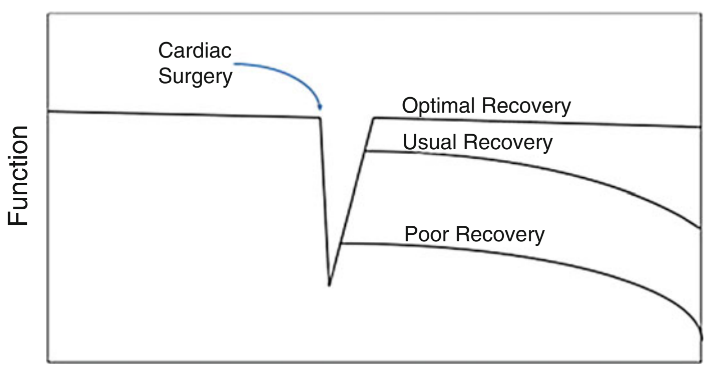

Fig. 1 Response to stressors. Following major stressor events such as cardiac surgery, a complete functional recovery (a return to the prior level of functioning) is anticipated. However, there is suboptimal recovery and patients attend a new "baseline" functional status. The patients with pre-existing vulnerability (i.e., frail) experience a disproportionate decline in their functional capacity and a poor recovery following cardiac surgery. (Reprinted from Experimental Gerontology, 87, Neupane, I., Arora, R.C., Rudolph, J.L., Cardiac surgery as a stressor and the response of the vulnerable older adult, 168–174, Copyright (2017), with permission from Elsevier)

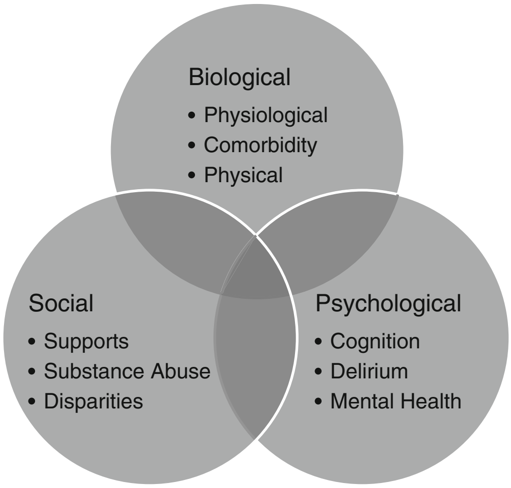

Fig. 2 Biopsychosocial Model for Frailty. (Reprinted from Experimental Gerontology, 87, Neupane, I., Arora, R.C., Rudolph, J.L., Cardiac surgery as a stressor and the response of the vulnerable older adult, 168–174, Copyright (2017), with permission from Elsevier)

requiring cardiac surgery [7]. This retrospective study reported that frail patients had a 1.5-fold increased risk of all-cause mortality, and frailty status (i.e., defined as an impairment in activities of daily living, ambulation, or documented history of dementia) was an independent predictor of in-hospital mortality (OR: 1.8, 95% CI: 1.1–3.0) and institutional discharge postoperatively (OR: 6.3, 95% CI: 4.2–9.4). The results of this retrospective analysis are supported by a recent systematic review conducted by Sepehri and colleagues, which suggests that frailty status, defined using multiple criteria, has a strong positive relationship with the risk of cardiac and cerebrovascular events following cardiac surgery (OR: 4.89, 95% CI: 1.64–14.60) [5]. The results of this systematic review are quite robust in that multiple definitions of frailty were assessed, including the multidimensional geriatric assessment, Fried phenotype criteria, and the comprehensive assessment of frailty [6, 9, 42, 50]. Another scoping review conducted by Beggs et al. reported similar associations between frailty and adverse perioperative outcomes in a variety of surgical populations, including cardiac, vascular, abdominal, and orthopedic procedures [49]. In addition to composite definitions of frailty, Afilalo and colleagues demonstrated the singular measure of gait speed to be an independent predictor of major morbidity and mortality (OR: 3.05, 95% CI: 1.23–7.54) and discharge to a health-care facility (OR: 3.19, 95% CI: 1.40–8.41) following coronary artery bypass graft or valve replacement surgery in patients over the age of 70 [3]. As part of this analysis, older patients were classified as having impaired gait speed if they required longer than 6 s to walk a distance of 5 m. This study is highly pragmatic in nature in that the simple gait speed assessment can be feasibly implemented in a clinical setting to support clinical decision-making during the preoperative period. The results of this initial prospective study have since been extended using the multicenter Society of Thoracic Surgeons Adult Cardiac Surgery Database in 15,171 patients over the age of 60 [20]. Compared to patients with a walking speed greater than 1.0 m/s, operative mortality is increased for those walking less than 0.83 m/s (OR: 3.16, 95% CI: 2.31–4.33). Even following adjustment, gait speed remained an independent predictor of operative mortality (OR: 1.11 per 0.1 m/s decrease in gait speed). Collectively, emerging evidence suggests that the frailty syndrome may be an important indicator of successful recovery following cardiac surgery. Strategies to optimize frailty status during the preoperative period may lead to improvements in postoperative outcomes.

Having a systematic approach to assessing and managing frailty is being examined in noncardiac surgery populations. Hall et al. published a large study in 2017 of a frailty screening initiative which included a screen of all patients undergoing elective major noncardiac surgery in a single center [51], in this case with the Risk Analysis Index tool [52]. The Risk Analysis tool combines many elements seen in other frailty tools and includes medical comorbidities, functional abilities, and cognition. Those identified as frail had their cases reviewed with interventions ranging from increasing awareness of the patient's frailty to changes in planned surgical and operative care approach to involvement of palliative care to clarify care goals. Researchers prospectively applied this approach over 54 months to 3878 patients

Table 1 Association of frailty with adverse postoperative outcomes

Source	N	Gender M/F	Age mean (SD) years	Frailty measure	Description	Primary study outcomes	Main outcome odds ratio/confidence interval
Sundermann et al. [9]	450	227/223	79 ± 4	CAF	6-domain questionnaire	30-day mortality, 1-year mortality	30-day mortality OR: 1.10 (95% CI: 1.06–1.20) 1-year mortality OR: 1.10 (95% CI 1.06–1.10) 1-year mortality independent of age OR: 1.091 (95% CI: 1.049–1.135) When added to known EuroSCORE, 1-year mortality OR: 1.089 (95% CI: 1.045–1.135) When added to known STS score, 1-year mortality OR: 1.087 (95% CI: 1.037–1.139)
Sundermann et al. [9]	450	227/223	79 ± 4	FORECAST	5-domain questionnaire	30-day mortality, 1-year mortality	30-day mortality OR: 1.30 (95% CI: 1.20–1.50) 1-year mortality OR: 1.30 (95% CI: 1.20–1.40) 1-year mortality independent of age OR: 1.265 (95% CI: 1.143–1.401) When added to known EuroSCORE, 1-year mortality OR: 1.271 (95% CI: 1.141–1.415) When added to known STS score, 1-year mortality OR: 1.264 (95% CI: 1.116–1.431)
Lee et al. [7]	3826	2828/998	65 ± 10	Katz index of ADL/ambulation independence/dementia diagnosis	5-domain questionnaire	In-hospital mortality and discharge to an institution	Adjusted in-hospital mortality OR: 1.80 (95% CI: 1.10–3.00) Adjusted reduced mid-term survival HR: 1.50 (95% CI: 1.10–2.20) Adjusted prediction for institutional discharge OR: 6.30 (95% CI: 4.20–9.40)
Afilalo et al. [42]	152	100/52	75.9 ± 4.4	Gait speed	5-m gait speed for more than 6 s	In-hospital mortality or major morbidity	Mortality or major morbidity OR: 2.63 (95% CI: 1.17–5.90) When added to STS-PROM, mortality or major morbidity OR: 2.53 (95% CI: 1.15–5.52)

(continued)

Table 1 (continued)

Source	N	Gender M/F	Age mean (SD) years	Frailty measure	Description	Primary study outcomes	Main outcome odds ratio/confidence interval
							When added to the Parsonnet score, mortality or major morbidity OR: 2.28 (95% CI: 1.02–5.21)
Afilalo et al. [42]	152	100/52	75.9 ± 4.4	Nagi scale	7 items	In-hospital mortality or major morbidity	Mortality or major morbidity OR: 1.28 (95% CI: 1.06–1.54) When added to STS-PROM, mortality and major morbidity OR: 2.66 (95% CI: 1.18–5.96) When added to the Parsonnet score, mortality or major morbidity OR: 2.17 (95% CI: 0.93–5.04)
Afilalo et al. [3]	131	87/44	75.8 ± 4.4	Gait speed	5-m gait speed for more than 6 s	In-hospital mortality or major morbidity	Adjusted mortality or major morbidity OR: 3.17 (95% CI: 1.7–2.59) Mortality or major morbidity after adjusting for STS risk score OR: 3.05 (95% CI: 1.23–7.54) Adjusted prolonged postoperative length of stay OR: 2.32 (95% CI: 0.95–5.67) Adjusted discharge to a health-care facility OR: 3.19 (95% CI: 1.40–8.41)
Robinson et al. [204]	129		73 ± 6	Katz index, Timed Up and Go test, Charlson index, Mini-cog, albumin, anemia, and fall	7 different frailty tools	Complications	Increase in complications for every 1 year increase in age OR: 1.015 (95% CI: 0.943–1.092) Likelihood for frail people to have complication OR: 6.697 (95% CI: 2.565–17.483)
Afilalo et al. [205]	131	86/45	75.8 ± 4.4	Fried scale, functional comorbidity, OARS instrumental ADL scales and Katz index of ADL	5 items	Mortality and major morbidity	When adjusted for STS risk score, mortality or major morbidity OR: 3.14 (95% CI: 1.02–9.68)

Abdullahi et al. [94], by permission of Oxford University Press

ADL, activity of daily living; CAF, comprehensive assessment of frailty; CI, confidence interval; FORECAST, frailty predicts death 1 year after elective cardiac surgery test; OARS, Older American Resources and Services; OR, odds ratio; STS, Society of Thoracic Surgeons; STS-PROM, STS predicted risk of mortality undergoing elective noncardiac major surgery. Only 6.8% of patients were identified as frail. Mortality increased with degree of frailty as identified by the Risk Analysis Index score. With intervention, mortality at 30 days improved in frail patients from 12.2% compared to 3.8% in a retrospective cohort ($p < 0.001$) and the benefit persisted to 365 days with improvement from 34.5% to 11.7% ($p < 0.001$) [51]. Interestingly, gains in mortality were observed in the non-frail population as well, attributed to the fact that care approaches were being measured and assessed more closely.

Strategies to Decrease Operative Risk

Improvements in surgical techniques and anesthesia have increased the confidence of cardiac surgeons performing operations in older adults with elevated perioperative risk. The two principal causes of stroke in older adult patients during cardiac surgery are embolization (air, atheroma, and calcific debris) and hypotension resulting in inadequate perfusion of the central nervous system. Preoperative evaluation of the ascending aorta and carotid arteries and intraoperative assessment of the proximal aorta using intraoperative transesophageal or epiaortic echocardiography may alter the conduct of the procedure, minimize surgical manipulation, and thereby significantly reduce the incidence of stroke [53–57]. Such information enables the surgeon to avoid cannulation or direct manipulation of heavily diseased portions of the aorta where atheromatous disease may dislodge or where plaque disruption may cause aortic dissection. The presence of extensive atheromatous or calcific disease, which precludes safe manipulation of the ascending aorta in patients with advanced coronary disease, leaves the surgeon with several choices:

1. Perform surgical revascularization on a beating heart (known as an off-pump coronary artery bypass (OPCAB)), using one or both internal thoracic arteries, radial artery, and/or non-aortic-based grafts [58–60].
2. Establish cardiopulmonary bypass via the femoral, axillary, or other systemic non-diseased artery and perform graft replacement or endarterectomy of the ascending aorta [53, 54]. The latter alternative is an aggressive, complex procedure, and in the older adult population, it should be reserved for the very good risk patient with no significant comorbidities.
3. Potential a "hybrid" procedure (i.e., a combination of coronary artery bypass graft to key target vessels and percutaneous coronary stents to other territories) [61–63].
4. Abandon the surgical procedure and consider nonoperative revascularization such as percutaneous coronary intervention (PCI) or transcatheter aortic valvular replacement (TAVR). This may require the acceptance of incomplete revascularization. If not suitable for PCI/TAVR, it may be necessary to ongoing medical management/palliative therapies.

Diffuse systemic atherosclerosis is more prevalent in the older adult than in younger patients; as such, special precautions should be taken to ensure adequate cerebral and renal perfusion both in the operating room and in the intensive care unit [64, 65]. Maintaining high perfusion pressures while on cardiopulmonary bypass can help decrease the incidence of ischemic stroke [66]. Managing blood pressure during the early perioperative period may also be beneficial in attenuating the incidence of postoperative delirium [67]. Control of atrial arrhythmias and avoidance of episodes of sustained arterial hypotension due to hypovolemia or medications are important during the immediate postoperative period, particularly in those patients with diastolic dysfunction who are increasingly reliant on the atrial contribution to cardiac output. Although there is still controversy regarding the management of asymptomatic carotid disease, it is believed that known carotid disease in the older adult population is a risk factor for postoperative stroke [53, 56, 68, 69]. Morris et al. recommended routine preoperative assessment of carotid artery disease in octogenarians and advocated carotid endarterectomy if significant disease is found; however this is still controversial and not the current standard of practice in most cardiac surgery centres [70, 71]. If symptomatic carotid artery disease is diagnosed prior to cardiac surgical intervention, consideration can be given to performing a staged or a combined cardiac/carotid procedure. If asymptomatic significant carotid disease is discovered by Doppler preoperatively (>75% stenosis bilaterally or lesser degrees of unilateral stenosis in the presence of an occluded contralateral artery), concomitant carotid endarterectomy may decrease the risk of perioperative stroke [72, 73].

Pre-habilitation

Older patients with multiple comorbid illnesses experience higher rates of in-hospital mortality after cardiac surgery when compared to younger patients [48]. Often surgery is required urgently, or the degree of cardiac compromise from valvular disease, angina, or heart failure precludes the ability to optimize preoperative status. However, in the setting of elective surgery, all possible measures must be taken to optimize the older adult patient preoperatively and in attempts to optimize their trajectory of recovery. Since the phenotype of frailty is characterized by reductions in muscle mass, strength, endurance, and activity level [22], cardiac rehabilitation programming is ideally suited to counteract impairments and improves frailty status among patients requiring cardiac surgery. Cardiac rehabilitation has previously been demonstrated to decrease morbidity and mortality in patients with established cardiac disease [74–78] and to be safe in older adults [79–82]. Furthermore, previous investigations conducted in nonsurgical populations of older adults suggest that the frailty syndrome is indeed modifiable through structured exercise interventions [83–86]. The concept of preoperative rehabilitation is well-established in many disciplines, including orthopedic, thoracic, and abdominal surgery [87–89]. Despite this, few clinical trials have evaluated preoperative exercise interventions in patients undergoing cardiac procedures. Herdy and colleagues conducted a randomized controlled trial in 56 patients undergoing coronary artery bypass graft (CABG) surgery, where participants randomized to a cardiopulmonary rehabilitation group received a minimum 5-day preoperative and 5-day postoperative progressive exercise program [90]. Notably, participants randomized to the intervention group presented with attenuations in atelectasis (RR: 0.15, 95% CI: 0.03–0.8) and atrial fibrillation (RR: 0.2, 95% CI: 0.05–0.8) and reduced their average postoperative hospital length of stay (5.9 ± 1.1 vs. 10.3 ± 4.6 days). Perhaps the strongest evidence supporting preoperative exercise interventions in patients undergoing cardiac surgery comes from a randomized trial conducted by Arthur et al., which investigated an 8-week supervised exercise program in 249 low-risk patients undergoing CABG [91]. The primary outcome of the study investigated postoperative hospital length of stay, while secondary outcomes examined exercise capacity, health-related quality of life, and anxiety levels. Notably, patients randomized to the intervention group reduced their hospital length of stay by a median of 1 day (95% CI: 0.0–1.0 day, $p = 0.002$) and spent an average of 2.1 less h (95% CI: 1.2–16 h, $p = 0.0001$) in the intensive care unit. Despite this evidence, routine clinical practice does not refer cardiac patients to cardiopulmonary rehabilitation programming until after their surgical procedure, leaving many patients to wait in fear [92] and experience further deconditioning. Currently, a multisite randomized controlled trial is being conducted in Canada to determine the efficacy of pre-habilitation among older adults undergoing elective CABG and/or valve procedures (NCT02219815) [93]. The pre-habilitation intervention will consist of twice-weekly exercise prescribed at 40–60% of heart rate reserve, for a period of 8 weeks. The primary outcome of the study will investigate the proportion of patients requiring a hospital length of stay greater than 7 days.

Predictors of Perioperative Morbidity and Mortality

A comprehensive preoperative assessment is essential to determine the relative risk and potential benefit of the surgical intervention in this patient population (Table 2). Current preoperative cardiac surgery risk scores, however, perform

Table 2 Key elements of preoperative evaluation

A meticulous history and physical examination	Documentation of acute and chronic (co-morbid) illnesses Baseline cognitive assessment Medication record including over the counter medications Baseline surgical risk score (i.e., STS-PROM or EuroSCORE II)
Routine laboratory tests	Cardiac workup: this typically included an electrocardiogram (ECG), chest radiograph, coronary angiography, and an echocardiogram Additional electrophysiology studies may be help define the patient's hemodynamic and physiologic profile The use of chest cardiac computerized tomography (CT) may be of benefit to determine degree of calcific atheromatous disease burden the ascending aorta and aortic arch Gated blood pool radionuclide studies or magnetic resonance imaging (MRI) may be necessary to define the coronary anatomy and myocardial viability Following evaluation of test results, the treatment format for surgical intervention is formulated
Frailty assessment	Frailty is highly prevalent in the older adult undergoing cardiac surgery. An optimal process of assessment in the cardiac surgery patients is still being determined; however the use of any frailty screening tool has been associated with improved prediction of outcome following cardiac surgery
Functional assessment	Identification of current living status and potential barriers to successful discharge and recovery should be identified in the preoperative setting to facilitate informed decision-making with patient-caregiver unit and to permit the health-care team to plan disposition arrangements

poorly in older adult patients [42, 94]. Cardiac surgery risk prediction tools, such as the Society of Thoracic Surgeons (STS) score [95] and the European System for Cardiac Operative Risk Evaluation (EuroSCORE II) [96], do not comprehensively account for preexisting frailty and disability, which is increasingly being recognized as critical determinants of health status with advanced age [42].

Frailty is a geriatric syndrome that reflects subclinical impairments in multiple organ systems impeding the body's ability to uphold physiological homeostasis in the face of stressors [97]. There are however >20 different frailty scales that have been developed, and new scales continue to emerge in the medical literature [94, 98]. Many scales are loosely based on Fried's core domains [22] and the Rockwood's frailty index [41]. The uncertainty regarding which frailty tool to use is compounded by uncertainty regarding which cutoff to use for each tool (e.g., gait speed [99]). As such, the choice of scale and cutoff can drastically modify the measured prevalence of frailty, which ranges from 6% to 44% in the same patients [100].

There is an unmet need to combine established cardiac surgery risk scores with measures of frailty and disability to provide a more complete model for risk prediction in older adult patients undergoing cardiac surgery. Despite this, there are some established risk factors for poor postoperative outcomes. Perhaps not surprisingly, in a prospective study of octogenarians undergoing cardiac surgery, the complexity and urgency of the surgery predicted poor outcome. The need to perform a CABG in addition to an (AVR) accorded surgical risk but is also a marker of the presence of extensive cardiovascular disease and more comorbidities. Independent of those factors, worsened creatinine clearance, previous MI, presence of atrial fibrillation, and chronic respiratory disease all independently predicted increased postoperative mortality [101].

Quality of Life Considerations

Although the short-term and intermediate survival for older adults undergoing cardiac surgery is less than younger cohorts, the long-term survival of octogenarians after open heart surgery compares favorably with survival for the general population of similar age. In a series of 600 consecutive patients 80 years of age or older undergoing various cardiac procedures, the 5-year actuarial survival, including hospital mortality, was 63 ± 2%. Survival in this group was identical to that for the comparable general US octogenarian population [68]. Excellent long-term results have been achieved by several groups in octogenarians after mitral valve surgery, aortic valve surgery, and coronary artery bypass surgery [102–104].

Another key determinant of "operative success" (and perhaps more importantly) is the consideration of post-discharge health-related quality of life (HRQoL) in older adults undergoing cardiac procedures. Several authors have shown that most (81–93%) of the octogenarians who survive open heart surgery "feel" as good and frequently better than before their operations [60, 68, 102, 104]. An equally high percentage (75–84%) of octogenarians believed in retrospect that having decided to have a cardiac surgical procedure after age 80 had been a good choice [68, 105]. Even so, the precise and objective measurements of quality of life may be difficult to quantify. Based on well-studied populations, it has been possible to construct instruments that reliably assess the various domains of daily living, thereby producing a meaningful, reproducible measurement of HRQoL [106]. A recent retrospective investigation of octogenarian patients undergoing cardiac procedures reported that 11.7% experience a prolonged stay greater than 5 days in the intensive care unit [107]. Of these patients experiencing prolonged stays in intensive care, 81.3% experienced functional survival (i.e., defined as alive at 1-year and living in their own home) as compared to 91.7% ($p < 0.01$) among those not experiencing a prolonged stay. A lack of physician visits in an outpatient setting within 30 days of discharge was associated with a fivefold increase in the risk of poor functional survival at 1 year (HR: 5.18, $p < 0.01$).

The Canadian Cardiovascular Society (CCS) and New York Heart Association (NYHA) angina scores and functional class and reflect symptom-free living with regard to chest pain and dyspnea [108, 109]. Octogenarians have consistently demonstrated substantial improvement in their NYHA functional class and cardiac failure functional class after cardiac surgery. In several reports, most (i.e., 68–92%) of the octogenarians who survived open heart surgery were in NYHA functional class I or II during long-term follow-up. When a well-validated HRQoL index, the SF-36, was employed to prospectively study a cohort of older adult and non-older adults, individuals over 75 years of age experienced identical long-term improvement in each of the seven domains of the SF-36. Indeed, many of the older adult patients had as low HRQoL SF-36 scores preoperatively as their younger cohorts; however while both age groups experienced improved SF-36 scores 6 months following surgery, the changes were even greater in the older adult population.

While most patients recovering from cardiac surgery will spend less than 48 h in the postoperative intensive care unit, some patients require a prolonged stay in the intensive care unit. Perhaps not surprisingly, patients with a prolonged postoperative intensive care unit stay experience increased rates of re-hospitalization and poorer HRQoL following their procedure. Many recent reports examining postoperative outcomes in the aging population undergoing cardiac surgery use hospital discharge as a metric to quantify surgical success. Even so, discharge from hospital may not necessarily translate to thriving in the community, particularly among older adults. There is an urgent need to consider patient-centered health outcomes, including functional capacity, quality of life, and activities of daily living, in addition to postoperative survival. Identifying patients at risk of poor functional survival would permit surgeons to improve the quality of informed consent and target modifiable risk factors in this vulnerable subset of the population both pre- and postoperatively.

Postoperative Complications

The vulnerable older adult patient, who is more susceptible to the complexity of surgical process, is at an elevated risk for complications of cardiac surgery and will be less likely to return to baseline function postoperatively [4]. In this section, perioperative complications that occur in all cardiac surgery patients will be addressed; however, a more detailed discussion of issue pertinent to the older adult will be undertaken later in the chapter.

With normal aging there is a reduction in both renal mass and glomerular filtration rate (GFR). In octogenarians this is more pronounced, with up to a 40% decrease in GFR and a 25% decrease in kidney mass [110]. Patients undergoing cardiac angiography should have pre- and post-angiography renal function assessed. Renal function may be made worse by transient hypotension that occurs during cardiopulmonary bypass, and in the older adult population, perioperative renal insufficiency is a strong positive predictor of postoperative mortality [110].

As individuals age, there is a decrease in adaptive immune function, primarily due to decreased production in naïve lymphocytes in the bone marrow [111]. This may be associated with increased susceptibility to infection in the geriatric population. This is particularly relevant in older adults undergoing cardiac surgery, where the use of monitoring lines, catheter, drainage lines, and central lines may provide further infection risk. Older age has been shown to be an independent risk factor for wound infection, including deep sternal wound infection [112]. Identification of postoperative infection can be delayed in the older adult population due to possible lack of leukocytosis and atypical presentation of infection, such as confusion or hypothermia [110].

General Postoperative Complications

Postoperative complications are associated with increased morbidity and mortality after cardiac operations [113]. The postoperative complications of cardiac surgery can be approached as complications that occur whenever one performs prolonged, complex surgery on a potentially vulnerable population and those complications that are very specific to cardiac surgery. The Society of Thoracic Surgeons (STS) is a large reporting body for more than 1800 international cardiac surgery programs (www.sts.org). The STS National Database is the largest and most representative data source in cardiothoracic surgery. The STS National Database currently identifies six major postoperative complications, including death, stroke, renal failure (defined as a threefold or greater rise in creatinine or new dialysis requirement), prolonged mechanical ventilation (>24 h), unplanned reoperation (for any reason), and deep sternal wound infection (DSWI). The STS National Database has further reported major morbidity or mortality outcome as a composite endpoint, defined as any of the outcomes listed in the six major complications.

With an increasingly complex population, there is an emphasis on ensuring there is an appropriate system of care in place, rather than focusing solely on developing the skills of a single clinician. When a complication occurs, how well it is assessed and managed is now a focus of attention. Failure to rescue (FTR) is increasingly recognized as an important quality indicator in cardiac surgery [113–116]. FTR refers to the prognosis of a patient cohort that has experienced a complication [117], and for the purposed of cardiothoracic surgery, FTR has been defined as the postoperative mortality rate after the occurrence of stroke, renal failure, reoperation, and prolonged ventilation [116]. For example, the STS National Database was used to develop FTR metrics and a predictive FTR model for CABG [116]. Recent work has shown that there is variation in FTR rates across cardiac surgery program in the United States [113]. This is an opportunity for improved systems for recognizing complications and improving team processes [113]. Postoperative care processes are evolving so that in many fields where the patient population is frail and complex, there is comanagement of care with a hospitalist. In vascular surgery, this process of care has been shown to decrease mortality and complications [118].

Major Bleeding, Transfusion, and Anemia

Postoperative bleeding is a relatively common complication after cardiac surgery. There are many factors that contribute to the development of major postoperative bleeding, including preoperative drug use and the effects of cardiopulmonary bypass [119]. Major postoperative bleeding, with associated allogenic blood product transfusion and perioperative anemia (the "deadly triad" of cardiac surgery [119]), is commonly experienced complications associated with poor postoperative outcomes [120–125]. In a retrospective study of 16,154 patients undergoing cardiac surgery, major bleeding, red blood cell transfusion, and anemia were all independent predictors of operative mortality. More specifically, patients with either major bleeding (OR: 3.453, 95% CI: 2.785–4.282) or red blood cell transfusion (OR: 2.916, 95% CI: 2.239–3.796) have an operative risk almost three times greater than patients without major bleeding or transfusion, even after adjustment for other covariates. Anemia is also associated with adverse outcomes after cardiac surgery, demonstrating an odds ratio of 2.0 (95% CI: 1.4–2.8) for a composite outcome of in-hospital mortality, stroke, or acute kidney injury [65]. As such, strategies to reduce postoperative major bleeds, anemia, and transfusion must be considered.

Complications Germane to the Older Adult Undergoing Cardiac Surgery

In 2016 the American College of Surgeons NSQIP and American Geriatrics Society coauthored the "Optimal Peri-operative of the Geriatric Patient: a Best Practice Guideline" which provides a practical and evidence-based foundation for approaching postoperative care [126]. In the postoperative period, the guideline focuses on delirium assessment and prevention, perioperative pain management, assessment of pulmonary complications, fall risk assessment, maintaining nutrition, urinary tract infection prevention, assessment and prevention of functional decline, and pressure ulcer prevention. General principles of having a structured approach to assessment, early mobilization, ensuring hearing and vision aides are available, early involvement of family and the multidisciplinary team, as well as avoiding inappropriate medications are all emphasized.

As preoperative comorbidities and frailty increase, so does the risk of complications, including delirium, acute kidney injury, and atrial fibrillation. Each of these complications has been determined to be an independent risk factor for both in-hospital morbidity and prolonged length of stay, but also poor long-term outcome [127–129]. Even with successful hospital discharge, in-hospital severity and duration predict increased long-term mortality.

Postoperative Atrial Fibrillation

New postoperative atrial fibrillation is a common complication that occurs in up to 33% of cardiac patients, with incidence increasing in combined procedures. It is often self-limited, with 80% of cases resolving within 7 days [130]. This is an area where there is still controversy over the optimal management approach, which includes either rhythm or rate control. A rhythm control approach results in accelerated resolution of the arrhythmia but has accompanying risks of toxicity from amiodarone. A rate control approach has less toxicity but slower resolution of the abnormal rhythm and a higher requirement for anticoagulation. Until recently, studies from nonsurgical settings have been used to direct practice in cardiac surgery. However, in 2016 Gillinov et al. published a trial specific to cardiac surgery. They prospectively followed 2109 patients undergoing a variety of surgeries; 33% developed atrial fibrillation, and 523 were randomized to either rhythm control or rate control as an initial management strategy. From a clinical effectiveness perspective, focusing on days in hospital, readmission rates, long-term atrial fibrillation, and need for cardioversion, the two approaches are equal [130]. Specific to the older adult, avoiding amiodarone because of the significant toxicity is a consideration. This consideration would favor a rate control approach, unless there is hemodynamic instability.

Stroke

Despite advances in surgical monitoring and management, stroke remains a devastating complication that typically occurs early in the patient course. As many as 30–40% of strokes occur intraoperatively, either from embolization (i.e., air, atheroma, and calcific debris) or hypotension, resulting in inadequate perfusion of the central nervous system. Postoperatively, they will occur in the first 1–2 days from a cardio-embolic source. LaPar et al. recently published a large retrospective study of all cardiac surgeries performed in Virginia over a 10-year period, who also had an STS score assessed at baseline (average age = 65 years). Of 57,837 patients undergoing surgery, 1.5% developed stroke as a complication [131]. In contrast, in a selected group of octogenarians undergoing elective surgery, the stroke rate was higher at 3.6% [101].

Stroke is more common after urgent and emergent surgeries, as well as isolated valve and combined CABG and valve procedures. Higher preoperative morbidity, as measured by the STS score, is a risk factor for stroke and reflects a higher burden of comorbidities, including peripheral arterial disease, diabetes, heart failure, and renal failure. Other independent predictors of postoperative stroke include prior cardiac surgery (OR: 1.33, $p = 0.05$), preoperative infection (OR: 2.39, $p < 0.0001$), and cardiopulmonary bypass time over 2 h (OR: 1.42, $p = 0.0004$) [132]. Being female is also an independent risk factor for postoperative stroke. In addition to immediate complications, having a stroke increases hospital mortality substantially. In a retrospective study by LaPar et al., mortality increased from 2% in those without stroke to 18% among those suffering a stroke. For those that survive, there is increased morbidity and often prolonged hospitalization as a result. A particular focus of LaPar's study was comparing stroke rates and FTR rates after stroke between institutions. As a clinical entity that can be readily diagnosed with a well-established management approach, it is expected that mortality rate would have little variability. It is concerning that institutional factors impacted both stroke rate and stroke mortality even after controlling for patient and procedure factors [131]. The next step is understanding variations in practice and sharing best practices between centers.

Delirium

Delirium is an acute change in cognitive function that negatively impacts outcomes in the cardiac patient. Delirium is a complication that remains frightening for the patient and equally upsetting for their caregivers. Delirium is the most common neurological complication in the cardiac patient [133, 134]. It is a marker of an injured or injury prone brain [135–137] that likely occurs secondary to alterations in cerebral blood flow [138, 139]. The existence of atherosclerotic vascular disease places the cardiac patient at an increased risk of delirium [140], with rates of delirium following cardiac procedures being reported as high as 78% [141], nearly twice the rate observed in other elective procedures [142–145]. Importantly, patients with heart failure [146] and valvular disease [147, 148] experience equal, if not higher, rates of delirium. Furthermore, while still commonly perceived as a transient syndrome with minimal adverse long-term impact, delirium in patients with acute cardiac illness and following cardiac procedures has been shown to be associated with higher probability of death, morbidity, falls, cognitive decline, and loss of functional independence [139, 149–155]. The burden of atherosclerosis is highly correlated with cognitive function [156]. Multiple studies have demonstrated decreased cognitive performance in patients undergoing cardiac surgery [157–159].

At present, a specific pathophysiology of delirium has yet to be identified and a single cause seems unlikely [160]. In a recent review, delirium has been characterized in three key determinants (also known as the "3-Strike Model"): an increased baseline vulnerability, suffering an acute cardiac event, and post-admission processes of care (Fig. 3) [161].

An important step in the prevention of delirium is the establishment of baseline risk. An advantage afforded to the cardiac surgery team is that they are often presented with the opportunity to obtain information on patients at baseline, prior to their procedure. While it is not clear what is "necessary" in the preoperative work up phase, there is value to the perioperative team to have an understanding of the baseline cognition using the Montreal Cognitive Assessment [162], Mini-Cog [163], or the Short Portable Mental Status Questionnaire [164]. Similarly, testing for frailty [44, 165], abnormal albumin [166, 167], anxiety, depression, and preprocedure pain [168–170] may also provide important information.

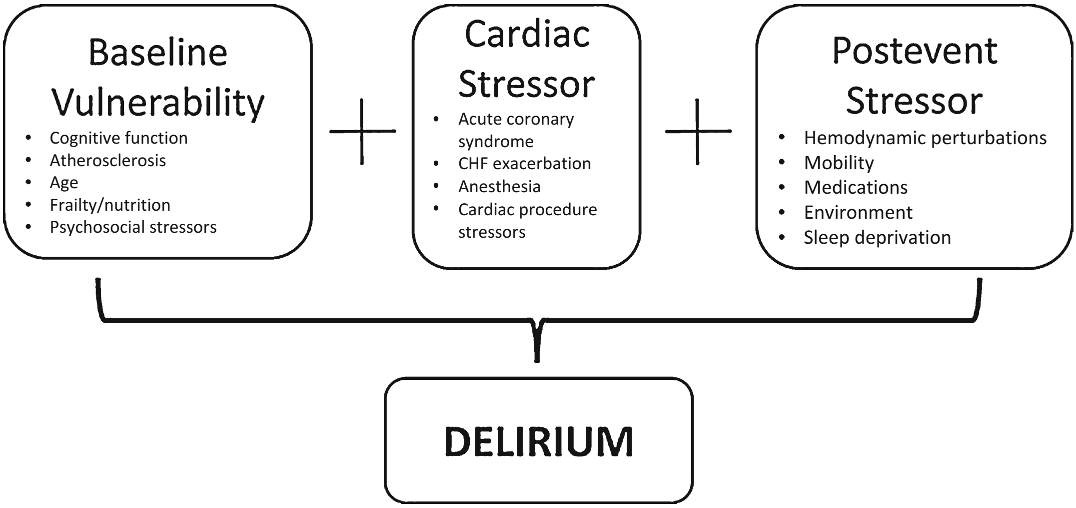

Fig. 3 The Cardiac "3-strike" paradigm- key factors leading to delirium. (Reprinted from Canadian Journal of Cardiology, 33, 1, Arora, R.C., Djaiani, G., Rudolph, J.L., Detection, Prevention, and Management of Delirium in Critically Ill Cardiac Patient and Patients Who Undergo Cardiac Procedures, 80–87, Copyright (2017), with permission from Elsevier)

Despite an increasing clinician awareness of the occurrence of postoperative delirium, under recognition continues to persist, particularly with hypoactive delirium [171, 172]. A system of daily assessment, specifically for delirium, should be in place. The ACS/AGS guidelines provide an excellent framework for approaching delirium [173]. In the postoperative ICU setting, two main screening tools for delirium have been developed and validated. The confusion assessment method adapted for the ICU (CAM-ICU) is a brief operationalized instrument that utilizes three assessments: the Richmond Agitation and Sedation Scale, the Attention Screening Exam, and five yes-no questions [174, 175]. The CAM-ICU has been validated in multiple studies and has been implemented in many ICUs. The Intensive Care Delirium Screening Checklist (ICDSC) consists of an eight-item checklist [176, 177]. Using the principles incorporated in the CAM-ICU screening tool, the ICDSC includes additional domains of perceptual differences, psychomotor agitation, sleep disturbances, and inappropriate speech. Both the CAM-ICU and ICDSC should be completed every nursing shift to potentially capture the fluctuations associated with delirium.

On the postoperative ward, there are several tools that have been developed for use of preoperative screening for postoperative delirium [167, 178, 179]. A rigorous study by Rudolph et al. [167] used the widely accepted confusion assessment method (CAM) [180] and included both a derivation and validation patient cohort as part of their analysis. This study, however, included the use of the Mini-Mental State Examination (MMSE) (which takes 15–20 min to administer), which may limit its clinical feasibility. This study serves to further highlight the urgent need for multicenter trials validating the current tools, which effectively screen for risk of delirium in cardiology and cardiac surgery environments.

A process for identifying individuals at high risk for delirium and counseling families preemptively is important. Principles of optimal perioperative care such as pain control, early mobilization, and fluid management are all relevant for prevention of delirium. If delirium emerges, in addition to considering surgical complications, infections, and electrolytes as precipitants, it is also relevant to reexamine pain control, review medications, and assess for urinary retention and fecal impaction. Once present, care includes meticulous attention to fluid balance to avoid dehydration and renal failure and close attention to pain control as the delirious patient may struggle to communicate needs. If delirium is hyperactive, then addition of an antipsychotic is indicated and should be used as a low-dose, scheduled drug rather than waiting for escalation. The ACS/AGS guidelines reference using haloperidol IM/IV initially which is appropriate in the ICU or if there is immediate risk to critical equipment. However more typically an oral agent can be used and risperidone or olanzapine can be used [97].

Deep Sternal Wound Infection

Deep sternal wound infections (DSWI) are infrequent but cause prolonged morbidity and hospital stays following cardiac surgery. Reports of occurrence are generally in the 0.5–2% range. One center publishing a large retrospective analysis of 13 years of cardiac surgery reported a DSWI rate of 0.77% [181]. The diagnosis is often made 2–3 weeks after the initial surgery with presenting symptoms consisting of wound dehiscence, wound discharge, or sternal instability; in one institutions review of all confirmed cases fever was present in only 29% [182].The formal definition follows the CDC classification for surgical site infections. There are also classifications systems for severity. On physical examination, local findings and fever are the main findings. The diagnosis requires a positive culture from the wound, mediastinum, or blood. Chest x-rays are not always helpful but can show damaged or misplaced sternal wires. Computerized tomography of the chest is useful for showing the extent of disease [181].

Preoperatively, risk factors for DSWI include male gender, obesity, diabetes, smoking, peripheral vascular disease, and advanced age. Intraoperative risk factors include prolonged surgery and bilateral internal thoracic artery grafting. The combination of diabetes and ITA grafting is considered particularly high risk for developing DSWI [181].

Traditionally, prevention of DSWI has included preoperative antibiotics and a short course of postoperative antibiotics. If infection is confirmed, treatment consists of wound debridement, primary sternal closure, and mediastinal irrigation, either with an antiseptic or antibiotic solution. Alternative approaches, such as secondary closure from granulation tissues, muscle flap reconstruction, secondary closure with omental flap transfer, and vacuum-assisted closure dressings, are also being used in some institutions. There is currently no consensus on the best practice approach to managing DSWI [181, 182]. Systemic antibiotics are continued for at least 6 weeks after the last positive culture.

Nonsurgical Alternatives

During the current era of health-care reform, there is considerable interest in providing the most appropriate care for patients more than 80 years of age at an “acceptable” cost [183]. As coronary bypass surgery is the most common major operation performed in the USA (more than 300,000 done annually), the use of coronary bypass in the very old adult is an important issue in the present cost-conscious environment. Medicare data from 1987 to 1990 indicated that the use of this operation in patients more than 80 years of age increased by 67% during that time period [184]. The projected rise in the number of coronary bypass procedures to be done in these patients and associated costs is impressive.

Several studies have attempted to compare the treatment results of less expensive and less invasive alternatives to coronary bypass surgery, particularly among older adults. In older adults, percutaneous coronary intervention (PCI) has the potential advantages of shorter hospital stay, less immobilization, and lower cost compared with coronary artery bypass; however, coronary bypass confers greater and more durable freedom from angina, less need for future repeat interventional measures, and overall improved health-related quality of life [185]. Although Mick et al. reported that the procedural complication rates in matched groups of patients undergoing coronary bypass versus PCI were similar, de Jaegere et al. identified that the extend of vessel disease is predictive of event-free survival [186, 187]. As mentioned above, compared with medical noninterventional therapy, coronary artery bypass provides a significant survival advantage and improved quality of life. Ko et al. compared 36 octogenarians who underwent coronary artery bypass with 29 octogenarians who continued medical noninterventional therapy and found that the functional class did not change in the latter group but improved significantly in the former group (NYHA functional class decreased from 3.4 to 1.2, $p < 0.01$) [185]. The 3-year survival rate of 77% for the surgical group was similar to the survival of octogenarians in the general US population and was significantly better than that of 55% for the medical group. In summary, coronary bypass surgery provides improved long-term survival and functional benefit compared with medical therapy and improved the quality of life compared with PCI.

Some high-risk patients diagnosed with severe symptomatic aortic stenosis may be suitable candidates for transcatheter aortic valve replacement (TAVR; also known as transcatheter aortic valve implantation (TAVI)) procedures. These TAVR procedures are conducted less invasively, via a small anterolateral thoracotomy, or more commonly now via the femoral vessels using a percutaneous technique. While the procedure is not without risk, it is generally hypothesized that high-risk patients undergoing TAVR will require a shorter hospital length of stay and experience an accelerated recovery period. Results from the prospective Placement of Aortic Transcatheter Valves (PARTNER) trial, which compared TAVR to standard therapy, identified that TAVR significantly reduced the rate of death at 1 year (30.7% vs. 50.7%, HR: 0.55, 95% CI: 0.40–0.74) among high-risk patients previously deemed inoperable by standard procedures [188]. The risk of all-cause mortality at 5 years is also significantly reduced among high-risk patients undergoing TAVR, compared to standard therapy (HR: 0.50, 95% CI: 0.39–0.65), with 86% of survivors having NYHA class I or II symptoms [189]. Collectively, the results of the PARTNER trail indicate that TAVR is more beneficial than standard therapy for the treatment of inoperable aortic stenosis. Even when compared to traditional surgical aortic valve replacement in high-risk patients, TAVR remains a comparable alternative with respect to 5-year survival rates (67.8% TAVR, 62.4% SAVR, $p = 0.76$) [190]. The results of the initial PARTNER trial have since been extended to intermediate-risk patients, reporting comparable 2-year outcome rates (i.e., death or disabling stroke) among patients undergoing TAVR and traditional surgical aortic valve replacement [191, 192]. Favorable 1–5-year survival rates for TAVR have also been reported among older adults (mean age 83 years), ranging from 83%, 74%, 53%, 42%, and 35% at 1, 2, 3, 4, and 5 years, respectively (Fig. 4) [193].

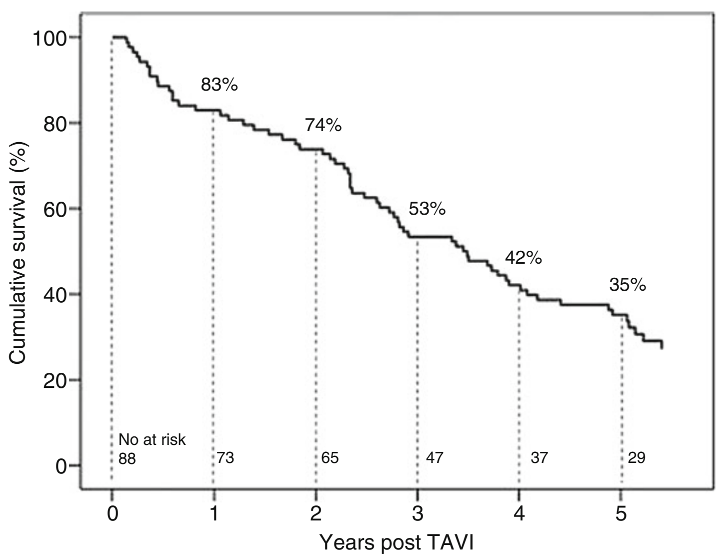

Fig. 4 Long-Term Survival After Transcatheter Aortic Valve Implantation. (Reprinted from Journal of the American College of Cardiology, 61, 4, Toggweiler, S., Humphries, K.H., Lee, M., Binder, R.K., Moss, R.R., Freeman, M., Ye, J., Cheung, A., Wood, D.A., Webb, J.G., 413–419, Copyright (2013), with permission from Elsevier)

Transplantation and Mechanical Circulatory Support

In the mid-1980s, implantable mechanical circulatory assist devices were introduced in FDA clinical trials for patients with severe left ventricular dysfunction who were awaiting transplant and would otherwise not survive. The most popular device in this early era, the HeartMate pneumatic left ventricular assist device (LVAD), enabled patients to ambulate and exercise on treadmills while in-hospital. The advantages of LVAD therapy for the often debilitated, deconditioned patients were significant and resulted in improved outcomes for heart transplant recipients who were able to optimize their physical and physiologic conditions prior to transplant. Since then, LVADs have become smaller (e.g., HeartWare (HeartWare) and HeartMate II (thoratec)), more durable, and associated with increased survival rates when compared with the earlier models [194]. The oldest patients with these smaller LVADs are octogenarians who, like their younger counterparts, are leading productive lives outside the hospital. For a selective group of older adults that are physically active who suffer hemodynamic compromise due to severe cardiac dysfunction, a temporary mechanical assist device can be implanted if there is hope of cardiac recovery, such as after a large myocardial infarction.

The seminal Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) trial demonstrated that implantation of LVAD's can provide survival advantages superior to optimal medical management in end-stage heart failure patients otherwise considered ineligible for transplant. Survival among patients receiving LVAD treatment at 1 year was 52% and 23% at 2 years, compared to 25% and 8% among patients randomized to optimal medical management ($p = 0.008$) [195]. There was a 48% reduction in the risk of all-cause mortality (RR: 0.52, 95% CI: 1.34–0.78, $p = 0.001$) in the group receiving LVAD as compared to patients receiving medical therapy [196]. The REMATCH trial also demonstrated significant improvements in functional status among patients receiving LVAD therapy, as assessed by the Minnesota Living with Heart Failure scores. Collectively, the results of the REMATCH trial demonstrated that the use of LVAD in patients with advanced stages of heart failure results in enhanced survival and clinically meaningful improvements in quality of life.

As the population ages, the number of older adults suffering from heart failure and associated pathologies is increasing. As a result, there is an increasing number of patients that are becoming candidates for heart transplantation procedures. Several studies have demonstrated encouraging survival rates among older adults (i.e., 60 years and older) requiring transplant procedures, although survival rates remain lower when compared to younger transplant recipients [197]. Even so, recent studies indicate the 1-, 5-, and 10-year survival rates among transplant recipients over 60 years to be 87.3%, 80.4%, and 68.0%, respectively [198]. Stringent patient selection and consistent follow-up is essential to ensure optimal outcomes are achieved. Predictors of survival among older heart transplant recipients include ischaemic cardiomyopathy (HR: 4.1) and postoperative complications, such as dialysis treatment (HR: 9.5) and mechanical circulatory support (HR: 4.2).

Strategies for Postoperative Follow-Up

In older adults, there are several considerations when transitioning from hospital back to the community after cardiac surgery. Although there are well-documented acute postoperative risks and considerations, there is less data and evidence for the best models of outpatient postoperative care. Similarly, postoperative mortality after cardiac surgery has been well studied; however, postoperative changes in functional status are less well documented in older adults after cardiac surgery.

Supportive follow-up that emphasizes collaborative and coordinated discharge planning among multidisciplinary team members (e.g., physiotherapy, nursing, occupational therapy, home care, pharmacy, dietician) is beneficial, particularly in frail and at-risk older adult patients [199]. Detailed discharge planning for older patients with medical conditions may help decrease readmission rates within 3 months of discharge from hospital, though fewer data are available to validate this model in cardiac surgery patients [200, 201]. Often detailed discharge planning is organized by an interdisciplinary team and executed by nurse specialists in the community. Successful discharge and community transition models use an individualized approach to the older adult patient. Aspects of these plans may include (1) recurring comprehensive functional assessments to include any changing needs of the patient while in hospital; (2) collaboration between patients, family members, cardiac surgery, cardiology, and primary care teams, including specific follow-up dates with surgical and primary care teams; (3) interdisciplinary discussion of patient's discharge plan and anticipated challenges; (4) clear and validated patient and caregiver education; (5) frequent reassessment of the discharge plan based on patient progress in hospital; and (6) post-discharge follow-up via visits or telephone calls to monitor whether patient's need further support or intervention once back in the community.

Despite the increasing proportion of older adults undergoing cardiac surgery, older survivors of critical care often have a decline in their functional status throughout their time in hospital. Delirium in the intensive care unit, intravenous narcotics, surgical complications, and device self-removal are all associated with functional decline and new institutionalization in critically ill older patients. This places more emphasis on continuous reassessment of discharge planning based on patient's changes in hospital [202].

Upon discharge and at all subsequent follow-up appointments, a thorough medication reconciliation is recommended to identify and prevent adverse drug errors. The immediate post-hospitalization period is a high-risk time for older adults due to in-hospital medication changes. In general, it is estimated that 12–17% of individuals have adverse drug interactions after hospital discharge, many of which are preventable [203]. Factors that contribute to medication management mistakes post discharge include poor patient-patient communication, poor education regarding medication use, poor or unclear therapeutic monitoring, incomplete or inaccurate transfer of information between health-care providers, and lack of prompt follow-up after discharge. Anticipating these difficulties during organized discharge planning is crucial to identify patients and families who may need more information, ensure discharge summaries are sent to appropriate primary care and specialist who will be following the patient, and identify patients who may need to be scheduled more urgent follow-up appointments.

Similarly, post-cardiac surgery clinic visits should include a medication review to ensure patients are taking their medications as prescribed and identify any side effects that may be preventing appropriate medication administration. Medications should be assessed for being stopped. Many older patients may leave hospital with prescriptions for benzodiazepines, antipsychotics, or aggressive bowel regimens that may have been needed acutely postoperatively but should be identified and stopped if there are no strong indications to have them prescribed. Finally, as the older cardiac patient transitions back to community, during follow-up visits, screen for caregiver burnout, acute changes in memory or mobility, and other clinical changes that may warrant a comprehensive geriatric assessment.

Conclusions

Within the last few decades, cardiovascular surgery in older patients, particularly in those older than age 80, has evolved from a relative rarity to a commonplace intervention. Throughout this course, it has been shown that older adults can not only tolerate, but have tremendous benefit from cardiac surgery, including improved symptoms, quality of life, and potentially increased survival. As nonoperative and less invasive interventions for coronary artery and valvular diseases continue to expand and the proportion of older adults in North America increases, it is expected that the number of older adults with cardiac disease that are candidates for procedures will continue to increase.

Due to the rising number of older adults that are undergoing cardiac surgery, there has been increasing attention to and consideration of this population's unique pre- and postoperative risks. Particularly since the 1900s, more attention has been focused on the identification and treatment of delirium in the postoperative cardiac surgery patient, preoperative cognitive assessment, detailed functional assessment, and the impact of preexisting frailty on surgical outcomes. Within the last decade this focus has been further expanded, and in some cases extrapolated to assessments of patients undergoing non operative cardiac interventions.

Further development of risk assessment tools in the older adult population undergoing cardiac surgery has emerged as a significant area of research. On a go forward basis, it will be crucial to continue to devise models to assess and risk stratify older adults undergoing cardiac surgery to further improve surgical outcomes in these individuals to ensure that patient not only survive but thrive after hospital discharge.

This shift toward a comprehensive approach to the older cardiac surgery patient has helped this population continue to thrive postoperatively. Compared to younger cohorts, older adults are often followed by multi- and interdisciplinary teams that include cardiac surgeons, primary care physicians and geriatricians, pharmacists, physiotherapists, and occupational therapists. This widely accepted collective approach to the cardiac surgery patient pre- and postoperatively will continue to help optimize these patients' symptoms and quality of life.

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Vascular Surgery

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Abstract

Cardiovascular diseases are the most common cause of morbidity and mortality in the world and account for 50% of deaths in people aged 65 and older. While there are many known modifiable risk factors, aging is as an independent and non-modifiable risk factor for worse outcomes in vascular diseases. The geriatric population is unique in their physiologic state, tolerance to stressors with serious risks to morbidity and mortality. Hence, it is essential for vascular surgeons and specialists in vascular interventions to consider the broader picture in older patients. This chapter delves into the geriatric-specific considerations for common vascular disease states. The first section studies the various preoperative risk factors and anesthesia considerations in older adults. Then, we dive into the various vascular maladies prevalent in the older population and their management approach including peripheral artery disease (PAD), carotid artery stenosis, and abdominal aortic aneurysms. Vascular atherosclerotic disease contributes to significantly high morbidity and economic burden in this cohort. Clinicians must carefully consider the decision to intervene, timing of intervention, as well as use of endovascular techniques for treatment of vascular disease. There is growing consensus to include frailty into the surgical workflow towards better planning for high risk patients. Preoperative frailty assessment using geriatric-specific tools could guide shared decision making and utilization of palliative services surrounding vascular care towards reducing morbidity and mortality.

Introduction

Cardiovascular diseases are the most common cause of morbidity and mortality in the world, and account for 50% of deaths in people aged 65 and older [1]. While there are many known modifiable risk factors, aging is as an independent and non-modifiable risk factor for worse outcomes in vascular diseases [1]. As the prevalence of atherosclerosis increases with advancing age, it comes as no surprise that the majority of vascular surgery patients are from the geriatric population [2]. In fact, increasing numbers of older people are undergoing emergency and elective arterial procedures [2]. Despite an overall improvement in the surgical outcomes of older adults, the combination of physiologic changes inherent to aging and the cumulative effect of comorbidities induces adverse postoperative outcomes in some of these patients [2, 3]. In addition to medical factors, the decision to intervene on these patients must also be weighed against several additional issues unique to the geriatric population including patient frailty, individual and family preferences, as well as quality of life. Because vascular disease primarily affects older adults, this is especially relevant to vascular surgeons and other practitioners who specialize in vascular interventions. As the population ages and life expectancy continues to increase, vascular surgery will play a key role in the treatment of geriatric patients. In this chapter, we will discuss perioperative factors, as well as some issues unique to each of the more common vascular maladies seen in contemporary geriatric populations (Table 1).

Perioperative Risk Factors and Anesthesia

Geriatric patients undergoing vascular interventions often have multiple perioperative risk factors, including diabetes mellitus (DM), coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), renal impairment, and cognitive decline. Preoperative assessment is extremely important in this population, and optimization of these factors will undoubtedly lead to improved

Table 1 Considerations in older adults with vascular diseases

1. Older adults are considered high risk for vascular surgery given their age, comorbidities, pathophysiology of occlusive/aneurysmal disease, poor functional status, muscle wasting, and risk for vascular dementia
2. Preoperative risk assessment using various risk-assessment measures and comprehensive geriatric assessments are associated with lower complication rates, shorter length of hospital stay, and decreased likelihood of being discharged to a facility with higher level of functional dependency
3. There is role for use of regional anesthetic techniques and multimodal opioid sparing analgesic pathways in vascular patients
4. Asymptomatic carotid disease should be carefully considered for medical management versus surgical intervention
5. Older adults often present late with PAD; have a high degree of suspicion for PAD with walking impairment and functional decline
6. Consider toe-brachial index (TBI) with suspected peripheral artery disease (PAD) given the high prevalence of medial calcific disease
7. Invasive diagnostic procedures with contrast should be approached with caution given incidence of contrast nephropathy
8. Consider high index of suspicion for abdominal aorta aneurysm (AAA) especially smokers, as they could present with chronic symptoms
9. Frail patients may be considered for watchful waiting for aneurysm repair if risk of surgery outweighs the risk of rupture
10. Decision to intervene should be patient and procedure specific with utilization of adjunctive medical therapies, palliative care, and shared decision-making

outcomes. To that end, observational and randomized studies have demonstrated that comprehensive preoperative geriatric assessment is associated with lower complication rates, shorter length of hospital stay, and decreased likelihood of being discharged to a facility with higher level of functional dependency [4].

Older adult patients with functional impairment are found to be at high risk for perioperative complications [4]. Efforts are often made to avoid general anesthesia in these patients, as it is considered to be riskier than other anesthetic options and may lead to higher rates of complications. However, this may not always be the case. A study by Moriera et al. [5] examined a geriatric cohort with functional impairment undergoing major lower extremity amputation and stratified outcomes by anesthetic type. The authors concluded that the mode of anesthesia did not have any significant effect on perioperative outcomes. On the contrary, several other studies have proved that regional anesthesia for lower extremity bypass in critical limb ischemia, as well as, for vascular access cases, improved cardiopulmonary outcomes and postoperative mortality when compared to general anesthesia [6, 7]. The decision regarding type of anesthesia should be individualized to the patient, associated comorbidities, and specific procedure. Communication between the surgical and anesthesia teams is of paramount importance in order to devise the safest anesthetic plan for each unique situation.

Peripheral Arterial Disease

The rate of peripheral arterial disease (PAD) is increasing, with a current prevalence of 10–14% in the Western world [8]. This is especially true of older adult patients: In a large database of over 3.6 million screened subjects, the prevalence of PAD increased with each decade of life [9] and nearly 25% of adults over the age of 80 years in the United States carry a diagnosis of PAD [10]. The economic burden related to this situation is significant. In 2001, 6.8% of U.S. Medicare recipients were treated for PAD, with an estimated cost of $4.3 billion [11]. Data from the REduction of Atherothrombosis for Continued Health (REACH) Registry estimated the total costs of vascular-related hospitalizations was $21 billion in the United States in 2008, with the majority of costs associated with revascularization procedures [12, 84]. A recent study found that annual costs attributed to chronic limb ischemia was ~$12 billion [85].

Symptomatic PAD can present either as intermittent claudication, ischemic rest pain, or tissue loss, with the latter two being grouped together as critical limb ischemia (CLI). As the median life expectancy has increased, the incidence of CLI has exponentially risen among the aging population [13]. Less invasive, endovascular procedures for CLI are attractive options for older patients since they can be performed without the need for general anesthesia. However, there is little objective evidence on the best management strategy for this cohort [13].

Currently, the US Preventive Services Task Force concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening in asymptomatic patients [14, 15]. Interestingly, owing to a more sedentary lifestyle, older adult patients may not present with symptoms of claudication and often present only when PAD is more advanced. In addition, comorbidities of older adults, such as neuropathy, vertebral injuries, cardiopulmonary disease, or degenerative joint disease, can mask or mimic symptoms of PAD. For this reason, aortoiliac disease may go undetected. Patients often develop multilevel disease by the time of onset of CLI and may not undergo their first vascular intervention until later in life [16]. Hence, there should be a high degree of suspicion for PAD in the older adults and more research is needed regarding use of routine ABI screening in older adults.

Noninvasive Imaging

Noninvasive testing of older adult patients is well tolerated and should generally be the first imaging modality employed. Ankle-brachial index (ABI) is an excellent screening test for PAD, although intervention will generally still be driven by symptoms. ABI also provides an objective measure of perfusion to follow revascularization. Older patients have higher propensity develop medial calcification in their tibial vessels, which is known to falsely elevate the ABI [16]. This is especially true in older adults with diabetics [86]. In such cases, the toe-brachial index (TBI) may be more helpful, with values of <0.7 are consistent with small vessel disease [17]. Waveform analysis by pulse volume recording (PVR) can also be particularly helpful in determining the degree of vascular compromise in calcified vessels (Fig. 1). In patients with abnormal screening tests, further noninvasive testing can be performed with arterial duplex ultrasound to localize the lesion. For patients with absent femoral pulses or suspicion of supra-inguinal disease on duplex or PVR testing, CT- or MR-angiography may be of some use (Fig. 2). However, these modalities are limited in their ability to evaluate smaller blood vessels, especially calcified vessels below the knee. Moreover, higher rates of renal dysfunction in the older population may portend increased risk from contrast administration.

Invasive Imaging

Angiography is considered as the gold standard for evaluating occlusive vascular disease and will often confirm the findings noted on ultrasound. However, there is currently little use for this invasive procedure for diagnostic purposes, given the high precision of noninvasive testing. Elderly patients generally have lower creatinine clearance and should be considered high risk for kidney injury regardless of their baseline creatinine [18]. For this reason, angiography as a diagnostic tool should be avoided whenever possible. However, there is one exception when the benefits of angiography outweigh its concern for use. It is when patients are being considered for bypass surgery; in this case, angiography is helpful in identifying an appropriate distal target and may be considered for investigation.

Decision for Intervention

Maximizing medical therapy is important in the geriatric population, given the inherent risks of intervention. Optimal management consists of lifestyle changes such as smoking cessation and exercise, control of comorbid conditions including diabetes and hypertension, and optimizing medications to include low dose aspirin and statins [14]. Perhaps owing to increased complexity, medical management of older patients by vascular medicine specialists has been shown to improve outcomes when compared to the management provided by standard primary care physicians [19]. Elderly patients with atherosclerosis are often not on optimal medical therapy [20].

The decision to intervene on an older adult patient with PAD follows a slightly different algorithm than for their younger counterparts. For patients with intermittent claudication, the bias should be towards noninvasive management.

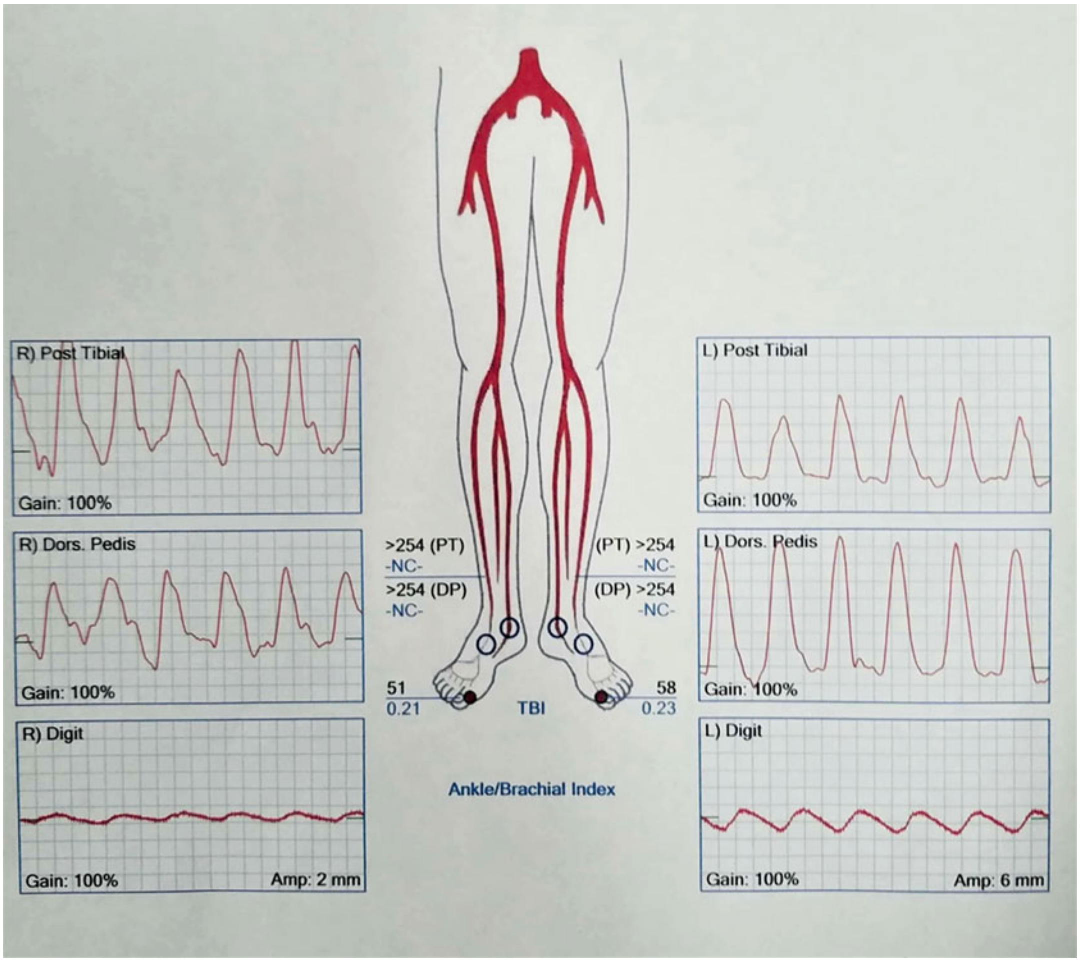

Fig. 1 Diagrammatic representation of a noninvasive methods of diagnosing peripheral artery disease (PAD) in the elderly population including the ankle-brachial index, toe-brachial index (TBI), and pulse volume recording (PVR) waveforms

Many studies have explained the benefits of supervised exercise programs with regard to disease stabilization and improvement in symptoms [21–23], and avoidance of invasive procedures in geriatric patients may be prudent. The use of oral agents such as cilostazol can also prove helpful in claudicants [21, 24]. For CLI, intervention should be undertaken in all but the sickest of patients due to the high risk of limb loss.

Endovascular Versus Open Surgical Revascularization

Although surgical bypass remains the gold standard for revascularization, more often than not a less invasive, endovascular approach is preferable [25]. Despite some positive institutional studies suggesting no increase in wound complications, amputations, or graft failures in octogenarians, many are reluctant to offer lower extremity bypass surgery to this cohort, attributed to the comorbidity burden in the older adults and risk of procedural complications such as wound complications, delirium, and high post-acute care needs [13, 26, 27].

When comparing octogenarians and nonagenarians with critical limb ischemia undergoing lower extremity bypass versus endovascular intervention, limb salvage at 1 and 2 years were similar between the two groups with a low associated mortality [13]. These and other authors have

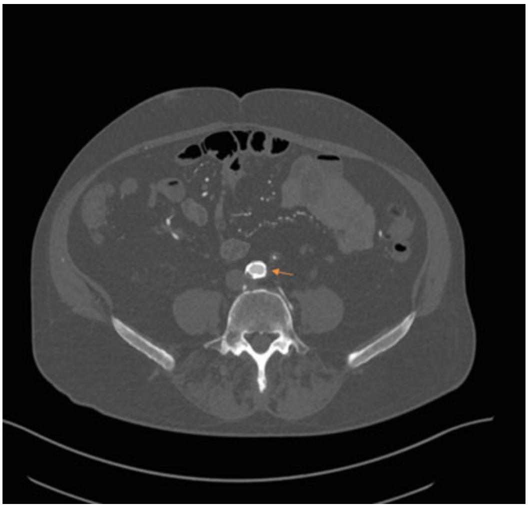

Fig. 2 Axial computed tomography showing vascular calcification present concentrically in the aorta (red arrow)

thus concluded that endovascular revascularization of this high-risk group is feasible and effective, with similar primary, assisted primary, and secondary patency rates [13, 27].

Geriatric patients for whom endovascular intervention is not an option should still be considered for bypass surgery and should not be excluded simply because of their age. For patients with intermittent claudication, the Society for Vascular Surgery (SVS) recommends that open surgery be offered if the patient will have reasonable likelihood of sustained benefit for at least 2 years [14]. Of course, this is particularly relevant to the older adult population. For elderly patients with multiple comorbidities though, less is often more. For example, geriatric patients with aortoiliac occlusive disease may be better served by a less invasive, extra-anatomic revascularization rather than inline reconstruction (e.g., axillo-bifemoral bypass versus aorto-bifemoral bypass). Additionally, for lower extremity disease, it may be appropriate to perform limb salvage procedures with non-autogenous conduits. This is often a more expedient approach to revascularization, and long-term patency rates are often overshadowed by the patient's short life expectancy. One institutional study looked specifically at outcomes in very elderly patients who underwent distal bypass for CLI. The authors found no difference in outcomes based on age alone, reporting similar data for patency, limb salvage, survival, and amputation-free survival. They recommended against using age alone as a determining factor for the decision to proceed with open surgery [27, 28].

Endovascular procedures can often be performed under local anesthesia, require less operative time, and have minimal blood loss [87]. However, endovascular therapy is not the panacea for geriatric patients, and they still must be optimized prior to these less-invasive interventions. Currently, there is a head-to-head trial underway in the United States, Best Endovascular versus Best Surgical Therapy in patients with Critical Limb Ischemia (BEST-CLI) to evaluate endovascular versus open first approach for patients with CLI that may provide contemporary data for treatment of older adults [29]. Overall survival and limb salvage rates are significantly reduced in older patients with poor nutritional status [30]. In addition, patients who are wheelchair bound, bedridden, or on dialysis all have increased risk of mortality following endovascular intervention for critical limb ischemia [30].

Amputation

Amputation has traditionally been reserved for patients without further revascularization options or for those with non-salvageable extremities due to extensive gangrene. However, amputation may also be considered first-line treatment in certain subsets of patients. Older adults who are non-ambulatory at baseline or whose functional status is so poor as to render revascularization senseless may benefit from primary amputation and faster discharge to home. Patients with comorbidities that prohibit extensive surgical revascularization should be considered for primary amputation, as well [31]. However, amputation is not without its own risks. A recent meta-analysis identified coronary disease, cerebrovascular disease, renal dysfunction, and dementia as independent predictors of increased mortality following major lower extremity amputation; these risk factors are more prevalent in the older adult population [32]. Even following successful amputation, rehabilitation programs can be challenging due to frailty and overall poor functional status. Geriatric patients also do poorly with amputation with regard to maintaining their independence [31]. Occasionally, patients will be deemed fit for neither an attempt at limb salvage nor an amputation, in which case terminal wound care is a potential alternative, with the goal to prevent infection and minimize pain and hospitalization time.

Acute Limb Ischemia

Acute arterial occlusion can also lead to significant morbidity in older adults, even in the absence of preexisting PAD. Patients may present with acute onset of unilateral pain, paralysis, and/or neurologic changes. Often, there will be a contrastingly normal vascular exam on the unaffected side. Atrial fibrillation, which is extremely prevalent in geriatric patients, is a significant cause of peripheral emboli [33]. In contrast to chronic PAD, and just as in younger patients, acute arterial occlusion is a surgical emergency and prompt restoration of blood flow is imperative to limb salvage. The age of the patient should not in itself be a factor in determining the strategy for revascularization in these instances: Limb salvage rates after surgical intervention for acute lower limb ischemia in the older adult population are comparable to those of the younger population [34]. However, thrombolysis has been associated with high risk of complications and should be undertaken with caution [20].

Extracranial Carotid Disease

Unsurprisingly, the overall increase in atherosclerotic diseases with age translates to an increased risk of carotid artery disease and ischemic cerebrovascular events [35]. However, finding the optimal treatment strategy for these patients is not always straightforward. In symptomatic patients, age was found to be an independent risk factor for stroke for patients treated with medical management alone, which would suggest that a more aggressive approach is warranted [36]. However, outcomes with carotid revascularization are poorer with advanced age as well. In the Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST) trial, older patients undergoing carotid stenting had a higher periprocedural stroke risk than their younger counterparts [37]. Furthermore, geriatric patients undergoing endarterectomy have demonstrated higher risk of in-hospital stroke and mortality [38]. Unfortunately, though, level 1 data is lacking, as most prospective and randomized trials have excluded patients older than 80 years old. One large registry study of over 1900 patients undergoing endarterectomy examined the 80-plus cohort and aimed to identify specific outcomes and survival [39]. The authors found no difference in stroke rates between patients older or younger than 80 years. However, the older group did have significantly higher perioperative mortality (1.9% vs. 0.8%), as well as a higher combined stroke/death rate. Interestingly, this was primarily attributable to differences among symptomatic patients on subgroup analysis, with asymptomatic octogenarians having similar stroke/death rates to the younger cohort. Ultimately, the authors concluded that despite the higher combined stroke/death rate, the outcomes fell within acceptable national guidelines and that geriatric patients could still derive benefit from surgery when compared to best medical therapy alone [39]

Another study from the Carotid Artery Revascularization and Endarterectomy (CARE) registry looked retrospectively at over 4000 patients, both symptomatic and asymptomatic. In contrast to the previously discussed study, there was a significant increase in mortality seen among asymptomatic patients over 75 years old, but no such difference was noted in symptomatic patients [40].

Given these contradictory findings in multiple studies, it is important to base the decision for revascularization on each patient's "physiologic age" and known risk factors, rather than their chronological age alone [39, 41–43].

As with younger patients, management of carotid arterial disease begins with risk factor modification. This is true both for patients receiving medical therapy alone and those undergoing revascularization. Hypertension, cigarette smoking, diabetes mellitus, left ventricular hypertrophy, increased age, prior stroke, transient cerebral ischemic attack, extracranial arterial disease, obesity, and coronary heart disease have all been shown to be risk factors for stroke among geriatric patients specifically [44–46]. Optimization of these factors is of paramount importance, and patients should universally be on daily low-dose aspirin and statin therapy.

Management of the Symptomatic Patient

The major prospective, randomized clinical trial for determining treatment of patients with symptomatic carotid stenosis was the North American Symptomatic Carotid Endarterectomy Trial (NASCET) [47]. Unfortunately, NASCET included an age cutoff of 80 years, which limits its applicability to patients over 80. However, some of this level 1 data can be extrapolated to those patients. NASCET was terminated early because of the high stroke rate seen in the medical therapy arm for high-grade stenosis (i.e., >70%), and the significant stroke reduction provided with CEA at only 3 months follow-up [43–47]. NASCET also showed that there does not appear to be an increase in operative risks owing to age alone, with the caveat again that this only applies to patients under 80 years old. In general, the majority of practitioners treating patients over 80 years old still follow the guidelines stemming from this pivotal trial. The Society for Vascular Surgery (SVS) currently recommends carotid endarterectomy as the first-line treatment for most symptomatic patients with stenosis of 50–99%, without any exception made for age [48].

Management of Asymptomatic Patient

The Asymptomatic Carotid Atherosclerosis Study (ACAS) demonstrated a significant decrease in 5-year stroke risk among asymptomatic patients with >60% stenosis who underwent carotid endarterectomy versus those who were treated with best medical therapy (11% vs. 5%) [49]. Like the NASCET trial though, ACAS only included patients less than 80 years of age. Again, this data must be extrapolated to the elderly population. Unlike in symptomatic patients, asymptomatic patients do not derive significant benefit in stroke reduction from CEA until approximately 5 years of follow-up. Currently, SVS and AHA guidelines recommend consideration of CEA for asymptomatic patients with stenosis of 60–99% provided the patient has a life expectancy of 3–5 years and perioperative stroke/death rates are ≤3% [48]. However, these guidelines lack specificity and are do not consider medical therapy, which according to many contemporary studies, now carries an annual stroke risk of <1% [50–52]. The ongoing Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis Trial (CREST-2) is a combination of two trial arms assessing treatment differences between intensive medical management alone compared to carotid endarterectomy (CEA) and carotid stenting (CAS) both with intensive medical management with no upper age limit to gather evidence for elderly carotid stenosis patients as well [53].

Endarterectomy Versus Stenting

Prior to the CREST trial, most assumed that stenting would be a better option for older patients given the less invasive nature of the procedure. However, overall outcomes in CREST were slightly better after carotid stenting in patients aged <70 years, and better after endarterectomy in the patients age >70 years [54]. Current SVS guidelines reflect this, recommending endarterectomy over carotid artery stenting in patients aged >70 years of age [48]. Additionally, a recent meta-analysis pooled data from four major randomized trials of stenting versus endarterectomy and found that older patients (≥65) had a significantly increased risk of periprocedural stroke and death with carotid stenting (HR = 2.16). The same was not true of CEA patients [55].

Although some smaller studies quote similar stroke rates between groups, the majority of carotid stent data has shown increased incidence of stroke in elderly patients compared to younger patients [43, 56–59]. However, carotid endarterectomy has been associated with increased mortality in older age groups [56, 58]. Data from CREST showed a higher myocardial infarction rate with CEA compared to stenting, which should disproportionally affect older patients with higher rates of underlying cardiac disease [60].

The most consistent data regarding safety and efficacy of carotid stenting remarks that the key to obtaining excellent results centers around high volume, experienced operators who exercise careful patient selection [57, 58]. According to the SVS guidelines, carotid artery stenting should be reserved for symptomatic patients with stenosis of 50–99% who are at high risk for carotid endarterectomy for anatomic or medical reasons [48]. Currently, carotid artery stenting is not recommended for asymptomatic patients. Again, without specific level 1 data, these guidelines should be applied to the geriatric population as well.

Aneurysm Disease

Epidemiology and Clinical Presentation

Abdominal aortic aneurysms (AAA) are a common disease of older adults with the greatest increase in incidence seen in men after the age of 55 and women after the age of 70 [61]. The epidemiology of abdominal aortic aneurysm is characterized by a large male predominance, and disproportionally affects Caucasian males [56, 61]. However, the incidence in women increases with age and approaches that of a male after the seventh decade of life [61]. The prevalence of AAA is five times higher in men than women and increases with age. AAA rates are reported as 1.3% in men and nearly 0% in women aged 45–54 years, and 12.5% in men and 5.2% in women aged 75–84 years [31].

The US Preventive Services Task Force recommends screening for AAA with abdominal duplex ultrasonography in all men aged 65–75 years old who have ever smoked and selectively in men who have never smoked [31]. Unless there is a family history of aneurysm, there is inconsistent evidence to support screening ultrasounds in women [31, 62].

While most often asymptomatic, presenting symptoms of AAA in older adults can be quite varied and include abdominal or back pain, failure to thrive due to mesenteric ischemia, acute renal failure, and distal thromboembolic disease (i.e., “blue toe syndrome”) [31, 63, 64]. A high index of suspicion is particularly important in the elderly population, as many older patients have chronic symptomatology, which can mask aneurysm-related findings. This may be one reason why octogenarians are more likely to present with ruptured aneurysms than are younger patients, in addition to the fact that octogenarians are more likely to have larger aneurysms [65].

Decision to Intervene

The Society for Vascular Surgery recently released updated guidelines on the management of abdominal aortic aneurysms [66]. Consistent with prior recommendations, there are no specific considerations for age as a determining factor for intervention. However, increasing age has been shown to correlate with poorer outcomes in a number of studies. A large, retrospective study of Medicare patients identified age as an independent predictor of mortality for both endovascular and open repair [67]. The Vascular Quality Initiative (VQI) now also includes age in its mortality risk prediction model for elective aneurysm repair, based on the results of a study from the Vascular Study Group of New England, which were subsequently validated against the VQI database [68]. The SVS guidelines include a recommendation to use this risk prediction model when determining overall fitness for aneurysm repair and therefore include age as an indirect factor to be considered. As such, the decision to intervene should be made on an individual, case-by-case basis. Age itself should be of secondary concern, with more emphasis placed on comorbid conditions and anatomic considerations. Frailty has been shown to be an independent risk factor for morbidity, mortality, and failure to rescue in abdominal aortic aneurysm repairs [69].

Open Versus Endovascular Repair

The consensus from the large, prospective, randomized trials of endovascular aneurysm repair (EVAR) versus open surgical repair of AAA indicate that there is an initial reduction in postoperative mortality with EVAR, with no difference in long-term mortality and increased rates of re-intervention. The mortality benefit may be more pronounced in older patients leading to an overwhelming majority of AAA repairs being done in the United States now being performed using an endovascular approach [70]. A recent analysis of over 45,000 propensity-score-matched Medicare demonstrated a lower mortality after EVAR than open surgical repair (1.2% vs. 4.8%), with the most pronounced and durable reduction in mortality seen in those of advanced age (80–84 years: 1.6% vs. 7.2%; $\geq$ 85 years: 2.7% vs. 11.2%) [71]. This difference among octogenarians is consistent with the anticipated benefits of a less invasive intervention, particularly among patients at high risk for perioperative morbidity and mortality.

Open abdominal aortic aneurysm repair in geriatric patients has largely been abandoned since the widespread adoption of EVAR, in part, owing to the perception that these patients are generally not fit for open surgery. In the United Kingdom Small Aneurysm Trial, increasing age was found to be an independent risk factor for perioperative mortality following open repair [72]. For octogenarians who have undergone open repair since the adoption of EVAR, the repair is often more complex: utilization of a retroperitoneal approach, suprarenal clamp position, ligation of the left renal vein, and longer operating room times have all become more common in the post-EVAR era [73]. This is presumably because more simple aneurysms are being preferentially treated with EVAR, with open repair relegated to those patients without a good endovascular option. However, open aortic surgery should not be totally dismissed based on age alone. Studies involving patients $\geq$80 years old undergoing elective open repair demonstrated an overall perioperative mortality rate of 5.6%, which was not statistically different from that of endovascular repair (4.5%) [65]. The authors do acknowledge a significant potential for selection bias though, and the EVAR mortality of 4.5% is much higher than one would anticipate. Nevertheless, in carefully selected patients with good perioperative risk profiles and good life expectancy, open AAA repair may provide a durable solution. A recent analysis of the national Vascular Quality Initiative (VQI) registry showed frail patients undergoing endovascular and open aneurysm having threefold higher long-term mortality with 1-year mortality rates being 15–20% for both open and EVAR repairs in frail patients, much higher than published randomized clinical trial data. Furthermore, 45.0% of patients underwent elective AAA repair at less than the recommended 5.5 cm diameter threshold. In frail patients, 35.6% underwent EVAR and 22.2% underwent open repair with aneurysms measuring <5.5 cm, suggesting a role for shared decision-making and possibly higher threshold for aneurysm repair in frail patients [74]. Ongoing studies show potential medical therapies for slowing progression of aneurysmal disease [75, 76].

Frailty

Frailty is defined as patient vulnerability to minor stressors due to physiological decline across multiple organ systems [2]. Predictably, many elderly patients undergoing vascular interventions meet this definition, especially given the multisystem effects of vascular disease in general [2]. Frailty is associated with several known atherosclerotic risk factors including hypertension, hypercholesterolemia, and smoking, and frailty itself is a known risk factor for adverse outcomes [2]. Frailty and sarcopenia are more prevalent in vascular surgery patients given the pathophysiology of vascular atherosclerotic and aneurysmal disease along with walking impairments, functional decline, and comorbid vascular dementia. Despite overlap of frailty and sarcopenia, diagnosis of frailty is an independent predictor of mortality and had the strongest prognostic significance in patients undergoing both surgical and nonoperative management [77].

Cognitive decline is an important factor in determining patient frailty. Eight percentage of critical limb ischemia patients 70 years old or greater suffer from dementia [78]; this frail group of older adults has high overall mortality rate of 52% within 1 year, and poorer limb salvage rates [78]. Even for those without overt cognitive issues preoperatively, postoperative delirium can often complicate the postoperative course. Delirium has been linked to higher mortality and longer institutionalization [79] and is most commonly seen following open aortic surgery, followed by peripheral arterial revascularization and amputation [79, 80]. Many factors have been associated with increased risk of delirium, including depression, smoking, alcohol use, visual and hearing impairment, ASA-score, biochemical abnormalities, and blood loss [79, 80]. The strongest risk factors for development of delirium are age and preexisting cognitive impairment [79, 80].

There are several frailty measures that can be employed during preoperative planning to ensure proper risk-stratification [81, 82]. One study, looking at preoperative risk factors for a nonhome discharge following elective vascular surgery procedures, concluded that frail patients are at a twofold increased risk of not returning home after surgery [83]. The authors therefore suggest that preoperative frailty assessments should be used to aid in counseling regarding postoperative disposition [83]. Preoperative assessment and optimization has also been shown to decrease hospital length of stay and increase chance of a home discharge [3]. Furthermore, preoperative risk stratification using geriatric specific tools can help shared decision-making and utilization of palliative care services in complex decisions surrounding vascular care of patients [84, 85].

Conclusion

The geriatric population has significant vascular disease prevalence. Clinicians specializing in vascular interventions should systematically consider geriatric-specific management pathways. The decision to intervene in older patients with vascular conditions should be carefully weighed in, and the type of intervention should be patient-specific. Further, preoperative risk assessment tools based on frailty have the potential of guide complex decisions surrounding vascular care of patients.

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36 Pulmonary Surgery for Malignant Disease in Older Adults

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Abstract

The majority of pulmonary surgery is performed for lung cancer, which is a disease of older adults. The median age of diagnosis of lung cancer in the United States is 71 years and over 65% of patients are diagnosed after age 65. Importantly, the decision to treat this cancer surgically should not be based on chronologic age alone, but on physiologic factors and a patient's personal goals of care.

Physiologic changes of normal aging include decreased chest wall compliance and strength, increased residual volume and functional residual capacity, and an attenuated response to both hypoxemia and hypercapnia. Therefore, preoperative evaluation must include, in addition to routine assessment of cardiac and renal function, an evaluation of respiratory capacity; this can range from basic spirometry to full cardiopulmonary stress testing and quantitative ventilation/perfusion scanning. Geriatric assessments of cognition, frailty, function, and nutrition should be added.

Operative risk in the older adult is largely attributable to loss of functional lung tissue and pain/stress of the thoracic surgical approach. There is growing evidence that minimally invasive surgery is beneficial in the older adult. Limited resections such as segmentectomy or wedge resection, compared to formal lobectomy, should be considered a compromise treatment but are acceptable in the older adult with major morbidity or shorter expected life span. Resection should also be considered for pulmonary carcinoid and pulmonary metastases.

Specialized multidisciplinary postoperative care and attention to detail perioperatively holds great benefit for the older adult thoracic surgery patient.

Case Study

Ms. Jones is a 78-year-old female who recently fell in her kitchen, striking her rib cage against the counter. X-rays in the emergency department showed no rib fractures but did reveal an incidental unsuspected lung mass in the middle of the left lung. This led to a CT scan that showed a 2 cm spiculated nodule in the superior segment of the left lower lobe with no mediastinal adenopathy.

Ms. Jones had an appendectomy at the age of 16 and a cholecystectomy at the age of 48. She has had no other surgeries. Four years ago, she had an episode of severe chest pain after a large meal that slowly resolved over the next day or so. She chose not to go to the hospital at that time. Ever since then she has developed swelling of her ankles that generally resolves when she lifts her legs to a stool at night. Not infrequently she awakens at night feeling shortness of breath and has trouble falling back asleep.

On evaluation Ms. Jones is generally in good health except for mild osteoporosis and arthritis affecting her hand and legs. She has no other constitutional symptoms. She slowly walks with assistance from a cane. Ms. Jones frequently has a glass or three of wine for dinner but has quit smoking after her fall last week. Recently, she was fitted for a hearing aid because she reports difficulty participating in conversations when she goes out to crowded restaurants with her family. She has been taking insulin over the past 2 years but sometimes forgets a dose. It seems to her that she takes a lot of pills and has trouble keeping them straight.

Ms. Jones is a widow and has been living alone for the past 6 years. Her two sons and their families live nearby. She prepares her own meals, cleans her home, and meets twice a week with the ladies in her building to play cards. Her older son has recently provided for a housekeeper to clean the apartment and help with the laundry once a week. She does not have a regular exercise program. She sees her grandchildren regularly. Of late, she has been relying on family and friends for help with grocery shopping and carrying bags into the apartment. She is no longer comfortable driving at night or for long trips. The recent fall was the second in the last 6 months. What are the next steps in managing Ms. Jones lung nodule?

Introduction

With the aging of the baby boomer population, the number of people in the United States over 65 is expected to nearly double by 2060. Currently 14.88% of the US population is over the age of 65, and this percentage is projected to increase to 23.55% by the year 2060. The average life expectancy in the United States is 78.9 and projected to increase to 85.6 by 2060 [1–4]. Older patients increasingly present for consideration of thoracic surgery, and determining the best management for this group of patients will be a more frequent challenge in the future. While elderly patients present with a spectrum of thoracic disease, both benign and malignant, patients with cancer comprise the largest and most studied subset of this population.

Lung cancer is a disease of the elderly. The median age of diagnosis for lung cancer in the United States is 71 years, and over 65% of patients are diagnosed after age 65. National Cancer Institute statistics indicate that lung cancer is the leading cause of cancer mortality in men and women [5, 6]. Between 2010 and 2014, the US death rate for ages under 65 was 12.4 per 100,000, while the incidence for 65 years and older was 268.5 per 100,000 [7].

Non-small cell lung cancer (NSCLC) comprises 80–85% of primary lung tumors, small-cell lung cancer (SCLC) makes up 15–20%, and 1–2% are pulmonary carcinoid [8–10]. SCLC is usually widely metastatic at time of diagnosis, and rarely under the purview of the surgeon, however, the percentage of lung cancer patients with SCLC histology falls with age [10]. Surgical resection of NSCLC and pulmonary carcinoid offers the best chance for oncologic cure. Additionally, retrospective evidence suggests that resection of isolated metastases to the lung may improve survival.

The decision to undergo surgical resection for malignant disease should not be based on age alone. An understanding of the unique qualities of this patient population has led to improved surgical outcomes for the elderly over the last several decades.

Patient evaluation, selection, and perioperative management must all be adapted to provide best possible care for the increasing numbers of aged patients undergoing surgery for cancer. Management of an elderly lung cancer patient requires a global consideration of the characteristics of aging, differences in tumor presentation and histology, and comorbidities that tend to accumulate over time. The initial interview with a patient and family members is used to elucidate important variables that may impact operative risk and expectations of the recovery process. These questions should elucidate the current independent status of the patient, social supports, mood, and signs of reduced activity or physical limitations. After all, the elderly population is a heterogenous group of patients ranging in functional reserve from the surprisingly well-preserved to the wheelchair-bound invalid.

Physiologic Changes of Age

Physiologic changes of the respiratory system associated with aging include reduced chest wall compliance with stiffening of calcified costal cartilages and narrowing of the intervertebral disc space. A progressively restricted rib cage is sometimes accompanied by increased diaphragmatic excursion. Postoperative weakness of a hemidiaphragm in this group can lead to otherwise unexplained respiratory failure. There is also a reduction of lung elastic recoil with loss of alveolar architecture producing a decreased alveolar gas exchange surface. Progressive atrophy creates weakness of the respiratory musculature. Additionally, there is a decrease in central nervous system responsiveness. The loss of lung elastic recoil and decreased lung compliance diminishes negative intrapleural pressure, which then prevents reopening of the small airways, resulting in air trapping and inadequate ventilation. Functionally this manifests in a gradual decline of vital capacity and partial pressure of oxygen (P_{02}), with an increase in residual volume. Decline in motor power of the accessory muscles and a stiffening of the chest wall also result in a declining forced expiratory volume in 1 s (FEV1). Changes in lung compliance are not uniformly distributed. Higher respiratory rates therefore increase ventilation-perfusion mismatch. The elderly also exhibit a blunted ventilatory response to both hypoxic and hypercapneic insults [11, 12]. Physiologic changes in lung mechanics make elderly patients particularly sensitive to narcotics and muscle relaxants, as well as to supine positioning. Elderly patients are also at increased risk for respiratory tract infections, due to waning immune responses [13]. Smoking in particular has been shown to cause bronchial mucociliary dysfunction [14], which has been associated with increased susceptibility to infection [15]. Finally, elderly patients with marked kyphosis and accompanying paraesophageal diaphragmatic hernias are at particular risk for postoperative aspiration.

Increasing age is associated with declines in other organ systems as well. There is a decline in glomerular filtration rate, an increasing incidence of heart disease, and an increasing incidence of cognitive dysfunction. Changes in body composition decrease the volume of distribution of water-soluble drugs [16]. Additionally elderly patients take more medications than younger patients and are vulnerable to adverse drug effects such as altered mental status.

Preoperative Evaluation

Elderly patients are at increased risk for preoperative morbidity and mortality due to both comorbid conditions and decreased ability to recover physiologic homeostasis after surgical stress. Older patients represent a heterogeneous population and should be offered surgery based on physiologic rather than chronological age. A thorough preoperative assessment is imperative to determine whether a patient is an appropriate surgical candidate and to predict and avoid postoperative complications. Numerous risk assessment tools have been created to define preoperative variables that correlate with poor outcomes; however an easy to use, strongly predictive tool has been elusive. Geriatric assessment tools aimed at predicting outcomes in the specific elderly surgical population remain under study.

All patients in consideration for lung cancer resection surgery require a complete history and physical exam with particular attention to characterization of symptoms, smoking history, and weight loss. At a minimum, patients should undergo a chest X-ray, electrocardiogram, a room air arterial blood gas, pulmonary function tests for patients undergoing lung resection, and basic laboratory work. Further workup can be determined based on symptoms or the status of comorbid conditions.

Accurate diagnosis and staging is of utmost importance to ensure that patients are appropriately chosen for operative resection. Elderly patients should have radiographic and surgical staging of suspected lung cancers in the same manner as younger counterparts. Only after the exact stage is known can rational treatment decisions be made. Therefore, elderly patients should have chest CT scans to image suspected lung nodules, PET scans to look for metastatic disease, brain scans to look for occult metastases, and (if indicated) cervical mediastinoscopy to stage mediastinal nodes. Elderly patients with suspected lung nodules should not be denied this standard workup unless their functional status is so impaired that treatment is not possible.

Cardiac Risk Assessment

The American Heart Association (AHA) and American College of Cardiology (ACC) published a readily accessible consensus practice guideline for perioperative cardiovascular evaluation for non-cardiac surgery that provides a template for assessing patients of all ages [17]. The AHA/ACC guidelines describe a stepwise approach to preoperative surgery with risk stratification and further imaging determined by utilizing symptoms, clinical predictors, and functional capacity. Clinical history should focus on assessment for coronary risk factors and physical capacity including the ability to climb two flights of stairs or walk one block. In general patients with poor functional status or patients with a history of angina or claudication should undergo noninvasive testing. In thoracic surgery patients, it may be difficult to determine if symptom etiology is the result of cardiac or pulmonary pathology; thus it is appropriate to have a low threshold for additional cardiac imaging and assessment by a cardiologist to assist with risk stratification.

Supraventricular tachycardias are very common after thoracic surgery, with increased risk for older patients or those with a faster preoperative heart rate [18]. The risk of postoperative atrial fibrillation is 19% in patients undergoing lung resection for cancer [19]. Randomized trials of thoracic surgery patients have determined that calcium channel blockers or beta-blockers can reduce the incidence of postoperative atrial fibrillation by 50–60%; however beta-blockers were associated with an increased risk of pulmonary edema. Neither class of medication reduced mortality. Three trials showed that digitalis increased the risk of atrial arrhythmias [20]. Beta-blockers and calcium channel blockers will both reduce postoperative atrial fibrillation; however beta-blockers are preferred by some due to their broader benefits of cardiac risk reduction. On the other hand, up to half the doses of postoperative beta-blocker may have to be held due to transient hypotension or bradycardia, leading others to recommend the use of calcium channel blockers.

Pulmonary Risk Assessment

All patients considered for lung resection surgery should have pulmonary function tests performed. FEV1 by spirometry is the most common measured value used to determine a patient's suitability for surgery. Data obtained in the 1970s from over 2000 patients showed a $<5\%$ mortality rate for patients with an FEV1 > 1.5 L for lobectomy and >2 L for pneumonectomy [21, 22]. Absolute values for FEV1 may create a bias against older people; however a value of $>80\%$ of predicted has been quoted by some as sufficient for a patient to undergo pneumonectomy without further pulmonary testing [23]. In reviewing more recent spirometry studies performed from 1994 to 2000, Datta and Lahiri concluded that in NSCLC patients, increased postoperative morbidity and mortality were predicted by an FEV1 of <2 L or $<60\%$ for pneumonectomy, an FEV1 of <1.6 L for lobectomy, and FEV1 of 0.6 L for wedge or segmentectomy [24].

Lung resections have of course been undertaken in patients with much poorer lung function. In 2005 Linden et al. published data from a series of 100 consecutive patients with preoperative FEV1 of $<35\%$ predicted undergoing lung tumor resection. In this series there were 1% mortality rate (single case of perforated colonic diverticulum) and 36% complication rate. Morbidity was dominated by 22% of patients with prolonged air leaks. Eleven patients were discharged with a new oxygen requirement, and four patients developed pneumonia. Only one patient was discharged on a ventilator, and three other patients required intubation for >48 h [25].

Ferguson et al. found preoperative diffusion capacity for carbon monoxide (DLCO) to be more predictive of postoperative mortality than FEV1 in a study of 237 patients. In this study a DLCO of $<60\%$ predicted was associated with increased mortality, and a DLCO of $<80\%$ predicted was predictive of increased pulmonary complications [26]. Other studies, however, have not found this parameter to be a significant predictor of postoperative complications [27, 28]. DLCO and spirometry may be used as complimentary tests, particularly in patients with diffuse parenchymal disease or dyspnea that is out of proportion to the FEV1, with a low DLCO prompting further evaluation [22] (Fig. 1).

Formal and simple exercise testing evaluates the cardiopulmonary system under induced physiological stress and also has been found to be predictive of postoperative complications. Girish et al. prospectively studied symptom-limited stair climbing

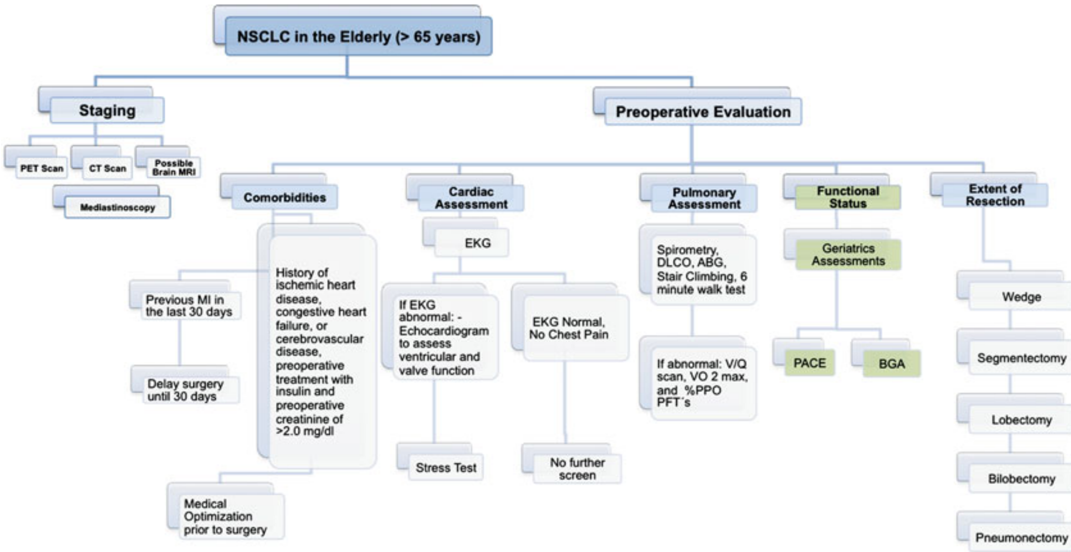

Fig. 1 Recommended pulmonary workup algorithm. *BGA* blood gas analysis, *CT* computed tomography, *EKG* electrocardiogram, *MI* myocardial infarction, *MRI* magnetic resonance imaging, *NSCLC* non-small cell lung cancer, *PACE* Preoperative Assessment of Cancer in the Elderly, *PET* positron emission tomography, *V/Q* ventilation/perfusion

in thoracic and upper abdominal surgery patients. No complications occurred in patients who could climb seven flights of stairs, while 89% of patients unable to climb one flight of stairs had complications. Inability to climb two flights of stairs had a positive predictive value of 80%. The ability of patients to climb stairs was found to be inversely related to the length of postoperative hospital stay [29]. The 6-min walk test (6MWT) measures the distance walked over a period of 6 min. In a qualitative review, Solway concluded that the 6MWT was easy to administer and more reflective of activities of daily living than other walk tests [30]. A normal patient should be able to cover 1400 ft in 6 min. While stair climbing and 6MWT are easy to perform, their use in elderly patients may be limited by orthopedic impairments, peripheral vascular insufficiency, or neurological impairments.

As published previously [31], a recommended preoperative pulmonary evaluation for an elderly patient should consist of spirometry, pulmonary diffusion capacity of the lung for carbon monoxide (DLCO), room air ABG, and exercise tolerance tests including stair climbing and 6-min walk. Patients with an FEV1 >1 L and no major abnormality of other tests (FEV1/FVC >50%, DLCO >50% predicted, ABG paO2 > 45 mm Hg, tolerance of exercise tests) may safely proceed with surgery, including pneumonectomy.

Further evaluations for patients who fall outside these criteria include VO2 max testing and ventilation/perfusion scans to calculate predicted postoperative (PPO) lung function. Measurement of maximal oxygen consumption (VO2 max) by formal cardiopulmonary exercise testing is helpful to further risk stratify patients with borderline lung function. A VO2 max value of <10 ml/kg/min had a very high operative morbidity (26% total in combined data) in several small case series. VO2 max values of 10–15 ml/kg/min had an intermediate perioperative morbidity (8.3% total), whereas patients with >15 mg/kg/min can proceed with lung resection surgery with an acceptable mortality rate [22].

A PPO FEV1 threshold of 0.8 L [32] or 0.7 L [33] has been suggested as a lower limit value for proceeding with lung resection. Absolute values of PPO FEV1 can underestimate postoperative lung function in people with small stature or the elderly and can thus be converted into percent-predicted postoperative (% PPO) lung function. Multiple studies have suggested that morbidity increases at a threshold % PPO FEV1 of <40% or a % PPO DLCO of <40% [26, 34–37].

Cognitive Assessment

One of the most important pieces of information for an elderly patient is the likelihood of returning to baseline physical and mental function after surgery. While patients and their families accept that there will be a postoperative recovery time in the hospital or rehabilitation setting, it is difficult to assess the magnitude of this functional decline and predict the risk of permanent loss of independence. There is a paucity of data assessing changes in quality of life after thoracic surgery in the elderly and few studies that assess whether surgery triggers postoperative loss of independence and change in need for assistance or living requirements. A study of 68 octogenarians undergoing pulmonary resections at Johns Hopkins Medical Institutions showed that 80% of patients were discharged directly home from the hospital rather than to rehab, offering some proxy information regarding immediate postoperative return to function [38]. Moller et al. published a study in 1998 that showed a 25% rate of cognitive dysfunction at 1-week postop from major non-cardiac surgery in elderly patients (average age 68), with continued dysfunction in 9% at 3 months [39]. Hshieh et al. found that elderly patients who experience postoperative delirium have a significantly worse trajectory of functional recovery [40]. Data from many studies verify a high incidence of postoperative cognitive dysfunction in the first week after surgery, and dysfunction does tend to increase with age. Only one other study has substantiated long-term declines over controls, and some have suggested that declines found in these studies may be due to random variation [41, 42]. Karneko et al. determined that preoperative dementia was a risk factor for postoperative delirium [43]. Furthermore, Fukuse et al. found that thoracic surgery patients with preoperative dementia, as estimated by the mini-mental status (MMS) exam, were fourfold more likely to have postoperative complications [44].

Geriatric Assessments

There are multiple assessment indices that have been applied to elderly patients to determine their risk for poor outcome. Functional status describes the ability to perform self-care, self-maintenance, and physical activities. Traditional measures used to assess functional status are activities of daily living (ADLs) and instrumental activities of daily living (IADLs). ADLs have six basic self-care skills, including the ability to bathe, dress, go to the toilet, transfer from a bed to chair, maintain continence, and feed one's self. IADLs include higher functioning skills that are used to maintain independence in the community. This scale assesses ability to use the telephone, go shopping, prepare food, perform housekeeping and laundry, use various modes of transportation, assume responsibility for medications, and handle finances. The need for assistance in these tasks has been predictive of prolonged hospital stay, nursing home placement, and home care requirements [45, 46]. Poor nutritional status, defined as a BMI <22 kg/meter squared, has been associated with increased need for assistance with ADLs and a decreased 1-year survival [47]. A lower ADL score is associated with postoperative complications [48]. The information source reporting a patient's functional status biases the results, with self-reported scores rating higher than scores reported by a significant other or nurse [49].

Performance status is a standardized scale designed to measure the ability of a cancer patient to perform ordinary tasks. There are two scales, the Karnofsky performance scale, which ranges from 0 (dead) to 100 (normal), and the ECOG scale that ranges from 0 (asymptomatic) to 5 (dead). Comparisons of the two scales have been validated with a large sample of patients [50]. Performance status has been used to select patients for entry into chemotherapy trials; however it is also well accepted to be associated with postoperative morbidity [51–53].

Postoperative Care

Postoperative management must be optimized specifically for the elderly population. Narcotic use should be minimized whenever possible to prevent delirium, and appropriate elderly patients should be assessed for preoperative placement of a thoracic epidural catheter for analgesia. Benzodiazepines and medications for sleep should also be minimized. Excellent pulmonary hygiene must

Fig. 2 Thoracic ambulation cart used to facilitate early postoperative ambulation. Forearms are supported by pads, while hands wrap around a handbrake. Oxygen tanks and ambulatory saturation monitors are stored along the sides. Pleural drainage systems can be suspended from the side rails. A cloth strap is used to secure the patient to the cart during ambulation

be maintained with frequent chest physiotherapy and early ambulation. At our institution, thoracic ambulation carts, as shown in Fig. 2, are used to facilitate walking patients who require oxygen and are otherwise tethered with multiple lines and catheters.

Non-small Cell Lung Cancer

Stage at Presentation

Elderly patients more frequently have early-stage disease, compared to younger patients with lung cancer. O'Rourke et al. used a database of 22,874 patients to demonstrate that percentage of patients with surgically resectable disease at diagnosis increases with age. The percent of lung cancer patients with local-stage NSCLC increased from 15.3% of those aged 54 years or younger to 19.2% of those aged 55 to 64 years, to 21.9% of those aged 65 to 74 years, and to 25.4% of those aged 75 years or older [54]. Data published from the Surveillance, Epidemiology, and End Results (SEER) database in 2005 analyzing a cohort of 14,555 patients with early-stage NSCLC showed that the frequency of stage I disease increased from 79% in patients <65 to 87% in patients age 75 or greater [55]. Thus, although the elderly are at higher risk of developing lung cancer, a higher proportion present with potentially curable disease.

Histology

Elderly patients are more likely to be diagnosed with squamous cell carcinoma (SCC) over other histology types [10, 56, 57]. Mery and colleagues' analysis of the SEER database showed that the frequency of SCC increased from 27% in patients less than 65 years old to 38% in patients 75 and older, with parallel decreases in frequency of adenocarcinoma from 61% to 50% in corresponding age groups, as depicted in Fig. 3 [55]. Squamous cell carcinomas are associated with a higher incidence of local disease [54], tend to have lower recurrence rates, and may have longer survival times than non-squamous cell cancers [58–60]. Squamous cell tumors are more likely to be centrally located however and thus are more likely to require pneumonectomy for curative resection.

Extent of Resection

Surgical resection for non-small cell lung cancer offers the best chance for cure. The extent of NSCLC resection in elderly patients has been extensively debated, with advocates for limited resections for the aged. Lobectomy, removal of one of the five lobes of the lung and associated lymph nodes within a single pleural membrane, is considered standard of care for surgical resection of early-stage NSCLC [61]. Unfortunately there are multiple studies that substantiate age as a risk factor for death after thoracotomy. Using data

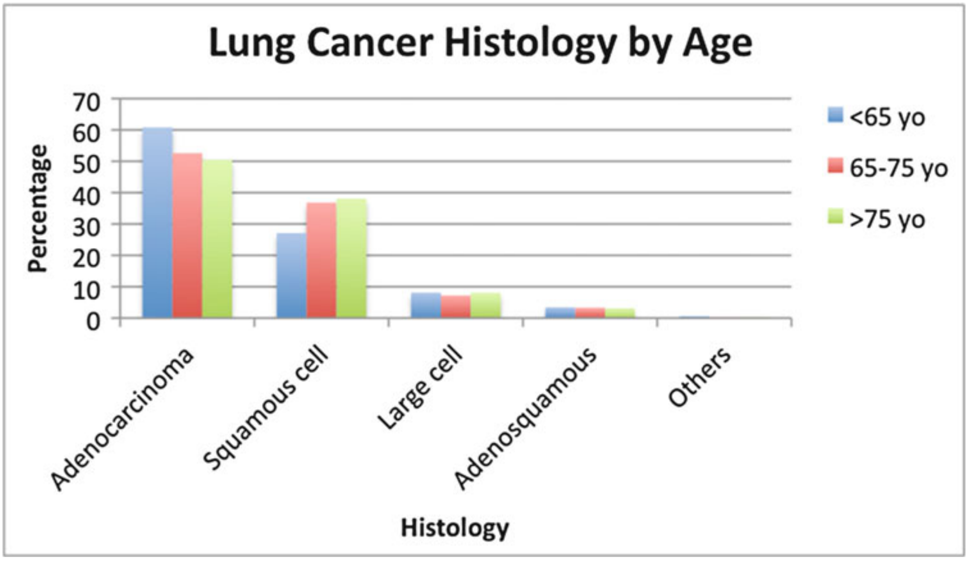

Fig. 3 Lung cancer histology by age. (Data from Mery et al. [55])

from the 1960s and 1970s, several small single-institution studies published operative mortality rates of 14 to 27% for the elderly depending on age and type of surgery [62–65]. These findings were confirmed by a multi-institution study by the Lung Cancer Study Group in 1983. Ginsberg et al. reviewed 2,200 cases of lung resection for cancer and found that operative mortality increased proportionally with age. Patients with age <60 had a 1.3% 30-day mortality rate, with increasing rates of 4.1, 7.0, and 8.1% mortality rates for the 60–69, 70–79, and 80 or greater age groups, respectively [66].

More recently Mery et al. determined a 30-day postoperative mortality rate of 14,555 patients who had undergone curative resections for treating stage I or II NSCLC over the period of 1992–1997. In an analysis of patients undergoing all types of surgery, there was a 0.45% mortality rate for those under age 65 years old, 0.6% for ages 65–74, and 1.2% for age 75 or older ($p = 0.001$). Mortality differences were found to be primarily due to differences in survival of patient undergoing lobectomy, with 0.3%, 0.5%, and 1.5% mortality, respectively, for these corresponding age groups ($p = 0.0001$). The difference in perioperative mortality was statistically similar for patients undergoing limited resection [67]. Prior published reports likewise did not identify a difference in expected operative mortality after thoracotomy if lung-sparing operations were performed [68–70].

The American College of Surgeons Oncology Group (ACOSOG) Z0030 Study published morbidity and mortality data in 2006 for 1023 clinically resectable T1 or T2, N0, or non-hilar N1 NSCLC patients randomized over a period from 1999 to 2004 to undergo lymph node sampling versus mediastinal lymph node dissection. Their age-stratified morbidity and mortality data is shown in Table 1. Notably, overall mortality was 1.4%, improved from Ginsberg's reported 3.8%, and was not statistically associated with age [71]. Ninety percent of patients in the ACOSOG Z0030 study underwent resection via a thoracotomy, with the remaining procedures performed as video-assisted thoracoscopic surgery (VATS) or VATS-assisted resections. Operative mortality reported by Ginsberg for pneumonectomy and lobectomy was 6.2% and 2.9%, respectively, compared with 0% and 1.3%, in the ACOSOG study. Notably the pneumonectomy rate of the earlier study was 25.6% versus 4% in ACOSOG, likely partially explaining the higher mortality rate of the earlier study. The complication rate did rise as age increased, with 49% of patients in

Table 1 ACOSOG Z0030 study age-stratified morbidity and mortality after resection for clinically resectable T1 or T2, N0, or non-hilar N1 NSCLC

Event	Age < 50 ($n = 35$)	50–59 ($n = 171$)	60–69 ($n = 386$)	70–79 ($n = 361$)	80+ ($n = 70$)
One or more complications	8 (23%)	50 (29%)	136 (35%)	162 (45%)	34 (49%)
Air leak > 7 days	1 (3%)	14 (8%)	24 (6%)	33 (9%)	6 (9%)
Chest tube drainage > 7 days	0	14 (8%)	42 (11%)	53 (15%)	9 (13%)
Chylothorax	1 (3%)	3 (2%)	3 (1%)	5 (1%)	1 (1%)
Hemorrhage	1 (3%)	3 (2%)	10 (3%)	16 (4%)	4 (6%)
Recurrent nerve injury	0	0	5 (1%)	2 (<1%)	0
Atrial arrhythmia	1 (3%)	13 (8%)	53 (14%)	68 (19%)	12 (17%)
Respiratory	4 (12%)	8 (5%)	30 (8%)	29 (8%)	3 (4%)
Death	1 (2.6%)	0	3 (0.8%)	8 (2.2%)	2 (2.9%)

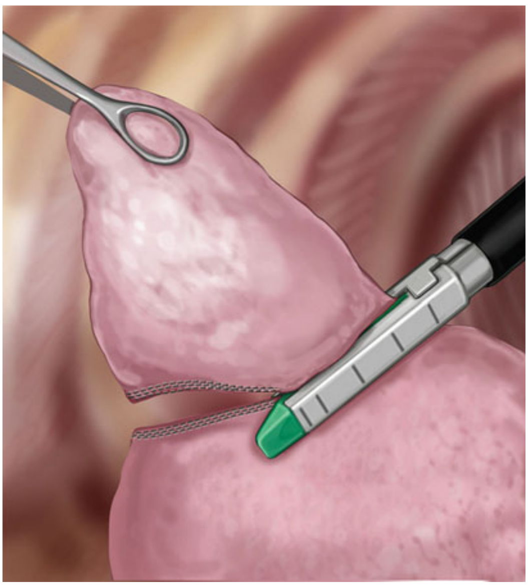

Fig. 4 Video-assisted thoracoscopic wedge resection surgery

the 80 and over age group experiencing one or more complications.

The operative risk of death after pulmonary resections is largely attributable to two anatomical disruptions. First there is the loss of functional lung tissue, and secondly there is the morbidity and mortality introduced by the access thoracotomy. Operative strategies particular to the elderly population have addressed both of these fronts, with use of video-assisted thoracoscopic surgery (VATS) to minimize the chest wall disruption of a thoracotomy and by consideration of limited resections for the most elderly. Figure 4 illustrates the difference in the disruption of chest wall musculature between thoracotomy and VATS approaches.

VATS is defined as surgery performed through two or three incisions that are 2 cm in length. A utility incision less than 10 cm long may be used, without spreading of the ribs. VATS procedures in the elderly have been shown to have lower morbidity, lower rates of postoperative delirium and result in earlier ambulation, a lower narcotic requirement, and a quicker recovery time [72–76].

Limited resections, consisting of either a segmentectomy or wedge resection, remove less lung tissue and are usually performed via VATS. These operations are associated with less perioperative morbidity and mortality but, however, do not completely remove draining lymphatics and may be associated with poorer oncologic outcomes. A randomized trial by the Lung Cancer Study Group of limited resection versus lobectomy for T1 N0 disease revealed a tripling of locoregional recurrence with limited resection and a trend toward improved survival in the lobectomy group [77]. Divergence of the survival curves between lobectomy and limited resection did not occur until 3 years after surgery, however, indicating a potential role for limited resection in patients with a shorter expected life span. Additional studies have concluded that limited resection remains a "compromise" treatment for elderly patients or those with limited cardiopulmonary reserve [78]. An age-stratified analysis of 14,555 patients in the SEER database showed no benefit for lobectomy over limited resection in patients over age 71 [55]. Figure 5 shows a schematic of

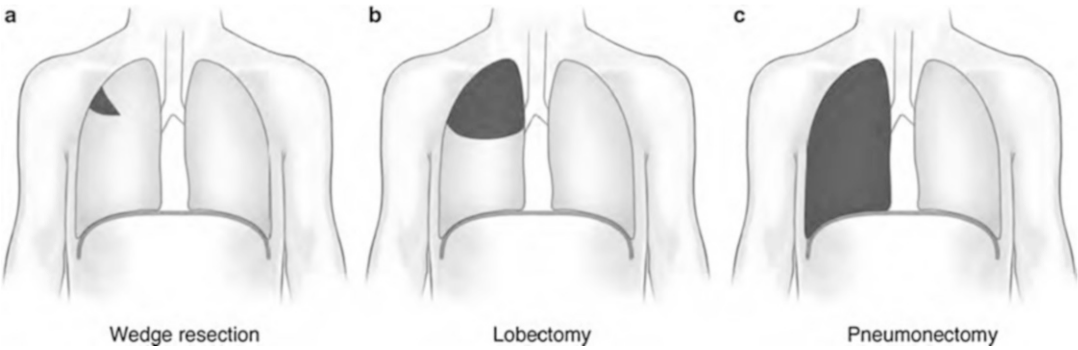

Fig. 5 Extent of resection: (**a**) wedge resection, (**b**) lobectomy, (**c**) pneumonectomy

the range of lung resections. The decision to perform a limited resection versus a lobectomy must take into account the patient's ability to tolerate a larger surgery and potential associated complications versus a smaller resection with less durable oncologic outcomes.

Pulmonary Carcinoid

Pulmonary carcinoids represent 1–2% of lung tumors. They consist of a spectrum of neuroendocrine tumors that are divided into those with typical (TC) or atypical (AC) histological features. While carcinoids tend to present in younger patients, atypical tumors are often diagnosed about 10 years later than typical carcinoid, occurring in the sixth decade. Atypical carcinoids tend to be larger, are usually localized to the peripheral lung fields, and are more aggressive than typical carcinoids. The 5-year survival is 40–60% versus 90% for indolent typical carcinoids [79]. Limited resection with wedge or segmentectomy is the preferred treatment for localized carcinoids. More extensive resection has been advocated for atypical carcinoids, with extent of resection mirroring recommendations for NSCLC [80, 81].

Surgical Resection for Pulmonary Metastases

Metastasis to the lungs is a common oncologic problem. Pulmonary metastases tend to be an indicator of widely metastatic disease; however in some patients metastases to the lungs may occur in isolation. Retrospective evidence suggests that highly selected patients may have improved survival after resection of pulmonary metastases. Indications for the procedure include (1) control of the primary site, (2) metastatic disease isolated to the thorax, (3) resectable disease, and (4) sufficient cardiopulmonary reserve for the operation [82]. Most studies have found that age does not have a prognostic influence on overall survival [83–87].

The largest evaluation of outcomes after lung metastasectomy comes from the International Registry of Lung Metastases. Established in 1990, the registry enrolls all patients who have undergone resection of lung metastases with curative intent. Of the 5206 patients enrolled between 1991 and 1995, 43% of lung metastases were epithelial in origin, 42% were sarcomas, 7% were germ cell tumors, 6% were melanomas, and 2% were other types. Single metastases accounted for 46% and multiple metastases 52%. Germ cell tumors had the best survival and melanoma the poorest survival at 5 and 10 years (68% at 5 years and 63% at 10 years vs. 21% and 14%, respectively). The survival rates for epithelial tumors and sarcomas did not differ significantly (37% at 5 years and 21% at 10 years vs. 31% and 26%, respectively). Rates of recurrence also varied by histology type, at 64% for sarcomas and melanoma, 46% for epithelial, and 26% for germ cell tumors with a median time to recurrence of 10 months. In a multivariate analysis, disease-free interval (DFI), number of metastases, and tumor type were highly prognostic of long-term survival.

Based on these findings, Pastorino et al. proposed four prognostic groupings to provide a framework for management. Group I consisted of patients with resectable metastases, a DFI $\geq$ 36 months, and a single metastasis. Group II patients had resectable metastases and a DFI of <36 months or multiple metastases. Group III again had resectable lesions and both a DFI of <36 months and multiple metastases. Patients with unresectable metastases made up group IV. Median survival for these four groups were 61 months, 34 months, 24 months, and 14 months for groups I thru IV, respectively [88].

The use of VATS over thoracotomy for lung metastasectomy is controversial, as the surgeon is not able to palpate the lung for additional lesions. In 1994, Collie et al. reported that conventional CT missed up to 50% of pulmonary metastases found at surgery [89]. Furthermore, McCormack et al. found additional malignant lesions at thoracotomy in 56% of patients after initial VATS exploration and thus concluded that thoracotomy with manual palpation was the gold standard for metastectomy [90]. Preoperative evaluation with PET has a reported sensitivity of up to 94% for lesions 1.1 to 1.9 cm; however it has limited ability to detect smaller lesions [91]. Other investigators, however, found no difference in rates of recurrence or survival between VATS and thoracotomy [92, 93]. As advances in imaging technology increase the ability to detect smaller lesions, it is likely that the use of VATS will become more commonplace, particularly in older patients. Elderly patients with isolated pulmonary metastases and adequate cardiopulmonary reserve should be considered for surgical resection.

Treatment Patterns of Elderly Cancer Patients

There are multiple studies that point to the undertreatment of cancer in the elderly, which is not limited to patients with lung cancer [94]. Published data from the SEER database showed that the frequency of limited resections increased with age, with a decline of pneumonectomies and lobectomies with age. Approximately 30% of the most elderly patients in the database were denied surgery or were offered only palliative surgery, in contrast with only 8% of the youngest patients [55]. Age is associated with declines in functional reserve and organ function, and optimal treatment is often affected by comorbid conditions. Adding to the complexity involved in treatment, the elderly have often not participated in clinical trials, often forcing clinicians to rely primarily on retrospective data for treatment decisions [95].

An analysis of the Brigham and Women's Division of Thoracic Surgery modern prospective database suggests a morbidity pattern in the elderly that is similar to that of younger patients. The database was designed to collect graded postoperative complications based on the Clavien-Dindo classification of surgical complications. When graded complications were compared based on age alone (<70 and $\geq$ 70), the elderly population had an increased number of complications. When comparing graded complications based on age (<70 and $\geq$ 70) and organ system, insignificant differences were found among complications of the pulmonary and gastrointestinal systems. Significant differences were found in the number of patients experiencing neurologic, cardiovascular, and genitourinary complications, which were mainly driven by an increased number of elderly patients experiencing delirium, atrial fibrillation, and urinary retention, in each of these categories, respectively. Preoperative evaluation of these systems may reduce morbidity and improve the postoperative course of elderly patients undergoing major thoracic surgical procedures.

Using 2004 data, the life expectancy of an 80-year-old in the United States is 9.1 years (8.2 years for males, 9.8 years for females), whereas the median survival for elderly patients with untreated early-stage lung cancer is only 14 months [96]. This suggests that life limitation for an 80-year-old with lung cancer is likely to be cancer related [97]. Table 2 [98] shows life table data from 2004 for patients older than 65.

Table 2 Life expectancy by age, United States, 2014 – Con

Age	Total	Male	Female
65	19.4	18.0	20.6
70	15.7	14.5	16.7
75	12.3	11.2	13.1
80	9.2	8.4	9.8
85	6.7	6.0	7.1
90	4.6	4.1	4.9

Case Reveal

Estimating prognosis, identifying comorbidities, and determining functional status are all essential in deciding the appropriate management of Ms. Jones' lung nodule. Ms. Jones' age and gender are good initial prognosticators. The size of the lesion and absences of mediastinal adenopathy will help determine T and N stages. Even without a tissue diagnosis, this nodule is highly suspicious for adenocarcinoma for which curative resection indicates the best possible survival [99].

Ms. Jones' comorbidities potentially include MI, PE, aortic dissection, esophageal reflux, or esophageal spasms due to her previous episodes of severe chest pain after large meals. Her swelling ankles may indicate MI, rheumatic disease, or pulmonary hypertension. Recent smoking cessation may lead to increased phlegm, slowing her recovery. Her polypharmacy, trouble keeping track of her medications, trouble sleeping, and frequent use of alcohol may indicate an altered mental status which could increase her risk for postoperative delirium and therefore affect her functional recovery.

Ms. Jones' functional status is multifactorial. It is encouraging to see that she prepares her own meals, cleans her home, and regularly spends time with family. Although she is widowed and has lived alone for 6 years, her sons are actively involved and she happily engages in social activities. Yet, the recent addition of a housekeeper and help from family with shopping and carrying bags shows a decline in functional status. Additionally, her trouble walking and multiple falls are concerning for poorer outcomes. Falling at age 65 or older is the 7th leading cause of death in the United States [100]. This leaves us to wonder how quickly Ms. Jones is declining.

Ms. Jones presents a difficult case given her declining cognition and functional status. It is recommended that she receive a geriatric assessment, EKG, stress test, echocardiogram, PET scan, bronchoscopy, possible brain MRI, PFTs, and a 6-min walk test. Additionally, it would be beneficial if her case was reviewed by a multispecialty tumor board that includes a geriatrician. If this workup results favorably, then Ms. Jones should be offered a segmentectomy to preserve lung function.

Conclusion

Resection of pulmonary malignancies has been shown to be safe in selected elderly patients, and age should not be a contraindication to a therapy that offers the best chance for cure for early-stage cancer patients. A targeted preoperative assessment can help individualize the morbidity and mortality risk of surgery for each patient and thus provide both surgeon and patient with the information needed for operative decision-making. Operative interventions in the elderly require coordinated attention to the specific requirements of the aged. Efforts must be made to balance complete oncologic resection with the elderly's limited tolerance for homeostatic insult. Specialized multidisciplinary care provided by primary care physicians, geriatric specialists, cardiologists, oncologists, surgeons, anesthesia, nursing, physical therapy and nutrition optimize care for the elderly thoracic surgery patient.

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Benign and Malignant Diseases of the Prostate

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Contents

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Abstract
A significant number of people will experience urologic disease with age. The breath of urology covers the entire urinary tract along with the retroperitoneum and male genital structures. Herein, we discuss diseases of the kidney, bladder, and prostate with a particular focus in malignancies of these organ systems.

Benign prostatic hyperplasia (BPH) and prostate cancer are two common disease processes that occur in elderly men. Both of these conditions are rare before the age of 50, but by age 80, more than 80% of men have pathologic evidence of benign hyperplasia and more than 50% have at least microscopic foci of prostate cancer [1]. While BPH-associated urinary symptoms will impact quality of life in most elderly men, the likelihood of prostate cancer resulting in significant morbidity remains low [2, 3]. This chapter reviews the incidence of these two diseases, the appropriate evaluation of elderly men, and surgical options available to the geriatric patient.

General Anatomical Considerations

The prostate is a glandular organ situated in the pelvis. The base of the prostate is in continuity with the bladder and the apex rests on the pelvic floor. The prostate gland surrounds the urethra immediately below the base of the urinary bladder and is located posterior to the inferior symphysis pubis, superior to the urogenital diaphragm, and anterior to the rectum. It is composed predominantly of glandular elements with an investing fibromuscular stroma. The outer capsule is a band of concentrically placed fibromuscular and vascular tissue that is inseparable form prostatic stroma and surrounding fascia. The urethra runs through the gland with anterior angulation at the verumontanum, representing the exit site of the ejaculatory ducts. The prostate can be defined by anatomical zones or surgical lobes which are subject to pathology at varying degrees. The transition zone consists of periurethral tissue situated proximal to the verumontanum. The central zone surrounds the ejaculatory ducts, extending posteriorly to the bladder base. The posterior zone encompasses the remainder of tissue posterior to these two areas adjacent to the rectal vault. The anterior fibromuscular stroma is devoid of glandular elements and runs from the anterior bladder neck to the pelvic floor. While BPH arises almost exclusively from the transition zone, 70% of prostate cancers originate in the peripheral zone, with approximately 25% and 5% of cases stemming from the transition and central zones, respectively. Surgical lobes have also been described in relation to BPH. Lateral lobes are typically seen on cystoscopy as bilaterally bulging elements impinging on the prostatic urethra. A middle or central lobe represents the hyperplastic component that protrudes superiorly into the floor of the bladder, sometimes creating a perceived ball valve effect on voiding. A true capsule does not separate the peripheral and transition zones, but the term “surgical capsule” has been used to delineate a plane of dissection when bluntly enucleating BPH nodules from the peripheral zone. The blood supply to the prostate is mainly from the inferior vesicle artery which arises from the anterior trunk of the internal iliac artery with venous drainage to the plexus of Santorini. The gland is innervated by the pelvic plexus with nerves seen in the periprostatic neurovascular bundle. Lymphatic drainage is mainly to the obturator and internal iliac nodes with secondary drainage to the external iliac nodes and to the presacral group.

Benign Prostatic Hyperplasia

In order to understand the diagnostic and treatment dilemmas facing practitioners caring for the older adult man with BPH, it is important to have working knowledge of the historical terminology used to describe the clinical symptoms. “BPH” represented an acronym for benign prostatic hypertrophy, as the majority of men with urinary symptoms were found to have enlarged prostates. However, from a histologic standpoint, the growth of the gland represents a hyperplastic process – with increase in both glandular and stromal elements. Two problems with this terminology were: (1) hyperplasia has been noted in prostates from men in their third decade of life who exhibit no urinary symptoms and (2) a linear correlation between prostate size and degree of urinary symptoms does not exist. Several other acronyms can be encountered that represent attempts to circumvent these issues. BPE (benign prostatic enlargement) and BOO (bladder outlet obstruction) represent such examples. Although BOO is pathophysiologically correct with regards to the underlying process, it remains a urodynamically defined element thus requiring a semi-invasive and costly test typically not viewed as necessary for treatment or diagnostic purposes. In order to get back to the clinical picture which leads patients to seek treatment, yet another acronym was coined being LUTS (lower urinary tract symptoms). This covered the constellation of symptoms (urgency, frequency, hesitancy, intermittency, straining, sense of incomplete emptying, and nocturia) that were associated with the original "BPH." However, LUTS may be resultant from a diverse list of diagnoses not limited to the obstructive processes of an enlarged prostate [4]. Today ICD-10 coding includes both BPH with and BPH without LUTS.

Epidemiology

The prostate is small at birth, enlarges rapidly at onset of puberty, and then remains at a constant size during the next several decades of life. The average weight of the prostate slowly increases after 50 years of age with an associated increase in the incidence of symptomatic BPH. Although the development of pathologic BPH is almost a universal phenomenon in aging men, the cause and pathogenesis of this disorder are poorly understood. While genetic susceptibility may play a role in younger patients, the relevance dramatically diminishes for those over the age of 60. Androgens are recognized as necessary for the development of pathologic BPH; however, they are not the cause of BPH. While individuals castrated prior to puberty do not develop pathologic BPH, prostate size can continue to increase with age when androgen levels typically decline, suggesting little correlation between the two [5]. Several other risk factors have been proposed, but today there is no evidence to suggest that BPH can be attributed to any specific factors. Series have investigated sociocultural variables including celibacy, specific blood groups, the use of alcohol or tobacco, and disease is commonly found among older adult men such as coronary artery disease, peripheral vascular disease, hypertension, and diabetes.

Pathophysiology

The pathophysiology of symptomatic BPH is complex involving both static and dynamic components. BPH is a true hyperplastic process with histologic studies demonstrating an increase in cell numbers throughout the gland. Hyperplasia occurs in the form of nodules that consist of stromal and epithelial elements. In addition, many nodules contain smooth muscle. Prostatic hyperplasia increases urethral resistance due to mechanical obstruction from tissue expansion. Presumably, the confinement created by the capsule transmits pressure to the urethra leading not only to increased resistance but also compensatory changes in bladder function. How the smooth muscle tissue contributes to symptomatic BPH is unknown, but the muscle fibers are regulated by the adrenergic nervous system. Receptor binding studies indicate that alpha receptors are the most abundant type of receptor in the human prostate and partially explain the ability of alpha-blocking medications to relieve BPH-associated LUTS. In addition, age-related functional changes in the bladder and nervous system have been reported to contribute to LUTS. At the ultrastructural level, normative aging and BOO both result in muscle loss and axonal degeneration with increased collagen deposition [6]. This can lead to both hyperactivity and impaired contractility, which manifest with clinical symptoms associated with symptomatic BPH. It is interesting to note that clinical LUTS are as common in age-matched women as they are in men.

Diagnosis and Evaluation of Prostate Disease

Physicians evaluating older adult men for obstructive urinary symptoms should begin with a detailed history that focuses on the urinary tract, previous surgical procedures, general health issues, and fitness for possible surgical procedures. Specific areas to discuss include a history of hematuria, urinary tract infection, diabetes, neurologic disorders such as Parkinson's disease or previous stroke, urethral stricture disease, urinary retention, and aggravation of symptoms by cold or sinus medications. Physicians should check all current prescription medications to determine whether the patient is taking any anticholinergic drugs (which impair bladder contractility) or a-sympathomimetics (which increase outflow resistance). A history of lower urinary tract surgery suggests the possibility of urethral or bladder neck stricture. The etiology of LUTS is multifactorial, and specific symptoms may be a poor indicator of underlying pathophysiology. This is particularly true in the elderly patient. While LUTS are most often attributed to prostatic obstruction, only two-thirds of men with LUTS meet the accepted diagnostic criteria for obstruction. Obstructive symptoms (hesitancy, weakened stream, intermittency, straining, and sense of incomplete emptying) do not reliably predict outlet obstruction. Researchers' have shown that many aspects of detrusor performance decline with aging and progress to detrusor underactivity (DU) in many older individuals [7–9]. DU can influence the clinical picture and may impede the therapy of many lower urinary tract disorders including BPH. Other contributing processes include detrusor overactivity, sensory urgency, sphincteric incontinence, polyuria, or nocturnal polyuria [10]. The use of certain drugs is also associated with increased risk for LUTS. A community-based cross-sectional study that included 2115 men between 40 and 79 years found that daily use of antidepressants or antihistamines was associated with an increase in symptoms [11]. A tool for symptom assessment has been established and permits objective data for evaluation that can be followed in a longitudinal manner. This is the AUA Symptom Score which should be obtained at initial consultation and routinely thereafter (Table 1). This instrument consists of a series of questions, correlating to common LUTS that have five-graded responses. Symptoms are considered mild, moderate, and severe with scores between 0 and 7, 8 and 19, and 20 and 35, respectively. The AUA symptom score should not be used to diagnose symptomatic BPH but rather to evaluate treatment response or disease progression. Symptom scores alone do not capture the morbidity of a prostate problem as perceived by the patient. The impact of symptoms on a patient's lifestyle must be considered as well. Intervening with medical or surgical therapy may make more sense in a patient with moderate symptoms he finds relatively troublesome compared with a patient with severe symptoms who is able to manage them fairly well. Thus, the critical question for all patients is how much bother these symptoms create and what are they willing to do to improve them. In addition, use of a voiding diary may help to identify patients with polyuria, nocturia, or other non-prostatic disorders. The physical examination should include a digital rectal examination (DRE) and a focused neurologic examination. The rectal examination establishes the approximate size of the gland and can help to guide which surgical approach is most appropriate should this be warranted. Because prostate size does not correlate with symptom severity or treatment outcomes, and DRE typically underestimates size by 50%, size by DRE should not be used to make a diagnosis and proceed with treatment. The DRE is helpful only for guiding management. A focused neurologic examination can be used to exclude neurologic problems that may cause the presenting symptoms and should include an assessment of rectal sphincter tone. A urinalysis should be obtained to screen for hematuria and urinary tract infection. Urinary cytology is no longer indicated in men with severe irritative symptoms, only those with gross hematuria, especially if they have a history of smoking [12]. Although localized prostate cancer typically does not

Table 1 AUA symptom score

Criterion	Not at all	Less than one time in five	Less than half the time	About half the time	More than half the time	Almost always	Your score
Incomplete emptying: Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?	0	1	2	3	4	5	
Frequency: Over the past month, how often have you had to urinate again less than 2 h after you finished urinating?	0	1	2	3	4	5	
Intermittency: Over the past month, how often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
Urgency: Over the past month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5	
Weak stream: Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5	
Straining: Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5	
Nocturia: Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?	0	1	2	3	4	5	
Total score							

produce urethral obstruction, it can coexist with BPH. Consequently, physicians may wish to consider assessing the serum PSA level should a diagnosis of prostate cancer alter the proposed management, although current guidelines recommend against screening for prostate cancer in men over age 75 [13]. Many patients advised to undergo surgical treatment may have cystoscopy and or a transrectal ultrasound. These examinations are not recommended to determine the need for surgery, but rather to help the surgeon determine the most appropriate technical approach based on prostate size. Formal urodynamic evaluation should be considered in elderly gentlemen who maintain high postvoid residuals, have a known or suspected neurologic disease that may affect the urinary tract, or have persistent symptoms after an invasive procedure. Clinicians should also perform a postvoid residual prior to surgical intervention.

Treatment of Benign Prostatic Hyperplasia

Prior to surgical management for BPH, behavioral therapy and medical therapy should be utilized. Behavioral therapies include double voiding, timed voiding, avoidance of caffeine, alcohol, use of nighttime diuretics, and fluid restriction at night.

Alpha Blockers

Alpha-adrenergic antagonists relax smooth muscle at the bladder neck and prostate helping to relieve BOO. They represent the most common initial therapy for treating LUTS associated with BPH. Alpha 1a selective blockers such as tamsulosin, alfuzosin, and silodosin are used commonly and avoid the systemic side effects associated with nonselective alpha blockade.

Common side effects associated with alpha blockade include hypotension that can result in dizziness (5–15% with $\alpha 1_a$-selective agents), retrograde ejaculation (6%), and rhinitis (12%) [14]. The cardiovascular effects are particularly seen when less selective drugs and higher doses of α-blockade are used (tamsulosin 0.8 mg daily). Silodosin is felt less likely to cause orthostasis given its high $\alpha 1_a$-selectivity. In regards to ejaculatory dysfunction, alfuzosin is thought to pose a reduced risk when compared to other means of alpha blockade [15]. The use of alpha blockers, in particular tamsulosin, has been associated with intraoperative floppy iris syndrome [16]. This problem leads to higher rates of iris trauma and posterior capsule rupture during cataract surgery and is associated with prior or concomitant use. Dosing regimens that can be used include but are not limited to tamsulosin 0.4–0.8 mg daily, or alfuzosin 10 mg daily, or silodosin 8 mg daily.

5-Alpha Reductase Inhibitors (5ARIs)

5ARIs suppress androgen synthesis by blocking conversion of testosterone to dihydrotestosterone. This is associated with reduction in prostate volume and a decrease in BOO. These drugs have a much slower onset of action when compared to alpha blockers and may take up to 6 months to see a benefit. The most common side effects associated with the use of 5α-reductase inhibitors include decreased libido (6.4%), erectile dysfunction (8.1%), ejaculatory disorder (0.8%), gynecomastia (0.5%), breast tenderness (0.4%), and rash (0.5%) in the first year of treatment [17]. Regimens that can be employed include finasteride 5 mg daily and dutasteride 0.5 mg daily.

It should be mentioned that alpha blockers and 5ARIs may be used in combination to augment therapeutic effect. Current guidelines published by the American Urologic Association (AUA) and the European Association of Urology recommend combination therapy with alpha blockers and 5ARIs for patients with moderate-severe symptoms, prostates above 40 cc, and advanced age. Sample regimens include finasteride 5 mg + 5 mg alfuzosin twice daily, dutasteride 0.5 mg + tamsulosin 0.4 mg daily, and finasteride 5 mg + doxazosin 8 mg daily.

Surgical Management of BPH

Men failing medical treatments can be offered surgery. Absolute indications for surgery include refractory urinary retention, recurrent urinary infections, recurrent gross hematuria, bladder stones, renal insufficiency caused by obstruction, and the concomitant presence of a large bladder diverticulum. Urologists have developed several surgical procedures to manage BPH. Open surgical excision, known as a simple prostatectomy, was developed more than 100 years ago. Although surgeons still utilize this approach to remove large glands, most urologists favor minimally invasive techniques for appropriately selected patients. Transurethral resection of the prostate (TURP) has been considered the treatment of choice for patients with glands less than 100 g in size. The procedure is typically performed under a spinal or general anesthetic with the patient placed in the lithotomy position. The resection is normally conducted in a fluid medium. Nonhemolytic solutions such as 1.5% glycine, sorbitol, or mannitol are commonly employed when monopolar resectoscopes are utilized. Bipolar electrodes have allowed the use of normal saline which helps to prevent dilutional natremia that can be seen with the use of hypotonic irrigants. The resection technique varies according to the size and configuration of the prostate. Resection is carried out in a circumferential manner from the bladder neck to just proximal to the verumontanum. Resection beyond this point risks damage to the external urinary sphincter. The majority of hyperplastic tissue exists between the 3 and 9 o'clock position with less noted anteriorly. The amount of intraoperative bleeding depends on the size of the prostate, the length of time required to resect the hyperplastic tissue, and the skill of the surgeon. Arterial bleeding is controlled by electrocoagulation. Venous bleeding may be apparent at the end of the procedure, when on irrigating the catheter the returning fluid initially clears but then turns dark red. Venous bleeding can be controlled by inserting a catheter and placing it on traction. Extravasation occurs in approximately 2% of patients, usually following capsular penetration. The symptoms associated with extravasation and fluid absorption include nausea, vomiting, and abdominal pain. Although TURP is considered the standard surgical procedure for treatment of BPH, several alternative surgical procedures have been developed. The majority involve a form of thermal energy transfer to the tissue which causes necrosis and desiccation with time, terminating the procedure and placing a urethral catheter. There has been a significant expansion in non-TURP procedures to assist with management of bladder outlet obstruction. Patients who absorb large amounts of fluid during TURP can become severely hyponatremic and may require treatment with hypertonic saline and diuretics. Over the past 50 years, there has been a steady decline in postoperative complications and mortality associated with TURP. These improvements can be attributed to several factors, including better medical management, better anesthesia, and better surgical equipment including improvements in optics and light sources. Wasson et al. reported that 91% of men undergoing TURP in the Veterans Affairs health care system experienced no complication during the first 30 days after surgery [18]. The mortality rate due to surgery was less than 1%. The most frequent complications reported included the need for catheter exchange (4%), perforation of the prostatic capsule (2%), and hemorrhage requiring transfusion (1%). Long-term complications at 3 years associated with TURP include bladder neck contracture requiring endoscopic surgery (3%), urethral stricture requiring dilation (3%), and secondary transurethral resection (3%).

Simple Prostatectomy

Simple prostatectomy is usually considered when the prostate gland is approximately 100 g or larger. This procedure should also be considered when other concomitant bladder conditions are present, such as a large diverticulum or a large, hard bladder calculus. The advantage of simple prostatectomy is a complete removal of the adenomatous tissue under direct vision without the risk of dilutional hyponatremia, which is often associated with a prolonged transurethral resection. The disadvantages include the need for a lower abdominal incision, a longer hospitalization, and an extended convalescence period. In addition, there may be an increased potential for intraoperative hemorrhage from the prostate fossa. Contraindications to this operation include a small prostate gland, a previous prostatectomy, previous pelvic surgery, and prostate cancer. An open simple prostatectomy can be accomplished using one of two approaches: retropubic or suprapubic. With the retropubic approach, the anterior prostatic capsule is incised and the hyperplastic adenoma enucleated. Advantages to approach include excellent anatomic exposure of the adenoma, precise transection of the urethra distally, clear and immediate visualization of the prostate fossa to control hemorrhage, and minimal trauma to the urinary bladder. The disadvantages of this approach include the inability to access the bladder and difficulty dealing with a large median lobe. A suprapubic prostatectomy is accomplished through an extraperitoneal incision in the lower anterior bladder wall. The bladder neck and prostate capsule are scored under direct vision and the adenomatous tissue enucleated. The urethra at the apex of the adenoma is transected sharply under surgeon feel. The major advantage of this procedure over the retropubic approach is that it allows better visualization of the bladder neck and bladder including the ureteral orifices. As a result, this operation is ideally suited for patients with a large median lobe protruding into the bladder, a concomitant symptomatic bladder diverticulum, or a large bladder calculus. It also may be the preferred approach in obese men when it is difficult to gain direct access to the prostate capsule and the dorsal vein complex. The major disadvantage of this approach is the inability to visualize the apical portion of the prostate directly. Both laparoscopic and robotically assisted laparoscopic approaches have been utilized. The robotic-assisted laparoscopic approach has the advantage of small incisions and less venous bleeding due to the use of intra-abdominal insufflation.

Recent advances in endoscopic technology including laser techniques have reduced the need to perform open simple prostatectomy. Enucleation with laser energy has reliably been shown to effectively treat glands >100 cc [19]. Both robotic surgery and enucleation are specialized techniques and may not be as widely available as TURP or other minimally invasive BPH treatments.

Transurethral Incision of the Prostate (TUIP)
Transurethral incision of the prostate capsule results in significant alleviation of the outflow obstruction, despite the fact that the volume of the prostate remains the same. This involves either unilateral or bilateral incisions, at the 5 and 7 o'clock positions, starting distal to the ureteral orifice ending just proximal to the verumontanum. The depth of the incision is generally described as down to the prostatic capsule. This has been considered an alternative to formal resection in elderly patients who are not deemed medical candidates for more invasive procedures.

Multiple other minimally invasive therapies have been developed. The majority of these involve energy transfer to the prostate causing tissue heating. Treated areas are either vaporized due to high temperatures or develop coagulation necrosis and slough after several days to weeks. Heat-generating elements include lasers (green light, holmium, Nd-Yag, and interstitial), high-intensity focused ultrasound (HIFU), or transurethral microwave thermotherapy (TUMT). Most of these procedures involve delivery of energy through a catheter placed transurethrally or under direct vision cystoscopically. The treatment area can be as long as 40 mm, as wide as 10 mm, and as deep as 10 mm. Laser prostatectomy has demonstrated several advantages over TURP, including technical simplicity, a forgiving learning curve, and the absence or minimization of complications such as intraoperative fluid absorption, bleeding, erectile dysfunction (ED), and incontinence. Patients can be continued on anti-coagulation/antiplatelet medications due to decreased risk of bleeding. The holmium laser has also been used extensively in enucleation of the prostate, described as HoLEP. Multiple patient series have described how large glands have been successfully treated by HoLEP, though a difficult learning curve as well as the need for morcellation to enucleate large lobes have restricted its wide adoption.

Prostatic Urethral Lift (UroLift®)
The prostatic urethral lift (UroLift®) involves implantation of tissue retracting implants inserted under cystoscopic guidance using the UroLift® delivery system. Appropriate patient selection based on prostate anatomy is critical for the success of this operation. An obstructive middle lobe is a contraindication due to the inability to treat this portion of the gland. Typically, 4–6 implants are placed in an anterolateral position that avoids the dorsal venous complex and neurovascular bundles. This system is an option for patients with LUTS attributed to BPH provided the prostate volume is less than 80 cc. Patients should be informed that the symptom reduction and improvement in flow is less when compared to TURP. The UroLift can also be offered to those patients concerned with erectile function for the treatment of LUTS attributed to BPH.

Prostate Cancer

Epidemiology

Prostate cancer is the most commonly diagnosed cancer in men. Nearly 240,000 men are diagnosed with prostate cancer (PCa) annually, and just over 80% of those cases represent localized disease [20]. Approximately 1 out of 7 US men will be diagnosed with PCa during their lifetime and nearly 2.8% of men will die from the disease (nearly 30,000 men) [21]. The majority of prostate cancer deaths (53%) occur among men age 80 and over [21]. Prostate cancer occurs much more frequently among African American men than in white Americans. Although the incidence rates are parallel for Whites and African Americans, the mortality from this disease is almost twice as high for African American men as for white men. Despite the significant mortality from prostate cancer, many men never experience symptoms from their disease. Many prostate cancers are indolent. Autopsy data from several countries have confirmed a high incidence of prostate cancer histology, suggesting that less than 1% of men with histologically identifiable cancer die from this disease [22]. Numerous studies have demonstrated that as many as 50% of men over the age of 50 years dying of causes other than prostate cancer have microscopic evidence of disease. These studies also demonstrated that the presence of these cancers increases with age. By age 75 years, more than 80% of men have microscopic evidence of prostate cancer at autopsy. The etiology of prostate cancer is unknown. The similar prevalence of latent disease among racial and ethnic groups at autopsy and the vast difference in the incidence of clinically significant disease suggest that the initiation of prostate cancer occurs frequently, but only some groups are susceptible to prostate cancer promoters. Known risk factors include familial inheritance. Several families have been identified with an apparent Mendelian pattern of inheritance, and several prostate oncogenes have been isolated [23]. A man with one first-degree relative with prostate cancer has a two- to threefold risk of being diagnosed with prostate cancer compared with the general population. A man with a first-degree and a second-degree relative may have a sixfold risk of developing prostate cancer [24]. Screening for prostate cancer remains controversial especially among older men. A greater understanding of the natural history of screen-detected prostate cancer suggests that as many as half of the screen-detected prostate cancers found among men age 70 and older are not clinically significant [25]. These findings led the US Preventive services Task Force to recommend against routine PSA testing in 2012. In 2013, the AUA released the following guidelines for prostate-specific antigen (PSA) screening:

- PSA screening in men under age 40 years is not recommended.
- Routine screening in men between ages 40 and 54 years at average risk is not recommended.
- For men ages 55–69 years, the decision to undergo PSA screening involves weighing the benefits of preventing prostate cancer mortality in 1 man for every 1000 men screened over a decade against the known potential harms associated with screening and treatment. For this reason, shared decision-making is recommended for men age 55–69 years that are considering PSA screening and proceeding based on patients' values and preferences.
- To reduce the harms of screening, a routine screening interval of 2 years or more may be preferred over annual screening in those men who have participated in shared decision-making and decided on screening. As compared to annual screening, it is expected that screening intervals of 2 years preserve the majority of the benefits and reduce over diagnosis and false positives.
- Routine PSA screening is not recommended in men over age 70 or any man with less than a 10–15 year life expectancy.

Table 2 Prostate cancer biomarkers

Test	When used	Result
PCA3	Post-DRE	Identification of clinically significant PCa
PHI	Negative biopsy	Identification of clinically significant PCa
4K score	Negative biopsy	Identification of clinically significant PCa
Oncotype DX	Post-biopsy	Identifies pT3 or Gleason 4
Prolaris	Post-biopsy or RP	PCa-specific mortality, biochemical recurrence, metastasis, biochemical failure, and biochemical recurrence
Decipher	Post-biopsy or RP	Identifies PCa-specific mortality, metastasis, and biochemical failure

Determining when to biopsy a patient based on PSA alone can be challenging and a number of adjunct biomarkers have been developed to determine the risk of prostate cancer in the pre-biopsy and post-biopsy setting. These are listed in Table 2.

Pathophysiology

Adenocarcinoma of the prostate is frequently diagnosed as a result of an elevation in PSA. In many cases, tumors cannot be palpated on rectal examination. Among men with clinically localized prostate cancer, the tumor is often multifocal, and most of the tumor mass is usually located in a peripheral location near the posterior edge of the prostate [26]. As prostate cancer grows, cancer cells invade the soft tissue surrounding the prostate directly and along the perineural pathways. Penetration of the capsule usually occurs posteriorly and posterolaterally, which may lead to extension into the seminal vesicles. The most frequent sites of metastatic spread are the pelvic lymph nodes and bone, especially the pelvis and vertebral bodies. In general, the size of a prostate cancer correlates with its extent [27]. Tumors are assigned a grade from 1 to 5, with 1 representing the most well differentiated and 5 the most poorly differentiated. A Gleason score is determined by summing the primary and secondary patterns. Men with high-grade disease (Gleason score 8–10) generally have a poor prognosis, whereas men with low grade disease (Gleason score 6) have an excellent prognosis. Once a diagnosis of PCa is made, risk assessment becomes paramount in guiding treatment decisions and for counseling patients accurately about expected oncologic and functional outcomes. Using clinical variables, men are commonly characterized into low-, intermediate-, or high-risk PCa categories. The AUA and the National Comprehensive Cancer Network (NCCN) both have similar risk stratification systems that are primarily based on PSA level, Gleason score, and clinical stage (Table 3).

Table 3 AUA and NCCN risk stratification

	AUA risk category	NCCN risk category
Very low	–	PSA $\leq$10 ng/mL, Gleason score $\leq$6, clinical stageT1c, <3 positive biopsy cores, $\leq$50% in each core, and PSA density <0.15 ng/mL/g
Low	PSA $\leq$10 ng/mL, Gleason score $\leq$6, and clinical stageT1c or T2a	PSA <10 ng/mL, Gleason score $\leq$6, and clinical stageT1-T2a
Intermediate	PSA >10–20 ng/mL, or Gleason score 7, or clinical stage T2b	PSA 10–20 ng/mL, Gleason score 7, or clinical stageT2b-T2c
High	PSA >20 ng/mL, or Gleason score 8–10, or clinical stage $\geq$T2c	PSA >20 ng/mL, or Gleason score 8–10, or clinical stage T3a
Very high	–	Clinical stage T3b-T4

Diagnosis and Evaluation

Unlike BPH, prostate cancer rarely causes symptoms early in the course of the disease because most prostate cancers arise in the periphery of the gland distant from the urethra. Symptoms in men with prostate cancer suggest locally advanced or metastatic disease. Growth of prostate cancer into the urethra or bladder neck can result in obstructive or irritating voiding symptoms. Metastatic disease that involves the bones can cause pain and anemia. Aggressive screening efforts have reduced the proportion of men with prostate cancer detected because of symptoms suggestive of advanced disease [28]. Because of the significant risk of prostate cancer, transrectal ultrasonography and prostate biopsy are recommended for all men who have an abnormality on DRE regardless of the serum PSA level. Unfortunately, in both screened and nonscreened populations, DRE misses 23–45% of prostate cancers that are subsequently found following prostate biopsy because of elevated serum PSA [29]. Routine use of the serum PSA assay increases the detection of prostate cancer over that achieved by a DRE alone. The use of serum PSA testing increases the lead time for prostate cancer diagnosis and the likelihood of detecting prostate cancers confined to the prostate. Recognizing that PSA elevations are common in aging men because of the high prevalence of BPH, investigators have focused on methods of improving the ability of the PSA test to distinguish between men with BPH and men with cancer. Recommendations include adjusting serum PSA levels for patient age, prostate volume, and the rate of change of PSA values [30]. With the advent of specific assays quantifying PSA molecular forms, the measurement of free, unbound PSA has been evaluated as a method of distinguishing between BPH [31]. A prospective analysis of more than 3600 men demonstrated that imaging studies are positive in fewer than 10% of cases when the serum PSA level is less than 20 ng/ml or the Gleason score is less than 8 [32]. Only men with serum PSA levels higher than 50 ng/ml are likely to have evidence of metastatic disease that can be identified on bone scan, CT scan, or MRI. Unfortunately, more than half of the men with newly diagnosed prostate cancer who have a serum PSA level over 10 ng/ml already have disease extension beyond the confines of the prostate [31].

Prostate MRI

Prostate MRI has been an increasingly utilized method for detection of suspicious areas of the prostate in men undergoing prostate biopsy for the first time and for those men who have had negative prostate biopsies but continue to have a rising or elevated PSA [33, 34]. The use of MRI-ultrasound fusion software platforms have allowed for targeted biopsy which has been shown to improve detection of clinically significant prostate cancer. Multiparametric MRI is often used pre-biopsy and images are acquired with at least one more sequence in addition to the anatomical T2 weighted images, such as DWI, or dynamic contrast-enhanced images. Based on the MRI, a PIRADS score is given to suspicious lesions from a grade 1–5, with grade 5 lesions being most likely to harbor clinically significant prostate cancer, and 1 signifying a normal prostate [35, 36]. A number of software platforms have allowed for the "fusion" of MRI images to real-time ultrasound allowing the operator to take targeted biopsies of the prostate using the MRI as a map. The negative predictive value of prostate MRI/US fusion prostate biopsy for detection of clinically significant prostate cancer on subsequent biopsy has been estimated at 97% [37]. The Precision trial was a large randomized trial that demonstrated prostate MRI, with or without targeted biopsy, was superior to standard 12-core biopsy in first-time prostate biopsy patients [38]. It is plausible that MRI-targeted prostate biopsy may become the standard in the future as operators and trainees gain familiarity with it.

Active Surveillance

Active surveillance (AS) is defined as a treatment strategy wherein men with low-risk prostate cancer are serially monitored for disease progression and then treated definitively (if needed), thereby avoiding or delaying the risk of treatment-related morbidity [39]. AS differs from observation or watchful waiting in that watchful waiting indicates a decision to avoid/forgo definitive therapy and palliate only if there is progression to symptomatic disease. Entry criteria for AS protocols vary from institution to institution. Men with very-low-risk and low-risk PCa per AUA and NCCN guidelines are typically candidates for AS. Similar to entry criteria, the monitoring protocols vary among institutions but typically involve routine history and physical with digital rectal exam, PSA testing, and prostate biopsy. As with AS selection and monitoring, indicators of progression and need for definitive treatment vary between institutions and continue to evolve. An increase in Gleason grade, number of positive cores, or percent of core positive on surveillance biopsy are common triggers for physicians to recommend treatment. Increasing PSA and subsequent patient anxiety/fear of cancer or even repeat prostate biopsies are other common triggers for patients to electively choose definitive treatment. In some cases, biomarker testing with the use of genomic markers (Oncotype DX Prostate, Prolaris, Decipher Biopsy) may help reveal patient mortality risk, disease stage, risk of progression, or biochemical recurrence or failure. Ultimately, 30–50% of patients on active surveillance ultimately undergo delayed treatment, though the vast majority will remain free of metastasis with a low risk of dying from prostate cancer [39].

Treatment of Prostate Cancer

The appropriate treatment of prostate cancer among elderly men remains controversial. Studies concerning the long-term outcomes of men treated conservatively for their disease have documented the relatively modest disease-specific mortality among men with low and moderate grade tumors [40, 41]. Alternatives to surgery include external beam radiation therapy and brachytherapy. When choosing therapy for an individual patient with clinically localized prostate cancer, the age and general health of the patient remain critically important because of the indolent progression of many prostate cancers. Death from a localized cancer left untreated is not likely to occur for 8–10 years, yet the risk of death from prostate cancer continues to increase for at least 15 years. As life expectancy decreases with older age, the potential benefits of surgical intervention decrease in parallel. Chronologic age is only one factor that influences life expectancy. Prostate cancer occurs frequently in elderly men who have associated comorbid conditions. Conversely, some older men are in excellent physical condition and have a life expectancy longer than average for their age group. The impact of comorbid conditions on long-term outcomes among men with localized prostate cancer has been assessed [42]. Men with significant comorbid disease, measured using one of several instruments, have a much higher probability of dying from causes other than prostate cancer compared with those men with no or relatively few competing medical hazards. Elderly patients must carefully assess the risks and benefits of surgical management compared with those of conservative management before making a decision concerning which therapy is the appropriate management for their localized prostate cancer.

Radical Prostatectomy

Radical prostatectomy (RP) is a curative treatment option for men with localized PCa and remains the gold standard of definitive therapy in patients that are surgical candidates. In addition to being curative in most patients, it allows for accurate pathologic grading and staging, and makes treatment failures easy to identify with PSA rises. Various surgical approaches for RP have evolved over the years and include robotic, open retropubic, laparoscopic, and open perineal RP. Currently, robotic-assisted laparoscopic and open retropubic are the most commonly performed RP procedures in the USA. More recent observational studies show that robotic surgeries may have better oncologic outcomes, less blood loss, and quicker convalescence.

Regardless of surgical approach, RP involves resection of the entire prostate and seminal vesicles, an urethrovesical anastomosis, and a pelvic lymph node dissection. Radical retropubic prostatectomy done open is performed with the patient in the supine position and laparoscopic or robotic with relatively steep Trendelenburg position to increase exposure to the prevesical space. The procedure is usually performed under general anesthesia. The lymphadenectomy may not be therapeutic but does provide additional pathology to stage the cancer more accurately. The procedure is performed by entering the prevesical space either directly through a lower midline incision or transabdominally, when a laparoscope or robot is employed. The Retzius-sparing approach has also been described and shown to improve return to continence while preserving oncologic control. The robotic approach usually approaches the prostate from the posterior, developing the plane between the seminal vesicles and the rectum. The prostate is separated from the bladder neck prior to controlling the dorsal vein complex and dividing the urethra at the level of the prostate apex. In younger selected men, care is taken to preserve the neurovascular bundles that lie on either side of the prostate from the base to the apex. Once the prostate and seminal vesicles have been removed, the bladder neck is repaired and secured to the stump of the urethra. Careful dissection around the apex of the prostate to avoid injury to the pelvic floor musculature should minimize the chance of incontinence. All techniques for performing a radical prostatectomy are associated with complications, which increase with the patient's age. An analysis of more than 100,000 Medicare claims has demonstrated that approximately one in four patients suffers a major or minor complication associated with these procedures [43]. The radical retropubic approach had higher risks of respiratory complications and miscellaneous medical complications and a lower risk of miscellaneous surgical complications. The perineal approach resulted in a 1–2% incidence of rectal injury, but this appears to be offset by the medical complications of the gastrointestinal tract with the retropubic approach. Short-term mortality following radical prostatectomy is low; approximately 0.5% for men under age 70 and about 1.0% for men aged 75 and older. Long-term complications associated with radical prostatectomy include impotence and incontinence. Although modern surgical techniques have decreased the incidence of postsurgical incontinence, reported rates of this complication vary widely. Patient reports of incontinence have been as high as 31%, whereas reports from tertiary medical centers suggest rates under 10% [44–46]. The age of the patient and whether an anastomotic stricture develops influence the recovery of continence. Patients over age 65 have a greater risk of incontinence compared to men under age 65. Return of erectile function has also been correlated with patient age. Quinlan et al. evaluated 503 potent men between the ages of 34 and 72 who underwent radical retropubic prostatectomy [47]. Among men under the age of 50, about 90% were potent if one or both neurovascular bundles were preserved. Among men age 65–69, only 27% recovered sexual function. Recovery of sexual function is likely to be even lower among men 70 years and older. Bill-Axelson et al. published 11-year outcomes from a randomized trial comparing radical prostatectomy against surveillance for men with clinically localized prostate cancer [48]. They found that all-cause survival was not significantly different between the two arms of the study, although there was a modest decrease in prostate cancer mortality from 18% in the watchful waiting arm to 13% in the radical prostatectomy arm. Interestingly, this benefit was only seen in men less than 65 years at the time of diagnosis and was achieved primarily during the first 5 years following treatment. Surgery in the setting of high risk and locally advanced disease has seen a resurgence. With improved imaging techniques and understanding of surgical anatomy, this can be completed with acceptable oncologic and functional outcomes. Consideration of disease location and burden may require altering surgical approach or surgical extent of dissection. Postoperative radiotherapy should be considered in this population as improvements in progression-free survival have been demonstrated in prospective trials [49, 50].

Radiation Therapy

Radiation therapy can also be used in the primary management of prostate cancer. Radiation therapy is frequently utilized for elderly men who have significant medical comorbidities which impose a high surgical risk but want treatment. There are various types of radiation treatment including external beam radiation therapy (EBRT), intensity-modulated radiation therapy (IMRT), stereotactic body radiation therapy (SBRT), proton therapy, and brachytherapy. External beam radiation is the directed delivery of high energy photons produced in a linear accelerator to the prostate, seminal vesicles, and, depending upon the patient's risk classification, pelvic lymph nodes. A simulation is a CT scan done with the patient placed in a position that is subsequently reproduced on each day of treatment (usually supine in an immobilization device designed to keep the pelvis still). Information from the CT scan with the patient in a reproducible position allows for the creation of the radiation delivery plan. IMRT is a specific type of EBRT delivery technique in which multiple metal leaflets pass across the path of a radiation beam while the radiation is being delivered. Small metal markers (fiducial markers) are often placed into the prostate prior to the SIM to allow for improved accuracy; this is termed image-guided radiation therapy. SBRT is a form of IMRT with even more precision and typically utilizing higher doses of radiation over fewer treatments. Proton radiation therapy is a specific type of EBRT in which protons are used instead of photons, the theoretical advantage being less effective to off-field targets compared to photon EBRT. Brachytherapy is the ultrasound-guided insertion of permanent, low-dose rate or temporary, high-dose rate radioactive sources directly into the prostate. Depending on the risk stratification of a patient's prostate cancer, radiotherapy may be used with or without hormonal therapy. The dose of radiation plays a role in acute and chronic toxicities. Acutely, patients can develop irritative and obstructive voiding symptoms due to bladder and urethral inflammation though may respond to alpha blockers such as tamsulosin. Late toxicities that occur greater than 3 months following treatment include stricture formation, hematuria from vascular changes in the bladder/urethra, and rarely incontinence. In addition, rectal toxicity such as radiation proctitis with rectal bleeding, urgency, and fistula formation may occur. Erectile dysfunction is also a late sequelae of radiation therapy and occurs in 30–40% of previously potent patients [51]. Recently, the use of rectal spacers between the prostate and rectum have been associated with significantly decreased rectal dosing of radiation and rectal toxicity. When assessing overall survival for men with less than 10 year life expectancy and localized prostate cancer, there is no difference in outcome whether receiving surgery or radiation [52]. As such, in those patients unfit for surgery due to competing medical risks but who would like to receive treatment, radiation represents an excellent primary therapy.

Ablative Therapy for the Treatment of Localized Prostate Cancer

Multiple energy modalities have been tested for the ablative treatment of localized prostate cancer; these include high-intensity frequency ultrasound (HIFU), cryoablation, laser ablation, photodynamic therapy, focal brachytherapy, radiofrequency ablation, and irreversible electroporation. The development of ablative techniques has been driven by its significantly lower side-effect profile when compared to whole-gland surgery or radiation. In addition, it is minimally invasive and can be performed in the outpatient setting with many returning to normal activities within a few days rather than weeks during or after radical therapy.

Cryoablation

Cryosurgical techniques have been used prostate treatment since the 1970s [53]. Cryoablation involves placing cryoprobes into the prostate to cause apoptosis and tissue destruction through extraction of heat from tissues below critical temperatures (−20 °C to −40 °C) with rapid freezing and thawing to prevent resistance and adaption. Patients with low- or intermediate-risk prostate cancer who cannot undergo surgery or radiation may opt for cryoablation. Several series have shown efficacy with cryoablation as primary treatment for localized prostate cancer. Ten-year progression-free survival for low-, intermediate-, and high-risk prostate cancer treated with cryoablation monotherapy has been estimated to be 81%, 74%, and 46%, respectively [54]. Complications of total cryoablation include erectile dysfunction, urinary incontinence, and in some very rare instances rectal urethral fistula formation. Following cryoablation, a prostate biopsy is recommended within 3–6 months. Focal cryoablation has also been used for patients with unilateral disease. In these instances, treatment consists of probe placement limited to the side of biopsy-proven disease in order to eradicate the cancer and preserve the contralateral neurovascular bundle.

High-Intensity Focused Ultrasound (HIFU)

HIFU is a noninvasive approach that uses precisely delivered ultrasound energy to achieve tumor cell necrosis without radiation or surgical excision [55]. Indications for HIFU use include those with localized prostate cancer who are unfit for surgery or radiation. In addition, focal HIFU therapy may be employed for patients in unilateral low-volume, low-grade tumors. Furthermore, HIFU has also been used in the high-risk setting and for postradiation salvage. The efficacy of HIFU in locally confined prostate cancer is comparable to those of radiotherapy and prostatectomy, characterized by failure rates of 63% at a mean of 38 months posttreatment and 30% at a mean of 34 months posttreatment [56]. Side effects of primary HIFU therapy can include prolonged voiding dysfunction and retention caused by edema, necrosis, or bladder outlet obstruction, as well as erectile dysfunction. In the same way as focal cryoablation, the goal of focal HIFU therapy is to provide oncologic control with a good side-effect profile in patients with unilateral, localized prostate cancer. The efficacy of HIFU and other focal therapies along with wider utilization will depend on precise diagnostic technologies as well as on accurate, safe, and easy applicable technologies to localize and ablate tumor foci [55].

Prostate Summary

Prostate diseases cause significant morbidity and mortality among elderly men. Both BPH and prostate cancer are relatively rare before age 50 but become increasingly common as men age into their 60s and 70s. For many patients with mild or moderate symptoms of bladder outlet obstruction, various medical therapies may prove beneficial. As symptoms worsen, however, surgical treatment may offer the best chance of relieving symptoms of urinary frequency, hesitancy, and slow stream. Most patients with symptomatic BPH should be offered therapy with an a-blocker or a 5a-reductase inhibitor before proceeding to surgery. Only patients with large prostates should be considered for simple prostatectomy. Minimally invasive therapies are available, but data on long-term efficacy outcomes are still needed. Prostate cancer poses a much more difficult problem for elderly men, especially men with well or moderately differentiated tumors. Prostate cancer in these men is frequently a slow-growing tumor, and other competing medical risks may become the dominant medical problem long before the cancer metastasizes. Patients must carefully assess the relative risks and benefits of a surgery. Elderly men with high-grade prostate cancers (Gleason scores 8–10) face a significant risk of dying from their disease even when it is diagnosed as a localized disease. These men may want to consider definitive treatment with radiation therapy or radical prostatectomy. Focal or subtotal ablative treatments may also be a viable option for elderly men as they provide effective short-term treatment with fewer associated side effects. For men with low grade and low-risk prostate cancer, active surveillance remains a widely utilized option with excellent cancer specific survival.

Kidney Cancer

Kidney Cancer Epidemiology and Etiology

Solid neoplastic lesions of the kidney are comprised of both benign and malignant pathology. Most solid lesions derived from the renal parenchyma are malignant in nature and are predominantly renal cell carcinoma (RCC) (80–90%) [57]. The World Health Organization (WHO) has classified benign renal masses based upon cell type of origin and histopathology (Table 4). The most common benign solid lesions of the kidney include renal cortical adenoma, metanephric adenoma, oncocytoma, and angiomyolipoma. Angiomyolipoma is the only benign tumor that can be readily distinguished by radiographic imaging from its malignant counterparts. Angiomyolipomas (AMLs) are a rare benign clonal neoplasm consisting of adipose tissue, smooth muscle, and blood vessels [58]. The presence of even a small amount of fat on CT is diagnostic of this tumor and can exclude RCC. Epithelioid AMLs lack macroscopic fat and are indistinguishable from other solid renal masses. Classic AMLs can occur either sporadically or in association with the tuberous sclerosis complex (TSC). Size greater than 4 cm and presence of intralesional vascular aneurysms >5 mm are associated with AML hemorrhage [59].

Table 4 WHO classification of benign renal tumors

Classification	Types
Epithelial tumors	Oncocytoma
	Papillary adenoma
Mesenchymal tumors	Angiomyolipoma
	Leiomyoma
	Hemangioma
	Reninoma
	Schwannoma
	Lymphangioma
Mixed epithelial and mesenchymal tumors	Mixed epithelial and stromal tumor
	Cystic nephroma
Metanephric tumors	Metanephric adenoma
	Metanephric adenofibroma
	Metanephric stromal tumor

Since the majority of solid renal masses are malignant and very few benign lesions can be characterized as noncancerous on imaging, it is the clinical assumption that solid lesions of the kidney are malignant until proven otherwise. RCC accounts for 2–3% of all adult malignancies and is considered the most lethal of all urologic cancers [20]. The majority of RCCs are sporadic in origin with hereditary etiologies (von Hippel–Lindau (VHL), hereditary papillary renal carcinoma syndrome, etc.) accounting for a small portion of RCC though the exact estimate of hereditary influence is controversial. RCC is a malignant disease of the elderly, occurring most commonly in the sixth and seventh decades of life [21]. Unlike bladder cancer, there are very few accepted environmental risk factors for RCC. Tobacco exposure is the only accepted factor, with an associated risk as high as 2.5, as compared to controls [60]. In contrast, the hereditary forms of RCC have given us an understanding of the genetic basis of renal carcinogenesis. In many instances, the genes responsible for the hereditary renal cancer syndromes play a role in the more commonly seen sporadic counterparts in the elderly. The most common variant of RCC is clear cell carcinoma. Molecular investigations have identified the inactivation of the VHL tumor suppressor gene located on chromosome 3p25 as the genetic cause of renal tumorigenesis in this subtype [61].

A high percentage of sporadic clear cell renal cancer seen in the elderly also demonstrates allelic loss of the VHL locus [62]. In a similar fashion, other hereditary renal syndromes have revealed the genetic etiology of various subtypes of renal cancer (Table 5).

Table 5 Familial renal cell carcinoma syndromes

Syndrome	Mechanism	Clinical manifestations
Von-Hippel Lindau (VHL)	pVHL tumor suppressor gene (3p25-26)	Clear cell or cystic RCC Retinal angiomas CNS hemangioblastomas Pancreatic cysts and islet tumors Epididymal cystadenomas Pheochromocytomas
Hereditary papillary RCC (HPRCC)	cMET proto-oncogene (7q31)	Type I papillary RCC
Hereditary leiomyoma RCC (HLRCC)	Fumarate hydratase tumor suppressor gene (1q42-44)	Type II papillary RCC (aggressive) Cutaneous leiomyomas Uterine fibroids
Birt-Hogg-Dube (BHD)	Folliculin tumor suppressor gene (17p12q11.2)	Chromophobe RCC or oncocytomas Fibrofolliculomas of head and neck Pulmonary cysts and spontaneous pneumothorax

Adapted from American Urologic Association, Renal Neoplasms

Natural History

A thorough understanding of the available knowledge regarding RCC behavior is important for treatment decisions in the elderly population. This special group of patients may have numerous confounding factors such as comorbid disease, which can impact life expectancy not related to their diagnosis of RCC. Therefore, it is imperative to understand the natural history of this tumor in the geriatric population. Although most clinical observations of RCC have been in patients in their late decades of life, these investigations do not specifically relate biology of tumor to age [63]. Factors such as tumor stage and grade are important prognosticators for RCC and can give insight into its clinical behavior [64]. Despite these important clinical parameters, the natural history of RCC in a particular patient can be highly variable. The clinical presentation of RCC can vary from an incidentally found solid renal mass, seen on imaging only, to a large rapidly growing mass with systemic metastasis. Prior to the advent of imaging techniques such as ultrasonography (US), CT, or magnetic resonance imaging (MRI), most of these kidney cancers were detected by clinical symptoms associated with RCC due to local tumor growth, hemorrhage, paraneoplastic syndromes, or metastatic disease. One prominent symptom, flank pain, is usually due to tumor hemorrhage and obstruction of the collecting system from clot. But in advanced disease, the symptom of pain may be the hallmark of local invasion. The classic triad of hematuria, flank pain, and an abdominal mass on physical exam is rarely seen in the modern era of advanced imaging [65]. Patients with advanced disease also complained of constitutional symptoms, such as weight loss, fever, and night sweats. On physical exam, they were often found to have palpable adenopathy, a nonreducing varicocele, and bilateral lower extremity edema. These tumors were often very large, and up to 25% were associated with metastases. Additionally, half of the patients who appeared to have organ-confined RCC

Table 6 Risk of harboring RCC at presentation

Tumor size (cm)	% Benign pathology	% Metastatic
<1	35–45%	<1%
1–2	20–25%	<1%
2–3	15–20%	<1%
3–4	15–20%	2%
4–5	~10%	2–3%
5–6	~10%	5–10%
6–7	~5%	5–10%
>7	~5%	15–20%

manifest asynchronous metastatic spread following an attempt at curative surgical extirpation, though contemporary series report a much lower rate [66, 67]. This malignancy preferentially spreads to the lungs, lymph nodes, and bone, although metastatic lesions are also found in less common sites such as brain, gallbladder, epididymis, and skin.

The increasing use of noninvasive imaging has shifted the presentation of this disease from a symptomatic course to that of a disease found incidentally in the elderly. The incidence of RCC has steadily increased during the last three decades, mainly due to the use of routine cross-sectional imaging for renal-related and nonrenal-related indications [68]. Now, most RCCs are detected incidentally as small tumors in patients without symptoms. The natural history of these neoplasms has not been investigated adequately, especially that of an incidentally found small renal mass. The risk of metastases at presentation and risk of harboring RCC at presentation are strongly associated with tumor size (Table 6) [49, 69]. As such, the American Urologic Association recommends active surveillance for small renal masses (<4 cm) detected in the elderly and infirm patients.

Management

Management of kidney cancer in the elderly may be a very complex decision process. Treatments must incorporate concerns about efficacy, comorbid illnesses, and complications, as well as physiologic effects on renal function and competing causes for future mortality. Surgery remains the mainstay for curative management of localized RCC. Patients with localized kidney cancer typically do not die of kidney cancer thereby underscoring functional aspects of therapy and survivorship. Features predictive of outcome after surgical treatment of localized RCC include T stage, tumor size, nuclear grade, presence of histologic necrosis, and performance status [70]. The foundation of surgical therapy for renal cancer is complete excision of all neoplastic tissue with an adequate surgical margin. This objective may be obtained by either complete removal of the kidney (radical nephrectomy) or via a nephron-sparing surgical approach (partial nephrectomy). In addition, many minimally invasive techniques, such as cryotherapy or radiofrequency ablation (RFA) can be used. Thermal ablative techniques can be applied during standard open or laparoscopic surgery but are better suited to a percutaneous approach under radiologic guidance (CT or MRI). When performed via the latter technique, a potentially curative treatment can be applied to a completely different patient demographic. Those with significant comorbid illnesses that were previously deemed unsuitable for surgical management can now be given treatment with curative intent, under local anesthetic or minimal sedation. Additionally, active surveillance may be an option especially for those elderly individuals with significant competing risk factors for non-RCC-related mortality. Renal biopsy may help delineate the natural history of RCC in this nontreatment group, to help identify aggressive renal cancers from those with minimal growth and metastatic potential [71]. There are several nomograms described in the published literature to help with competing risk counseling, including a Fox Chase competing risk calculator that is available online.

Radiologic Evaluation

The current radiologic modalities used to diagnose and evaluate renal masses include intravenous pyelography (IVP), renal ultrasound (US), CT, and MRI. In the past, the standard IVP was a commonly used test for the evaluation of hematuria. However, due to the lack of sensitivity and specificity for the detection of renal parenchymal tumors, this technology has been supplanted by multidetector computed tomography urography (CTU), for the evaluation of hematuria [72]. More than 70% of asymptomatic renal masses are found to be simple cysts. The prevalence of benign renal cysts increases with age and are found in over 50% of patients older than 50 years of age, thus a significant finding in the elderly [73]. These lesions are easily characterized by US and CT, and the most common “simple” variety requires no further workup or surveillance [74]. A dedicated renal protocol CT, which entails thin-slice images through the kidney with and without administration of contrast, is the single most important radiologic test to evaluate for RCC. Any renal mass with enhancement characteristics of more than 15 Hounsfield units (HU) after administration of contrast material should be considered an RCC, until proven otherwise [75]. Gadolinium-enhanced MRI is also an excellent modality equal to contrast-enhanced CT that can be utilized for patients with renal insufficiency, a significant problem in the elderly population. The gadolinium-based contrast agent (GBCA) used in MRI lacks significant nephrotoxicity, though previous formulations were shown to have an association with nephrogenic systemic fibrosis, a debilitating and potentially life-threatening disease, with the use of GBCA in renal failure patients [76]. Due to this finding, widespread transition to contrast agents that do not cause nephrogenic systemic fibrosis has been underway. Current precautions involve informing the patients regarding the potential risks of gadolinium-enhanced MRI versus performing a standard CT with iodinated contrast media and understanding the risk of contrast medium nephropathy.

Treatment of Kidney Cancer

Radical Nephrectomy

The radical nephrectomy is the standard of care for localized tumors not amenable to nephron-sparing technique such as partial nephrectomy. While nephron-sparing surgery is recommended by national guideline committees, the only randomized trial to compare partial and radical nephrectomy did not demonstrate any survival benefit to partial nephrectomy [77]. Radical nephrectomy may be the preferred modality for higher risk kidney tumors if there is a high tumor complexity with risk of complication even in experienced hands, there is no existing kidney disease, and postoperative GFR is anticipated to be well preserved. When compared to a partial nephrectomy, radical nephrectomy poses less risk of urinoma and hemorrhage but can lead to a relatively higher risk of chronic kidney disease. Removal of the adrenal gland during RN is generally not indicated unless there is clinical suspicion for involvement based on preoperative imaging and or gross involvement visualized intraoperatively. Regional lymph node dissection does not improve cure rate or survival in patients with low stage, localized RCC based on the results of the EORTC 30881 phase III randomized trial [77]. However, a lymph node dissection improves staging, and may potentially improve survival, albeit with the potential for added complications, in patients with clinical suspicion of positive nodes [78]. Another variable to consider is the choice of surgical incision, which can affect morbidity in the elderly. The radical nephrectomy can be performed through a variety of surgical incisions. The surgical approach is determined by the size and location of the tumor, body habitus, history of previous abdominal surgeries, and morbidity of the patient, all important considerations in the elderly population. This operation is usually performed through a transabdominal approach, which allows abdominal exploration for metastatic disease and early visualization of the renal vasculature with minimal mobilization of the tumor. The principal disadvantage is a slightly longer postoperative ileus and possible long-term complications related to adhesions. Other approaches include the flank incision, most commonly at the eleventh and twelfth rib, and a thoracoabdominal incision. The flank incision is an extraperitoneal approach that may be beneficial in the elderly or in patients with poor surgical risk, but exposure of the renal vasculature is limited especially in large tumors. The thoracoabdominal incision extends from the flank anteriorly, involving an incision through the diaphragm. This approach allows excellent visualization of the tumor and vessels but often requires placement of a tube thoracostomy for management of the consequent pneumothorax. Although large RCCs may be removed from this incision, the postoperative morbidity is high and should be avoided in patients with poor pulmonary function, and is rarely indicated in the elderly. The cancer-specific survival following this procedure is dependent on a number of variables, with pathologic stage proving to be the single most important prognostic factor for RCC [64]. Approximately 70–90% of patients with organ-confined RCC (TNM stage T1–2) are alive without disease at 5 years [64]. Survival decreases significantly once the tumor is locally advanced or when lymphatic and systemic metastases are discovered.

Laparoscopic nephrectomy or robotic nephrectomy for both benign and malignant disease has become the standard of care at most centers. This minimally invasive surgery is associated with less postoperative discomfort and improved recovery, and costs compare favorably with the open approach [79]. A variety of approaches are utilized laparoscopically which include transperitoneal, retroperitoneal, and hand-assisted approaches, each dependent on the skill and comfort level of the surgeon. In the elderly population, this technique is attractive due to decreased convalescence and pain. These benefits have been shown to result in improved pulmonary function among patients treated by LRN as compared to the open counterpart, suggesting that that this procedure may be particularly useful in patients with poor pulmonary reserve [80]. One exception is the patient with severe chronic obstructive pulmonary disease with CO_2 retention. These patients may develop significant hypercarbia or acidosis and will require close monitoring.

Partial Nephrectomy

Postoperative morbidity of radical nephrectomy includes renal dysfunction in the both the short- and long-term setting. This occurrence has prompted surgeons to investigate alternatives to complete removal of the kidney, especially in the patient with a solitary kidney, impaired renal function, or those that present with bilateral renal masses. In the past, parenchymal-sparing partial nephrectomy was performed only for the above reasons due to concerns about incomplete resection and recurrence. In addition, the renal transplant literature concerning donor nephrectomy (patients with a normal contralateral kidneys) have shown that donors do not have a higher rate of kidney failure during their lifetime [81]. However, distinct differences exist between donors and RCC patients. Renal donors tend to be carefully selected for medical comorbidities and are generally young, whereas those patients with RCC tend to have more comorbidities. These changes are reflected in the renal function of RCC patients who choose complete nephrectomy. A landmark study by Huang et al. highlighted the impact of radical nephrectomy on future renal function. The incidence of chronic kidney disease (stage 3) was much higher in patients who underwent radical nephrectomy (65%) than after partial nephrectomy (20%) [82]. This highlights the importance of considering partial nephrectomy even with a normal contralateral kidney. The classic partial nephrectomy for RCC involves removing the tumor with an adjacent 1 cm margin. A margin this size is easily obtainable for exophytic tumors but is not technically feasible for neoplasms located intraparenchymally or near the renal sinus/vasculature. More contemporary data has shown that a histologic tumor-free margin is more important; the width of the resection margin has no biologic or prognostic significance [83]. In fact, enucleation of the tumor with negative macroscopic margins has similar recurrence rates to wider resection. Partial nephrectomy is now considered an acceptable therapeutic approach in patients with a single, small T1a (<4 cm) RCC and a normal contralateral kidney. In an elderly patient, the choice of a partial nephrectomy is an accepted practice to avoid chronic renal dialysis. However, in the setting of a normal contralateral kidney, one must weigh the additional risk of complications unique to this procedure. These include increased bleeding, urinary fistula, positive margins, local recurrence, arteriovenous fistula, and nonfunction of the remaining portion of the kidney. Though it should be mentioned that studies have shown no difference in 30-day mortality for elderly patients who undergo partial versus radical nephrectomy [84].

Thermal Ablative Therapies

Many elderly patients with RCC have significant comorbidities that make them poor surgical candidates. This group of patients is often treated conservatively with active surveillance and not given an option for curative treatment. It is assumed that the patient will most likely have a non-RCC mortality. With improvements in health care, these elderly patients are living longer which would allow a subset of these RCCs to grow and metastasize. In addition, many elderly patients are very anxious about not treating RCC in their kidney, especially for such a chemo-/radiation-resistant tumor. Thermal ablative therapies are a minimally invasive option for curative treatment of RCC. These modalities include renal cryotherapy and radiofrequency ablation (RFA); both are different forms of ablative energy focused on the renal lesion.

Thermal ablation is an option for cT1a renal masses <4 cm in diameter. A core tumor biopsy is recommended and counseling about ablation should include a discussion regarding potentially higher risk of local recurrence, potential need for reintervention, need for long-term abdominal imaging, lack of proven parameters for success, and potential for difficult surgical salvage. Both cryotherapy and RFA use needles to transmit their energy to the tumor and can be placed percutaneously or through laparoscopic exposure. The percutaneous approach can be performed with local anesthetic alone or with intravenous sedation which would allow most patients who are poor surgical risks a chance at curative treatment. These focused thermal ablative therapies allow RCC treatment with minimal morbidity while maximizing posttreatment renal function. Percutaneous thermal ablative therapies are performed with image guidance: CT, MRI, and ultrasound. The most important principle in all the described therapies is precise localization and treatment application of the energy. In this regard, cryotherapy has an advantage because the treatment area or "iceball" is easily visualized on imaging unlike RFA. Ablative therapies have a slightly higher risk of recurrence compared to surgical removal; however, retreatment is an option.

Adjuvant Therapies for Localized RCC

There have been a number of kidney cancer trials that have explored the benefit of systemic therapies following surgery for high risk localized RCC. Although demonstrating promise in the metastatic setting, most adjuvant localized studies thus far have failed to show a benefit.

Management of Advanced RCC

About one-third of patients diagnosed with kidney cancer present with metastatic disease. Patients with advanced RCC present with a wide spectrum of disease varying from indolent to rapidly progressing. The majority of these patients are candidates for systemic therapy. Elderly individuals with advanced RCC are unlikely to benefit from surgical therapy unless a radical nephrectomy is performed with palliative intent. Therefore, systemic agents offer the most rational treatment options for older patients with this disease. Although categorical recommendations for the therapy of cancers based on chronologic age are neither appropriate nor reasonable, many decisions for or against administration of systemic therapy are often based on the age of the individual. Variability among aging individuals with regard to physiologic senescence and comorbidities suggests that a more practical approach for the clinician is the use of guidelines and performance scores to assess the elderly patient's functional and physiologic tolerability for potentially toxic therapy. First, it is important to define those who are considered elderly. Without readily usable markers of a patient's physiologic age, Balducci recommended that the clinician consider those individuals over 70 years as elderly and should undergo some form of geriatric assessment [85]. These individuals have an increased occurrence of the following: decreased musculoskeletal mass, functional limitations, geriatric syndromes (dementia, malnutrition, polypharmacy, incontinence, delirium), and multiple comorbidities.

Minimizing the occurrence of side effects from chemotherapeutic drugs in the elderly requires careful clinical assessment for functional ability and preexisting neuropathy, cardiac/hepatic/renal function, bone-marrow reserve, nutrition, polypharmacy, and cognitive function. Interventions should include adjusted doses of renally excretable agents to GFR, use of support agents such as growth factors and cytoprotective agents when indicated, appropriate nutritional support, and the preferential use of safer agents when indicated. Traditional cytotoxic chemotherapeutic agents and hormonal therapies have been ineffective in the treatment of metastatic RCC. An improved understanding of the molecular biology underlying metastatic RCC has led to the development of targeted agents to treat this disease. Vascular endothelial growth factor (VEGF) overexpression in RCC is a result of inactivation of the VHL tumor suppressor gene, which occurs in the majority of clear cell RCC cases. Insufficient or inactive VHL leads to constitutive activation of HIF and overproduction of HIF-related proteins, including VEGF. VEGF overexpression drives angiogenesis in RCC. Strategies to target the VEGF pathway include small molecule tyrosine kinase inhibitors (sunitinib, sorafenib, pazopanib, and axitinib) that target VEGFRs and anti-VEGF directed antibodies (bevacizumab). Nivolumab is an anti-programmed death (PD)-1 monoclonal antibody. Nivolumab acts as an immunomodulator by blocking ligand activation of the PD-1 receptor on activated T cells. VEGF and mTOR-targeted therapies have improved patient outcomes and represent the mainstay of treatment for advanced untreated RCC. The use of immunotherapy for advanced RCC in the aged must be approached cautiously due to the significant toxicities associated with its use. Improved understanding of the biology of RCC, especially through the VHL pathway, has led to the many "targeted therapies" for treatment of metastatic kidney cancer. Since 2005, two broad-spectrum TKIs (sunitinib malate and sorafenib tosy-late), one mTOR inhibitor (temsirolimus), and one VEGF antibody (Bevacizumab) in combination with interferon have been approved for the treatment of advanced RCC. In addition, another mTOR inhibitor (everolimus) has received FDA approval for patients with advanced RCC after failure of treatment with sorafenib or sunitinib, i.e., second-line therapy [86]. Sunitinib is well tolerated when compared to interferon and has become standard first-line therapy for metastatic RCC. In addition, data from an expanded access trial has revealed that sunitinib is safe and efficacious in subgroups of patients including those with poor performance status [87]. In current practice, most patients with treatment-naïve good/intermediate risk clear cell RCC receive sunitinib or pazopanib, while those with poor risk disease receive nivolumab+ipilimumab. Following failure of first-line treatment for metastatic RCC, treatment recommendations for patients with relapsed or recurrent disease are primarily limited to targeted agents. Everolimus, an mTOR inhibitor, is approved for the treatment of advanced RCC following treatment failure with sunitinib and sorafenib. Nivolumab, an anti-PD1 antibody was recently approved for use in previously treated patients (one or two lines of antiangiogenic therapy). All targeted agents can be used in the elderly metastatic patient with consideration of the caveats mentioned earlier (careful evaluation, GFR dose adjustment, use of growth factors, etc.) to minimize the side effects and improve the tolerability of toxic systemic therapy.

Bladder Cancer

Tumors of the bladder are among the most common oncological issues managed by urologists. Few conditions illustrate the link between cancer and aging better than urothelial cell carcinoma of the bladder (UCC). There is a distinct increase in incidence with age such that men over 70 have a 3.7% probability of developing bladder cancer compared with 0.92% of men 60–69 and 0.38% for men 40–59 [88]. As one ages, the risk for higher stage and grade disease increases. This raises the probability of developing invasive cancer and therefore affecting survival [89]. The basis for this phenomenon has triggered molecular research aiming to explain the influence of biological changes associated with the aging processes on the development and/or progression of UCC.

Urothelial cell carcinoma represents a broad spectrum of pathologic processes, extending from indolent low-grade papillomas to invasive poorly differentiated tumors with rapid metastatic capability. Age and performance status play a major role in the election of therapy and outcomes. Therefore, successful management of UCC of the bladder in the elderly patient requires an understanding of the natural history of UCC and the quality-of-life implications of each therapeutic approach.

Diagnosis

Bladder cancer represents an important consideration in the differential diagnosis of voiding complaints in the elderly individual. The presence of a neoplastic lesion within the bladder may be heralded by irritative symptoms such as urinary urgency, frequency, or dysuria. Hematuria, microscopic or gross, may also announce the existence of malignant bladder lesions. It has been estimated that 5–15% of patients, predominantly men, with hematuria harbor unsuspected bladder cancer [90]. The 2008 US Preventive Services Task Force found no high quality evidence that screening would impact mortality from bladder cancer. Although screening for UCC specifically is not recommended, many patients do routinely have urinalysis for the above symptoms or by their primary care physician. Any asymptomatic hematuria (>3 red blood cells per high power field in the absence of a benign cause) requires urologic evaluation with cystoscopy as well as urothelial tract imaging, typically excretory urography or with the more contemporary computed tomography urography. The cost implications of this approach, given the incidence of voiding symptoms and hematuria, are obvious. In the absence of a clear etiology such as infection, it is difficult at the present time to identify a subpopulation of patients not requiring a cancer evaluation.

Natural History

Epidemiologic and experimental evidence favors a strong role for environmental exposure as an etiology of bladder cancer in the elderly. However, since many cases arise in patients with no obvious exposure, it is important to understand the molecular basis of this disease. Several inherited tumor syndromes are associated with bladder cancer development including Lynch syndrome and Li–Fraumeni syndrome. Patients that have a strong family history of cancer, that have a syndromic phenotype, or that have bladder cancers occurring at a young age and without known risk factors should be referred to a geneticist for consideration of genetic testing.

The most important epidemiologic risk factors associated with urothelial carcinoma are chemical carcinogens, which are derived from tobacco products or a spectrum of industrial and environmental agents. Urothelial cell carcinoma of the bladder represents a broad spectrum of pathologic processes, thus preventing a linear description of the natural history of this disease.

Table 7 TNM staging of bladder cancer

Stage	Characteristics
Tx	Unknown
T0	No carrier
Ta	Noninvasive
Tis	Carcinoma in situ
T1	Invades lamina propria
T2	T2a – invades detrusor muscle superficially
	T2b – invades detrusor muscle deeply
T3	T3a – invades perivesical fat microscopically
	T3b – invades perivesical fat macroscopically
T4	T4a – invades prostate stroma (i.e., direct invasion and not only prostatic ducts) or vagina/uterus
	T4b – invades pelvic side wall or abdominal wall
Nx	Unknown
N0	No cancer in nodes
N1	1 positive pelvic node in the true pelvis (internal iliac, obturator, external iliac, presacral, perivesical)
N2	$\geq$ 2 positive pelvic nodes in the true pelvis
N3	Positive common iliac nodes
Mx	Unknown
M0	No metastases
M1a	Nonregional nodal metastases
M1b	Other distant metastases

To better understand the development and progression of UCC, it is important to make a distinction between superficial or non-muscle invasive bladder cancer and invasive carcinoma. Superficial UCC exhibits an overall low risk of progression (to a life-threatening cancer), but recurrences are very frequent. A minority of these recurrences may eventually progress into high-grade disease, which can then be locally invasive. The management of high-grade/invasive disease in the elderly is costly and challenging. Treatment options for patients with muscle-invasive disease or recurrent high-grade superficial disease include cystectomy (with or without chemotherapy), radiation and chemotherapy (bladder-sparing therapy), and a palliative approach. It is important to understand the difference between a superficial and invasive lesion when considering treatment of a geriatric patient with bladder cancer. The staging system for a primary bladder UCC is shown in Table 7.

Non-muscle Invasive Bladder Cancer

Approximately 75–80% of all bladder UCCs are classified initially as non-muscle invasive or superficial. This group of lesions encompasses indolent papillary lesions confined to the urothelium with high recurrence frequency (stage Ta), a poorly differentiated flat cancer called carcinoma in situ (CIS) with higher invasive potential (Tis), and neoplasms invading the lamina propria of the bladder wall (stage T1). Information regarding the recurrence and possible progression of superficial UCC is available after a complete transurethral resection of the bladder tumor (TURBT) has been performed. The pathologic specimen allows incorporation of information regarding the depth of invasion, histologic grade, and presence or absence of multicentric disease. The remainder of this discussion refers to the biologic behavior of each of these lesions in elderly patients. Stage and histological grade are central determinants of the disease-specific outcome for superficial UCC [91]. In general terms, a stage Ta lesion exhibits a 50–90% recurrence rate at 5 years with a 2–25% rate of progression to muscle-invasive disease. Within this same category (Ta), pathologic grade-1 and 2 cancers exhibit a recurrence rate of approximately 30%, whereas grade-3 lesions recur in over 70% of cases, exemplifying the importance of histologic grade [92].

Muscle Invasive Bladder Cancer

The concept of muscle-invasive disease refers to lesions that have invaded beyond the lamina propria into the muscle wall of the bladder (stage T2). The literature suggests that approximately 50% of individuals who present with stage T2–T4 TCC will develop distant metastasis within 2 years [93]. Most patients who develop T2 lesions of the bladder present initially with this muscle-invasive disease de novo rather than from a previous superficial cancer (Ta-T1). It appears that the proportion of patients with muscle-invasive TCC increases with age. Approximately 18% of patients aged 40–44 years have locally advanced TCC at presentation, whereas 39% of patients over 84 years of age present with this stage disease [68]. As a result, the elderly patient more often faces a life-threatening cancer compared to their younger counterparts. Unfortunately, this elderly patient will have a higher surgical risk due to comorbidities. Data extracted from SEER database found that individuals of 75 years of age and older with muscle-invasive bladder cancer had a higher prevalence of cardiac disease, prior cancer diagnosis, chronic anemia, and poor American Society of Anesthesiologists Physical Status Classification (ASA) [89]. These factors have a direct impact on treatment choices, especially when surgical options may involve significant morbidity.

Radiologic Evaluation

Once the diagnosis of a stage T2 UCC has been established through transurethral biopsy or resection, the patient should be thoroughly examined for evidence of lymphatic or hematogenous spread, as well as invasion into adjacent tissues. The primary sites for the dissemination of UCC include the pelvic lymph nodes (within the obturator and hypogastric regions), lung, liver, and bone. Pertinent radiologic studies include a chest radiograph and an abdominal/pelvic CT or MRI scan. A bone evaluation with skeletal scintigraphy (bone scan) is indicated in individuals with complaints of musculoskeletal pain or an elevated alkaline phosphatase level [94]. Approximately

5–15% of patients with invasive UCC harbor metastatic bone lesions, which obviate an attempt at curative (surgical) therapy. Computed tomography is about 80% accurate in differentiating locally advanced tumors involving perivesical fat or surrounding structures from those with less invasive tumors. However, since CT is often performed after a transurethral resection, interpretation of perivesical fat invasion becomes involved. It may be difficult to distinguish inflammatory or postsurgical edematous changes from true extravesical tumor extension. Another important limitation of CT is that it may miss tumors <1 cm in size, particularly those in the bladder trigone or dome. Tumors located in these areas may be better evaluated by gadolinium-enhanced MRI. The use of positron emission tomography (PET) in the evaluation of patients with localized TCC remains investigational, largely due to confounding factors from urinary excretion of the glucose-labeled tracers. MRI may ultimately be the preferred study over CT in the older patients since they often present with a suboptimal creatinine clearance.

Treatment: Non-muscle Invasive Disease

The presence of any feature displayed on Table 8 is associated with an increased risk of recurrence or progression for non-muscle invasive bladder cancer.

This is encouraging for the geriatric patient with comorbidities who does not present with these risk factors, since they can be managed conservatively. Management would involve intermittent resection or even fulguration of recurrent lesions without any additional treatments. In this context, patients who do not develop another tumor within 3 months of the initial resection for UCC have an 80% probability of never demonstrating another tumor in the bladder [95]. However, patients who experience ten or more recurrences exhibit a high rate of progression and death from TCC [96]. Therefore, in this instance, the conservative algorithm for stage Ta UCC with endoscopic resection alone should be complemented by intravesical therapy. CIS presents as a flat formation of poorly differentiated UCC confined to the mucosal surface of the bladder. This CIS lesion (Tis) may appear as a solitary primary lesion or accompanied by another form of UCC. Tis may also display a diffuse involvement of the mucosa and extend into the distal ureters or prostatic ducts. This pattern of superficial spread is associated with particularly aggressive disease, with the majority progressing to invasive cancer. Common presenting manifestations of CIS include severe irritative voiding symptoms and hematuria. But, many of these patients may be relatively asymptomatic with only an abnormal finding on urine cytology. In addition to recurrence, the literature supports an especially high rate of progression to invasive disease after endoscopic resection [97]. Therefore, patients with primary or concomitant Tis cannot be treated with endoscopic resection alone, regardless of their age. Intravesical therapy should be used in conjunction with TURBT. If this combination therapy fails to control the disease, cystectomy should be considered in the elderly individual with a good performance status. The final type of superficial UCC is a lesion that invades the lamina propria of the bladder wall but not the muscularis propria. This stage T1 lesion exhibits a high rate of recurrence (67–81%) and progression (12–49%). Patients presenting with this stage disease have a cancer-specific mortality ranging from 17% to 71% [97]. Virtually, all of these tumors are of high grade and require therapy beyond standard endosurgical resection due to the risk of progression [98]. T1 tumors are often treated adjuvantly with instillation of chemotherapeutic or immunotherapeutic agents in addition to endoscopic ablation. The intravesical

Table 8 Features associated with an increased risk of recurrence or progression

Multiple papillary recurrences (two or more in a given year)
More than three lesions or any tumor >3 cm in diameter, sessile or with a thick stalk invasion of the lamina propria (T1 tumor) or poorly differentiated histology
Incomplete resection due to diffuse bladder involvement and/or unfavorable location
Diffuse Tis alone or in association with papillary tumor

instillation of Bacillus Calmette–Guérin (BCG) has been shown to be efficacious in reducing the recurrence rate by 30–40% and may also reduce progression of T1 tumors [99]. Elderly individuals with significant comorbidities and solitary T1 disease may comprise a subpopulation of patients for whom endoscopic resection may be adequate. Nevertheless, intravesical immunotherapy in addition to TURBT should be standard practice for T1 lesions in the geriatric population given the high risk for progression and recurrence. A second-look (repeat) TURBT is done within 2–6 weeks of the first TURBT for T1 tumors and if the first TURBT is incomplete, if the tumor is high grade, and larger than 3 cm or multifocal.

An aggressive approach of early cystectomy for de novo T1 disease has been advocated by some as immediate cystectomy at the time of initial diagnosis of a T1 cancer can improve survival [100]. The selection of an adequate therapeutic plan for an elderly patient with T1 TCC must involve performance status, comorbid illness, and impact of the treatment on their quality of life.

Intravesical Therapy

Intravesical therapy permits high local concentrations of a chemotherapeutic or immunotherapeutic agent within the bladder to eradicate residual tumor cells that remain viable after TURBT, thus preventing recurrence. Conceptually, this application is provided after complete resection as a specific strategy against recurrence or progression. Less commonly, intravesical therapy is instituted for residual tumor following incomplete TURBT. These instilled agents may cause symptoms of bladder irritation as a side effect. Furthermore, systemic absorption can occur if the bladder mucosa is damaged and results in systemic toxicity. Treatments, therefore, are generally initiated 2–4 weeks after tumor resection, allowing the re-epithelialization of the bladder mucosa. The most commonly used agent for intravesical therapy is Bacillus Calmette–Guerin (BCG). A number of other agents also have activity, including mitomycin, thiotepa, gemcitabine, and docetaxel. The intravesical administration of an antineoplastic agent within 24 h of TURBT has been shown to reduce the bladder cancer recurrence rate by about 35% [101]. Anthracyclines (epirubicin, doxorubicin, pirarubicin) and mitomycin C have been used. The AUA guidelines state that in a patient with suspected or known low- or intermediate-risk bladder cancer, a clinician should consider administration of a single postoperative instillation of intravesical chemotherapy within 24 h of TURBT. Patients with bladder perforations should not receive perioperative IVC since systemic toxicities and severe cystitis reactions may develop.

The AUA guidelines state that in a low-risk patient, a clinician should not administer induction intravesical therapy. In an intermediate-risk patient, a clinician should consider administration of a 6-week course of induction intravesical chemotherapy or immunotherapy. In a high-risk patient with newly diagnosed CIS, high-grade T1, or high-risk Ta urothelial carcinoma, a clinician should administer a 6-week induction course of BCG followed by maintenance therapy [102].

Bacillus Calmette–Guérin is a live attenuated Mycobacterium that has been found to incite an immune response within the bladder, which appears to be responsible for its therapeutic efficacy against UCC. The immune activation may persist for a number of months facilitating an ongoing antitumor response. BCG has also demonstrated effectiveness when administered as therapy for CIS of the bladder. At the author’s institution, BCG maintenance therapy is the standard intravesical regimen, and the majority of elderly patients complete the full protocol duration with reduction doses if necessary. Lowering the dose of BCG for this population of patients still maintains its efficacy and can be utilized during time of nationwide BCG shortages. Patients that recur despite BCG should be offered bladder removal, but clinical trials and salvage intravesical therapy with a chemotherapy agent are alternative options albeit at a higher risk of recurrence and progression.

In summary, non-muscle invasive bladder cancer presents frequently in the aged population often with a protracted natural history and a low risk of progression. Most stage Ta lesions may be managed with endoscopic resection with subsequent outpatient follow-up utilizing cystourethroscopy and urine cytology. Surveillance protocols for such patients often involve cystoscopy every 3 months for 2 years, every 6 months for 2 years, and then every year thereafter with variation based on risk of disease. The intensity of this approach may be reduced for individuals in ill health or with favorable lesions at low risk for recurrence and progression. Patients who present with Tis or T1 cancers will benefit from a course of intravesical immunotherapy with BCG, following surgical resection. Again, these patients should be carefully followed with an organized surveillance protocol. Individuals with recurrent or refractory Tis or T1 lesions should be considered for curative radical cystectomy.

Treatment: Muscle-Invasive Bladder Cancer

Therapeutic approaches to muscle-invasive UCC of the bladder are determined by the presence or absence of clinically detectable lymphatic or hematogenous metastases. Multimodality curative therapy should be applied only in individuals whose cancers are confined to the bladder wall or associated with minimal-volume regional lymphatic disease. Neoadjuvant chemotherapy prior to radical cystectomy is considered the current standard of care for muscle invasive bladder cancer.

Surgical Therapy

The perioperative morbidity associated with radical cystectomy and the substantial impact of urinary diversion on the quality of life has led to the use of less radical approaches for the management of muscle-invasive bladder cancer in the elderly. Alternatives to radical cystectomy include radical transurethral resection (TURBT), partial cystectomy, or chemotherapy/radiation, which combines radical TURBT followed by external-beam radiation therapy with concurrent chemotherapy (cisplatin used as a radiation-sensitizing agent). In general, bladder preservation approaches are considered by many to produce inferior oncologic outcomes compared to radical cystectomy. It appears that solitary tumors confined to the muscle wall are ideal candidates for these alternative treatments with intermediate and long-term cancer-specific survival rates approaching that of radical cystectomy. An attempt at complete endoscopic resection of a solid muscle-infiltrating lesion within the bladder represents the most conservative surgical treatment approach. However, radical TURBT is applicable only to a small minority of patients with muscle-invasive disease and demands intensive, long-term cystoscopic follow-up due to local recurrence. This follow-up may represent a challenge for the geriatric population. Another surgical option, the partial cystectomy, allows complete pathologic staging of the primary tumor with an extended pelvic lymph node dissection. This technique preserves urinary function and avoids the need for diversion, therefore minimizing the impact on the elderly patient's quality of life. As with the radical TURBT, only a few patients are optimal candidates for this partial resection, and the risk of recurrent tumor in the residual bladder remains. Complete surgical extirpation with radical cystectomy remains the treatment of choice for locally advanced UCC in patients of all age groups. The contemporary surgical approach includes thorough pelvic lymph node dissection followed by complete removal of the bladder, uterus, and anterior vaginal wall in women or bladder with the prostate and seminal vesicles in men. A urinary diversion with either an ileal conduit (non-continent) or a continent reservoir (orthotopic or nonorthotopic) is constructed following the cystectomy. Radiotherapy prior to surgery increases the risk of operative complications and makes the creation of an internal urinary reservoir using irradiated bowel more difficult. Therefore, radical cystectomy alone has become established as satisfactory monotherapy for most patients with locally advanced UCC of the bladder. The impact on survival from a radical cystectomy performed in a healthy surgical patient is clear. The benefit of this extensive surgery, as we age, depends largely on competing risks for death. In the elderly individual, who typically carries a high burden of comorbid diseases and disability, the benefit of radical cystectomy versus radiation therapy is less dramatic. The largest case series involving contemporary data evaluated the benefit of cystectomy in different age groups (<60, 60–69, 70–79, >79), without correlating outcomes to physiologic measures, such as performance status [103]. A total of 8034 patients underwent cystectomy, while 2077 had radiation therapy as their primary treatment for muscle-invasive UCC. They found that older patients were less likely to have a cystectomy and that a sizeable survival advantage was seen with cystectomy in all age groups except for the octogenarian (15 vs. 18 months). The small benefit of cystectomy was lost when the elderly patient had a limited or no pelvic node dissection, highlighting the importance of a full lymph node dissection in locally advanced UCC. Another multicenter trial evaluated 888 patients over a 19-year period [104]. Thirty percent of the patients were 70–80 years of age, but only 6% were over 80. Age was an independent predictor for adverse outcomes. Currently, only two small studies have utilized functional geriatric assessment as it relates to radical cystectomy outcomes. Weizer et al. correlated a Karnofsky Performance Status (KPS) score with cystectomy in 106 patients with muscle-invasive disease [105]. Patients with a KPS score below 80 had an overall 4-year survival of 14% versus 33% for those with a KPS score above 80. This functional assessment tool was validated as the only independent predictor of overall survival in a multivariable analysis that included age, marital status, treatment type, mobility, and stage. These findings demonstrate the importance of functional age of the patient in contrast to their chronologic age when dealing with muscle-invasive TCC. It is, therefore, not justified to withhold a potentially curative therapy such as radical cystectomy on the basis of age alone. Historically, many individuals are willing to undergo intensive therapy and endure significant morbidity if the likelihood of cure from a disease is high. As discussed earlier, the ability to eradicate bladder cancer is directly related to the stage at presentation, particularly the presence or absence of lymphatic metastasis. Most reports demonstrate that lymph node metastasis at the time of radical cystectomy is associated with a 6–23% 5-year survival [106]. For the elderly patient with an otherwise asymptomatic stage T2–T4 bladder cancer with borderline nodal enlargement on CT, an accurate identification of lymphatic disease could dissuade them from undergoing radical cystectomy and make more palliative approaches attractive. Finally, minimally invasive alternatives such as laparoscopic radical cystectomy or robotic-assisted radical laparoscopic cystectomy, with the potential for reduced morbidity and more rapid convalescence, are being adopted in many centers worldwide. Reports have demonstrated the technical reproducibility and safety of these techniques, although extensive experience with these procedures is required to achieve optimal results. Advantages include faster reactivation of gastrointestinal motility and shorter hospital length of stay. Although this appears as a promising alternative for the geriatric population, data regarding the long-term oncologic outcomes is lacking at the present time, especially with regard to the adequacy of the pelvic lymph node dissection by these techniques.

Multimodality Therapy for Muscle Invasive Bladder Cancer

A viable alternative to radical cystectomy is combination chemo/radiation. Chemotherapy is widely used for therapy in advanced or metastatic bladder cancer and remains an area of active research as an adjuvant or neoadjuvant treatment with definitive local therapy. The 2017 AUA guidelines recommend that for patients with muscle-invasive bladder cancer who have elected multimodal bladder preserving therapy, clinicians should offer maximal transurethral resection of bladder tumor, chemotherapy combined with external beam radiation therapy, and planned cystoscopic reevaluation. It is unclear what proportion of patients who, having initially chosen bladder preservation, ultimately require cystectomy in a non-study setting. The reported bladder preservation rates may be dependent upon the degree of initial patient evaluation and selection. Thus, currently the AUA guidelines panel proposed that multimodal bladder preserving therapy is the preferred treatment in only those patients who desire bladder preservation and understand the unique risks associated with this approach or those who are medically unfit for surgery.

Metastatic Bladder Cancer

Although prognosis is poor for patients with metastatic bladder cancer, metastatic bladder cancer is generally responsive to palliative chemotherapy. Since Sternberg et al.'s original report of a 72% response rate in metastatic bladder cancer patients using methotrexate/vinblastine/doxorubicin/cisplatin (M-VAC) [107], the incorporation of newer and highly active agents, such as gemcitabine and paclitaxel, has led to the development of new combination regimens. One combination, gemcitabine plus cisplatin (Gem-Cis) demonstrated comparable efficacy but was significantly less toxic than MVAC and has become a commonly prescribed regimen for bladder cancer [108]. However, elderly patients may not be fit for intensive cisplatin-based chemotherapy regimens. A retrospective review of 381 patients with advanced urothelial carcinoma who were treated with one of several platinum-based regimens identified 116 who were 70 years of age [109]. The elderly experienced more frequent neutropenia and renal toxicity compared to patients <70 years of age. However, toxic death rates were similar in both age groups, and median survival did not differ significantly. Immunotherapy is currently a hot top in advanced bladder cancer. Antibodies targeting PD-1 and PD-L1 are thought to generate anti-tumor immunity by inhibiting these negative T cell signaling in the PD-1/PD-L1 axis. PD-1/PD-L1 therapies are now a principal component in the management of metastatic bladder cancer and are expected to impact less advanced disease states as well. There are at least five immune checkpoint inhibitors currently approved for patients on second-line therapy for metastatic bladder cancer or for those who cannot tolerate cisplatin-based regimen, this includes atezolizumab, nivolumab, darvalumab, avelumab, and pembrolizumab. It is a consensus among the medical oncology community that all immune checkpoint inhibitor have comparable activity in bladder cancer. However, pembrolizumab is the only drug with data from phase III trial demonstrating overall survival benefit as compared to chemotherapy in second-line setting for metastatic bladder cancer. As many patients will still progress on immunotherapy, there are ongoing trials assessing the efficacy of radiation combined with chemo-immunotherapy, immunotherapy with chemotherapy, dual checkpoint inhibitor, and immunotherapy in combination with vascular endothelial receptor tyrosine kinase inhibitors.

Conclusions

Improvements in diagnostic imaging, surgical techniques, advanced instrumentation, and systemic chemotherapy/immunotherapy have been combined to offer older individuals a wide array of treatment options for renal, prostate, and bladder malignancies. However, the myriad issues confronting these people serve only to complicate the choice of therapy. The literature suggests that aging may affect negatively the treatment response of superficial disease and the outcomes of curative surgery. Comprehensive geriatric assessment tools that incorporate not only age but also physiologic and biologic considerations, such as comorbidities, functional status, renal function, and hemoglobin are necessary to help stratify the elderly into "fit" and "frail" populations, allowing tailoring of appropriate therapy. Clinicians must avoid the unconscious bias against curative treatment for an elderly individual and thoroughly address all potential options and the impact of these in the patient's context of quality of life. Age-specific investigations in conjunction with comprehensive assessment tools are needed before the best treatment options for geriatric patients are identified.

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Gynecologic Disorders in the Older Woman

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Abstract

Nonmalignant and malignant genital tract conditions as well as pelvic floor disorders including pelvic organ prolapse and incontinence are common gynecologic problems encountered by the older woman. With the rapidly increasing population of active older American women, physicians can expect to provide evaluation and treatment of these conditions with increasing frequency. These conditions are typically amenable to both medical and surgical therapies making individualization of treatment approaches important. An evidence-based review of evaluation and treatment approaches of benign and malignant gynecologic conditions of the lower and upper genital tract as well as of pelvic floor disorders common in the older woman is presented.

Keywords

Menopause · Vulvovaginal disorder · Pelvic organ prolapse · Incontinence · Gynecologic malignancies · Research in older woman

Benign Gynecologic Conditions

Introduction

Nonmalignant and malignant genital tract conditions as well as pelvic floor disorders including pelvic organ prolapse and incontinence are common gynecologic problems encountered by the older woman. With the rapidly increasing population of active older American women, physicians can expect to provide evaluation and treatment of these conditions with increasing frequency. These conditions are typically amenable to both medical and surgical therapies making individualization of treatment approaches important. An evidence-based review of evaluation and treatment approaches of benign and malignant gynecologic conditions of the lower and upper genital tract as well as of pelvic floor disorders common in the older woman is presented.

Menopause

Menopause is defined as 12 months of amenorrhea secondary to cessation of ovulation. It can also be induced by surgical oophorectomy, chemotherapy, or radiation [1]. The transition into menopause (perimenopause) typically begins 4 years prior to the last period [2] and starts with irregular cycle lengths during which estrogen levels can be normal or elevated. Ultimately, estrogen and progesterone levels decrease with subsequent increase in follicle-stimulating hormone (FSH) levels. Postmenopausal estradiol levels, the most potent estrogen, are typically <20 pg/mL, while FSH is most often >70 mU/mL. Testosterone production, however, is maintained by the ovaries and adrenal glands maintaining serum levels of testosterone at 2–40 mg/dL. Even though estrogen production declines dramatically with menopause, a small amount of production continues via peripheral conversion of androgens by aromatase in adipocytes [2]. The natural process of aging results in increased fat body mass and decreased lean body mass such that obese postmenopausal women can manifest conditions due to estrogen excess, such as endometrial hyperplasia and carcinoma. In the United States, the mean age of menopause is 51 years [2] with cigarette smoking and low socioeconomic status being risk factors for premature (<40 years old) menopause [1].

Symptoms attributed to menopause include vasomotor (hot flushes and night sweats), vaginal atrophy (itching, dryness, and painful intercourse), urinary incontinence, sleeping difficulty, depression, anxiety, mood changes, cognitive decline, and somatic complaints. However, only vasomotor symptoms, atrophy symptoms, and trouble sleeping are consistently related to menopause in longitudinal studies [1–3]. A hot flush is the sudden feeling of warmth of the chest, neck, and/or face. It lasts for approximately 4 min, usually no longer than 5 min, and may have concurrent perspiration followed by a chill [1, 2]. Hot flushes occur most commonly in the late perimenopause (~65% of women). Symptoms decrease in intensity over time with up to 90% of women having complete resolution in 5 years [1]. The physiology behind hot flashes is poorly understood, but theories center around hypothalamic control in relation to hormonal changes with the transition to menopause [1, 2]. Studies have demonstrated that menopausal symptoms vary by race and ethnicity. For example, African Americans tend to have an increased prevalence of vasomotor symptoms compared to Caucasians [4, 5] and also have a higher level of bother from these symptoms [6]. At the same time, African American women may be less inclined to bring these symptoms up in the medical encounter [7]. It is important for providers to appreciate these racial differences and screen every menopausal patient for symptoms so that appropriate treatment can be provided.

Estrogen therapy is the most effective treatment for vasomotor symptoms [8]. However, use of systemic estrogen has been complicated by results from the Women's Health Initiative (WHI), which found that systemic estrogen alone increased the risk of stroke (relative risk 1.39), while the addition of progestin increased the risk of coronary events (relative risk 1.28), breast cancer (relative risk 1.26), and pulmonary embolism (relative risk 2.13) [2]. The absolute increase in risk for these events is lower in the younger menopausal women [2]. A description of the criticisms and various organizational guidelines regarding hormone replacement therapy is beyond the scope of this chapter.

The American College of Obstetricians and Gynecologists and the North American Menopause Society recommend that the lowest effective dose of systemic estrogen (plus progestin if the uterus is present) should be used and estrogen replacement should not be used for disease prevention [1, 2, 8, 9]. Alternative medicines for the treatment of vasomotor symptoms, especially when estrogen is contraindicated, include paroxetine, clonidine, and gabapentin [1, 2].

Connective tissue, in general, is sex-hormone-sensitive. Therefore, menopause may also be associated with a loss of skin elasticity and strength of bone because of the estrogen-sensitive collagen of these structures. Postmenopausal women who are given a combination of estrogen and testosterone have been reported to have greater skin collagen content and greater skin thickness than do untreated women [10]. In untreated women, skin collagen content is inversely proportional to the amount of time since menopause. It also has been shown that oral or transdermal estrogen given together with medroxyprogesterone acetate significantly increases skin collagen content in postmenopausal women [10].

Lower Genital Tract

Vulva

The vulva includes the portions of the genitalia that are externally visible: the mons pubis, labia majora and minora, clitoris, and vestibule. Within the vestibule are the hymen, vaginal orifice, urethral meatus, and the openings of Skene's and Bartholin's ducts [11]. The vulva is covered by keratinized stratified squamous epithelium with the exception of the vestibule which, like the vagina, is not keratinized. Skin changes that occur with menopause and the accompanying decrease in ovarian estrogen production are evident on the vulva as they are on all skin surfaces. These changes include dryness, roughness, wrinkling, and loss of turgor. Structurally, there is flattening and decreased thickness of the epidermis and dermis, an overall decrease and change in distribution of subcutaneous fat, and loss as well as depigmentation of hair. These changes lead to functional loss of the skin's barrier function, elasticity, mechanical protection, and wound healing [12].

Lichen Sclerosus

Lichen sclerosus is a chronic, benign epithelial condition associated with characteristic skin changes as well as vulvar pain and pruritus. The vulva is the most common site at up to 96% of cases, but lesions can be seen on any skin surface [13]. The condition typically occurs in postmenopausal women, with a mean age of 52.6 years at time of diagnosis in one study, but can also be seen in children, premenopausal women, as well as men [14]. The etiology is unknown, but possible mechanisms include genetic and/or local vulvar factors as well as immunologic abnormalities [15, 16]. Patients typically complain of vulvar pruritus, the hallmark symptom of the condition, along with pain or irritation; however, some women are asymptomatic. Other common symptoms include dysuria and painful defecation if fissures are present and dyspareunia associated with introital stenosis. On physical examination, the classic features of the disease are thin, pale, wrinkled (often described as "parchment paper") skin on the labia (Fig. 1). Excoriations may be present secondary to scratching, and fissures can be seen perianally or between the labial folds and around the clitoris. More advanced disease can lead to the destruction of labial and clitoral architecture, with nearly complete midline fusion of the labia.

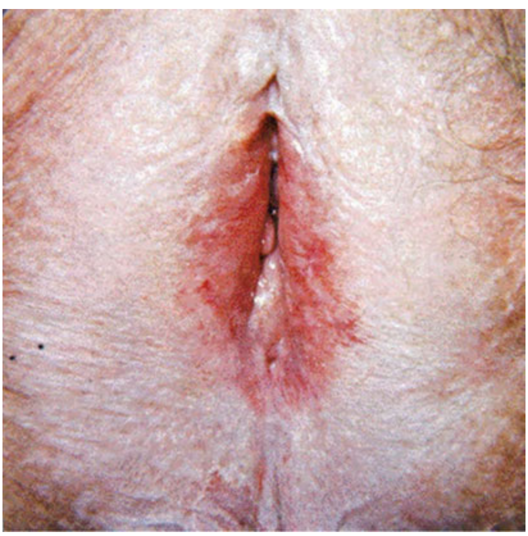

Fig. 1 Lichen sclerosus. Note the destruction of normal architecture and "parchment paper" skin

One important distinctive feature of lichen sclerosus is that the vagina and cervix are not involved [17]. Diagnosis is based on high-clinical suspicion and confirmatory 3 mm punch biopsy, as other vulvar dystrophies can have a similar appearance. Women with lichen sclerosis have a high prevalence of hypothyroidism (up to 30%) regardless of age, so we suggest screening for thyroid dysfunction in all women with biopsy-proven disease [18]. Women with lichen sclerosus are also at an increased risk of developing invasive squamous cell cancer of the vulva [19]. High-potency topical corticosteroids are the mainstay of therapy for lichen sclerosus, typically with clobetasol or halobetasol propionate 0.05% ointment nightly for at least 4 weeks followed by a slow taper when symptoms resolve. The ointment vehicle is preferred to the cream because the alcohol and preservatives in the creams irritate the skin [20]. Approximately 95% of patients will have complete or partial resolution of their symptoms with this regimen [21, 22].

Maintenance therapy with twice-weekly dosing may decrease flares or recurrent symptoms, though some experts recommend stopping therapy with resolution of symptoms and only retreating for recurrences [23]. It is unclear whether maintenance therapy reduces the chance of malignant evolution, so any recurrent or persistent lesions should be re-biopsied to rule out cancer [24]. Topical immunosuppressants have shown some promise in lichen sclerosus but are currently considered second-line therapy for disease that is unresponsive to high-potency corticosteroids [17].

Lichen Simplex Chronicus

Lichen simplex chronicus is an eczematoid disease of hyperkeratotic, scaling plaques of varying pigmentation that is associated with severe vulvar pruritus. It may commonly be seen in conjunction with a number of other vulvar skin disorders and is ultimately brought about by chronic scratching and irritation from both environmental and dermatologic processes [25]. Lichen simplex chronicus has been found to be associated with a history of atopic disease in up to 75% of patients and typically presents later in adult life though it can be seen in children. Initiating events range from chronic heat and excessive sweating to candidal infection or other dermatoses such as lichen sclerosus [17]. Diagnosis of lichen simplex chronicus is based on a history of vulvar irritation, pruritus, and typical hyperkeratotic lesions on examination. Ulcers and excoriations are sometimes seen due to chronic scratching. Biopsy may be done to identify the underlying disease (e.g., lichen sclerosus), and vaginal yeast cultures may also be helpful in this regard [17]. First-line therapy involves treatment of any underlying conditions, and topical corticosteroids may be used for symptomatic relief of inflammation and itching. Combination of steroid and antifungal ointments can be used as a convenient first-line therapy, if underlying yeast infection is suspected. Additionally, hygiene measures are important in controlling chronic vulvar wetness and avoiding potential irritants (strong soaps, perfumes, or detergents) that might exacerbate or prolong the condition.

Lichen Planus

Lichen planus is another inflammatory condition involving the genital mucosa that is thought to be caused by a cell-mediated autoimmune mechanism [26]. Unlike other vulvar dermatoses, lichen planus is more commonly found on non-vulvar skin or the mucosal membranes, especially the buccal mucosa [27]. Oral lichen planus is present in approximately 1% of the population, and up to one-fourth of women with oral disease will also have genital disease. The condition generally presents from 30 to 60 years, and the typical lesions seen are white reticulate striae on the buccal mucosal surface (Wickham's striae). Vulvar and skin lesions tend to consist of shiny, pruritic, violaceous papules; vulvar lesions can be less well demarcated and may even appear as white patches that are difficult to distinguish from lichen sclerosus [17]. The erosive form of lichen planus can lead to extremely painful erosions of the posterior vestibule and labia minora, with eventual architectural destruction and scarring and narrowing of the introitus; patients with such advanced disease complain of dyspareunia and difficulty voiding [17].

Diagnostic biopsy specimens are usually nonspecific, but classic findings in lichen planus include liquefactive degeneration of the basal cell layer and a band-like lymphocytic dermal infiltrate [28]. However, biopsy does help to rule out immunobullous diseases as well as cancer. There are a number of treatment options for lichen planus; unfortunately, though, response is typically poor, and therapy goals should focus on long-term maintenance of symptoms rather than complete control. Patient education, behavioral modification, and emotional support are all important components of any treatment plan. Medication options include topical and/or systemic high-potency corticosteroids, topical and oral cyclosporine, as well as a number of other immunemodulators [17]. In our experience, tacrolimus (Protopic) 0.1% ointment applied twice daily has been used with some success.

Bartholin's Cysts and Abscesses

Bartholin's glands, also called the greater vestibular glands, are pea-sized and located near the 4 and 8 o'clock positions on the posterolateral aspect of the vaginal opening. They function to provide vulvar and vaginal lubrication by way of mucous production [29]. The glands are connected to the vestibule of the vagina via ducts. The obstruction of the duct orifices can lead to Bartholin's cysts, which are typically asymptomatic unless they become large. These ducts and cysts may also become infected and evolve into polymicrobial abscesses, which generally present with exquisite pain and swelling. The treatment for symptomatic Bartholin's cysts or abscess is incision and drainage and placement of a word catheter, which allows for epithelialization and decreases the risk of recurrence. Other treatment options include marsupialization and CO_2 laser therapy [29]. The incidence of Bartholin's cysts or abscesses is up to 2% over a woman's lifetime but tends to be less common during the postmenopausal years [30]. Due to the possibility of underlying Bartholin's gland carcinoma, cysts and abscesses in women over the age of 40 should be drained and biopsied at the first occurrence, followed by complete excision of the gland for recurrent disease [31].

Vulvodynia

Vulvodynia is defined as chronic pain in the vulvar area lasting at least 3–6 months [32]. In 2003, the International Society for the Study of Vulvovaginal Disease classified vulvar pain into two categories: (1) vulvar pain related to an underlying disorder (infection, inflammation, neoplasm, or neurologic disease) and (2) vulvodynia, defined as vulvar burning or discomfort in the absence of any identifiable cause [33]. The true prevalence is unknown, but has been reported to be between 10% and 16% over a woman's lifetime, and tends to be more common in older patients [34, 35]. The etiology of vulvodynia is also unclear but is thought to have a neuropathic basis related to long-term tissue damage; it may also be related to changes in hormonal status, possibly explaining its temporal association with menopause [36].

While all patients present with complaints of pain, their descriptions may be widely variable with respect to location, timing, character, and provocations. Many patients believe that they have – and may have – been treated for chronic, recurrent yeast infections. Vulvodynia has been associated with coexisting conditions such as depression, interstitial cystitis, fibromyalgia, irritable bowel syndrome and frequent urinary tract, and yeast infections [35]. Incidence rates vary by demographic factors such as age, ethnicity, and marital status [37]. The diagnosis of vulvodynia is one of exclusion, and many times vulvar erythema, tenderness to palpation, and/or allodynia may be the only physical exam findings; vaginal pH, wet mounts, and yeast cultures may help to exclude other causes.

Vulvodynia can also be a frustrating treatment dilemma, as specific triggers for the pain patients experience are often difficult to identify. General measures should include education, emotional support, hygiene measures, and behavioral therapy; referral to a pain specialist may be helpful, and physical therapy involving pelvic floor muscle rehabilitation can be effective in patients with vaginismus and pelvic floor hypertonicity [38]. First-line pharmacologic therapy consists of tricyclic antidepressants (e.g., amitriptyline 10 mg nightly, increasing by 10 mg weekly until symptoms improve) with or without a topical anesthetic. Topical lidocaine gel may be used on a scheduled basis up to six times a day or on an as needed basis for intercourse. With the tricyclic antidepressants, care must be taken to watch for anticholinergic side effects as they may be more pronounced in the geriatric population. Other pharmacologic options include gabapentin, duloxetine, and the addition of topical estrogen if atrophy is present. For pain unresponsive to these therapies, local nerve block with a corticosteroid and lidocaine has been found to provide temporary relief, and referral to a pain management specialist may be appropriate in this case [39].

Cervix

In the geriatric patient, the appearance of the cervix changes in comparison to that of premenopausal patients as the transformation zone is usually found high within the endocervical canal. The cervix may also atrophy and become flush with the vaginal vault. While problems arising from the cervix are rare, two of the more common conditions in menopausal women are cervicitis and cervical stenosis.

Cervicitis in postmenopausal females is typically related to atrophic changes rather than an infectious process and can be a common cause of vaginal bleeding in this patient population. If there is no evidence of sexually transmitted or superimposed infection, treatment with vaginal estrogen should be started. A wet mount slide and/or cultures should be performed to evaluate any associated suspicious discharge and appropriate antibiotics prescribed for any infectious process.

In addition to cervicovaginal atrophy, the menopausal decrease in estrogen also induces changes in the endocervical canal that may lead to the agglutination of the cervix, ultimately resulting in complete stenosis. This can obstruct the outflow of secretions and debris from the atrophic endometrial cavity, leading to hematometria or hydrometria; pyometria can occur if this accumulation of debris becomes infected.

Urogenital Atrophy and Vaginitis

During menopause, the vagina, in particular, thins and loses elasticity. In addition, the vagina undergoes a decrease in blood flow and secretions. For one-third of women, this results in dryness, discomfort, itching, and/or painful intercourse early in menopause and is often referred to as atrophic vaginitis. On exam, an atrophic vagina appears pale and has decreased rugae. The vaginal introitus is often narrow, and the urethral meatus is prominent, simply because of the decreased bulk of the surrounding vulvar tissue. Unlike vasomotor symptoms, atrophy symptoms continue or worsen, and the prevalence increases to about one-half of women with aging. Additionally, lack of estrogen changes the vagina from an acidic to a more basic environment, which favors colonization with enteric potentially uropathic bacteria [1–3]. Low doses of transvaginal creams, pessaries, tablets, and rings are likely equally effective in treating symptoms of vaginal atrophy and are not associated with significant systemic absorption [3]. Vaginal estrogen therapy is usually prescribed in tapering doses: from nightly for the first 2 weeks of therapy to maintenance doses of twice weekly. Reversing vaginal atrophy before vaginal surgery is often performed (Fig. 2).

Other less common forms of vaginal irritation in the older women include bacterial vaginosis (BV) and candidiasis. In the atrophic vagina with a higher pH, lactobacilli and yeast are less commonly found likely explaining the decreased incidence of candidiasis [40]. Differentiation between these causes of vaginal irritation is important. Increased vaginal pH is found with both BV and atrophy. The discharge with BV is malodorous, thin, homogenous, grayish, and adherent to the vaginal walls. Candidiasis is odorless and "cottage cheese-like" in appearance; the labia can be erythematous and edematous with satellite lesions. BV also has a characteristic fishy odor with the application of potassium hydroxide. On saline wet mount, BV has clue cells (epithelial cells stippled with bacteria), while candidiasis has pseudohyphae [41]. With atrophy, the wet mount is predominantly intermediate and parabasal epithelial cells with few or no superficial cells [42]. Antibiotic treatment for BV and anti-candidal regimens is effective and routinely prescribed by practitioners caring for older women [41].

The lower urinary tract is also estrogen sensitive, as estrogen receptors are found in the bladder and urethra. Symptoms of dysuria, urethral discomfort, overactive bladder (OAB), hematuria, urinary tract infections (UTIs), and urinary incontinence (UI) are associated with aging. Estrogen had been a mainstay of treatment of urinary tract symptoms, generally based on small observational studies [43]. However, a 2003 Cochrane review called into question the routine use of systemic estrogen as a therapeutic agent for UI. Fifteen of the 28 trials in this review favored estrogen use to treat UI, but the results from the

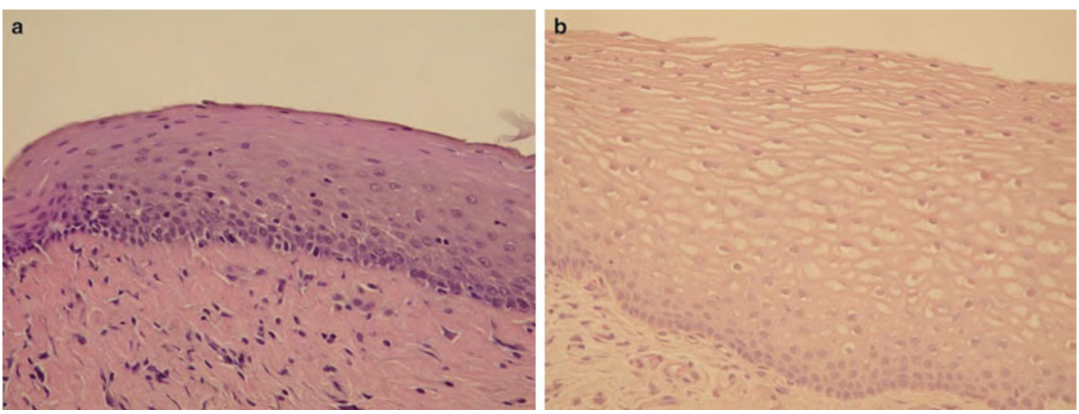

Fig. 2 Vaginal atrophy treated with estrogen cream. (**a**) A thin vaginal epithelium (0.075 mm) where the estrogen-sensitive superficial cell layer (flatter cells with smaller nuclei) composes a smaller proportion of the epithelium. (**b**) Epithelial changes after nightly treatment with 50 μg of estrogen cream. The thicker epithelium (0.4 mm) contains a larger proportion of superficial cells

Heart and Estrogen/Progestin Replacement Study (HERS) swayed the analysis toward estrogen worsening UI [44]. This review was followed by the negative findings in the Women's Health Initiative which showed increased or worsening of UI in women taking estrogen and progesterone or estrogen alone [43]. It is important to note that the influence of different estrogen formulations and route of delivery, in particular transvaginal estrogen, has yet to be elucidated. However, it is clear that systemic estrogen has not been shown to improve OAB or urinary incontinence and may actually worsen them [1, 43]. There is a role for transvaginal estrogen in preventing recurrent UTIs [45].

Genitourinary Syndrome of Menopause (GSM)

The previous section describes the effects of hypoestrogenism on the lower genital and urinary tract. In 2013, the Board of Directors of the International Society for the Study of Women's Sexual Health (ISSWSH) and the Board of Trustees of The North American Menopause Society (NAMS) convened to develop an all-encompassing and medically accurate nomenclature to describe these changes. From this meeting, the term "genitourinary syndrome of menopause" was born. GSM describes a collection of symptoms involving changes to the vulva, vagina, urethra, and bladder that occur solely because of menopause [46].

Upper Genital Tract

Uterus

Many of the changes evident in the postmenopausal uterus are a direct result of decreasing estrogen levels. There is an estimated 95% decline in blood estrogen concentration from the premenopausal to postmenopausal state [47]. The postmenopausal uterus undergoes involution and gradually becomes smaller with age. Benign abnormalities of the uterus, especially abnormalities of the uterine cavity, may result in postmenopausal bleeding, and endometrial cancer must be ruled out when it occurs in this age group. The primary causes of postmenopausal bleeding include vaginal atrophy with friability, endometrial atrophy, endometrial hyperplasia, endometrial and cervical polyps, and invasive cancer. The initial evaluation of postmenopausal bleeding should include either a transvaginal ultrasound or a biopsy of the endometrium. If the endometrial thickness is less than 4 mm on ultrasound, then a biopsy is not required. When a biopsy is attempted in the postmenopausal patient, either as the initial assessment of bleeding or as a follow-up assessment when the endometrium is >4 mm thick on ultrasound, providers often encounter cervical stenosis because of atrophic changes. In this case, endometrial sampling in combination with hysteroscopy in the operative setting may be beneficial [48].

Endometrial Atrophy

Endometrial atrophy is a frequent cause of postmenopausal uterine bleeding. The surface epithelium of the uterine cavity, otherwise known as the endometrial layer, is known to undergo cellular and glandular loss, likely as a result of lowered estrogen levels [49]. This ultimately thinned endometrial surface is subject to bleeding, especially as a result of trauma. The collapsed, atrophic endometrial surfaces contain little or no fluid to prevent intracavitary friction [50]. Microerosions of the surface epithelium then develop that are prone to light bleeding or spotting.

The diagnosis of endometrial atrophy is confirmed by endometrial biopsy or by ultrasound (double-layer thickness less than 4 mm). Adequate estrogen therapy is nearly always effective in relieving symptoms of both endometrial and vaginal atrophy. Although many oral preparations are available for the treatment of endometrial atrophy, local vaginal estrogen therapy has also been shown to be effective and well-tolerated in the treatment of endometrial atrophy but should be accompanied by a progestin for doses greater than 50 μg [3, 51].

Endometrial Polyps

Endometrial polyps, which are hyperplastic overgrowths of endometrial glands and stroma, develop from the endometrial basalis layer and are likely the result of estrogenic stimulation. The known association of large endometrial polyps with tamoxifen [52], a selective estrogen receptor modulator, strengthens this likelihood. The incidence peaks in the fifth decade of life; fortunately for most postmenopausal women, the incidence of endometrial polyps greatly decreases after menopause. They may be solitary or multiple and are usually pedunculated. Most are benign, with an estimated 1.5% being malignant [53]. In addition, while most are asymptomatic, they account for 12–25% of cases of postmenopausal bleeding [54, 55].

Endometrial polyps are diagnosed only by microscopic evaluation of the specimen post removal, although they can be further evaluated and characterized using sonohysterography (Fig. 3). Saline infusion sonography has been shown to be more accurate than ultrasound alone in diagnosis, with a sensitivity and specificity of 93% and 94%, respectively, compared to 65% and 76%, respectively, for ultrasound alone [56]. Treatment of symptomatic polyps is removal by dilatation and curettage (D&C) or hysteroscopic-guided polypectomy. Excision of symptomatic polyps is essential to rule out carcinoma because imaging characteristics cannot adequately distinguish between benign and malignant polyps [53].

Fig. 3 Saline infusion sonohysterogram of a perimenopausal patient with abnormal uterine bleeding. A polypoid lesion is seen extending near the anterior fundal region. This measures 10.2 × 6.7 mm (calipers). At the time of D&C with hysteroscopy, a polyp was identified and confirmed by pathology

The management of asymptomatic patients with incidentally found polyps remains controversial [57–59].

Leiomyomas (Fibroids)

Benign uterine leiomyomas, otherwise known as fibroids, are hormonally responsive and typically decrease in size after menopause [60]. Although leiomyomas tend to atrophy as the woman ages, their presence can cause concern during bimanual exams or with their appearance on imaging studies. Medical therapy to decrease fibroid size is generally not indicated in the older postmenopausal woman. Additionally, surgical interventions for simple uterine fibroids in the postmenopausal female usually are not indicated. However, while most uterine masses ultimately prove to be benign fibroids, a rapidly enlarging pelvic mass may represent a uterine leiomyosarcoma. These are relatively uncommon, accounting for only 1–2% of postmenopausal uterine masses [61]. With any enlarging or persistent uterine mass, evaluation in the form of ultrasonography, computed tomography, and referral to a gynecologic specialist is warranted to exclude sarcoma.

Endometrial Hyperplasia and Cancer

Endometrial hyperplasia, or excessive proliferation of the uterine endometrium, can occur from many conditions, almost all associated with long-term unopposed estrogen stimulation. Risk factors for endometrial hyperplasia, other than direct unopposed estrogen stimulation, include obesity, nulliparity, diabetes, early menarche, late menopause, polycystic ovarian syndrome, and tamoxifen therapy for greater than 2 years [62]. According to the World Health Organization (WHO), endometrial hyperplasia is classified as either atypical hyperplasia or hyperplasia without atypia. These classes are further subdivided into two categories: simple and complex, with complex and atypical classifications having higher risks for malignancy. Because of interobserver and intraobserver variability inherent in the WHO classification system, the Endometrial Intraepithelial Neoplasia (EIN) classification system was developed [63]. The EIN system uses molecular genetics to identify precancerous or cancerous endometrial lesions and to provide standardization [64]. Endometrial hyperplasia or EIN is made from direct tissue sampling in the form of an office endometrial biopsy sampling or dilation and curettage. Treatment strategies center around the use of progestins or hysterectomy, depending on the pathology. Hysterectomy is often the first management choice in patients with complex atypical hyperplasia or EIN given that the risk of concurrent malignancy is 26% and 24%, respectively [64].

Ovary

As women progress into menopause, there is a marked depletion of ovarian follicles resulting in decreased synthesis of circulating estrogen. The ovaries become atrophic becoming smaller in size than those of the premenopausal woman and are typically not palpable on bimanual examination. The risk of ovarian cancer increases with age, but unfortunately there is no validated way to screen for the disease. Educating patients on the signs and symptoms of ovarian cancer and encouraging them to present for evaluation should they develop those symptoms is paramount. Benign ovarian enlargement or benign cysts are rarely found in the postmenopausal female, as the ovary is inactive. Benign teratomas missed at an earlier age are sometimes found, but in general, most postmenopausal ovarian masses are suspect for malignancy.

Urogynecologic Conditions

Introduction

Pelvic floor disorders including pelvic organ prolapse and incontinence are common gynecologic problems encountered by the older woman. With the rapidly increasing population of active older women, physicians can expect to provide evaluation and treatment of these conditions with increasing frequency. These conditions are typically amenable to both medical and surgical therapies making individualization of treatment approaches important. Evidenced-based evaluation and treatment suggestions are provided.

Urethra

The female urethra is typically 4 cm in length and 6 mm in diameter. The proximal urethra is lined by urothelium, whereas the distal mucosa is lined by nonkeratinized stratified squamous epithelium which is continuous with the vulva externally. The urethra is composed of mucosa and submucosa, surrounded by smooth and striated muscles. The epithelium and submucosa are estrogen sensitive. The submucosa is highly vascular, and this vascular cushion helps the urethra to intrinsically remain sealed [65]. The periurethral glands are located in the distal two-thirds of the submucosa, and most of these glands drain into the distal one-third. Of the periurethral glands, the Skene's glands are most distally located, which drain outside and lateral to the external urethral meatus [66].

The urethral sphincters are composed of the urethral smooth muscle layers: an inner oblique and longitudinal layer and an outer circular layer; the outer skeletal muscle layer is most prominent in the middle third of the urethra. The urethra is supported by fibromuscular connective tissue which is suspended to the pelvic sidewall [66, 67].

Urethral Prolapse

Urethral prolapse is a circumferential eversion of the urethral mucosa at the external meatus, often appearing as a beefy red ring around the meatus. This condition is relatively rare and typically seen in postmenopausal women and prepubertal girls. The etiology has been linked to a lack of estrogen. Urethral prolapse can be asymptomatic. However, bleeding is the most common symptom, followed by voiding symptoms such as dysuria, urgency, frequency, and nocturia. If strangulated, suprapubic pain can occur. Concurrent infection can occur [67].

Since urethral prolapse is rare, careful examination is needed to confirm the diagnosis, as the more common urethral caruncles and rare malignancy are in the differential diagnosis. Urethral prolapse is distinguished by the circumferential prolapse with a central opening, which can be catheterized to confirm the presence of the urethra. Significant swelling can lead to anatomical distortion, strangulation, and potentially necrosis and may necessitate examination under anesthesia to confirm the diagnosis with possible surgical correction. Imaging studies are seldom necessary once the diagnosis has been confirmed with catheterization; otherwise, malignancy should be considered. Histologically, inflammatory infiltrates are seen in the underlying connective tissue.

Treatments include warm sitz baths, transvaginal estrogen cream, topical steroids to reduce inflammation, and antibiotics for infection [68, 69]. Estrogen has been reported to resolve the prolapse within 6 weeks [69]. If conservative management fails or if strangulated, surgical excision and short-term catheterization (less than a week) should be performed [70]. Surgical techniques include cauterization, ligation around a urethral catheter, and circumferential excision with reapproximation of the healthy urethral mucosa to the vagina. Complications include infection and urethral stenosis. Long-term transvaginal estrogen should be included in the postoperative care.

Urethral Caruncles

Urethral caruncles are benign, usually small, reddish exophytic lesion in the distal posterior urethra visible at the external meatus. These lesions are often asymptomatic and an incidental finding but can present with dysuria, tenderness, or bleeding especially if they enlarge to 1–2 cm (Fig. 4). Rarely, the large lesion can thrombose, which presents as a dark periurethral mass. The etiology likely starts with incomplete urethral prolapse, which becomes chronically irritated and takes a polypoid form. Like urethral prolapse, its origins are attributed to estrogen deficiency and more common in older women. Cystoscopy is generally unnecessary. Treatment of symptomatic urethral caruncles is conservative and consists of sitz baths, transvaginal estrogen therapy, and anti-inflammatories when necessary. When clinical differentiation from cancer is difficult, such as a large (1–2 cm) lesion, there is a failure of medical therapy, or in the presence of severe symptoms, surgical excision biopsy should be considered [71]. Intestinal metaplasia, melanoma, and lymphoma have all been reported to either coexist with or mimic urethral caruncles [72–74].

Fig. 4 Urethral caruncle. Note that it is a reddish, exophytic lesion off of the posterior urethra

Urethral Diverticulum

A urethral diverticulum is an outpouching of the urethra within the fibromuscular connective tissue protruding into the anterior vaginal wall. This defect often appears as cyst-like structure connected to the urethral lumen. In more complicated cases, the diverticulum can have a saddlebag shape or circumferentially around the entire urethra [66]. The prevalence of urethral diverticulum is difficult to estimate; however up to 1–6% has been reported [66, 75]. It is uncommon past 60 years of age. The diverticulum is thought to be the result of obstruction of periurethral glands and is most commonly found in the posterolateral distal one-third of the urethra. The classic symptoms include dysuria, dribbling, urgency, frequency, and dyspareunia. Other symptoms include hematuria, urinary incontinence, voiding dysfunction, hematuria, and pyuria. These women can have recurrent cystitis or urinary tract infections.

Up to 20% of patients with diverticulum may be completely asymptomatic. On examination, it feels like a suburethral mass expanding in the anterior vaginal wall; however, some may also expand laterally or even dorsally [66, 75]. It can be hard if a stone is present, mostly of calcium oxalate or phosphate, which can occur up to 10% [76]. Urine or purulence may be expressed from the meatus when massaged. The differential diagnosis includes vaginal wall cysts from an embryologic remnant or local gland and ectopic ureterocele. Malignancy has been reported in 6–9%. The most common type is adenocarcinoma [77]. Magnetic resonance imaging (MRI) is the diagnostic imaging modality of choice to confirm the diagnosis, location, and size. Three-dimensional ultrasound technique has been investigated as an alternative to MRI [78, 79]. Surgical excision is recommended treatment [76]

Pelvic Floor Disorders

Introduction

The national prevalence of symptomatic pelvic floor defects including pelvic organ prolapse (POP), urinary incontinence (UI), and fecal incontinence (FI) has been estimated to be 25%. Older women are far more affected, with rates up to 53% in women 80 years old and older [80]. The prevalence of anatomic stage II–IV POP using the Pelvic Organ Prolapse Quantification (POPQ) [81] (see Table 1 and Fig. 5) examination in the general population was reported to be 37%; prevalence in an older population of women with a mean age of 68 years was 64.8% [82].

Table 1 Stages of pelvic organ prolapse

Stage 0	No prolapse is demonstrated. Points Aa, Ap, Ba, and Bp are all at −3 cm, and point C is between total vaginal length (TVL) and −(TVL −2 cm)
Stage I	The most distal portion of the prolapse is >1 cm above the level of the hymen
Stage II	The most distal portion of the prolapse is <1 cm proximal or distal to the plane of the hymen
Stage III	The most distal portion of the prolapse is <1 cm below the plane of the hymen but no further than 2 cm less than the total vaginal length
Stage IV	Complete to nearly complete eversion of the vagina. The most distal portion of the prolapse protrudes to> + (TVL −2) cm

Clearly, these are highly prevalent conditions and contribute significantly to older women's overall quality of life. Despite the availability of effective evaluation and treatment methods, women continue to suffer needlessly, with nearly 50% of affected women neglecting to inform their healthcare providers about their symptoms [83].

Pelvic Organ Prolapse and Urinary Incontinence

The etiology of POP and incontinence is complex and multifactorial, involving potential injury to, or attenuation of, the many ligaments, muscles, connective tissue, and innervation of the pelvis. These conditions are associated with several risk factors including age, parity, forceps use at the time of vaginal delivery, abdominal circumference, and body mass index. Vaginal support defects as defined by DeLancey include Level I apical support defects (the cardinal-uterosacral ligament complex providing proximal support), Level II defects including cystocele, rectocele, or paravaginal defects (a defect in vaginal support at the level of the arcus tendineous fascia pelvis), or a Level III defect, detachment of the perineal body (Fig. 6) [84].

It is common for the older woman to be affected by more than one pelvic floor condition. POP can be associated with urinary as well as bowel dysfunction and fecal incontinence. Women with advanced POP may experience voiding dysfunction caused by urethral obstruction. Older women are at risk for coexisting urinary and fecal incontinence (accidental bowel leakage) or "dual incontinence." The reported prevalence of dual incontinence in community-dwelling adults ranges from 3% to 15% [85, 86]. A thorough history will elucidate these associated symptoms. An evaluation for occult urinary incontinence may be warranted in cases of advanced prolapse, as an incompetent urethra may be masked by the urethral kinking associated with advanced pelvic organ descent.

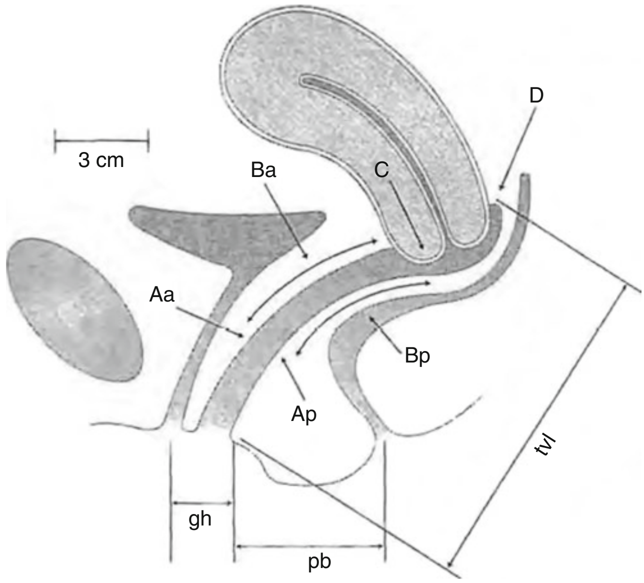

Fig. 5 Six sites (points Aa, Ba, C, D, Bp, and Ap), genital hiatus (gh), perineal body (pb), and total vaginal length (tvl) used for pelvic organ support quantifications. (From Bump et al. [81]. Reprinted with permission from Elsevier)

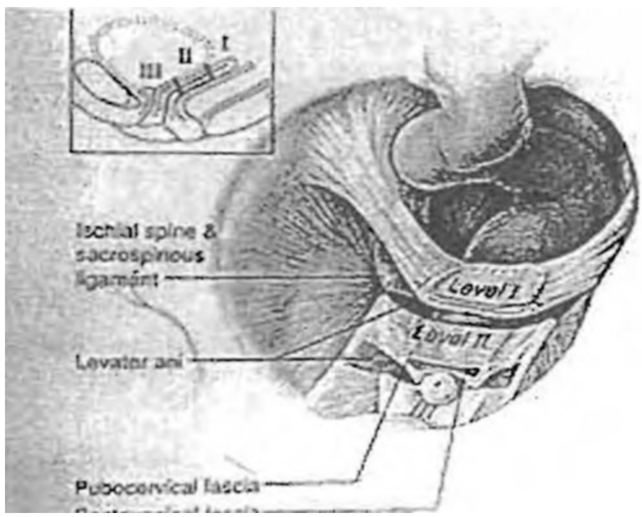

Fig. 6 Vaginal support defects as defined by DeLancey include Level I apical support defects (the cardinal-uterosacral ligament complex). Level II defects include cystocele, rectocele, or paravaginal defects (a defect in vaginal support at the level of the arcus tendineous fascia pelvis), or a Level III defect, detachment of the perineal body. (From De Lancey [84]. Reprinted with permission from Elsevier)

The diagnosis of POP is made during a pelvic examination. The full extent of the prolapse may not be appreciated unless the patient stands or uses a strong Valsalva force. Bladder and bowel dysfunction may require the use of further diagnostic testing such as urodynamics, anal manometry and ultrasound, or electromyography of the pelvic floor.

Urinary incontinence (UI) is defined as the complaint of any involuntary leakage of urine [87]. Diagnostic categories of UI include stress incontinence (leakage associated with episodes of increased intra-abdominal pressure), urgency urinary incontinence (leakage associated with urgency and involuntary detrusor muscle contractions), and overflow incontinence (seen when bladder emptying is insufficient).

Initial evaluation techniques center on the treatment of reversible causes of UI, for example, infection, inappropriate medication use, and mobility issues. After a thorough history, the examination focuses on pelvic/bladder anatomy and neurologic status. Bladder physiology and function may be further characterized using a stress test or urodynamic assessment, a diagnostic means of observing bladder neurologic and motor/muscle physiologic function. As overflow incontinence can mimic the symptoms of stress or urgency incontinence, it is important to check a post void residual volume with the use of a bladder scanner or in and out catheterization, as older women can have impaired bladder emptying.

Treatment of POP and UI

Management should be individualized based on the patient's health status, clinical setting, and preference. It is important to discuss the expectations and goals of therapy with the patient and her caregiver, when applicable. The first step is to determine if the patient has symptoms that are bothersome. Asymptomatic patients with pelvic floor disorders that are found incidentally on examination can be managed expectantly.

Nonsurgical Treatment of POP and UI

Nonsurgical treatment of POP and UI includes behavioral therapy (pelvic floor muscle exercises including stress and urgency incontinence strategies), medications, as well as the use of intravaginal supportive devices. A conservative treatment approach is usually considered in older women who do not desire a surgical intervention or where surgery may not be an ideal choice due to medical comorbidities causing increased surgical risk.

Pelvic floor muscle exercises may limit the progression of mild prolapse and related symptoms; however, less response has been noted with prolapse beyond the vaginal introitus [88]. This method of treatment is often employed to treat accompanying urinary and/or fecal incontinence. Results are generally dependent on patient motivation and adherence to the exercise program.

The use of an intravaginal device such as a pessary is an excellent option for nonsurgical treatment of POP and UI. Patient acceptance is relatively high with appropriate counseling. Pessaries are available in different shapes and sizes, the majority of which are made of silicone. Risk factors for failed fitting include a large genital hiatus and short vaginal length. Pessaries provide pelvic organ support within the vaginal vault. Two categories of pessaries exist for prolapse: support and space filling. The ring pessary (with diaphragm) is a commonly used support pessary, and the Gellhorn pessary is a commonly used space-filling pessary (Fig. 7). Most women with stage II and III prolapse were successfully fitted with ring pessaries, whereas women with stage IV prolapse usually required a Gellhorn pessary [89].

Possible complications associated with pessary use include vaginal discharge and odor. There may be failure to retain the pessary, or conversely the pessary may be too large, which could lead to excoriation or irritation. There may be de novo or increased stress incontinence [90] with the reduction of vaginal prolapse and in rare instances more severe complications such as fistula development.

Surgical Treatment of POP

The decision for surgical versus conservative intervention for the treatment of pelvic floor disorders should not be based on chronologic age alone. Prior to the selection of a specific treatment or procedure, all existing pelvic floor defects should be evaluated. The older woman can expect similar operative risks as well as subjective and objective anatomic and quality-of-life outcomes as that of younger women undergoing pelvic floor disorder treatment.

In the United States, 300,000 surgeries are performed annually for the treatment of POP [91]. Demand for the care of pelvic floor disorders has been projected to increase significantly in the coming years due to significant shifting of American age demographics. Women aged 80 years and older are the most rapidly growing segment of the older US population. A woman's lifetime risk of having surgery for either POP or UI by age 80 is 11.1% [92]. Women who have undergone a procedure for UI or POP are at risk for recurrence, with a reoperation rate of approximately 30% [92, 93].

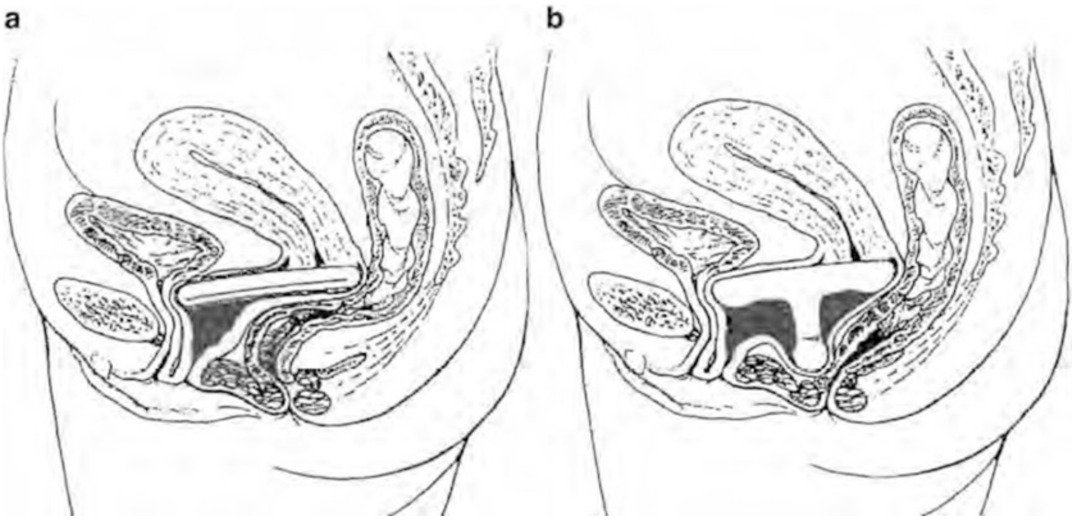

Fig. 7 (**a**) Ring pessary without support in place; patient with cervix and uterus. Note that the pessary rests at the level of the bladder neck anteriorly and behind the cervix posteriorly. (**b**) Gellhorn pessary in place; patient with cervix and uterus. Note that the disk of the Gellhorn pessary rests at the level of the bladder neck anteriorly and behind the cervix posteriorly similar to the position of a ring pessary and that the knob rests behind the perineal body. (From Weber and Richter [88]. Reprinted with permission from Lippincott Williams & Wilkins)

The ideal procedure in the older woman would robustly repair symptomatic pelvic floor defects, be performed efficiently, allow for rapid postoperative recovery including return to baseline or improved functional status, and conform with the sexual activity desires of the patient. Although many studies have included older women when examining outcomes after pelvic floor surgery, limited studies exist to specifically address POP surgery outcomes in older women. Older women undergoing elective pelvic floor surgery face risks similar to patients of all ages undergoing elective general surgery. Pelvic floor surgery is considered an intermediate risk procedure with a perioperative mortality rate <5%. A review of recent studies that examine outcomes of the older woman undergoing pelvic floor surgery shows mortality rates from 0.0% to 4.1% and complication rates from 15.5% to 33.0% [94]. Complication rates vary and may be due to the heterogeneous definitions of complications throughout the studies. However, the majority of complications were related to urinary tract infections, febrile morbidity, and blood loss requiring transfusion.

Presurgical preparation should include optimization of the urogenital epithelium. Topical estrogen improves the quality of vaginal tissue in postmenopausal women. The effects of vaginal estrogen on surgical outcomes in postmenopausal women undergoing transvaginal prolapse repair are currently being investigated in a multicenter placebo-controlled randomized trial (NCT02431897).

Surgery to correct POP and UI should address the specific pelvic floor defects that are present including the anterior vaginal wall (cystocele), posterior vaginal wall (rectocele), and apical vaginal support defects (enterocele) (Figs. 8 and 9). Surgical techniques to address anterior defects are the anterior colporrhaphy and paravaginal repair. Symptomatic anterior wall prolapse repair outcomes were compared at a 21-month average (12 months minimum) follow-up between 31 patients aged 80 years or more and 234 younger patients. They demonstrated similar rates of symptomatic failure between the groups, 6 versus 5%, respectively. Recurrence of any vaginal support defect in the older group was 10% [95].

The most efficacious technique to repair posterior defects is the traditional midline colporrhaphy [88]. Perineorrhaphy should be performed when there is separation of the perineal

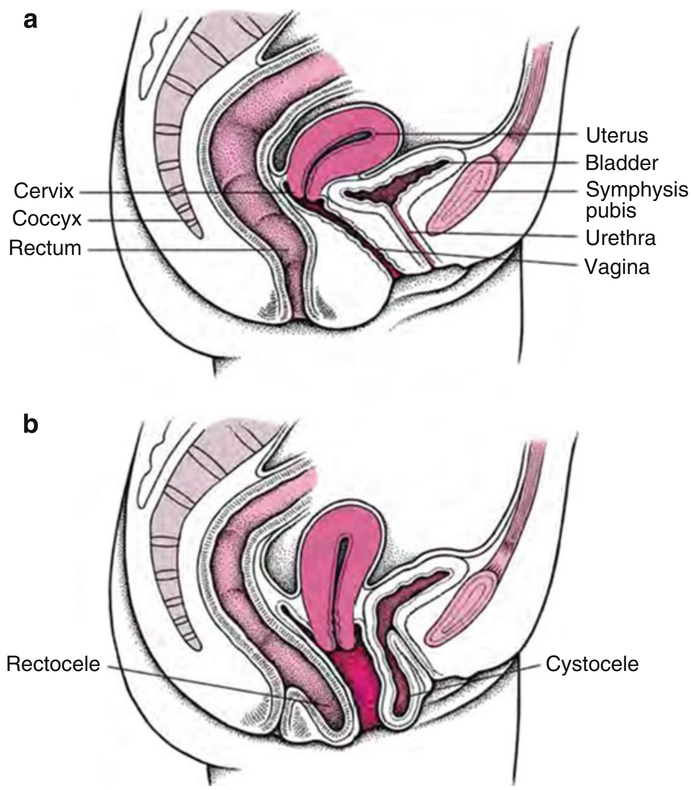

Fig. 8 Sagittal section showing normal anatomy (**a**); cystocele and rectocele (**b**). (Reprinted with permission from Beers and Berkow [12]. Copyright 2000 by Merck & Co, Inc., Whitehouse Station, NJ.)

muscles. The posterior rectovaginal connective tissue should be reattached to the perineal body if separated. However, careful attention should be paid to avoid excessive vaginal narrowing (unless desired) as postoperative dyspareunia is a common complication. Anatomic success is high with this procedure; however, functional success rates may be considerably lower regardless of age.

Surgical techniques to address apical vaginal defects include the abdominal sacrocolpopexy (ASC), uterosacral ligament suspension (ULS), iliococcygeus fixation, and sacrospinous fixation (SSLF). The ASC employs graft material to suspend the anterior and posterior walls of the vagina to the anterior longitudinal ligament of the sacrum. Published ASC apical cure rates range from 78% to 100% [88]. However, this surgery requires a laparotomy or laparoscopic surgery with or without the robot; has a longer operative time and, if performed by laparotomy, a longer recovery period; and has higher postoperative complications when compared with vaginal approach surgeries. A recent RCT demonstrated similar perioperative complication rates as well as subjective and objective outcomes in women aged 70 years and older compared to a younger group undergoing ASC [96]. ASC may be safely performed laparoscopically, even in the older woman.

The two most common vaginal native tissue apical suspension procedures are ULS and SSLF. ULS is an intraperitoneal technique that attaches the vaginal vault to the uterosacral ligaments at the level of the ischial spine bilaterally (Fig. 10). The SSLF is an extraperitoneal approach that attaches the vaginal vault to the sacrospinous ligament. A recent randomized controlled trial examined a direct comparison of outcomes from a ULS versus SSLF and demonstrated that there was no significant difference in success rates (ULS 59% vs. SSLF 61%, OR 0.9 [95% CI 0.6, 1.5]) or serious adverse event rates (ULS 17% vs. SSLF 17%, OR 0.9 [95% CI 0.5, 1.6]) [97].

Colpocleisis or colpectomy (narrowing or closure of the vaginal tissue and introitus) may be offered to the older woman who has no desire

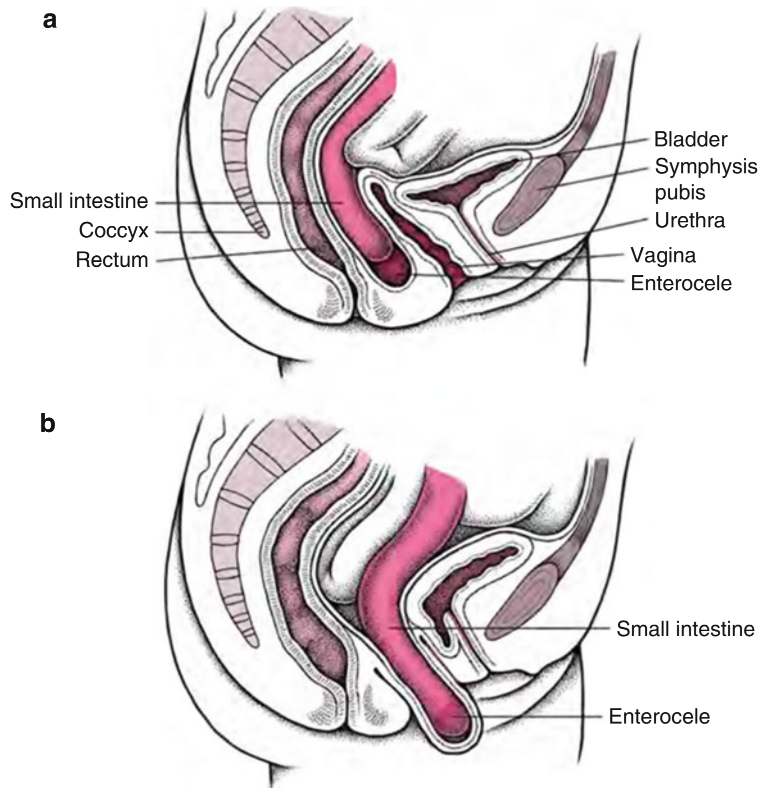

Fig. 9 Posterior enterocele without eversion (**a**); enterocele with eversion (**b**). (Reprinted with permission from Beers and Berkow [12]. Copyright 2000 by Merck & Co, Inc., Whitehouse Station, NJ.)

for vaginal function. These obliterative procedures have been shown to have shorter operative times and have fewer perioperative complications compared to reconstructive repair [98]. Patient satisfaction is high and prolapse recurrence is low [99]. Preoperative assessment and operative treatment for occult stress incontinence may help avoid this unwanted postoperative complication.

Transvaginal mesh augmentation is another approach for POP repair. The use of synthetic mesh to augment a repair addresses potentially and reduces the risk of recurrent prolapse; however, this approach is controversial. Mesh-related complications include erosion or exposure, infection, and de novo dyspareunia. A detailed discussion of the use of surgical mesh for prolapse repair is beyond the scope of this chapter.

Little information is available to guide us about which procedure should be considered in the older woman versus the younger woman. A multicenter three-arm randomized trial (NCT02676973) is currently undertaken to determine the efficacy and safety of three existing surgical approaches (native tissue vaginal repair with ULS or SSLF, sacrocolpopexy, and transvaginal mesh augmentation). The ultimate decision on which approach and which procedure to employ in the treatment of POP in older women should take into consideration the patient's overall health and physical activity status, her specific pelvic floor defects and her future sexual activity desires, as well as the surgeon's training, skills, and preference.

Surgical Treatment of Urinary Incontinence

Surgical management options for UI depend on the types of UI, which can be divided into two categories: stress or urgency urinary incontinence (SUI or UUI). Surgical approaches for the treatment of SUI include the midurethral sling (retropubic or transobturator), colposuspension, pubovaginal sling (autologous, synthetic, or allograft), and bulking agents.

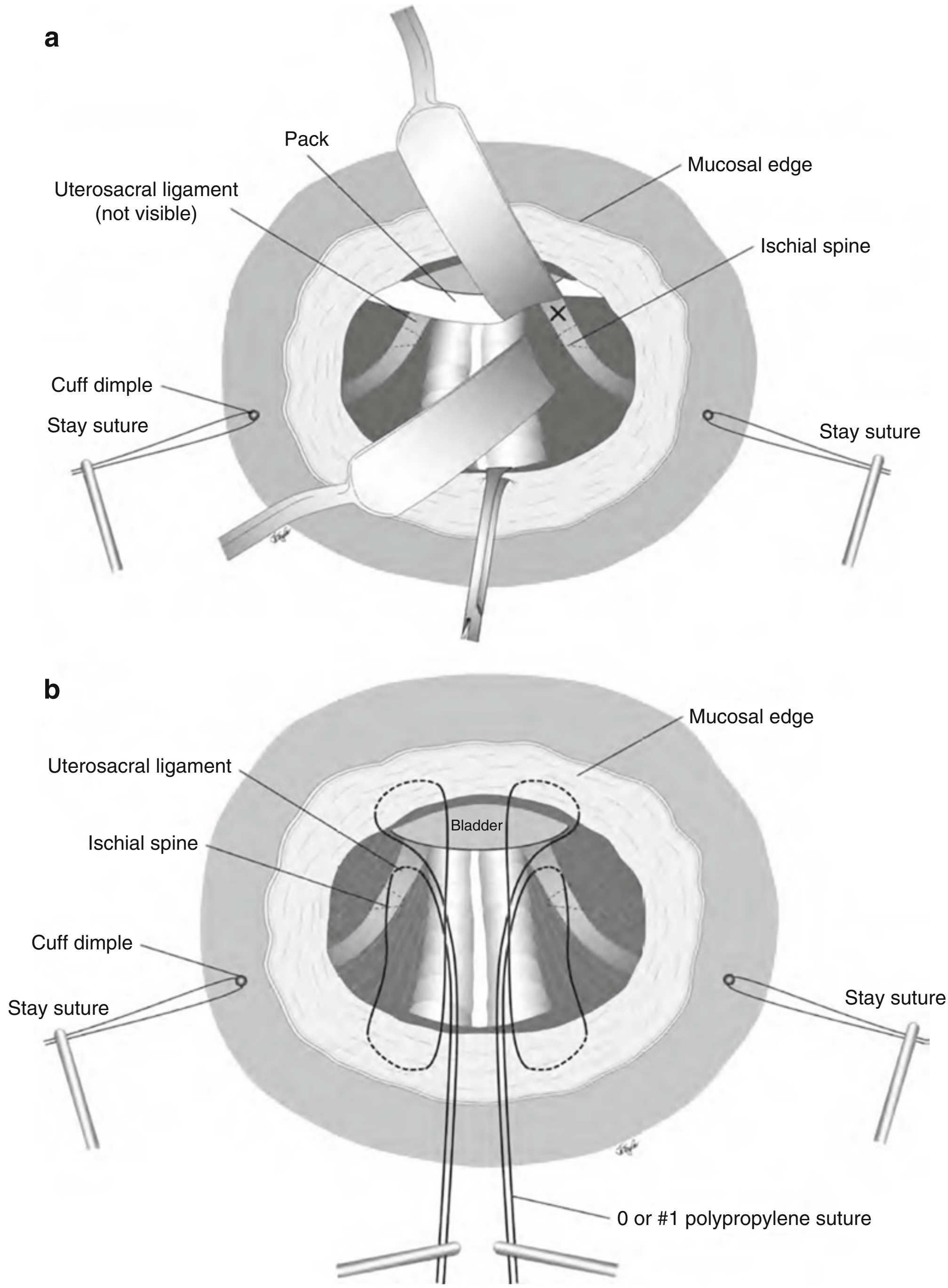

Fig. 10 Diagrams illustrating open vaginal apical area with (**a**) exposure of site for suture placement or lateral pelvic side wall and (**b**) suture placement through ligament and then through the posterior and anterior paravaginal tissue where they are locked to enable pulley action to the ligaments when tied. (From Berek JS (ed) [60]. Reprinted with permission from Lippincott Williams & Wilkins)

Older woman undergoing incontinence surgery can expect continence rates that in general compare favorably to those of younger women. The choice of incontinence surgery will depend upon patient history, physical examination, urethral and bladder function, and whether other concomitant procedures will be performed.

The midurethral sling (MUS) is a minimally invasive surgery and has become the gold standard for the treatment of SUI. Two main types of MUS are the retropubic and transobturator approaches. A recent randomized controlled trial directly compared the two approaches and demonstrated that the objectively assessed success for the treatment of SUI was equivalent between the two approaches (71% retropubic vs. 78% transobturator; 95% confidence interval [CI] −3.6 to 9.6). Subjective success rates were similar between the two and, however, did not meet the predefined equivalence criteria of 12% (62.2% retropubic vs. 55.8% transobturator; 95% CI −1.6 to 14.3) [100]. Existing data regarding the impact of aging on surgical outcomes are limited. A retrospective cohort study demonstrated no difference in treatment success of suburethral slings based on age groups (≤50 years, 51–69 years, ≥70 years of age) [101]. Another study using the British Society of Urogynaecology database including 7600 women undergoing a midurethral sling procedure (757 women ≥70 years and 119 women ≥80 years of age) reported that advanced age was associated with significantly lower subjective impression of improvement for the 70–79 year-old and 80–89 year-old groups (70%) compared to women younger than 50 (93%). Reassuringly, no difference was noted in the intraoperative and postoperative complication rates, except for short-term voiding dysfunction that was higher in the group of women older than 80 years of age [102].

Periurethral bulking injections may be offered in the treatment of SUI in older women. Regardless of the agent, cure and improvement rates are poor and appear to decline with time. The advantage of urethral bulking is that the injection can be performed in the office or operating room. Given the low risk of the procedure, this may be a reasonable option in the medically compromised patient or in the patient who has failed other approaches. Currently available bulking agents include carbon-coated zirconium oxide beads, cross-linked polydimethylsiloxane, and calcium hydroxylapatite. Existing data suggest insufficient evidence for one specific agent to be superior in treatment outcomes, long-term efficacy, and complication rates [103].

More invasive surgical approaches are available such as Burch colposuspension or pubovaginal sling procedure using autologous fascia. A secondary analysis of data from the Stress Incontinence Surgical Treatment Efficacy Trial (SISTEr), a randomized trial of Burch colposuspension versus autologous rectus fascial sling, addressed 2-year outcomes in older women (≥65 years of age) versus those younger [96]. Older women had a slightly longer time to normal activities (50 days compared with 42 days, $P=0.05$), but there was no difference in time to normal voiding (14 days compared with 11 days, $P=0.42$). Older women were more likely to have a positive stress test at follow-up (odds ratio [OR] 3.7, 95% confidence interval [CI] 1.70–7.97, $P=0.001$), less subjective improvement in stress urinary incontinence (eight-point lesser decrease, 95% CI 1.5–14.1, $P=0.02$), and urgency urinary incontinence (seven-point lesser decrease, 95% CI 1.5–12.2, $P=0.01$) as measured by the Medical and Epidemiologic Social Aspects of Aging questionnaire and were more likely to undergo surgical retreatment for SUI (OR 3.9, 95% CI 1.30–11.48). Perioperative adverse events and length of stay did not differ between groups.

The mainstay of treatment for overactive bladder (a condition including urinary frequency and urgency and nocturia with or without urinary urgency incontinence) includes a combination of pelvic floor muscle rehabilitation and medication. Patients refractory to these conservative therapies may be candidates for intravesical botulinum toxin A injections or neuromodulation techniques including posterior tibial nerve stimulation (PTNS) and sacral neuromodulation (SNM).

Fecal Incontinence

Treatment of fecal incontinence (FI) or accidental bowel leakage (ABL) in the older woman should include evaluation for possible functional, anatomic, and neurologic deficiencies in the lower gastrointestinal tract. Behavioral therapies that include diet modification with fiber supplementation and fluid rehabilitation should be considered. Fiber is a bulking agent and thus improves stool consistency, promotes complete evacuation of stool, and improves sensation of the need to defecate. It is beneficial for low-volume, loose-stool-associated FI. Severe constipation can lead to overflow FI; therefore, older women should avoid fecal impaction and have a good bowel regimen. Other conservative management includes pelvic floor muscle training with or without concurrent biofeedback and pharmacologic treatment with anti-diarrheal agents. Devices for the management of FI, such as anal and vaginal inserts, to provide temporary occlusion of the anal vault to prevent leakage have recently become available [104, 105].

Surgery is considered if conservative management is not tolerated or ineffective. Current data regarding surgical management of FI in older women are limited. Perianal bulking is a minimally invasive option. Bulking agents can be injected into the anal submucosa to increase the proximal anal sphincter volume to create a tighter seal. Currently, the most studied bulking agent is non-animal stabilized hyaluronic acid/dextranomer (NASHA/Dx). It is offered typically in the office with little morbidity. Long-term efficacy and safety of this agent is limited.

If an anatomic defect such as a sphincter disruption is identified, anal sphincter repair could be considered. Little studies address the efficacy of this approach in the older woman; however "good" short-term outcomes in all age ranges are achieved in approximately 70% of patients. Unfortunately, longer-term results may not be as robust, with one study reporting only 23% of patients with "good" results at 10-year follow-up [106]. Advanced age at the time of repair has been suggested as a risk factor for long-term surgical failure [107].

Other surgical approaches to consider for the treatment of refractory FI include sacral neurostimulation (SNS). The proposed mechanism of SNS is to reduce colonic activity, change rectal sensitivity via somato-visceral reflex pathway, to increase sphincter tone, and to improve rectal compliance. A recent analysis with a median follow-up of 44 months including patients with FI over 65 years of age demonstrated a significant reduction in FI episodes over 2 weeks, from 10 to 1 [108]. As the device often requires adjustment with the patient programmer, it may not be suitable for older women especially with cognitive or vision impairment or decreased dexterity.

Gynecologic Malignancies in the Older Woman

Introduction

Gynecologic malignancies are those that arise in the female reproductive tract including the uterus, ovaries, cervix, vulva, or vagina. The incidence of most of these cancers increases with age, and outcomes are worse for elderly women across all disease sites. This section outlines the presenting symptoms, diagnostic workup, and treatment for the most common gynecologic malignancies and reviews some of the unique challenges involved in diagnosis and treatment of these cancers in older patients.

Uterine Cancer

While cervical cancer is the most common gynecologic cancer worldwide, cancer of the uterine corpus is the most common malignancy of the female reproductive tract in developed countries. An estimated 61,380 new cases of uterine cancer are diagnosed annually in the United States, and 10,920 women die per year as a result of this disease [109]. Patients 65 and older account for 44.3% of new endometrial cancer diagnoses and 66.6% of endometrial cancer deaths [110].

Endometrial Adenocarcinomas

The most common type of uterine corpus cancers are the endometrial adenocarcinomas, which arise from the uterine lining. These have classically been divided into type 1 and type 2 endometrial adenocarcinoma. The more common type 1 endometrioid adenocarcinomas are endometrioid histology, associated with unopposed estrogen exposure, and generally have a good prognosis. Compared to type 2 adenocarcinomas, these tend to occur more commonly in younger, obese patients and arise in a background of endometrial hyperplasia [111].

In contrast, the type 2 adenocarcinomas are high-grade, non-estrogen dependent, more common in older patients, arise in a background of atrophy, and are associated with a poor prognosis [111]. Type 2 histologies include grade 3 endometrioid adenocarcinoma, uterine papillary serous carcinoma, clear cell carcinoma, and carcinosarcoma (previously malignant mixed mullerian tumor). These tumor types account for a small percentage of endometrial cancer cases but a disproportionate number of endometrial cancer deaths [112].

The majority of older patients with endometrial cancer present with postmenopausal vaginal bleeding. While endometrial cancer is not the most common cause of postmenopausal bleeding, any patient presenting with this complaint should have a diagnostic evaluation to rule out malignancy as a cause. A typical initial workup would include a pelvic exam and a transvaginal ultrasound and/or endometrial biopsy. In a postmenopausal patient, an endometrial stripe >4 mm or persistent or recurrent bleeding regardless of endometrial thickness warrants further evaluation with an endometrial biopsy [113]. Particularly in older patients, cervical stenosis may preclude office endometrial biopsy. If adequate tissue cannot be obtained in the clinic setting, a dilation and curettage is indicated.

Endometrial hyperplasia is the precursor lesion for type 1 endometrial cancer and is classified as simple or complex hyperplasia with or without atypia. While simple hyperplasia rarely progresses to invasive cancer and can be observed in elderly patients, 30% of patients with complex atypical hyperplasia (CAH) will ultimately progress to invasive cancer, and nearly 50% of patients with CAH on biopsy are found to have an invasive cancer on final pathology at the time of hysterectomy [114, 115]. Given the high likelihood of invasive cancer, the finding of CAH on endometrial biopsy should prompt referral to a gynecologic oncologist. Complex hyperplasia without atypia has a much lower risk of progression and can be treated with progestin therapy [115].

Endometrial cancer is surgically staged (Table 2), and primary treatment consists of a total abdominal hysterectomy, bilateral salpingo-oophorectomy, and pelvic and para-aortic lymphadenectomy. Because the majority of endometrial cancers are limited to the uterus, preoperative imaging to evaluate for metastatic disease is typically not indicated prior to surgery. Due to advances in minimally invasive surgical techniques, the majority of these cases can now be performed laparoscopically or robotically with substantially less postoperative morbidity than traditional laparotomy [116]. Lymphedema and other morbidity associated with lymph node dissections can be minimalized through use of sentinel lymph node biopsy, which has been shown to have a high sensitivity for detection of metastatic disease and a low false negative rate [117]. For older women with significant comorbidities or poor functional status that precludes surgical management, primary radiation therapy can be used [118, 119].

Table 2 Carcinoma of the endometrium [222]

Stage I	**Tumor confined to the uterine corpus**
IA	Less than ½ myometrial invasion
IB	Greater than ½ myometrial invasion
Stage II	**Cervical stromal involvement**
Stage III	**Regional metastases**
IIIA	Uterine serosa or adnexal involvement
IIIB	Vaginal and/or parametrial involvement
IIIC	Lymph node involvement
IIIC1	Pelvic lymph node involvement
IIIC2	Para-aortic lymph node involvement
Stage IV	**Distant metastases**
IVA	Invasion of bladder and/or bowel mucosa
IVB	Distant metastases

The need for adjuvant therapy is determined by final pathology results. Patients with low-grade, superficially invasive tumors confined to the uterus do not require adjuvant therapy and have an excellent prognosis (5-year survival >90%) [120]. High-intermediate risk has been defined as stage I endometrial cancers that are high-grade (grade 2 or 3), deeply invasive (outer third myometrial invasion), and/or have lymphovascular space invasion identified. Women >70 who have one of these risk factors, women 50–70 with two risk factors, and women of any age with all three risk factors have been shown to have decreased recurrence risk and improved progression-free survival with adjuvant brachytherapy [121, 122]. Adjuvant chemotherapy is indicated for patients with type II endometrial cancers, regardless of stage, and for patients with advanced-stage disease [123, 124].

Management of recurrent endometrial cancer is variable and depends on histologic subtype and site of recurrence. Isolated vaginal cuff recurrences can be successfully treated with salvage radiation therapy in a high percentage of patients [125]. Chemotherapy or hormonal therapies are options for treatment of more widespread disease. In older patients who are unable to tolerate chemotherapy, hormonal therapy may allow for disease stabilization and improved progression-free survival with minimal toxicity [126].

Uterine Sarcomas

The uterine sarcomas are a rare and aggressive group of soft-tissue sarcomas that typically occur in middle-aged to older women. These cancers account for <10% of all uterine malignancies and typically present as incidental findings at the time of surgery for presumed leiomyoma. Preoperatively, patients may present with vaginal bleeding or a rapidly enlarging pelvic mass [127, 128]. The two major pathologic subtypes are leiomyosarcoma and endometrial stromal sarcoma. Carcinosarcoma was previously thought to be a type of uterine sarcoma; however, it is now understood to be an aggressive, dedifferentiated carcinoma and as such is best grouped with the type II endometrial adenocarcinomas [129].

Uterine sarcoma is primarily a surgically treated disease, and complete surgical resection has been associated with improved survival [130]. Staging differs from that of the endometrial adenocarcinomas and is presented in Table 3. Unlike endometrial adenocarcinomas, sarcomas tend to metastasize hematogenously rather than via lymphatics; therefore, lymphadenectomy is not always required for surgical management of sarcomas [131]. There is limited data to guide adjuvant therapy of uterine sarcomas. Chemotherapy may confer some benefit for patients with leiomyosarcoma, while patients with endometrial stromal sarcomas may derive benefit from hormonal therapy [132, 133]. Radiation therapy does not appear to have a role in the treatment of uterine sarcomas [134].

Key Points in Uterine Cancer Affecting Older Women

- Any patient with postmenopausal bleeding should have a diagnostic evaluation to exclude uterine malignancy.
- Uterine cancers in older women are more likely to be the more aggressive type II histologies (papillary serous, clear cell, carcinosarcoma).
- Primary treatment for both endometrial adenocarcinoma and uterine sarcoma is surgical.

Table 3 Uterine sarcoma [222]

Stage I	**Tumor confined to the uterine corpus**
IA	Tumor <5 cm
IB	Tumor >5 cm
Stage II	**Pelvic extension**
IIA	Adnexal involvement
IIB	Extension to extrauterine pelvic structures
Stage III	**Abdominal metastases**
IIIA	One site
IIIB	More than one site
IIIC	Pelvic or para-aortic lymph node involvement
Stage IV	**Distant metastases**
IVA	Invasion of bladder and/or bowel mucosa
IVB	Distant metastases

Ovarian, Primary Peritoneal, and Fallopian Tube Cancers

With a 5-year survival of only 46.5%, ovarian cancer is the deadliest of the gynecologic cancers and is the fifth leading cause of cancer death in women in the United States [135]. Approximately 1 in 70 women will be diagnosed with ovarian cancer in their lifetime. In 2017, an estimated 22,440 women will be diagnosed with ovarian cancer in the United States, and 14,080 will die from this disease [109]. Forty-five percent ovarian cancer diagnoses and 65% of ovarian cancer deaths occur in women >65 years [135]. Ninety percent of ovarian cancers are epithelial in origin, and as epithelial ovarian, primary peritoneal, and fallopian tube cancers have similar pathogenesis, clinical behavior, and treatment, these are treated as a single clinical entity [136, 137]. As epithelial cancers are the most common malignancies of the ovary, they will be the focus of this chapter. Common histologic subtypes of epithelial ovarian cancer include serous, mucinous, endometrioid, and clear cell cancers.

It was previously thought that only 5% of ovarian cancer patients had a hereditary predisposition to develop the disease; however, we now know that as many as 15–20% of epithelial ovarian cancers are genetic. BRCA1 and BRCA2 are the most common – 40% of patients with a *BRCA1* mutation and nearly 20% of patients with a *BRCA2* mutation will develop ovarian cancer by age 70 [138]. Lynch syndrome is more commonly associated with colorectal and endometrial cancer but also carries a 10% lifetime risk of ovarian cancer. Other less common genes associated with hereditary ovarian cancer include *TP53*, *BRIP1*, *CHEK2*, and *RAD51C* [139]. As nearly one in five women with epithelial ovarian cancer may have a hereditary cancer syndrome, current guidelines recommend that all women diagnosed with epithelial ovarian cancer be referred for genetic counseling and offered genetic testing [140]. Other risk factors for ovarian cancer include nulliparity, early menarche or late menopause, and endometriosis [141]. Multiparity, oral contraceptive pills, tubal ligation, and breastfeeding have all been shown to be protective [142–145].

Because there is no effective screening test and ovarian cancer lacks early warning symptoms, approximately 70% of women have advanced disease (stage III or IV) at the time of their initial presentation [146]. The most common presenting symptoms are vague abdominal complaints, such as bloating, constipation, early satiety, and nausea. Diagnosis is often made by imaging obtained for evaluation of these complaints, which may show ascites, omental caking, and an adnexal mass. Physical exam may be notable for abdominal distension with visible fluid wave or a palpable abdominal or adnexal mass [147]. While not useful as a screening test, the tumor marker CA125 is often markedly elevated in patients with epithelial ovarian cancer and can be used both to support the diagnosis and to monitor response to treatment [148].

Ovarian cancer is surgically staged (Table 4), and survival is directly related to stage at diagnosis. Five-year survival for stage I patients is 81%, for stage II 57%, for stage III 30%, and for stage IV is 14% [149]. Treatment of ovarian cancer is typically a combination of cytoreductive surgery and chemotherapy, most often a platinum/taxane doublet [150]. Surgical staging of ovarian cancer includes total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, pelvic and para-aortic lymphadenectomy, washings, and resection of any other visible disease. The goal of surgery is debulking to no gross residual disease (NRD) as this is associated with improved survival. If debulking to NRD is not feasible, the goal is to have no residual disease >1 cm [151]. Traditionally, patients were treated with surgery followed by adjuvant chemotherapy. As most patients present with advanced-stage disease, up-front cytoreductive surgery is often extensive and can be associated with high postoperative morbidity and mortality. More recently, there has been a shift toward use of neoadjuvant chemotherapy to decrease disease burden prior to proceeding with cytoreduction.

Patients typically have confirmation of diagnosis by either cytology or diagnostic laparoscopy with peritoneal biopsies, receive 3–4 cycles of chemotherapy, and then have an interval debulking surgery followed by an additional 3–4

Table 4 Carcinoma of the ovary [222]

Stage I	**Tumor confined to the ovaries**
IA	Limited to one ovary, capsule intact, no surface involvement, negative washings
IB	Both ovaries involved but capsules intact with no surface involvement, negative washings
IC	Limited to 1 or both ovaries, plus:
IC1	Surgical spill
IC2	Capsule rupture prior to surgery or surface involvement
IC3	Malignant cells in ascites or peritoneal washings
Stage II	**Pelvic extension below the pelvic brim or primary peritoneal cancer**
IIA	Extension to uterus and/or fallopian tubes
IIB	Extension to other pelvic intraperitoneal tissues
Stage III	**Extension to extrapelvic peritoneum and/or retroperitoneal lymph nodes**
IIIA	Positive retroperitoneal lymph nodes and/or microscopic extrapelvic disease
IIIA1	Positive retroperitoneal lymph nodes only
IIIA1(i)	Metastasis $\leq$10 mm
IIIA1(ii)	Metastasis >10 mm
IIIA2	Microscopic extrapelvic peritoneal involvement $\pm$ positive retroperitoneal lymph nodes
IIIB	Macroscopic extrapelvic peritoneal metastases $\leq$2 cm $\pm$ positive retroperitoneal lymph nodes. Includes extension to capsule of the liver or spleen
IIIC	Macroscopic extrapelvic peritoneal metastases >2 cm $\pm$ positive retroperitoneal lymph nodes. Includes extension to capsule of the liver or spleen
Stage IV	**Distant metastases excluding peritoneal metastases**
IVA	Pleural effusion with positive cytology
IVB	Hepatic and/or splenic parenchymal metastases or metastases to extra-abdominal organs

cycles of chemotherapy. For patients at high risk of suboptimal debulking, neoadjuvant chemotherapy is associated with less surgical morbidity and mortality, higher rates of interval NRD, and equivalent survival [152, 153]. Neoadjuvant chemotherapy can also be used to treat patients who are unable to tolerate extensive and lengthy surgery due to advanced age or significant medical comorbidities [154, 155].

With a combination of surgery and platinum-based chemotherapy, the majority of patients will achieve remission; however, recurrence rates are high with over 75% of patients eventually experiencing a relapse [156]. The majority of patients with recurrent ovarian cancer are treated with chemotherapy. There are numerous chemotherapy regimens that can be used for the treatment of recurrent ovarian cancer [157], and while survival can be prolonged, once ovarian cancer recurs, it ultimately leads to the patient's demise. Patients with an isolated recurrence following a long disease-free interval are candidates for surgical management of recurrence [158].

There are several important considerations in the management of ovarian cancer in the older woman. Age is an independent prognostic factor in ovarian cancer – older women are known to have a significantly worse prognosis than younger women [159, 160]. It is not clear whether this difference is due to old age and its associated comorbid conditions or to differences in treatment of elderly women. Elderly patients are more likely to receive primary chemotherapy, less likely to ever have surgery, and more likely to be treated with single-agent platinum rather than combination chemotherapy [161]. While some older patients may experience increased toxicity with chemotherapy, there is evidence that many elderly patients tolerate combination chemotherapy well. Assessing functional status with tools such as the Instrumental Activities of Daily Living (IADL) assessment may help differentiate between elderly patients who are likely to tolerate therapy well and those who are not [162].

Key Points in Ovarian Cancer Affecting Older Women

- Due to the lack of an effective screening test and nonspecific symptoms, the majority of patients present with advanced disease.
- Ovarian cancer is typically managed with a combination of surgery and chemotherapy.
- Resection to no gross residual disease confers the best prognosis.
- In patient with advanced disease, neoadjuvant chemotherapy increases rates of optimal debulking and decreases postoperative morbidity with affecting overall survival.

Cervical Cancer

Cervical cancer is the most common gynecologic cancer and the fourth most common cancer overall in women worldwide; however, the majority of diagnoses and 87% of cervical cancer-related deaths occur in less-developed countries due to the lack of access to appropriate screening and treatment of preinvasive disease [163]. In the United States, there are an estimated 12,820 cervical cancer diagnoses and 4,210 deaths annually [109]. Unlike the other gynecologic cancers discussed in this chapter, the incidence of cervical cancer is actually highest in women in their 30s and 40s and decreases with age [164]. While the incidence is lower in older women, survival also tends to be worse in this cohort [165, 166].

Persistent human papillomavirus (HPV) infection is the most important risk factor for the development of cervical cancer and causes >99% of these cancers worldwide [167]. The most common HPV subtypes implicated in the development of invasive carcinoma are HPV 16 and 18, which together are responsible for over 70% of cervical cancers [168]. The most common histology is squamous cell carcinoma (63.6%), followed by adenocarcinomas (25.1%) [169]. In addition to HPV infection, cigarette smoking, multiple sexual partners, young age at first intercourse, and immunosuppression have been established as risk factors for the development of invasive cervical cancer and its precursor lesion, cervical intraepithelial neoplasia (CIN) [170].

The incidence of cervical cancer in the United States has been steadily declining since the introduction of the Pap smear in the 1950s [169]. Current cervical cancer screening guidelines recommend cytology every 3 years from age 21 to 29. From age 30–65, both cytology and HPV co-testing are recommended at 5-year intervals. If all prior screening has been normal, continued routine screening is not recommended for patients >65. Abnormal cytology or the diagnosis of persistent HPV infection should prompt referral for colposcopy, a microscopic examination of the cervix and vagina, with directed biopsies [171]. The majority of CIN and cervical cancers originate in the transformation zone, where the squamous epithelium of the ectocervix meets the columnar epithelium of the endocervix. Careful evaluation of the transformation is critical for detection of CIN at time of colposcopy. If the entire transformation zone is not visible, endocervical curettage (ECC) is recommended. Of note, the transformation zone tends to recede into the endocervix after menopause; therefore, ECC is often required to exclude endocervical CIN in older women. High-grade CIN (CIN2 or CIN3) detected on biopsy can be treated in a variety of ways, including excision of the transformation zone with either cold knife cone (CKC) or loop electrosurgical excision procedure (LEEP), CO_2 laser ablation, or cryotherapy [171]. Large high-grade lesions or those with an appearance concerning for microinvasive disease should be treated surgically with either CKC or LEEP to allow for pathologic evaluation.

While most early cervical cancers are asymptomatic and detected via screening, patients may present with complaints of irregular or postcoital vaginal bleeding, pelvic pain, or malodorous vaginal discharge. Because cervical cancer typically spreads by direct extension, locally advanced disease may also cause bladder or bowel symptoms, including urinary hesitancy or frequency, constipation, or even vesicovaginal or rectovaginal fistulas. Any of these symptoms should prompt a pelvic exam with biopsy of any suspicious lesions. A screening Pap smear is not appropriate for evaluation of a visible mass.

Cervical cancer is clinically staged (Table 5), and treatment primarily involves surgery or chemoradiation, depending on the extent of disease. While advanced imaging modalities are not used to determine staging, CT, MRI, or 18-F FDG PET scans can be used to help guide treatment decisions.

Patients with stage I cervical cancer are primarily managed surgically, while stage II and higher are best served by primary chemoradiation therapy. Stage IA1 cervical cancer, which has ≤3 mm stromal invasion, can be adequately treated with an excisional procedure such as CKC or LEEP or with a simple hysterectomy given low risk of lymph node involvement (<0.5%) and low risk of recurrence (1.7%) [172]. Stage IA2 disease is typically treated with a type II (modified radical) hysterectomy and bilateral pelvic lymphadenectomy. Historically, stages IB1–IIA

Table 5 Carcinoma of the cervix [222]

Stage I	**Tumor confined to the cervix**
IA	Microscopic cancer with depth of invasion ≤5 mm and horizontal extension ≤7 mm
IA1	Stromal invasion ≤3 mm and horizontal extension ≤7 mm
IA2	Stromal invasion 3–5 mm and horizontal extension ≤7 mm
IB	Clinically visible or exceeds dimensions for stage IA disease
IB1	≤4 cm in diameter
IB2	>4 cm in diameter
Stage II	**Extension beyond the cervix but not to pelvic sidewall or lower 1/3 of vagina**
IIA	Extension to upper 2/3 of vagina
IIB	Parametrial involvement
Stage III	**Extension to pelvic sidewall, lower 1/3 of vagina, and/or causing hydronephrosis**
IIIA	Extension to lower 1/3 of vagina
IIIB	Extension to pelvic sidewall or hydronephrosis
Stage IV	**Extension beyond the pelvis or to mucosa of bladder or rectum**
IVA	Invasion of bladder and/or bowel mucosa
IVB	Distant metastases

were treated with a type III radical hysterectomy; however, patients who require adjuvant radiation due to positive margins or other pathologic risk factors have higher associated morbidity than those treated with either surgery or radiation alone [173, 174]. For this reason, patients with bulky IB2 or IIA tumors are often treated with primary chemoradiation. Advances in laparoscopic and robotic surgery and the increasing use of sentinel lymph node biopsy have resulted in decreased surgical morbidity for patients treated with radical hysterectomy [175–177].

For patients with locally advanced disease or who are not surgical candidates, the cornerstone of treatment is radiation therapy (external beam and brachytherapy) in combination with radiosensitizing chemotherapy. While both hydroxyurea and 5-fluorouracil have also been studied, cisplatin appears to confer a superior survival benefit and has become the chemotherapy of choice in this setting [178–180]. Patients with distant disease at time of diagnosis (stage IVB) have a poor prognosis and are typically treated with palliative chemotherapy. Radiation therapy can be used for palliation of bleeding and bulk symptoms in this population. Five-year survival for women with cervical cancer ranges from over 90% with women with early-stage disease to only 17% for women with stage IVB disease [169].

Treatment of recurrent disease depends on the site of recurrence and the primary treatment modality. In general, recurrent cervical cancer is difficult to treat and portends a poor prognosis. Patients with a pelvic recurrence who had surgery as their primary therapy can be treated with salvage chemoradiation. For patients who were treated with primary chemoradiation and develop a central pelvic recurrence, exenterative surgery is a potentially curative option; however, exenteration has high associated postoperative morbidity and mortality and can have significant detrimental effects on patients' quality of life. Patients with recurrent pelvic disease not amenable to exenteration or with distant disease can be offered palliative chemotherapy, although best response rates remain <50% [181]. Best supportive care is also a very reasonable option in this patient population.

There are significant differences in the management of cervical cancer in older patients compared to younger women. Older patients with early-stage cervical cancer are far less likely to undergo surgery as a primary treatment and less likely to have a lymphadenectomy if they do have surgery. Older women with locally advanced disease are far more likely to undergo no cancer-directed therapy at all compared to younger women. If treated with primary radiation, they are less likely to have concurrent brachytherapy, despite evidence that it is well-tolerated in older patients [111, 166].

Key Points in Cervical Cancer Affecting Older Women

- >99% of cervical cancers are related to human papillomavirus.
- Current guidelines recommend discontinuing routine cervical cancer screening at 65 in patients with a history of normal screening.
- Despite a lower incidence of cervical cancer in patients >65, survival is significantly worse in older women.
- Older women are less likely to receive standard of care treatment than younger women.

Vulvar Cancer

Vulvar carcinoma is a rare malignancy, representing less than 5% of all cancers of the female genital tract [182]. While vulvar carcinoma remains uncommon, the incidence is increasing [182, 183]. There were an estimated 6,020 new cases of vulvar carcinoma diagnosed in the United States in 2017 and an estimated 1,150 deaths from the disease [109]. The mean age at diagnosis is 68.7, and 70% of vulvar cancer diagnoses occur in women over the age of 60 [183].

Squamous cell carcinomas of the vulva are by far the most common histologic subtype, accounting for 90% of vulvar cancers [182]. There are two distinct pathways involved in the pathogenesis of squamous cell carcinoma of the vulva and its precursor lesion, vulvar intraepithelial neoplasia (VIN). Previously, VIN included grades 1–3; however, the nomenclature recently changed, and VIN now refers only to high-grade lesions of the vulva [184]. Human papillomavirus (HPV)-associated VIN, also referred to as usual-type VIN, occurs more frequently in younger women and is predominantly associated with the carcinogenic HPV genotypes, most commonly HPV 16 [185]. HPV-independent VIN, or differentiated VIN, occurs more frequently in older women and is associated with chronic inflammation often secondary to an underlying dermatologic condition such as lichen sclerosus or lichen planus [186, 187]. The clinical behavior of these two pathogenic subtypes is very different. HPV-associated VIN typically develops slowly and may spontaneously regress, while HPV-independent VIN is more likely to progress rapidly to invasive squamous cell carcinoma [185]. While 80% of VIN is associated with HPV infection, only 20–50% of vulvar squamous cell carcinoma can be attributed to HPV, indicating that most invasive squamous cell carcinomas of the vulvar actually arise independently of HPV infection [186].

Patients with VIN or vulvar carcinoma most often present with vulvar burning or pruritus and may report a visible lesion [188]. Diagnosis is made via careful inspection of the vulva with biopsy of any suspicious lesions. Usual-type VIN is multifocal in as many as 49% of cases, while differentiated VIN is more likely to be unifocal [185]. There are several options for treatment of usual-type VIN. Wide local excision, laser ablation, and topical treatment with imiquimod have all been shown to be effective [189]. Surgical management is recommended for patients with large lesions that have an appearance worrisome for invasive disease and for women with differentiated-type VIN given the higher likelihood of progression [184].

Vulvar cancer is surgically staged (Table 6). The presence or absence of lymph node metastasis is the most important prognostic factor for women with this disease. Five-year overall survival in the absence of nodal metastasis is 91% compared to only 57% for patients with node-positive disease [190]. Regardless of nodal status or stage at

Table 6 Carcinoma of the vulva [222]

Stage I	**Tumor confined to the vulva**
IA	≤2 cm in size with stromal invasion ≤1.0 mm
IB	>2 cm in size or with stromal invasion >1.0 mm
Stage II	**Tumor of any size with extension to adjacent perineal structures, including lower 1/3 of urethra or vagina and/or anus**
Stage III	**Positive inguinofemoral lymph nodes**
IIIA	1 lymph node metastasis ≥5 mm or 1–2 lymph node metastases <5 mm
IIIB	2+ lymph node metastases ≥5 mm or 3+ lymph node metastases <5 mm
IIIC	Positive lymph nodes with extracapsular spread
Stage IV	**Invasion of upper urethra or vagina or distant spread**
IVA	Tumor invading upper urethral, vaginal, bladder, or rectal mucosa, fixed to pelvic bone, or with fixed or ulcerated inguinofemoral lymph nodes
IVB	Any distant metastases, including pelvic lymph nodes

initial diagnosis, vulvar cancer-specific mortality increases with age. Women >65 years have a fourfold higher risk of death, and women >80 have a sevenfold higher risk of death compared to women <50 [191].

Historically, vulvar cancer was treated with en bloc radical vulvectomy with bilateral inguinofemoral lymphadenectomy; however, this approach was associated with substantial postoperative morbidity, including wound breakdown, lymphedema, and sexual dysfunction. Given these risks, there has been a trend toward less radical surgical management. Patients with tumors ≤2 cm with ≤1 mm depth of invasion can be treated with wide local excision to a 1 cm free margin alone as their risk of lymph node metastasis is exceedingly low [192]. Well-lateralized tumors <4 cm in size can be treated with wide local excision and ipsilateral groin node evaluation; however, midline or deeply invasive (>5 mm) lesions should have bilateral groin node assessment [193, 194]. Given the substantial infectious morbidity and lymphedema risk associated with inguinofemoral lymphadenectomy, sentinel lymph node biopsy using a combination of isosulfan blue and radiocolloid was investigated and found to have a high sensitivity for detection of metastatic disease and significantly less morbidity than full groin dissection [195, 196]. In many institutions, sentinel lymph node biopsy is now the standard method of groin node assessment for patients with early-stage vulvar cancer. For patients who are found to have positive groin nodes on final pathology, adjuvant radiation to the pelvis and groin with or without concurrent chemotherapy significantly decreases risk of recurrence and improves survival [197, 198].

Similar to changes in the management of early-stage disease, treatment of advanced vulvar cancer has also shifted to a less radical approach. Traditionally, patients with advanced disease were treated with pelvic exenteration; however, this procedure was associated with significant morbidity and high postoperative mortality. Neoadjuvant chemoradiation has been shown to eliminate the need for exenterative surgery for patients with locally advanced disease and to improve outcomes in patients with previously unresectable nodal metastases [199, 200]. Radiation with concurrently weekly cisplatin leads to high rates of complete pathologic response, and for these patients, subsequent surgical resection may be unnecessary [201]. Older women with vulvar cancer are much less likely than younger women to be treated surgically and are more likely to receive primary chemoradiation [191].

The prognosis and treatment of recurrent vulvar cancer depend on the site of recurrence. Isolated vulvar recurrence can be treated with surgical excision [202]; however, the optimal treatment for patients with nodal or distant recurrence is unclear. Prognosis for these patients is poor regardless of choice of therapy. Chemotherapy and palliative care are both reasonable options in this setting [203].

Other Vulvar Malignancies

Vulvar melanoma is the second most common malignancy of the vulva after squamous cell carcinoma and makes up 5–10% of vulvar malignancies. The majority of vulvar melanomas occur in elderly patients, and it is much more common in Caucasian women [204]. Compared to cutaneous melanoma and other mucosal melanomas, prognosis for patients with vulvar melanoma is poor with a 5-year overall survival rate of less than 50%. Forty percent of women with vulvar melanoma will have metastatic disease at the time of initial presentation [205]. Similar to cutaneous melanomas, wide local excision with sentinel lymph node biopsy has been adopted as the treatment of choice for these patients [206, 207].

Extramammary Paget's disease of the vulva is an intraepithelial adenocarcinoma that occurs most commonly in postmenopausal Caucasian women and may be associated with underlying adenocarcinoma of the vulva. Invasive Paget's disease of the vulva is rare, accounting for only 1–2% of vulvar malignancies [208]. Patients classically present with pruritus, and physical exam shows an erythematous plaque with white scaling. Ulceration may also be present [208, 209]. Diagnosis is typically made by biopsy, which shows intraepithelial mucin-producing cells known as Paget cells [208]. Treatment is typically wide local excision, which may be extensive given the propensity for multifocal disease. Positive margins are common, and re-excision is indicated to ensure complete resection [208].

Bartholin gland carcinomas are rare adenocarcinomas of the vulva that are frequently misdiagnosed as cysts or abscesses as these are common abnormalities of the Bartholin gland. Any suspected Bartholin cyst or abscess in a postmenopausal patients warrants biopsy [210].

Key Points in Vulvar Cancer Affecting Older Women

- Vulvar cancer in older women is more likely to be associated with vulvar dermatoses than with HPV infection.
- Ninety percent of vulvar cancers are squamous cell carcinomas.
- Older women have a worse prognosis than younger women regardless of stage at diagnosis.
- Lymph node status is the most important prognostic indicator.

Vaginal Cancer

Primary cancer of the vagina is rare, accounting for only about 2% of all gynecologic cancers. The incidence increases with age with 50% of patients presenting at age 70 or older [211]. By definition, vaginal tumors that involve the cervix or vulva are classified as primary cervical or vulvar malignancies; thus, the most common tumors involving the vagina are actually metastases. Over 50% of primary vaginal carcinoma occurs in women with a previous hysterectomy [212]. Similar to cervical cancers, the majority of primary vaginal cancers are squamous cell carcinomas (80%) and are related to HPV disease, especially HPV-16. Adenocarcinomas account for 15% of vaginal carcinomas, and the remaining 5% are made up of rare histologies including melanoma and sarcoma [211, 213].

The most common presenting complaints in women with vaginal cancer are vaginal bleeding and abnormal discharge; although, patients with more advanced disease may also present with pain and/or urinary or rectal symptoms [214]. These symptoms should prompt a careful pelvic examination with biopsy of any suspicious lesions. Patients who have had a hysterectomy for cervical intraepithelial neoplasia may present with abnormal findings on vaginal cytology. If no visible lesion is seen, colposcopy with Lugol's iodine solution can be used to identify areas of vaginal intraepithelial neoplasia (VAIN) or microinvasive disease.

The prognosis for vaginal carcinoma correlates with the stage of disease, which is determined according to the FIGO staging of vaginal cancer. Similar to cervical cancer, vaginal cancer is clinically staged rather than surgically staged (Table 7). Five-year overall survival ranges from near 80% for patients with stage I disease to less than 15% for patients with stage IVB disease [213].

Because vaginal carcinomas are such a rare disease, there are no large randomized trials to guide management. Choice of primary therapy depends largely on stage, tumor size and location in the vagina, and patient factors [214]. The majority of patients are treated with primary

Table 7 Carcinoma of the vagina [222]

Stage I	Limited to vaginal wall
Stage II	Involves subvaginal tissue but does not extend to pelvic wall
Stage III	Extension to pelvic sidewall
Stage IV	Extends beyond the pelvis or involves bladder or rectal mucosa
IVA	Invasion of bladder and/or bowel mucosa
IVB	Distant metastases

radiation or chemoradiation. Surgical management with a radical upper vaginectomy and pelvic lymph node dissection appears to be superior to radiation for patients with stage I or small stage II tumors that are limited to the upper third of the vagina [211, 215]. For patients with early-stage disease who are not surgical candidates, radiation therapy is an effective treatment option that results in excellent local control and long-term disease-free survival. The majority of patients are treated with a combination of external beam and either interstitial or intracavitary brachytherapy [216–218]. Patients with advanced disease are often treated with chemoradiation, which is extrapolated from data showing improved survival with the addition of chemotherapy in cervical cancer [180, 219]. Although there is no prospective data showing a benefit with chemoradiation, available retrospective data suggests a significant benefit over radiation therapy alone [220].

Management of recurrent vaginal cancer is similar to that of recurrent cervical cancer. Central recurrences can be managed surgically with a pelvic exenteration, while distant recurrences are managed with chemotherapy or best supportive care. Prognosis for recurrent disease is poor [221].

Key Points in Vaginal Cancer Affecting Older Women

- Primary vaginal carcinomas are rare. The majority of vaginal tumors originate from the cervix or vulva.
- The majority of vaginal cancers are squamous cell carcinomas and are related to HPV.
- Select patients with early-stage disease may be candidates for surgical management, but the majority are treated with radiation therapy or chemoradiation.

Research Involving Older Woman

Given the growing geriatric population along with the high prevalence of both benign and malignant gynecologic disorders, there is a pressing need for information on the nonsurgical and surgical treatment outcomes in older women. Understanding aging-related physiologic and anatomic changes as well as unique challenges such as cognitive and functional limitations in the geriatric population is critical in providing effective therapy. There is a relative paucity of literature that addresses the older woman. In fact, older women have been excluded from many of the trials that have examined outcomes. In the area of pelvic floor surgery, a systematic review found the median percentage of women aged 70 or older who participated in surgical trials for SUI was 3.8%, while the number of surgeries for SUI performed on this population of women is estimated at 16% [223]. Less invasive treatment options have recently become available, yet long-term data on efficacy and safety specifically in the geriatric population are still lacking.

Another unique challenge for research on aging-related conditions is that there is no discrete age to define “old.” Research has suggested the use of different age groups: young old (65–75), old-old (75–85), and the oldest old (>85). Among these groups, the oldest old is the most rapidly growing population. It is essential to consider not only the chronological age but also the functional status and “physiologic age” of the patient when discussing treatment with patients. Continued effort in research initiatives should be made to increase high-quality data to improve evidence-based management of all gynecologic issues in the older women.

Conclusion

This chapter summarized an evidence-based review of the evaluation and treatment of benign and malignant gynecologic and urogynecologic conditions. Optimization of gynecologic health in the older woman may involve the spectrum of gynecologic subspecialties. Evidence-based treatment approaches are important to appreciate and can result in marked improvement in quality of life. Increasingly, the older woman is seeking to continue to be active in the workforce as well as physically and socially. Being proactive in the care of our older female patients should be a priority for all providers of care to women.

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39 Anesthetic Management

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Abstract

Elderly patients will constitute 20% of the population in the USA by 2030. This phenomenon has clear implications for healthcare including perioperative care. While this group consumes approximately 35% of the surgical services, their perioperative outcomes lag behind other age groups.

While traditional anesthetic management focused in the intraoperative portion, it is peremptory to provide comprehensive and coordinated care along the perioperative continuum. In the preoperative phase, a systematic review of systems and comorbidities remains most important. However, the concepts of frailty as a determinant of outcomes and pre-habilitation in order to further optimize those presenting for anesthesia and surgery provide new perspectives in the care of these patients. Intraoperative, assuring organ perfusion, proper ventilation, and minimizing the physiological responses to surgery are key aspects. In addition prevention of awareness and movement are also important goals. Postoperatively, assessing and treating pain properly; avoiding, recognizing, and treating postoperative delirium; preventing falls; and assuring proper hydration and nutrition are important aspects in the management of these patients.

The care of the surgical geriatric patient is complex and requires excellent coordination and communication across all healthcare providers involved in their care. The perioperative surgical home promotes such collaborative effort and has proven results in different surgical service lines. This approach might prove useful when caring for the older adult across all the phases of the perioperative continuum.

Keywords

Perioperative continuum · Perioperative surgical home · Frailty · Pre-habilitation · Anesthesia · Perioperative complications

Introduction

In America, about 10,000 people turn 65 years of age every day. This phenomenon started in January 2011 and is estimated to last for 19 years. By the time it ends in 2030, 18% of the population will be older than 65 years of age, compared with only 13% in 2013 [1]. Combined with the fact that the fastest growing segment of the population encompasses those older than 85 years of age [2], it is clear that there is a socioeconomic impact of such demographic change at all levels. Healthcare, including perioperative care, is no exception. Older adults receive 35.3% of the inpatient surgical procedures and 32.2% of all outpatient procedures performed in the USA [3, 4]. In 2002, this age group consumed 36% of the healthcare expenditures [5]. It has been estimated in the USA that this group will have at least one procedure done before dying [5].

This increase on demand for perioperative service in this demographic group has not been paired by improvement in outcomes. A prospective observational study in patients undergoing noncardiac surgery found that the 1-year mortality of those over 65 years of age was 10.3%, almost twice of those below that age (5.5%) [6]. The authors reported that in this cohort of 1064 patients, being over 65 years of age implied a relative risk of 1-year postoperative mortality of 4.459, which was the highest risk factor after having three or more comorbidities or having an ASA classification of 3 or 4. Others identified age as one of nine independent predictors of a cardiac adverse event after general vascular and urological surgery in a cohort of 7740 patients of 68 years of age or older [7]. Similarly, a review of the National Surgical Quality Improvement Program database from February 24, 2002 through June 30, 2005, showed an overall 28% morbidity rate and 2.3% mortality rate among 7696 surgical patients. However, for those older than 80 years of age, the morbidity rate was 51% and the mortality 7% [8].

If we consider that the cost of care in the USA on those older than 65 years of age is significantly higher than other developed countries, it is not difficult to infer that there are opportunities to enhance the care we provide to our older adult patients [9]. In this chapter, we will cover current trends in the anesthesia care in the older adult. While we will follow a traditional format of preoperative, intraoperative, and postoperative care, we will also discuss the need of better coordination of care for these patients along the whole perioperative continuum.

Preoperative Evaluation

The need to improve outcomes in the older adult undergoing surgery and anesthesia is obvious. Although age seems to be related to these not-so-desirable outcomes, it is not the only cause. Physiological changes of aging, comorbidities, occurrence of complications and type of surgery also play a role. As perioperative evaluation, frailty, and rehabilitation are explored in detail in other chapters of this book, we will only highlight some of the important aspects.

The expected physiological changes of aging are noted in Table 1. In terms of the impact of existing comorbidities, Tiret et al. demonstrated that as patient ages, the presence of one or more comorbidities is correlated with a higher incidence of complications [10]. The importance of this data resides in the impact that complications have in these patients. In a publication looking at patients older than 80 years of age undergoing noncardiac surgery, 20% had one or more postoperative complications. Furthermore, in those who suffered complications, the 30-day mortality was higher than those who did not (26% vs. 4%, $P < 0.001$) [11]. Therefore, optimization of pre-existing comorbidities is most important when caring for the older adult in the perioperative period. Additionally, quality of life should not be forgotten as an important outcome measure. Postoperative complications in the elderly have been

Table 1 Physiological changes of aging

Organ system	Changes with aging
Central nervous system	Loss of neural tissue: 26% reduction of white matter 10–20% Reduction in cerebral blood flow Decreased number of serotonin, acetylcholine, and dopamine receptors Decline in memory, reasoning, perception Disturbed sleep/wake cycle Prone to delirium and cognitive dysfunction
Cardiovascular	Diastolic dysfunction and loss of compliance of vascular bed Less responsive to catecholamines Autonomic tissue is replaced by fat and connective tissue: Prone to arrhythmias – most commonly atrial fibrillation and AV block
Respiratory	Loss of pharyngeal reflexes Decrease in chest wall compliance Decline in lung elasticity Alteration in control of ventilation Decreased diaphragm strength Increased A-a gradient Increased closing capacity
Renal	Loss of renal tubular mass Decreased renal blood flow by 50% Decreased glomerular filtration rate (by 80 years old, decreased by 45%) Reduced ability to dilute and concentrate urine and conserve sodium Decreased drug clearance
Pharmacological	Decrease level of proteins Decreased protein binding Decreased lean and increased fat body mass Decreased circulating blood volume

correlated to with decreased independency on activities of daily living [12].

The type of surgery performed also impacts outcomes. Schwarze et al. reviewed two cohorts of patients from 2001 and 2007 and looked at procedures that had a mean crude inhospital mortality of at least 1% [13]. About 227 procedures were identified; most of them are in high-risk cardiac, vascular, gastrointestinal, neurosurgical, urological, and vascular case. The need for emergency interventions also seems to play a role in outcomes. A Canadian retrospective study looking at patients 80 years or older undergoing emergency surgery in a tertiary care institution found that the inhospital mortality was 14.7% and that over 60% of patients require additional services or an alternate level of care upon discharge [14]. Another report form this group reported an inhospital mortality of 12%, which not surprisingly correlated with higher ASA classification and inhospital complications [15].

When assessing a patient presenting for surgery and anesthesia, it is important to consider all the above aspects. The American College of Surgeons, in collaboration with the American Geriatric Society, has published comprehensives guidelines for the perioperative care of the geriatric patient [16, 17]. A chapter devoted to perioperative assessment can be found elsewhere in this book.

While a thorough assessment of all organ systems is of great importance during the preoperative evaluation, one of the most important factors in determining outcomes is the assessment of the patient's functional capacity. As we age – and even when in health – the capability to respond to stress is progressively lost. This process does not necessarily correlate well with chronological age [18]. Perioperative functional and performance status may be predictive of postoperative outcomes, including incidence of delirium, surgical site infections, discharge institutionalization, and 30-day and 6-month mortality [16]. Assessment of functional status is relatively easy and could be achieved with a short series of screening questions assessing a patient's ability to independently perform activities of daily living, e.g., the ability to get out of bed or chair, dress, bathe, prepare meals, and shop. Lack of capacity on any of these should prompt further evaluation, consider physical and/or occupational therapy referral, and start proactively planning the hospital discharge. Worsening self-reported mobility has been found to correlate with negative outcomes [19]. Other functional aspects to evaluate include hearing, vision, swallowing, gait or mobility deficits, as well as screening for falls or risk of falling [16–20].

More recently, the concept of frailty has emerged as a good indicator of the patient's functional capacity and has been shown to correlate well with increasing the risk for adverse postoperative outcomes. Frailty is a syndrome independent of disability and comorbidity that is highly prevalent in the geriatric population; some estimate that up to 50% of those over 85 years of age may be frail.[16] Multiple measures of frailty exist, but one widely recognized definition was put forth by Fried et al. [21]. This group suggested that a clinical syndrome is present when three or more of the following criteria were met: unintentional weight loss (10 pounds in the past year), self-reported exhaustion, weakness (grip strength), slow walking speed, and low physical activity.

Based on this definition, Malaky et al. reported their finding using these criteria scale in patients presenting for surgery [22]. They classified patients with a score of 2 or 3 as intermediately frail and those with a score of 4 or 5 as frail. They found that in this cohort of patients, preoperative frailty was associated with an increased risk for postoperative complications (intermediately frail: odds ratio [OR] 2.06, 95% CI 1.18–3.60; frail: OR 2.54, 95% CI 1.12–5.77), prolonged length of stay (intermediately frail: incidence rate ratio 1.49, 95% CI 1.24–1.80; frail: incidence rate ratio 1.69, 95% CI 1.28–2.23), and higher likelihood of discharge to a skilled nursing or assisted-living facility after previously living at home (intermediately frail: OR 3.16, 95% CI 1.0–9.99; frail: OR 20.48, 95% CI 5.54–75.68). Robinson and colleagues used a different frailty scale in patients undergoing cardiac or colorectal surgery [23]. They used seven criteria: Katz score less than or equal to 5, Timed Up and Go test greater than or equal to 15 s, Charlson index greater than or equal to 3, anemia less than 35%, Mini-Cog score less than or equal to 3, albumin less than 3.4 g/dL, and 1 or more falls within 6 months. Based on the number of positive traits, patients were classified as nonfrail, 0 to 1 traits; prefrail, 2 to 3 traits; and frail, 4 or more traits. Their findings were similar to the Malaky study as frailty was associated with increased postoperative complications after colorectal (nonfrail: 21%; prefrail, 40%; frail, 58%; $P = 0.016$) and cardiac operations (nonfrail: 17%; prefrail, 28%; frail, 56%; $P < 0.001$). It is important to mention that this finding was independent of advancing age. Additionally, frail individuals had longer hospital stays and higher 30-day readmission rates in both groups. A recent systematic review of the literature recently published suggests that there is strong evidence that frailty in the elderly patient undergoing surgery and anesthesia predicts outcomes such as mortality, complications, and extended length of stay [24]. It is pertinent to mention a recent study looking at the association of hospital volume of frail surgical patients presenting for elective major noncardiac surgery and outcomes. Survival among frail patients was better at institutions that care for larger number of frail surgical patients [25].

A remaining challenge is how to collate all this information in terms of age, comorbidities, type of surgery, frailty, and other factors and estimate the risk of postoperative complications. As a tool to help with this issue, the American College of Surgeons created a Surgical Risk Calculator that is accessible to the physicians and the public [26]. Physicians and patients can enter perioperative information about the patient to help estimate the risk of postoperative complications and make better informed decisions.

Associated to the concept that the presence of frailty or decrease functional status has been associated with worse outcomes, the notion of pre-habilitation as a way to optimize patients in preparation for surgery is an emerging concept. Currently, there are studies which suggest that an exercise program aimed to improve the functional status of patients before surgery might improve recovery and overall outcomes, including in the geriatric population [27–29]. Some studies also propose that there might be benefits in the cognitive domain as well [30]. This concept of pre-habilitation and perioperative optimization is not only a focus in the management of elderly patients: the State of Washington has a program entitled "Strong for Surgery," demonstrating the interest that those paying for healthcare (in this case a particular state) have identified pre- and perioperative care as an area of focus for improving surgical outcomes [31].

Intraoperative Management

Anesthetic Goals

Intraoperative management focuses on the immediate surgery, but consideration should also be given toward promoting postoperative recovery whenever possible. An adequate anesthetic prevents painful stimuli from being sensed by the brain, thereby preventing patient awareness of pain in attempt to minimize the body's physiologic responses to painful stimuli. The latter implies the goal of a stable blood pressure, maintained organ perfusion, appropriate ventilation, controlled body temperature, and, hopefully, a minimal hormonal response to the pain and trauma of surgery. Lastly, a relaxed, immobile patient is important.

Central Nervous System Management

In the operating room, one of the first goals to be considered is the desired state of consciousness. The goal will vary depending on the type of anesthetic employed. With a general anesthetic, the patient should remain unconscious and have no awareness of the surgery postoperatively. In contrast, when a regional block is used as the primary anesthetic, there should be no pain experienced by the patient. Sedation is therefore an optional component. How much sedation is used becomes heavily dependent on the patient's desires and expectations. World War II veterans rarely needed anything at all, whereas anxious patients often state that they do not want to be aware of anything. Such a request can be accommodated, but it requires levels of sedation that essentially constitute a general anesthetic and raises the question of why utilize a regional anesthetic unless it is provided for postoperative analgesia as well. Regional anesthetic techniques that can be used as the primary anesthetic include spinal or epidural anesthesia with high concentrations of local anesthetics to achieve complete neural blockade and peripheral nerve blocks that completely numb and paralyze an extremity. MAC, or monitored anesthesia care, cannot be considered as a primary anesthetic technique. In MAC cases, the surgeon is responsible for blocking painful stimuli, typically via injection of local anesthetics into the surgical field. Theoretically, with MAC, sedation, is optional, although most patients desire some degree of sedation. Anesthesia personnel often provide MAC not so much for the administration of sedation but to closely keep track of the patient's vital signs because of the patient's severe systemic disease.

Whenever an anesthetic does not involve a general, consideration must be given to what needs to be done if the regional block and/or the local anesthetic provides inadequate pain control. More sedation and opioid analgesia is typically administered, but increasingly deeper levels of sedation increase the risk of an obstructed airway. The older patient is at increased risk for obstruction due to changes in anatomy, muscle tone and control, and concurrent obesity. In short, as the "sedation" progresses to a largely unresponsive or even unconscious patient, at some point the airway may need to be secured. It is therefore important to recognize that if local anesthetic agents are unlikely to provide successful analgesia, it is likely riskier to the older patient to be essentially under a general anesthetic with an unsecured airway than to have proceeded with a general anesthetic that includes a laryngeal mask airway or endotracheal tube.

All drug administration is usually given to effect rather than a fixed dose. Nevertheless, the anesthesia caregiver will likely at least start with smaller drug doses in the elderly patients. A rough rule of thumb is that opiate and induction agent dosing should be approximately half that of a young adult, whereas benzodiazepine dosage may only require modest reductions until very old age at which point dosage should be markedly reduced.

Cardiovascular System Management

All anesthetics tend to lower blood pressure, primarily by reduction of sympathetic tone. Older patients typically have much higher sympathetic tone than in young adults, both at rest and in response to stimuli [32]. General anesthesia suppresses sympathetic outflow from the brain. Spinal or epidural anesthesia blocks the pain signals from reaching the spinal cord, although when low concentrations of local anesthetics are used for epidural analgesia that blockade is not complete. Local anesthetic action also blocks sympathetic outflow over a dermatomal range that may extend well above the level of sensory blockade, especially with spinal anesthesia. A given dose of local anesthetic is likely to spread to more dermatomes in older patients as well. However, blockade of a single extremity typically has a minimal effect on blood pressure, not only because of the limited area of sympathetic blockade but because the rest of the sympathetic nervous system is intact and can be involved in the baroreflex control of pressure. When sympathetic outflow is high, as is often the case in the elderly, central nervous system or direct nerve blockade of most the sympathetic nerves can result in quite extreme effects, and the resultant hypotension appears to be more from a decrease in vascular resistance than a decrease in cardiac output (Fig. 1) [33].

Although propofol and all of the potent volatile anesthetics possess some direct depression of the vascular smooth muscle and the myocardium, significant myocardial depression is highly unlikely, even when there is baseline myocardial dysfunction. It is important to recognize that even drugs with no direct hemodynamic effects can cause profound hypotension in an acutely ill patient who is surviving on intense vasoconstriction and tachycardia. Any drug affecting the brain will decrease sympathetic nervous system outflow and indirectly decrease vascular resistance and possibly cardiac output. In this sense, the older, frail patient is similar to a young, healthy trauma patient. Where the difference between these two classes of patients resides is typically in their volume status. The young trauma patient is most likely severely hypovolemic. At baseline, the elderly

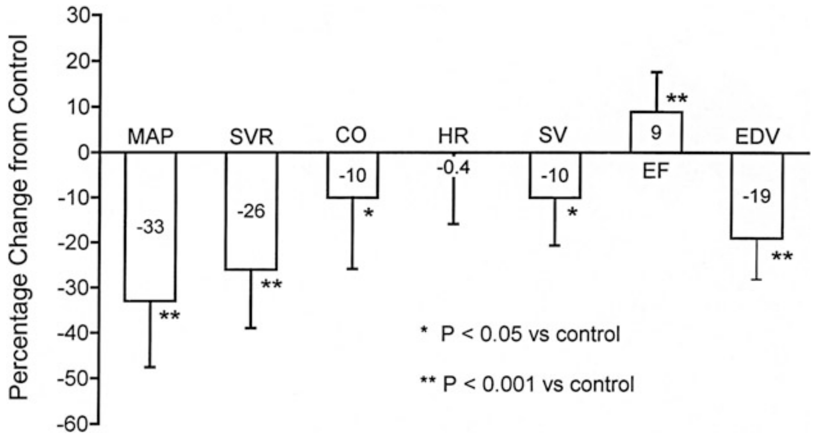

Fig. 1 The effect of total sympathectomy from spinal anesthesia is demonstrated in older men with varying degrees of cardiac disease. The large decrease in systemic vascular resistance (*SVR*) accounted for the majority of the decrease in mean arterial blood pressure (*MAP*). Although cardiac filling (*EDV*, end-diastolic volume) decreased significantly, the overall increase in the ejection fraction (*EF*) prevented an equal decrease in stroke volume (*SV*) and cardiac output (*CO*) (Reprinted from Rooke GA, Freund PR, Jacobson AF: Hemodynamic response and change in organ blood volume during spinal anesthesia in elderly men with cardiac disease. Anesth Analg 1997; 85: 99, with permission)

patient may be slightly hypovolemic but likely has a high degree of vascular tone that will disappear with an anesthetic. Management of hypotension should therefore be quite different for these two groups. Fluid administration for the trauma patient is a key aspect of resuscitation, but volume alone is not the primary therapy for the older patient: the improvement in cardiac output will be modest at best and is not capable of compensating for a large decrease in vascular resistance. The better therapy is a drug that causes vasoconstriction and will restore systemic vascular resistance, such as phenylephrine. Besides causing direct arteriolar vasoconstriction, venoconstriction will shift peripherally pooled blood back to the central circulation and improve ventricular preload and cardiac output, although the effect on vascular resistance likely accounts for most of the effect on blood pressure.

Not only is volume administration often poorly effective in older patients, but it may prove harmful in the long run. Venous stiffening leads to greater swings in cardiac filling for a given change in intravascular volume. This instability is made worse by the ventricular stiffening and diastolic dysfunction that occurs from both aging and chronic hypertension [34]. Although overt hypovolemia and inadequate ventricular filling must be avoided, fluid overload is dangerous. The amount of crystalloid that remains in the blood vessels is highly dependent on the volume status of the patient. Most of the fluid given to a hydrated patient ends up in the interstitium. The jury is still out as to how harmful tissue edema is, but where that fluid unequivocally can be deleterious is when the third-space fluid starts to mobilize. The stiffened cardiovascular system poorly buffers the increased intravascular volume and can lead to pulmonary congestion if not outright pulmonary edema and clinical heart failure. The best volume administration strategy in older patients may well be to give volume for preexistent hypovolemia, basic metabolic needs (minimal), and blood loss but not to make any guesses on third-space fluid requirements. Instead, administer volume challenges when there is physiologic evidence of hypovolemia.

Respiratory System Management

General anesthesia suppresses ventilatory drive and, along with the ciliary suppression of an endotracheal tube, suppresses elimination of secretions [35]. Controlled ventilation is common during general anesthesia and is particularly useful for preventing atelectasis. The decrease in lung tissue stiffness with age leads to an increase in closing capacity. With induction of general anesthesia, functional residual capacity (FRC) decreases and further increases the volume that must be given to the lungs to get from FRC to above the closing capacity. Therefore, either a large tidal volume must be used or positive end-expiratory pressure (PEEP) must be applied to raise FRC. Serious respiratory complications are reduced when a strategy is to employ a modest tidal volume and add PEEP as needed to prevent atelectasis [36].

Another risk factor for perioperative respiratory complications is residual neuromuscular blockade [37]. The phenomenon occurs more often than is commonly appreciated and the elderly are at increased risk [38]. The mechanism behind the increased risk with aging is not clear but may involve the poorer muscular control of swallowing and protection from aspiration that develops with age. Residual neuromuscular blockade certainly would not help. Avoidance of this phenomenon requires rigorous attention to the state of neuromuscular blockade present at the end of surgery. Complete reversal of neuromuscular blockade with neostigmine can only be achieved if the level of existing blockade is modest [39]. Administration of neostigmine too soon into the natural resolution of the blockade can actually make things worse and increase the duration of residual blockade. Concern over the ability to reverse the blockade is the likely basis for disagreements between the surgeon and anesthesiologist over the management of "tight" muscles toward the end of the surgery. Frequently, merely deepening the anesthetic can muscle relaxation without having to resort to more non-depolarizing muscle relaxant. Proper management of significant residual blockade at the end of the case requires waiting for neuromuscular blockade to wear off to a point where neostigmine can work effectively. This can take a long time, even an hour or more. Whether the use of sugammadex, at present a very expensive drug, will have a significant effect on avoiding residual neuromuscular blockade has yet to be determined.

Temperature Management

The operating room is a cold environment and presents a stress to all patients. Inhalational anesthetics, many intravenous agents, and even spinal anesthesia lower the temperature at which vasoconstriction and shivering commence. Aging further impairs these thresholds. In addition, the older patient has a lowered metabolism and therefore produces less heat. Hypothermia has been associated with adverse outcomes including myocardial ischemia, coagulopathy, and wound infections [40]. Shivering may place a significant stress on a patient with low pulmonary or cardiac reserve. Prevention of hypothermia has been greatly aided by the widespread use of active warming, not only in the operating room but also in the preoperative holding area and the recovery room.

Stress Response to Surgery

The physical response to trauma is complex and can be deleterious to the patient [41]. The adverse consequences may include the brain, though the evidence for that is weak. Reduction of the stress response to surgery should begin in the operating room [42]. It can be argued that improvements in surgical technique that limit trauma and improvements in analgesia are responsible for the ability to perform surgeries on increasingly frail patients with reasonable outcomes.

Regional anesthesia may limit the hormonal response more effectively than general anesthesia, but this advantage goes away postoperatively when the regional anesthetic wears off. At present, there are no good studies showing an overall improvement in outcomes with regional anesthesia over general anesthesia. Postoperative epidural analgesia has had some limited success in reducing complications in some situations, but the only definitive statement is that epidural analgesia has the potential to produce the best possible analgesia [43]. The methods available for analgesia and therefore stress reduction continue to evolve.

Controversies in Geriatric Anesthesia

There are always controversies over the "best" anesthetic management, but most of the current controversies in anesthesia principally affect the older patient. This discussion presents "pro" evidence only as this section is only meant to introduce the topics and not to present a comprehensive evaluation. No definitive conclusions are possible without additional studies, but it is likely that these topics will be studied and debated for some time to come.

Perhaps the most extensively examined concern is the contribution of anesthetic management to delirium and postoperative cognitive dysfunction (POCD). Certainly any drug that obtunds the brain can contribute to delirium. What is controversial is to what extent the depth of anesthesia contributes to delirium. One provocative study found that general anesthesia monitored with bispectral index was associated with approximately a 25% lower incidence of delirium than when bispectral index was not used [44]. Even with just propofol sedation, deep sedation levels were associated with more delirium than from low levels of intraoperative sedation [45]. The impact of anesthesia on POCD is discussed later and is far more confusing a picture than with the relationship to delirium.

Intraoperative hypotension as a risk factor for adverse outcome is another important topic. Risks include adverse cardiac events, acute kidney injury, stroke, and death) [46, 47]. In addition to hypotension alone, hypotension in combination with low levels of anesthetic gas administration and low bispectral index values constitutes a mortality risk [48]. What is less clear is the causal relationship beyond the seeming logic that hypotension is bad. It is entirely possible that intraoperative hypotension, especially in the elderly, is merely a marker of a patient with diminished reserve who is less able to withstand the stress of a surgical procedure.

Recent studies indicate that many older patients have postoperative troponin leaks [49], those that do demonstrate an increased risk of both short-term and long-term mortality. Most of the troponin elevations occur in the absence of symptoms, making the diagnosis of the damage after the fact. Furthermore, many patients present for elective surgery with recent troponin elevations, and they, too, are at increased risk of adverse outcomes [50]. Clearly more needs to be known about these phenomena and what can be done to ameliorate the subsequent increased risk.

Postoperative Care of the Surgical Geriatric Patient

The core competencies of anesthesiology include optimization of comorbidities and volume status, management of pain and sedation, as well as postoperative nausea and vomiting (PONV) prophylaxis. Consequently, given the growing and medically complex geriatric population, there is an increased emphasis on anesthesia care in the postoperative period [17, 51–54]. Geriatric care is quickly becoming an area where anesthesiologists can have an impact on postoperative outcomes. In addition to traditional outcomes such as ambulation, nutrition, cognition, and length of stay, anesthesiologists can directly affect the subjective patient experience, including their emotional well-being, overall translating into increased satisfaction with their care and the surgical team [54]. In short, the goal of postoperative anesthesia care should be to keep the elderly patient:

- Mentally and physically active (using multimodal pain control and avoiding sedation) to prevent complications (e.g., DVT, infections, functional deconditioning, or cognitive problems)
- Normothermic
- Well fed (PONV, ileus, and pain prevention) to facilitate their recovery and wound healing
- While being cognizant of reduced renal/hepatic function and the prevalent polypharmacy

A multidisciplinary approach is the way to do it [17, 51, 54]! To accomplish these goals, the healthcare provider needs to be familiar with the unique considerations in the elderly patient and the key concepts of pain management as well as understand the most prevalent issues and complications in this medically complex population [52]. The recently published best practice guidelines by the American College of Surgeons provide an excellent overview of managing the older adult in the perioperative period [17].

Anesthesia Considerations for Postoperative Care in the Elderly Patient

As mentioned earlier in the chapter, aging affects baseline physiological functions as well as the response to stressors and medications [54]. The key changes accompanying the normal aging process include [17, 51, 54, 55]:

- Pharmacokinetics and pharmacodynamics: The combination of increased adipose tissue mass accompanied by a loss of skeletal muscle mass, lean body mass, and total body water, together with the prevalent malnutrition (low albumin), leads to [54]:
  - Increased reservoir, protracted clearance, and an increased duration/effect of lipid-soluble medications, including inhalational anesthetics, opioids, and benzodiazepines [56]
  - Decreased volume of distribution and therefore higher plasma concentrations and greater clinical effects of water-soluble drugs [57, 58]
  - Decreased reservoir for albumin-bound drugs, like diazepam or propofol, potentially leading to high plasma concentration of the free drug [59]

Consequently, the elderly patient frequently requires a reduction in the dose of the postoperative medications. Additionally, polypharmacy is highly prevalent, with an estimated 40% of geriatric patients using ≥ 5 medications and up to 19% taking ≥ 10 medications per week [60].

Organ Anatomy and Physiology

- The aging brain can be associated with a decline in thinking and memory after surgery, including postoperative cognitive dysfunction and/or delirium. The clinician taking care of a geriatric patient should be particularly cognizant of the increased sensitivity to analgesics and sedatives [54, 61, 62], placing the elderly patient at risk for respiratory depression [62]. Furthermore, the geriatric patient was found to have a 40–50% reduction in response to hypoxia and hypercapnia [63]. The data on age-related changes in pain sensitivity are contradictory and inconclusive. While some groups suggested that pain perception decreases in old age, others showed an increase in the pain threshold with aging [64–67].
- Liver function is decreased due to the reduction in hepatic mass and blood flow, leading to an overall decline in metabolism and clearance of medications commonly used in the postoperative period [68].
- Kidney function decreases throughout life. In fact, the clinician should assume a 30–50% decrease in glomerular filtration rate (GFR) in a geriatric patient [57, 60–72]. The elderly surgical patient has a higher risk of electrolyte or fluid shifts, acid-base abnormalities, as well as of an acute renal failure after surgery [73–75]. Lastly, the elderly surgical patient has a decreased ability to correct for iatrogenic fluid overload or under-resuscitation [54, 71, 73, 76].
- GI tract is another organ that can undergo changes relevant for postoperative care. For one, the gastric drug absorption is commonly delayed, i.e., there is an inconsistent dose-time-response relationship [59]. Second, the elderly patient has a higher risk of aspiration, as swallowing dysfunction and the loss of the coughing reflex are commonly reported in this population; up to 30% carry the diagnosis of GERD [77]. Third, up to 50% of patients >60 years of age are seropositive for *Helicobacter pylori* [78]. Fourth, gastric atrophy is prevalent, thus increasing the risk of GI

bleed. Finally, up to 30% of the geriatric population takes laxatives preoperatively for chronic constipation [79, 80]. Consequently, the clinician needs to be familiar with the side effects and interactions of the commonly used medications to treat GI issues, including antacids (diarrhea, plasma levels of sodium and magnesium), sucralfate (constipation), misoprostol (diarrhea), antibiotics (changes in metabolism, absorption), proton pump inhibitors (risk of hip fractures in patients at risk, community-acquired pneumonia, C difficile infection, hypomagnesemia), histamine-2 receptor antagonists (changes in metabolism, absorption, tachyphylaxis, cognition) [54, 81–85].

- Other comorbid conditions, including COPD, CAD, heart failure, diabetes, etc., are prevalent and place the geriatric patient at higher risk for perioperative morbidity and mortality [55].

Postoperative Pain Management

Effective pain control is one of the essential interventions to reduce or even prevent postoperative complications in the elderly. Pain can negatively affect vital aspects of recovery, including time of ambulation, nutritional intake, respiratory and GI function, risk of venous thromboembolism, cognition, as well as the emotional well-being. However, effective postoperative pain control can be challenging in the geriatric population, given the age-related changes in physiology, the prevalent comorbidities, and polypharmacy, overall placing the elderly at a higher risk of drug-comorbidity and drug-drug interactions [56, 86–88]. Lastly, exposure to surgery has been reported to exacerbate chronic nonsurgical pain, like back pain.

The two principles of postoperative pain control in the elderly are (1) multimodal, "balanced" approach using different analgesics with additive or synergistic properties to minimize the use of opioids and (2) individualization of the medications and doses used, to account for the less predictable onset, delayed effect, and protracted clearance [86, 87, 89–91]. The multimodal approach is anchored in the observation that postoperative pain involves multiple different mechanistic pathways. Consequently, combining different types of analgesics while limiting the use of narcotics improves the quality of analgesia while reducing potential complications [86, 89–91].

Though the full scope of multimodal, "balanced" analgesia is beyond the scope of this chapter, here are a few clinically relevant pearls [17, 51, 54, 55, 86, 89–91]:

- Acetaminophen (PO or IV) is one of the safest analgesics in the elderly, typically needing no dose adjustments.
- NSAIDs, while effective, should be used with caution as they may increase the risk of GI bleed or renal failure. In this context, cyclooxygenase-2 (COX-II) inhibitors may represent an effective short-term alternative (long-term use is associated with cardiovascular complications) [92].
- There is a plethora of nontraditional drugs that have been found to effectively reduce postoperative pain and deserve consideration on individualized basis, including gabapentin, ketamine, clonidine, and dexmedetomidine.
- Opioids remain an important pillar in the postoperative pain management as part of a "balanced" anesthetic plan. In patients with kidney or liver dysfunction, opioids should be used cautiously since they can cause a variety of side effects and/or complications. As a general rule of thumb, the clinician should start with a lower dose at regular (or extended) intervals first and subsequently adjust the dose and interval based on the clinical picture and signs of drug accumulation [93].

In Patients with Renal Dysfunction

- Should not be used [94, 95]
  - Codeine and meperidine: accumulation of active metabolites with risk of cardiorespiratory depression as well as neuroexcitatory effects.
- Should be used cautiously, possibly requiring dose adjustment

  - Morphine: active metabolites accumulate in renal failure (risk of cardiorespiratory depression as well as neuroexcitatory effects).
  - Oxycodone: 10–20% excreted unchanged in the urine, 80% metabolized in the liver
  - Hydromorphone: metabolized in the liver, but hydromorphone-3-glucuronide metabolite can accumulate and produce neuroexcitatory effects (agitation, confusion, and hallucinations).
  - Hydrocodone: metabolized to hydromorphone. Parent drug and active metabolite can accumulate and produce neuroexcitatory effects.
- Considered safe
  - Remifentanil: metabolized by nonspecific plasma esterases. No active metabolites.
  - Fentanyl, sufentanil, and alfentanil: seem to be safe in renal impairment. Metabolized by the liver without clinically relevant active metabolites.
  - Methadone: mostly metabolized in the liver to an inactive metabolite. Considered by some as one of the opioids of choice in dialysis patients [96].

In Patients with Hepatic Dysfunction

- Should be avoided [93, 94, 97]
  - Codeine: prodrug with no analgesic activity that needs to be converted to morphine in the liver to exercise analgesic effect. Consequently, in patients with hepatic failure codeine may fail to produce analgesia.
  - Meperidine: reduced clearance in liver failure with risk of seizures.
- Should be used cautiously, possibly requiring dose adjustment
  - Morphine: while morphine is not a pre-drug, the conversion to active metabolites as well as hepatic excretion may be affected.
  - Hydromorphone: the half-life time may be increased.
  - Hydrocodone: pre-drug metabolized into hydromorphone and oxymorphone.
  - Oxycodone: plasma concentration may be increased.
  - Methadone: clearance is reduced with increased half-life.
- Considered safe
  - Remifentanil: metabolized by nonspecific tissue and plasma esterase; no hepatic metabolism.
  - Fentanyl: recommended by some as the opioid of choice in liver failure.

Peripheral nerve blocks using local anesthetics can provide effective postoperative analgesia and reduce narcotic use; rebound pain is, however, a possibility as is the documented higher risk of permanent nerve damage [54, 98–100]. The addition of a glucocorticoid steroid (dexamethasone) and/or alpha-2-agonist (clonidine, dexmedetomidine) may further improve the quality and extend the duration of the block [99, 100]. Finally, a continuous perineural infusion of local anesthetics using a catheter should be considered as it has been found to reduce postoperative pain and improve sleep quality and overall patient satisfaction [99]. On the other hand, it has been recently suggested that prolonged quadriceps femoris blockade may prevent early mobilization and increase the fall risk [101, 102]. In their article, entitled, "Femoral nerve block for total knee replacement – A word of caution," the authors noted, "The literature, which is largely in anesthetic journals, reflects the high quality of analgesia of femoral nerve block, but makes little or no mention of the delays or dangers in early mobilization. We believe that the potential risks to orthopedic patients are underestimated" [101]. Consequently, while quality of analgesia is important, every effort should be made not to negatively affect patient's ability to ambulate early.

Epidural anesthesia is another option to address postoperative pain, especially for thoracic and abdominal procedures [32, 103, 104]. The main advantage of this technique is the reduced narcotic effect, leading to less sedation and/or respiratory depression. In addition, given the typically excellent quality of analgesia, the epidural technique is associated with better respiratory mechanics. Despite the many advantages, epidural anesthesia should be used cautiously in the elderly patient since it can cause a pronounced sympathetic and muscular blockade, leading to a higher risk of hypotension, dizziness, delayed ambulance, and urinary retention postoperatively. The frequently required intravenous administration of fluids to correct for hypotension can lead to congestive heart failure, while the use of vasoactive agents, such as the alpha-agonist phenylephrine, can be detrimental in patients with reduced arterial perfusion or with vascular grafts. Epidural anesthesia using only opioids without local anesthetics in order to avoid sympathetic blockade can be associated with respiratory depression [104].

Postoperative Complications in the Elderly Patient

While the full scope of postoperative complications in the elderly patient is beyond the scope of this chapter, here is a brief and pragmatic overview of common postoperative complications in the geriatric patient from an anesthesiologist's perspective.

As was previously mentioned, postoperative cognitive decline (POCD) is of concern to physicians and patients alike. POCD is a common complication that can present as two separate entities; postoperative delirium and postoperative cognitive dysfunction.

Postoperative delirium (POD) is defined as an acute, early-onset, and transient disturbance of consciousness that is characterized by inattentiveness and cognitive impairment with a fluctuating course [105]. POD is one of the most common complications in the elderly surgical patient. The reported incidence of postoperative delirium ranges from 5% to 15%, with rates as high as 16% to 62% in high-risk groups, such as hip fracture patients [17, 106]. Clinically, POD can present in three different subtypes: hyperactive delirium (i.e., the "prototypical" combative and agitated delirious patient), hypoactive delirium (calm and quiet patient with decreased motor activity), and mixed subtype [17]. Typically, POD is diagnosed using the Confusion Assessment Method for the ICU (CAM-ICU) [for ICU patients] or Confusion Assessment Method (CAM) [for ward patients] [107]. The POD diagnosis requires an acute onset or fluctuating course, plus presence of inattention, and either altered level of consciousness (i.e., anything other than alert and calm) or presence of disorganized/incoherent thinking [17, 55, 107, 108]. Multiple risk factors for development of postoperative delirium have been identified, with preexisting cognitive impairment and advanced age being the strongest predictors of postoperative delirium [17, 109]. The development of delirium is associated with increased mortality,[109] increased risk of institutionalization [110], the development of dementia [110], increased length of stay [109], as well as increased risk of major complications [109]. The occurrence of delirium can predict long-term cognitive impairment [110].

It has been estimated that 30–40% of cases of delirium are preventable using multicomponent interventions, including individualized care, pain management, cognitive reorientation, daily mobilization/activity, attention to sensory deprivation, constipation prevention, facilitation of sleep, geriatric-focused training of staff, etc. [111–113]. In terms of treatment, it is recommended to start with the abovementioned multicomponent non-pharmacological interventions, followed by antipsychotic agent like haloperidol starting at 0.5–1 mg PO. However, the results for haloperidol have been mixed [113]. When used as prophylaxis in a randomized, double-blind, placebo-controlled study of 430 elderly patients (≥70 years of age) undergoing elective hip surgery, haloperidol failed to decrease the incidence of postoperative delirium [114]. Haloperidol prophylaxis did, however, significantly reduce the duration and severity of postoperative delirium [114]. In contrast to haloperidol, the atypical antipsychotic drug olanzapine significantly decreased the incidence of the postoperative delirium, while significantly increasing the duration and severity of postoperative delirium [115]. Collectively, the data on the role of antipsychotic drugs in prevention of postoperative delirium are too limited to draw any firm conclusion. Similarly, the cholinesterase inhibitors donepezil hydrochloride and rivastigmine failed to reduce the incidence of postoperative delirium [116, 117] or length of hospital stay [117]. Finally, there is no clear evidence that melatonin or melatonin agonists reduce delirium incidence compared to placebo [112].

Postoperative cognitive dysfunction (POCD) is defined as a longer-lasting decline in the level of cognitive performance after surgery as compared to preoperative baseline [118]. It includes acute (weeks), intermediate (months), and long-term (years) cognitive decline. Up to 50% of surgical patients suffer from POCD in the early weeks following a major noncardiac surgery [119, 120]. Although the majority of patients gradually recover over time, permanent cognitive decline has been described [121]. Advanced age, history of cerebral vascular accident, lower educational level, and alcohol abuse have been shown to be independent risk factors for POCD at 3 months [119–122]. POCD was found to be associated with poor short- and long-term outcomes including depression, decrease in daily functional ability, loss of independence, premature unemployment, and possible permanent dementia [120, 123]. Here are few clinically relevant pearls [124]: There is currently no strong evidence in humans that anesthetic agents or anesthetic techniques are a risk factor for POCD [125–130]. Two meta-analyses comparing general anesthesia (GA) vs. regional anesthesia (RA) failed to demonstrate that GA is a risk factor for POCD [126, 128]. In two recent clinical trials, the incidence of POCD in patients undergoing an intervention under RA or monitored anesthesia care was at least as high as in the GA group [125, 129]. Furthermore, while volatile anesthetics have been found to promote and accelerate AD-neuropathology in animal models, all human studies examining this subject have failed thus far to show such a relationship [131–133]. The mechanism underlying POCD is unknown. In terms of prevention and treatment, currently there no prophylactic/therapeutic interventions that consistently and predictably reduce the incidence of POCD.

Another issue affecting the older adult is immobility, and the risk of falling [17, 51, 54, 55]. It has been estimated that 1.5% of surgical inpatients suffer a fall after surgery [17]. Many elderly patients have preexisting conditions that place them at higher risk of immobility or falls, including baseline functional deconditioning, malnutrition, sarcopenia, arthritis, or poor sensory input (vision, hearing, etc.). In addition, surgery and anesthesia may add surgical pain, sedatives, analgesics, and/or muscle weakness due to peripheral nerve blocks that may make mobilization more challenging while increasing the risk of falls. Early ambulation, daily physical activity, and avoidance of falls are the key steps to prevent functional decline as well as prevent respiratory, thromboembolic, and cognitive complications after surgery [17, 51, 54, 134–136]. Multicomponent interventions are recommended, including early assessment, early involvement of physical therapy, supervised and assisted exercises, maintaining call light within reach, placing handrails in relevant areas, using nonslip footwear, and geriatric-focused training of staff. Obviously, early ambulation with a low risk of a fall is more likely in a patient with normal cognition who is not in pain – so effective pain control and prevention of delirium are a must.

Hydration in the postoperative period is also an important aspect of the care [17, 51, 54, 55]. As mentioned above, age-related physiological changes place geriatric patients at higher risk for decreased glomerular filtration rate (GFR), urinary concentration ability, and free water clearance. A reduced sense of thirst is a common problem in the elderly. Consequently, the elderly patient is at higher risk for electrolyte and acid-base abnormalities as well as fluid disorders. Finally, given the frequently impaired renal function already at baseline, the elderly patient is also at higher risk for acute postoperative renal impairment. Therefore, an early return to oral intake, balanced approach to fluid management, maintaining appropriate blood pressure, and avoiding nephrotoxic drugs are essential – especially in the context of the highly prevalent polypharmacy. When measuring electrolytes after surgery, the clinician should be aware that even normal creatinine plasma levels of in the elderly patient might indicate a decreased GFR due to the decreased skeletal muscle mass.

Postoperative problems with nutrition are notorious in the elderly [17, 51, 54, 55]. In fact, up to 40% of hospitalized patients are malnourished. Chronic constipation, poor appetite, and/or social isolation are additional factors that increase the risk for malnutrition in the elderly. Finally, exposure to surgery, sedatives, and analgesics further compounds this problem with the attendant risks of ileus, nausea/vomiting, and loss of appetite. Early return to oral intake plus nutritional supplementation in undernourished patients is key to reduce the risk of malnutrition [137]. In addition, early ambulation, opioid-sparing pain management, and normal fluid intake should be considered to prevent postoperative ileus. Whether early enteral feeding is warranted in patients in whom oral intake is not possible remains controversial. A recent multicenter, single-blind clinical trial that randomized 1372 ICU patients expected to remain in the ICU longer than 2 days with relative contraindications to early enteral nutrition to either standard care or early parenteral nutrition failed to demonstrate a difference in day-60 mortality, ICU, or hospital-stay duration [138]. According to the accompanying editorial, "This article joins several articles that suggest either benefit or harm from supplemental parenteral nutrition or whether 'trophic feeding' is 'just as good' in patients in the ICU during the first 7 days of their hospitalization" [139].

The older adult can also face issues with wound healing and the development of pressure ulcers. The prevalent comorbid conditions, such as poor nutritional state, sarcopenia, circulatory and oxygenation problems, and diabetes, can impair wound healing in the elderly. Thus, it is imperative to avoid fluid overload, hypotension, hypoxia, hypothermia, ileus, or hyperglycemia after surgery and provide appropriate antibiotics. Similarly, the elderly are at higher risk to develop postoperative pressure ulcer. Early involvement of physical therapy, turning patients regularly, oral/tube feeding, nutritional supplementation, and optimization of comorbidities can be instrumental.

Finally, cardiovascular and pulmonary complications are common in the geriatric patient during the perioperative period [17, 51, 54, 55]. The burden of cardiovascular and pulmonary disease increases as the body ages. In fact, cardiac pathology is the most common cause of death in the elderly surgical patient. In addition to the obvious maintenance of stable hemodynamics, oxygenation, and electrolytes, postoperative management should focus on early restarting of preoperative medications for preexisting comorbidities. The care should include vigilant management of fluids (especially avoiding fluid overload), prevention of atelectasis and pneumonia (incentive spirometer, upright position, pulmonary toilet, respiratory therapy), early mobilization, and oral intake of fluids and food.

Long-Term Outcome in the Elderly Patient

Some authors have argued that the long-term outcomes have been improving [17, 54, 140, [141], with a morbidity and mortality in the elderly undergoing elective surgery ranging from 7% to 20% and 0% to 5.4%, respectively, which is comparable with outcomes in younger patients [54, 141–145]. However, the outcomes of emergent surgeries in the elderly are markedly lower, with morbidity and mortality ranging from 30% to 68% and 13.6 to 31%, respectively [142, 145].

A key difference exists when assessing the long-term success between the non-geriatric and geriatric population. In the younger patient, the outcome is typically defined using standardized measures like morbidity (e.g., stroke, MI, creatinine, troponin, length of stay, etc.) and mortality, while in the elderly patient, the long-term success is defined using much more subjective criteria, like quality of life, cognitive function, the subjective perception of health, and the return to preoperative baseline level of functioning allowing the patient to live an independent and fulfilling life. Overall, the long-term postoperative outcome based on quality of life and independence, while increasingly important, is still a developing field with paucity of data. Disconcertingly, studies from the 1980s and 1990s examining this field reported that [54, 146–150] up to 75% of geriatric patients who were independent at hospital admission were not independent at hospital discharge, that 33% of patients sent to a nursing home after suffering a hip fracture remained there for ≥1 year, and that, of those who enter nursing home, 55% spend ≥1 year and 21% spend ≥5 year of total lifetime in the nursing home.

More research is required in this important area to help us guide the postoperative care in the elderly surgical patient.

Putting All Together: The Geriatric Perioperative Surgical Home

The Institute of Health (IHI) Triple Aim calls to improve the quality of care, reduce the healthcare expenses, and improve the overall health of the population [150]. Considering the characteristics of the older adult population, it seems that initiatives aimed to improve all those domains should be a priority. The American Society of Anesthesiology has introduced the concept of the perioperative surgical home (PSH) as a patient-centered, physician-led, team-based coordination of care along the perioperative continuum [151]. This initiative aligns well with goals of the Triple Aim. They both share common goals, namely, to improve the quality of care, reduce the global healthcare expense, and improve the overall health of the population. Most of the literature in PSH has been related to specific service lines [152]. However, a geriatric PSH has to be able to be embedded into PSH service lines and also be able to stand alone to care for the geriatric population regardless of the type of surgery [153].

Conclusions

The rapidly growing geriatric population imposes challenges to the healthcare system, and perioperative services are not the exception. The outcomes in the older adult presenting for surgery lag behind improvements in surgical and anesthesia. While age and the physiological changes of aging play a role, other factors such as comorbidities, type of surgery, and the occurrence of complications also weigh heavily in patient outcomes. Recently, the concept of frailty has emerged as a reliable marker for outcomes in this population. The concept of pre-habilitation to further optimize patients prior to surgery is also becoming more prevalent.

Meticulous intraoperative and postoperative care is fundamental to avoid complications and improve outcomes. However, it seems apparent that those efforts should occur in concert and should involve all the teams that participate in the care of the patient. The concept of a geriatric perioperative surgical home aimed to enhance the quality of care, decrease costs, and improve the overall health of this population is likely the future for care of geriatric patients embarking in the perioperative continuum.

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Skin Lesions and Pressure Ulcers

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Abstract

The skin is the body's largest organ and is the most conspicuous. It plays not only an integral role in self-perception and outward attractiveness but very often conveys the earliest diagnostic signs of internal disease. Attention to and care of the skin contribute not only to the elderly patient's health and physical comfort but also to their quality of life, psychological well-being, and dignity. In this chapter, we review age-related mechanical and functional changes in the skin. The prevalence of skin malignancies and pressure sores is increasing in the growing elderly population. These conditions are often curable, if not preventable, in their early stages. Therefore, caregivers and surgeons must be vigilant for the subtle skin changes inadvertently ignored or neglected by the elderly patient experiencing impaired vision, sensation, mobility, or cognition.

Common Benign and Malignant Skin Lesions

The elderly patient presents with a variety of benign and malignant skin lesions. The ability to differentiate various cutaneous neoplasms is especially important in the geriatric population because of the higher incidence of malignant skin tumors that arise in aging skin. The aim of this chapter is to acquaint the surgeon with normal skin anatomy, with changes in the skin anatomy during aging, and with the pathophysiology, diagnosis, and treatment of common benign and malignant skin tumors of the elderly.

In general, we recommend an annual total body skin examination for the elderly patient who has any of the following independent risk factors: fair skin color; history of blonde, red, or light-colored hair; green, gray, or blue eye color; a family or personal history of skin cancer; chronic occupational or recreational exposure to the sun; a history of sunburns; or anyone with numerous or atypical nevi. Patients with a personal history of skin cancer should be seen every 6–12 months.

Basic Skin Anatomy

The skin is composed of two layers: a stratified squamous epithelial layer, or epidermis, and an underlying connective tissue layer, or dermis. The cell types making up the epidermis provide skin protection and include keratinocytes, melanocytes, Langerhans cells, and Merkel cells. Keratinocytes are the predominant cell type of the epidermis and form a mechanical barrier. Melanocytes produce pigmentation important in UV protection. Langerhans cells function in antigen presentation and immunity. Merkel cells sense pressure and two-point discrimination [1].

Dermis

The mesoderm-derived dermis sits just below the avascular epidermis, supplying it with a rich neurovascular system. Histologically, the dermis can be divided into two layers. The superficial papillary dermis is composed of a loosely woven arrangement of connective tissue bundles. Beneath it lies the reticular dermis, so named for its denser, interwoven pattern of connective tissue fibers. The resident cells of the dermis are mostly fibroblasts, which secrete collagen, elastin, and ground substance. Collagen and elastin give the skin its tensile strength, distensibility, and flexibility. Ground substance, which is comprised of polysaccharides and proteins, provides a supportive matrix for the connective tissue fibers. The overall structure accommodates the network of vascular, lymphatic, and nerve plexi that supply the skin. Other cellular constituents of the dermis include mast cells, macrophages, lymphocytes, and other leukocytes.

The dermal–epidermal junction is characterized by downward folds of the epidermis into the dermis. These folds, called rete ridges, provide mechanical support against shearing forces. Beneath the dermis lies a fatty layer of subcutaneous tissue that serves to insulate and protect the underlying structures.

Epidermal Appendages

During embryologic development, epidermal cells invaginate and migrate into the dermis forming adnexal structures such as hair follicles, sebaceous glands, and eccrine and apocrine sweat glands collectively termed epidermal appendages. Hair follicles are composed of modified keratinocytes that form a tubular structure enclosed by a collagenous sheath. Each hair follicle is associated with one or more sebaceous glands, which secrete sebum, an oily viscous fluid composed of triglycerides, free fatty acids, wax monoesters, squalenes, and sterols. Sebum functions to help moisturize and waterproof skin and hair. Apocrine glands are modified sweat glands located in the axillae and groin. Like sebaceous glands, they secrete their product into the follicular lumen. With the exception of the groin and axillae, the remainder of the skin is covered by eccrine sweat glands. These glands are thermoregulatory in their capacity to secrete sweat and immunologic in their capacity to excrete active cytokines [2].

Skin Function

The basic functions of the epidermis, dermis, and epidermal appendages include that of a physical barrier as well as homeostasis, thermoregulation, immunologic defense, communication, and sensation. As a physical barrier, the skin protects the body from ultraviolet radiation-associated DNA damage, microorganisms, and toxic chemicals. Far more than simply a sheet of protective wrap, the skin continually regenerates itself by sloughing off damaged cells and providing a fresh interface for the ever-changing environment. Central to its barrier function is the maintenance of water balance and protection against dehydration. Not all water loss is damaging, however, and eccrine gland-mediated evaporative water loss is critical to thermoregulation. In the battle against microbial invaders, the skin provides the first line of defense. The skin hosts both adaptive and innate immune functions; in the skin itself, circulating lymphocytes and antibodies encounter foreign materials and activate antigen-presenting cells. Cathelicidins, neutrophil-derived polypeptides resident in the skin, also function in antimicrobial defense and cell–cell signaling [3]. Additionally, it is often a fundamental disruption in the immunologic function of the skin that facilitates the development of cutaneous malignancies. In social interaction, the communication and sensory functions of the skin are intertwined. The skin and hair are central to our mechanisms of physical attraction. Neural modulation of the cutaneous blood supply conveys information in interpersonal communication, and the skin is the organ through which touch, temperature, itch, pleasure, and pain are perceived.

Changes in the Skin Associated with Aging

The intrinsic changes that occur in aging skin are important for understanding the pathophysiology of benign and malignant lesions that affect senescent skin.

Epidermis

Between the third and seventh decades, the turnover rate of keratinocytes is reduced by 50% [4]. The slower epidermal turnover rate increases the duration of keratinocyte exposure to carcinogens such as ultraviolet radiation, making the epidermis more susceptible to the development of keratinocytic neoplasms. Decreased proliferative capacity of keratinocytes also prolongs wound healing.

The aging epidermis also undergoes structural alterations. The rete ridges at the dermal–epidermal junction retract, making elderly skin more susceptible to shearing forces. Keratinocytes in the basal layer of the epidermis become increasingly pleomorphic, displaying variations in size, shape, and staining pattern [5]. With age, the most superficial layer of the epidermis, the stratum corneum, increases in thickness due to a slower rate of desquamation. This thick stratum corneum has reduced intercellular lipid content and reduced water-binding capacity, predisposing aging skin to xerosis, or drying, with cracking, compromised mechanical barrier function, and subsequent irritation and inflammation [6, 7].

Melanocytes also undergo age-related decrease in number over time. After age 30, the surviving population of melanocytes drops by 8–20% each decade [8]. As a result, less melanin is produced which allows greater penetration of ultraviolet radiation and results in an increase in the risk of developing skin cancer. Like melanocytes, Langerhans cells decrease in number with age. Langerhans cells are especially sensitive to UV radiation and are further functionally impaired by the age-related decrease in protective melanin. This UV-induced immune suppression compromises the cell-mediated immune response in elderly skin, increasing its vulnerability to the development of tumors.

Dermis

As the skin ages, the dermis thins and becomes less vascular. Collagen fibers become thickened and less resilient, and the dermis becomes more susceptible to shearing injuries. Elastin fibers display structural degradative changes, resulting in skin laxity and wrinkle formation [5]. The amount of ground substance decreases, reducing the supportive dermal matrix, and so structures such as blood vessels become more susceptible to damage. This manifests clinically as easy bruising in the elderly. Thinning of vessel walls may also contribute to the increased susceptibility to ecchymoses. Other changes in cutaneous vasculature include a decrease in the density of vessels. Diminished cutaneous circulation can lead to impaired clearance of foreign material, delayed wound healing, and diminished thermoregulatory capacity. The aging skin also loses its ability to mount an inflammatory response, leading to muted clinical presentations of cutaneous disease.

Benign Epidermal Lesions

Seborrheic Keratoses

Seborrheic keratoses are common, benign, flat-topped papules or plaques composed of hyperproliferating keratinocytes. They typically appear during the fifth decade, although early lesions can present in the fourth decade. Early lesions manifest as discrete 1–3 cm skin-colored to dark brown patches that progress to form slightly elevated, warty, greasy plaques. Their exophytic growth pattern makes them appear waxy and “stuck on.” [9] Although seborrheic keratoses can be found on any part of the body, they are most prevalent on the face and upper trunk (Fig. 1). These lesions are not UV induced and sometimes present with itch. They occur more frequently in Caucasians and affect males and females equally.

A histologically identical variant of the seborrheic keratosis, dermatosis papulosa nigra, is commonly found in patients with darkly pigmented skin. Clinically, these lesions present as multiple 0.1–1.0 cm rough brown to black papules of the face. They are especially common on the malar cheeks, forehead, neck, back, and chest.

Seborrheic keratoses remain unchanged for the lifetime of the individual once they appear. They are benign lesions with no malignant potential. However, the eruption of multiple lesions in a short duration of time, known as the sign of Leser–Trelat, has historically been thought to point to internal malignancy, particularly gastrointestinal adenocarcinoma, breast carcinoma, and lymphoma. Despite a large number of case reports and anecdotal evidence in support of an association between widespread eruptive seborrheic keratoses and internal malignancy, the data to support this phenomenon as a true paraneoplastic process is largely lacking [10].

Fig. 1 Seborrheic keratosis, the most common benign cutaneous tumor in the elderly. Its significance lies in its potential to mimic malignant melanoma. Although treatment is not normally indicated, the lesion, which may appear rough or greasy, may be irritated necessitating removal. Alternatively, if there is suspicion about melanoma, biopsy is indicated

For an atypical seborrheic keratosis resembling a malignancy such as a pigmented basal cell carcinoma (BCC) or melanoma, surgical excision is appropriate for diagnostic purposes. Otherwise, treatment options include curettage, cryotherapy, or trichloroacetic acid (TCA).

Epidermal Appendages

Marked age-related changes also occur in the epidermal appendages. There is an overall reduction in the number and function of both eccrine and apocrine sweat glands, leading to a decrease in thermoregulatory capacity [6]. Sebaceous glands enlarge with age, but their sebum production is paradoxically reduced. These changes in sebaceous glands manifest clinically as sebaceous hyperplasia and xerosis.

Solar Lentigo (Senile Lentigo, Actinic Lentigo)

Chronic sun exposure can induce melanocytes to proliferate locally forming multiple 0.5–2.0 cm brown macules known as solar lentigos, “liver spots,” or “age spots.” Their presence in more than 90% of individuals over the age of 70 has led to the unflattering descriptive term “senile lentigo,” but they are often found on light-skinned persons of any age. These lesions are localized to sun-exposed areas, such as the cheek, forehead, nose, dorsa of hands and forearms, upper back, and chest (Fig. 2). They are more commonly seen in Caucasians than in Asians and affect males and females equally.

Solar lentigos have virtually no malignant potential although a small proportion of lesions occurring on the face rarely develop into lentigo maligna [9]. Solar lentigos can be confused with other benign lesions, such as early seborrheic keratoses, and premalignant lesions such as pigmented actinic keratoses and lentigo maligna. To differentiate solar lentigos from seborrheic keratoses and pigmented actinic keratoses, the lesion must be examined with a hand lens in oblique light. Seborrheic keratoses and pigmented actinic keratoses generally display features of epidermal change, whereas solar lentigos are completely flat. Lentigo maligna, like solar lentigo, may not show epidermal changes. However, it has distinct variations in color from light brown to dark brown with flecks of black. A biopsy is taken to exclude melanoma from any solar lentigo that develops a highly irregular border, increase in pigmentation, or thickening.

If the patient finds these “age spots” cosmetically unacceptable, treatment can be accomplished in several ways. Bleaching agents like hydroquinone are not particularly effective. Cryotherapy and topical retinoids, particularly 0.05% retinoic acid, have demonstrated efficacy in randomized controlled trials. Among laser treatments, Q-switched ruby and 532 nm Nd:Yag have been shown effective in controlled trials without randomization [11]. Regardless of treatment methods chosen, the preventive use of sunscreen to prevent new lesion should be emphasized.

Melanocytic Nevi (Moles)

Melanocytic nevi or moles are small, well-circumscribed macules and papules that vary in color from skin-colored to tan and brown (Fig. 3).

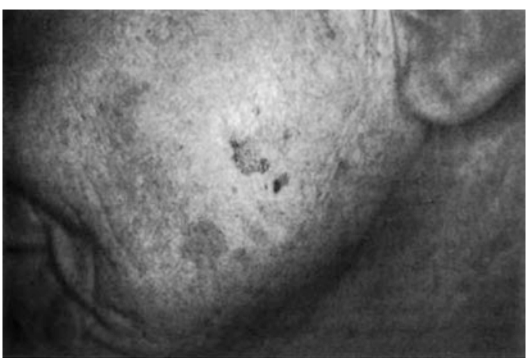

Fig. 2 Solar lentigo, seen mostly on the face and dorsa of the hands, has tan to brown pigmentation and is flat. They may be of cosmetic concern and occasionally must be biopsied to rule out lentigo maligna

Fig. 3 Nevi of medical significance are uncommon in the elderly, but new pigmented lesions that are not seborrheic keratoses should be evaluated

They are composed of nests of melanocytes located in the epidermis, dermis, and rarely subcutaneous tissue. If the cluster of melanocytes is localized to the dermal–epidermal junction, the nevus is classified as a junctional nevus. Junctional nevi tend to have smooth regular borders and are often found on the palms and soles. Intradermal nevi are found on the face and are also skin-colored, homogenous, and dome-shaped. Compound nevi combine the feature of both junctional and intradermal nevi and may appear very dark. They are round or oval and raised above the epidermal surface.

Melanocytic nevi are acquired during childhood and early adulthood. They typically increase in number up to the age of 40, after which they begin to involute. With the exception of dermal nevi, most nevi disappear by the age of 60. As some junctional and compound nevi age, their melanocytes migrate into the dermis and assume features of dermal nevi. Nevi are rarely premalignant. However, if new melanocytic nevi are acquired after mid-adulthood, they should be regarded with a high degree of suspicion and followed closely to rule out the development of malignancy [12].

Benign Dermal Lesions

Acrochordons (Skin Tags)

Acrochordons or skin tags are composed of loose fibrous tissue and usually occur as multiple skin-colored pedunculated lesions typically 2–3 mm in diameter and located on the neck, axillae, or major flexures. Skin tags are prevalent in postmenopausal women, pregnant women, and obese individuals, suggesting a hormonal influence on their development [13]. The exact etiology of skin tags is unknown, though some familial groupings have been noted.

Skin tags have no malignant potential but may cause pain or itch in areas exposed to friction such as the belt line. They can also cause considerable discomfort when infarcted. Treatment consists of simple excision requiring no local anesthetic.

Xanthelasma Palpebrarum (Eyelid Xanthomas)

Xanthelasma palpebrarum develop in adults in their fourth to fifth decade. They present as yellow velvety plaques confined to the eyelids. The lesions often begin as small yellow spots that initially may be confused with milia or senile closed comedones. They grow over a span of months coalescing into plaques on the upper eyelids and around the inner canthus (Fig. 4). Once growth stabilizes, these plaques are permanent. Histologically, xanthelasma palpebrarum is characterized by lipid-laden macrophages in the superficial dermis.

Approximately 50% of elderly patients who present with these xanthelasma palpebrarum have an underlying disorder of lipid metabolism, such as familial hypercholesterolemia or familial dysproteinemia. Patients with these disorders typically have elevated low-density lipoprotein (LDL) and apoprotein E levels and are prone to atherosclerotic cardiovascular disease. Patients who present for the first time with xanthelasma palpebrarum should have their serum lipoproteins and apolipoproteins checked. If the levels are within normal limits, no further testing is needed.

The etiology of xanthelasma palpebrarum in patients with no lipid disorder is unknown. Systemic therapy with lipid-lowering agents rarely affects the appearance of these lesions. Prior to the advent of laser therapy, excision, cryotherapy, and topical application of 30% trichloroacetic acid were the preferred methods of treatment. With most of these treatments, however, recurrence is

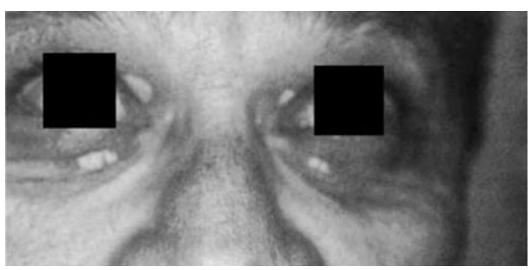

Fig. 4 Xanthelasma. These cholesterol deposits occur on the upper and lower lids and can best be removed surgically. They are yellowish with a smooth surface

common. Excision with primary closure is effective in only 60% of patients and is limited by the location of the lesions [14]. Some authors have advocated excision with secondary intention healing, thereby minimizing the risk of ectropion and complications with skin grafting. Healing by secondary intention may allow greater margins of resection and therefore minimize the rate of recurrence to as low as 7% [15]. Recently, various laser modalities including erbium:YAG [16], argon [17], and 1064 Q-switched Nd:YAG [18] have been utilized in the treatment of xanthelasma with good cosmetic outcomes. Ultrapulse CO_2 laser in only one treatment session has shown excellent results without complications or recurrence at 1-year follow-up [19].

Sebaceous Hyperplasia

Sebaceous hyperplasia is a benign lesion that is often found on the face of older patients. It typically presents as a cream- or yellow-colored umbilicated papule on the forehead, cheeks, eyelids, and nose of individuals over the age of 30 (Fig. 5). 25% of patients over the age of 65 carry these lesions, and the incidence increases with age. The etiology of sebaceous hyperplasia is unknown, but genetic factors likely play a role in its pathogenesis. Most lesions occur independent of sun exposure and arise in patients of northern European heritage.

Fig. 5 Sebaceous hyperplasia. These lesions represent benign hypertrophy of the sebaceous glands. With their central umbilication and rounded edge, they are occasionally confused with basal cell carcinoma

Sebaceous hyperplasia often begins as a small, 2–3 mm papule with a central depression. This depression represents the opening of a wide sebaceous duct that is surrounded by enlarged sebaceous glands, lending the lesion its characteristic lobular configuration. Some lesions of sebaceous hyperplasia contain central telangiectasias. This feature, combined with the papule's translucent appearance, often leads clinicians to confuse sebaceous hyperplasia with basal cell carcinoma (BCC). A clue to the correct diagnosis can be obtained with diascopy (applying pressure on the lesion with a glass slide), which reveals the yellow-white color of sebaceous hyperplasia. However, relying on diascopy for diagnosis is not perfect: the yellow-white color sometimes leads to the incorrect diagnosis of xanthoma. Xanthomas can usually be differentiated by their larger size and absence of umbilication [20].

When the clinical diagnosis is uncertain, a biopsy should be performed to rule out malignancy. Otherwise, no treatment is necessary for sebaceous hyperplasia unless cosmetically desirable.

Chondrodermatitis Nodularis Helicis

Chondrodermatitis nodularis helicis (CNH) typically presents as a painful, erythematous nodule on the helices of men over the age of 40. Approximately 30% of cases of CNH occur in young individuals and in women, but the location varies to include the antihelix, tragus, antitragus, and concha [21]. The tender nodule, which often displays central crusting and ulceration, is typically surrounded by hyperemic skin. It enlarges within a few months to reach a size of 0.5–2.0 cm and then remains unchanged without evolution to malignancy (Fig. 6).

This disorder is thought to be due to compromised local blood supply as a result of pressure or cold temperatures. It often arises in individuals who habitually sleep on one side. Aggravating factors include cold temperatures, pressure from head gear, and trauma.

Despite the characteristic exquisite tenderness of these lesions, CNH is often mistaken for squamous cell carcinoma (SCC). Biopsy is indicated

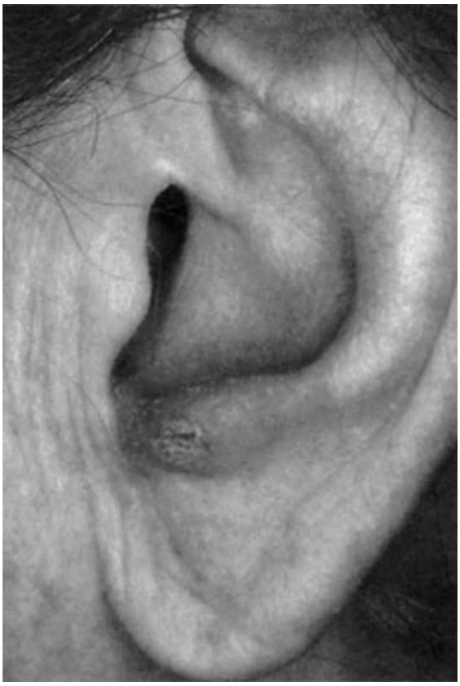

Fig. 6 Chondrodermatitis nodularis helicis. This benign condition of the ear is painful and may present with eroded epidermis. It can be confused with squamous cell cancer of the ear, which usually is not painful

only if there is high suspicion for SCC. Histopathology of CNH reveals degenerated collagen surrounded by vascular granulation tissue with a central ulcer and overlying acanthotic epidermis. The thickened perichondrium shows a lymphocytic infiltrate.

Treatment of CNH may be medical or surgical. Medical therapies include intralesional injection of steroids and collagen [21] and cryotherapy. Conservative management has been advocated as the first line of treatment [22]. Techniques for surgical excision vary widely: some advocate removal of abnormal auricular cartilage only [23–26], whereas others recommend removal of the skin overlying the involved cartilage as well [4, 27]. A cure rate approaching 100% over a 2-year follow-up period has been reported using CO_2 laser surgery [28, 29], but recent data from large-scale comparative trials are not yet available. To prevent recurrence, the patient should be instructed to minimize pressure and trauma to the ear.

Fig. 7 Hemangioma. This deep-seated hemangioma on the upper lip is benign, but in the absence of the ability to blanch on compression, it should be biopsied to rule out other tumors

Cherry Hemangioma (Campbell de Morgan Spots)

Cherry angiomas are small, benign, bright red to violaceous, dome-shaped papules that are commonly found in middle-aged and older adults. They are distributed over the trunk and proximal extremities, vary in size from 2 to 8 mm in diameter, and become more numerous with age (Fig. 7). Their etiology is unknown.

Histologically, cherry angiomas are characterized by the presence of numerous dilated capillaries lined by flattened endothelial cells with edematous surrounding stroma and collagen homogenization. The overlying epidermis is frequently thinned with fenestrations.

Cherry angiomas are diagnosed clinically and require no treatment. If nodular melanoma or metastatic carcinoma is suspected, an excisional biopsy should be performed. If a cherry angioma is at a site of recurrent trauma and therefore prone to ulceration or if it is at a site that is cosmetically unacceptable to the patient, it can be treated by shave excision, cryotherapy, electrodesiccation, or laser ablation.

Venous Lakes

Venous lakes are angiomatous dilations of venules occurring on the face, lips, and ears of patients who are usually above the age of 50.

They manifest clinically as dark blue to violaceous papules with an irregular, cobblestone appearance. After an initial growth phase, venous lakes stabilize and do not regress. The etiology of these lesions is unknown and they occur with equal incidence in both sexes. Microscopically, the lesion reveals small, single-layered interconnected vessels (or one large dilated space) in the upper dermis surrounded by a thin wall of fibrous tissue. A venous lake can resemble a pyogenic granuloma or a nodular melanoma, requiring excisional biopsy for definitive diagnosis. In most instances, however, venous lakes can be distinguished clinically by applying prolonged pressure to the lesion, which causes it to lose its violaceous hue as the venous bed empties.

Treatment of venous lakes is cosmetic. They can be obliterated with electrocoagulation or laser; the long pulse Nd:YAG has recently shown promise [30]. Alternatively, they can be surgically excised with the risk of a cosmetically unacceptable scar.

Premalignant Lesions

Actinic Keratoses (Solar Keratoses)

Actinic keratoses (AKs) are discrete, scaly, pink to red papules that are found on chronically sun-exposed skin of the face, ears, neck, forearms, and dorsal hands. They have a rough quality, allowing them to be more easily felt than seen. Typically, they arise in middle-aged individuals, though they may occur at younger ages in people living in latitudes closer to the equator. Actinic keratoses are generally considered premalignant lesions with a conversion rate to invasive SCC ranging between 0.075% and 0.096% per lesion per year [31]. For the average person with multiple actinic keratoses, the chance of developing invasive SCC has been estimated at 10–20% over a 10-year period if those AKs are left untreated [32]. An alternate viewpoint characterizes actinic keratoses not as premalignant lesions but rather as malignant lesions akin to SCC in situ [33] (Fig. 8).

Fig. 8 Actinic keratoses. This is one of the most common sun-related lesions in the elderly. It is biologically and clinically premalignant and should be treated because of the risk of malignant transformation. The lesions can vary in size from 1 to 2 mm up to more than 1 cm and have a rough surface overlying a reddened background

Because AKs are considered premalignant, treatment is ablative and the method determined by the number and location of lesions. If a patient presents with fewer than 10 AKs, cryotherapy is the method of choice. Flat to slightly raised lesions are treated with liquid nitrogen until frosted. For lesions that are thick and hyperkeratotic, 3–5 s of freezing may be necessary. With this technique, cure rates as high as 98% have been reported [33, 34]. Light electrodesiccation and curettage and CO_2 lasers are other effective methods for scattered lesions but have the disadvantages of requiring local anesthesia and may increase the risk of scarring.

For more than 10 AKs, topical fluorouracil (5-FU), which selectively targets abnormal keratinocytes, is an effective treatment option. It is applied as a 1%, 2%, or 5% cream or solution once or twice daily until the AKs become inflamed and ulcerate. The treatment period can last 2–6 weeks and can cause significant discomfort, which may hamper patient compliance. Inflammation can be minimized with mid-potency topical steroids during the healing phase without affecting the efficacy of the treatment.

Clinical investigation of daily topical imiquimod has revealed clinical clearance rates ranging from 45% to 84% [35–37].

Growing data support the use of photodynamic therapy (PDT) in the treatment of actinic keratoses with response rates better than cryotherapy and 5-FU. A number of prospective trials have been performed with clearance rates ranging from 77% to 99% with recurrence rates as high as 30% after 1 year [38].

Patients presenting with AKs usually have a history of chronic sun exposure, which places them at increased risk for developing other skin cancers. Therefore, it is important to follow these patients at regular intervals and to emphasize preventive care by recommending sun protection strategies.

Actinic Cheilitis

Actinic cheilitis is a premalignant disorder of the lip. It usually localizes to the mucosal surface of the lower lip where sunlight exposure is greatest but occasionally occurs on the upper lip (Fig. 9). The lesion initially presents as an edematous erythematous patch that progresses to an indurated, scaly plaque with a whitish-gray to brown discoloration. Vertical fissuring and crusting can occur and become painful. Vesicles may arise and burst, giving rise to superficial ulcerations, which may then become secondarily infected. Eventually, warty nodules may form that can undergo malignant transformation to SCC.

The main risk factor for developing actinic cheilitis is chronic sun exposure, as evidenced by a higher incidence of the lesions in light-skinned individuals who work outdoors. Its decreased incidence in women may be due to the protective effects of lipstick [4].

The propensity for actinic cheilitis to develop into SCC should alert the clinician to look for

Fig. 9 Actinic cheilitis. This confluent, hyperkeratotic tumor of the lip is sun-induced. It can be asymptomatic or develop painful fissures. It is premalignant and biologically analogous to actinic keratoses on nonmucosal skin

features associated with malignancy such as ulceration, persistent flaking, or crusting. Any lesion with suspicious features should be biopsied. If the lesion is not indurated, a trial of conservative therapy with opaque zinc oxide or titanium dioxide containing sunscreens and topical steroids may be initiated. Because of the sensitivity of the lip area, ablative treatments can be painful and problematic. Topical agents can be used but can also cause a painful reaction. In one approach, topical 5% fluorouracil can be applied three times daily for 9–15 days resulting in brisk ulceration followed by a 2–3 week period of healing. Even with good compliance, recurrence rates range from 17% at 22 months to 60% at 50 months [39, 40]. Vermilionectomy, which involves excision of the vermilion border down to orbicularis oris muscle with subsequent advancement of a labial mucosal flap, is reserved for cases of actinic cheilitis that recur or do not respond following topical 5FU, laser, or photodynamic therapy [41].

Leukoplakia

Leukoplakia appears as a white plaque on the oral mucosa and is the most common precancerous lesion of the oral cavity. These lesions must be differentiated from those resulting from chronic irritation (usually from smoking), candida, or HPV infection. Malignant transformation occurs in 10–20% of patients and should be biopsied if growth or ulceration of the plaque is present.

Cutaneous Horn

Cutaneous horn is a clinical term used to describe a hard, yellowish brown, conical outgrowth of skin, resembling an animal's horn. Cutaneous horns develop on sun-exposed areas such as the scalp, upper part of the face, tips of the ears, and dorsum of hands; they may grow as long as 20 cm [41]. They can arise from benign, premalignant, or malignant epidermis.

More than 60% of cutaneous horns derive from benign lesions of epithelial hyperplasia, such as warts, skin tags, seborrheic keratoses, and nevi; 24% arise from premalignant lesions including actinic keratoses, and the remaining 16% arise from mostly squamous cell cancer. Horns arising from basal cell cancer and metastatic and sebaceous carcinomas have also been reported.

A cutaneous horn, characterized histologically by a compact hyperproliferation of keratin, is considered a premalignant variant of actinic keratosis. Surgical excision is indicated as approximately 15% of cutaneous horns contain SCC [41, 42].

Bowen's Disease (Squamous Cell Carcinoma In Situ)

Squamous cell carcinoma in situ localized to the epidermis is referred to as Bowen's disease. It typically arises in individuals over the age of 60 and demonstrates a slow, indolent course.

Although not invasive into the dermis, it must be considered a variant of squamous cell cancer. Approximately 5% of the lesions progress to invasive SCC [43].

Bowen's disease initially presents as a solitary, slowly enlarging, erythematous macule with a sharp border that can evolve into a scaling, crusting plaque usually 2–6 cm in diameter (Fig. 10). When this lesion develops on the penis, it is known as erythroplasia of Queyrat. Its etiology has been associated with chronic irritation, HPV infection, and immunosuppression [44]. Ulceration or bleeding may be a sign of invasive malignancy. Bowen's disease can be treated with excision, Mohs micrographic surgery, or destructive therapies such as cryotherapy, electrodesiccation and curettage, topical 5-FU, imiquimod, and photodynamic therapy. Histologic confirmation should be obtained before using one of the destructive modalities. Cure rates of 90–97% have been reported using cryotherapy [34, 45].

Fig. 10 Bowen's disease. This large plaque is an extreme example of squamous cell carcinoma in situ or Bowen's disease. This noninvasive cancer may extend down the hair follicles, so failure to eradicate cells at this level, surgically or otherwise, may result in recurrence of the tumor

Lentigo Maligna (Hutchinson's Freckle)

Melanoma In Situ

Lentigo maligna is a noninvasive disorder of atypical melanocytes limited to the epidermis. This flat, pigmented lesion develops into invasive melanoma in about 1 of 750 cases per year [46]. As a result of its malignant potential, most authors view lentigo maligna as a melanoma in situ [47]. The major risk factors for developing lentigo maligna are chronic sun exposure and light skin color. Additional risk factors include a history of severe sunburn, radiation exposure, estrogen and progesterone therapy, and use of nonpermanent hair dyes [48]. The incidence of lentigo maligna, which is slightly higher in women, peaks during the seventh and eighth decades, with the average age of onset around 65 years.

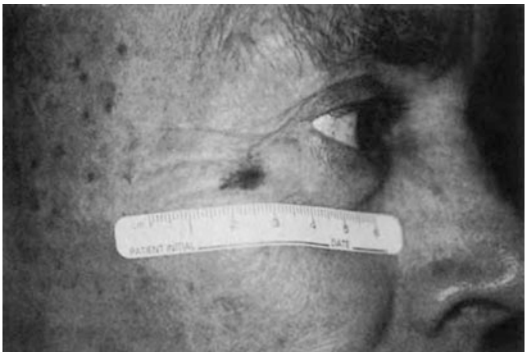

Fig. 11 Lentigo maligna is melanoma in situ on sun-exposed skin. Although this lesion is small and easy to excise, these lesions are often long-standing in the elderly and can reach sizes that make excision unfeasible

Clinically, lentigo maligna presents as a uniformly flat macule ranging in size from 3 to 20 cm with intralesional variations in color (Fig. 11). The color often appears as a disorganized array of dark browns and black on a background of light browns, pinks, and white. The borders of the lesion tend to be irregular with a notched, "geographic" shape.

Biopsy of lentigo maligna reveals cytologically atypical melanocytes proliferating in distinct units throughout the basal layer. These atypical melanocytes can extend far beyond the clinical margin, leading to a high recurrence rate. The black areas of the lesion often display the most advanced histologic changes, whereas the white areas show signs of regression. Regions with surface irregularity may signify invasion.

Several lesions can simulate lentigo maligna, including seborrheic keratoses, solar lentigos, pigmented actinic keratoses, pigmented Bowen's disease, and pigmented BCC. However, these lesions tend to be more uniform in color and rarely contain black pigment. Seborrheic keratoses can usually be distinguished based on their characteristic verrucous surface. Solar lentigos do not exhibit variations in color as seen with lentigo maligna. Pigmented carcinomas tend to be raised. To confirm the diagnosis, an incisional punch or shave biopsy that includes the most darkly pigmented area is recommended.

Complete excision is the treatment of choice for lentigo maligna. Conventional surgery, which provides a 91% cure rate [49], should be performed with 0.5 cm margins if feasible [50]. Depending on the clinical circumstance, mapped serial excision may be required to ensure removal of what can often be very large lesions. This approach is especially helpful for periocular and other cosmetically sensitive areas of the face [51–53]. Cure rates as high as 97% have been achieved using Mohs surgery [54, 55]. However, the technical issues related to frozen section interpretation of melanocytic lesions make use of conventional margin analysis preferable at this time, either in a staged fashion or single excision where feasible.

Some lesions of lentigo maligna do not lend themselves to excision because of their size, location, or the patient's comorbid conditions. In such cases, destructive therapies such as CO_2, ruby laser, electrodesiccation and curettage, radiation therapy, cryotherapy, topical azelaic acid, and topical imiquimod have been used [56]. The major disadvantage of these methods is that they do not provide a specimen to confirm that the cancer has been properly and completely eliminated. These methods may also fail to treat the adnexal melanocytes, which can lead to recurrence. This is suggested by the high recurrence rate of lentigo maligna that occurs with these modalities: 20–25% for electrodesiccation and curettage, 6–36% for cryotherapy, up to 100% for azelaic acid, and up to 38% for irradiation [48].

Malignant Lesions

Squamous Cell Carcinoma

Squamous cell carcinoma (SCC) accounts for 15–20% of all skin cancers in the United States. SCC is a malignant tumor of keratinocytes arising on sun-damaged skin and mucous membranes. The incidence is higher in men but occurs more frequently on the extremities in women. Individuals over the age of 55 are most frequently affected, with the mean age of onset at 60 years.

Approximately 3,000 patients die from SCC annually in the United States, and the incidence of more aggressive or advanced tumors is increasing [57].

The biggest risk factor for SCC is chronic sun exposure. This is evidenced by the fact that SCC occurs most frequently in geographic areas that have sunny climates, such as California and Florida. Also, the incidence of SCC is higher in people who work outdoors. Other predisposing factors include prior trauma, frostbite, ionizing radiation, PUVA therapy, exposure to chemical carcinogens (arsenic, topical hydrocarbons, nitrogen mustards), viruses (human papilloma virus strains 16,18,31,33, and 35), and chronic immunosuppression following organ transplantation which increases the risk of SCC up to 250 times the general population [58, 59].

SCC may arise from preexisting pathology, such as the chronic inflammatory lesions of discoid lupus, burn scars (Marjolin's ulcer), osteomyelitis sinuses, lichen planus, and chronic stasis dermatitis. SCC of the lip is associated with tobacco use.

Up to 80% of SCC tumors arise in association with a preexisting actinic keratosis, although <1% of all actinic keratoses undergo malignant transformation annually [60–62]. Malignant transformation in these lesions is associated with increased induration and inflammation. Patients often notice that the lesion is growing or changing. Well-differentiated SCC typically presents as an indurated papule, plaque, or nodule with overlying adherent hyperkeratosis. It may become ulcerated or bleed with formation of a central crust surrounded by a firm, scaly margin. If the carcinoma is undifferentiated, it may appear as a fleshy, granulating nodule with central ulceration and a necrotic base [63].

Clinically, SCC may resemble actinic keratoses, amelanotic melanoma, granulomatous disease, or adnexal tumors.

If a lesion appears suspicious for malignancy, it must be biopsied (Fig. 12).

SCC has the capacity to metastasize. For SCC arising from actinic keratoses, the metastatic propensity is low (approximately 0.5%) [64], whereas for those developing de novo, the risk is 7.7–13.7%. Tumors arising from preexisting pathology, such as a burn scar, have a much higher rate of metastasis, estimated to be 20–40%. Patients presenting with an SCC should have regional lymph nodes examined clinically, as regional lymphadenopathy is often the first sign of metastasis. The prognosis for tumors that have spread is poor, with an estimated 5-year survival rate of 26% if the metastasis is localized to regional lymph nodes and 23% if it has spread systemically [65].

Fig. 12 Squamous cell cancer. This large lesion was present for many months. Occasionally, when the lesion arises over a 6-week period, keratoacanthoma, a variant of squamous cell cancer, must be considered

Although primary tumors can be locally invasive, SCC is frequently diagnosed in the early stages when it is a highly curable disease. Simple excision of low-risk lesions with 4 mm margins is often adequate for most lesions up to 0.5 cm. Six to ten millimeter margins are recommended for larger or higher-risk lesions. For tumors that are large, deep, and recurrent and demonstrate aggressive histology or are located in areas with high metastatic potential (e.g., lips or ears) or anatomically complex areas of the face, Mohs micrographic surgery is the treatment of choice.

Mohs surgery is a tissue-sparing, office-based procedure that involves the sequential excision and mapping of the cancer. The final defect can be repaired immediately or is allowed to heal by secondary intention. Mohs excision has a 3% recurrence rate compared to an 8% recurrence rate with simple excision.

As an alternative to excision, small, superficial tumors (<0.5 cm) can be destroyed by electrodesiccation and curettage, which yields a 5-year cure rate of approximately 90%. Radiotherapy can also be effective but is typically reserved for patients who cannot undergo surgery or as adjunctive therapy in high-risk areas with perineural invasion. This method relies on patient compliance. If used properly, however, it has a 5-year cure rate similar to that of electrodesiccation and curettage [66]. Topical retinoids have also been shown to be effective for some inoperable lesions [67]. Lymph node dissection is not indicated unless nodes are clinically involved.

Sentinel lymph node biopsy to determine staging is indicated for high-risk SCC without palpable nodes. However, more controlled prospective randomized trials are required to determine whether detection of subclinical nodal metastasis results in better clinical outcomes [68]. Chemotherapy is reserved for patients with distant metastasis or advanced local disease not amenable to surgery or other treatment modalities.

Keratoacanthoma

Keratoacanthomas (KAs) represent a well-differentiated or low-grade variant of SCCs. Interestingly, in some cases, they involute and resolve spontaneously. KAs most often appear as isolated lesions on sun-exposed areas in middle-aged or older individuals. The lesion begins as a small papule that rapidly enlarges over 4–8 weeks to form a painless nodule often containing a central keratin-filled crater. KAs occur twice as often in men as in women and are most commonly found in Caucasians.

The cause of keratocanthomas is unknown. They are usually solitary, but multiple lesions may arise as part of a syndrome such as Muir–Torre, Ferguson-Smith, or generalized eruptive KAs of Grzybowski [69].

Unlike most other SCCs, KAs have a history of rapid onset and are not usually associated with regional adenopathy. The history of rapid onset (4–6 weeks) is key to making the diagnosis of KA. While KAs can spontaneously regress, they have also been shown to metastasize and ultimately be fatal [70]. Therefore, surgical excision is warranted.

Basal Cell Carcinoma

Basal cell carcinoma (BCC) is the most common type of skin cancer, constituting 75% of all non-melanoma skin cancers. BCCs are not thought to be associated with a premalignant lesion. Though they are slow-growing tumors that rarely metastasize, they can be locally invasive and destructive. BCCs most commonly present on habitually sun-exposed skin of the head and neck in fair-skinned individuals over the age of 40. Aside from chronic sun exposure, race, and age, other predisposing factors include genetic defects (basal cell nevus syndrome, xeroderma pigmentosum, Bazex syndrome, Rombo syndrome), radiation exposure, immunosuppression, and prolonged contact with chemical carcinogens such as arsenic. The incidence of BCC in the United States has been estimated at approximately 150 cases per 100,000 per year, with men more frequently affected. One exception to this trend is in the lower extremities where the lesion arises three times more commonly in women.

Morphologically, BCCs can be classified into at least five subtypes: noduloulcerative, cystic, pigmented, superficial, and morpheaform. The most common is the noduloulcerative variant, which usually starts as a small papule that slowly enlarges, appearing translucent and pearly with a rolled border and overlying telangiectasias (Fig. 13). As the tumor continues to grow, it eventually exceeds its own blood supply and becomes necrotic and centrally ulcerated (“rodent ulcer”). Most lesions are asymptomatic, though some are pruritic. Noduloulcerative BCC may resemble melanocytic nevi, sebaceous

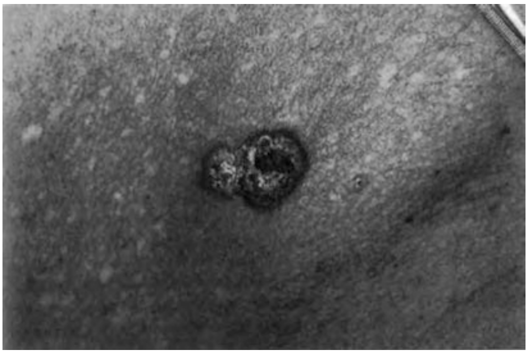

Fig. 13 Basal cell cancer. The large nodule on the chest is a neglected basal cell cancer. Actinic keratoses and severe solar damage are noted on the rest of the chest

hyperplasia, molluscum contagiosum, SCC, verruca vulgaris, keratoacanthoma, amelanotic melanoma, atypical fibroxanthoma, or an adnexal tumor.

Cystic BCC presents as a smooth, pearly, erythematous nodule that rarely ulcerates. The cystic cavity may contain necrotic debris or mucin. This BCC variant can mimic other cystic lesions, such as epidermal inclusion cysts and hidrocystomas.

Excess melanin from epidermal melanocytes can cause BCCs to become pigmented. Pigmented BCCs often occur in dark-skinned individuals and can be clinically confused with melanoma. Unlike melanoma, the border of this BCC variant is often rolled, and the color is browner in contrast to the black–brown hue of malignant melanomas.

Superficial BCC is the second most common type and appears as an erythematous, scaly plaque with irregular borders on the trunk and extremities. This tumor does not invade beyond the superficial dermis. It is often confused clinically with benign processes (e.g., localized eczema, psoriasis, or fungal infection). Superficial BCC can be differentiated by biopsy.

The most aggressive BCC subtype is the morpheaform, or infiltrative/sclerosing, variety, usually found on the head and neck. This locally destructive lesion typically appears as a whitish, sclerotic patch, resembling a scar without history of trauma. Morpheaform BCC is firm upon palpation due to the extensive fibrous stroma associated with the tumor. The strands of tumor cells can travel well beyond the clinical margins into the deep dermis, making these tumors notoriously difficult to treat without Mohs surgery.

Rarely, BCC will metastasize with a reported incidence of 0.0028–0.5% [71]. Metastatic BCC tends to occur more frequently in Caucasian men, occurs on the head and neck, and has no increased risk with a particular histologic subtype although many so-called metastatic basal cell cancers have had squamous features. In contrast to the relatively benign course of primary BCC, metastatic BCC has a 5-year survival of 10% [71] and commonly affects the lymphatics, lungs, bone, and skin.

Knowledge of the pathology of these five primary BCC subtypes is important when choosing the appropriate method of treatment. In addition to taking the morphologic type into account, the proper treatment modality also depends on the size and location of the tumor, the age and comorbid conditions of the patient, and patient preference. For patients who can undergo surgical procedures, electrodesiccation and curettage, simple excision, and Mohs surgery are the methods of choice. With the exception of the morpheaform subtype, most small, nonrecurrent varieties of BCC can be treated with simple excision, achieving a cure rate exceeding 95% [72, 73].

For tumors <1 cm, an excisional margin of 4–5 mm is recommended. Wider margins of 5–10 mm are recommended for tumors >1 cm [74].

For recurrent BCC, infiltrative subtypes, or tumors involving complex or aesthetically sensitive areas of the face, Mohs surgery is recommended. It has the added benefit of being tissue-sparing and offers a cure rate approaching 99% for nonrecurrent lesions [75]. Based on a recent randomized clinical trial, Mohs surgery resulted in better outcomes for treatment of recurrent basal cell tumors, compared to direct excision [76].

Nonsurgical treatment methods include radiotherapy, photodynamic therapy, and topical chemotherapy with agents such as 5-FU and imiquimod. Both topical agents are reserved for the superficial type of BCC because they cannot readily penetrate beyond the dermis. The treatment course can last from 2 to 6 weeks or more, thus requiring high patient compliance. For 5-FU, clinical clearance rates up to 90% have been reported with extended treatment courses of up to 12 weeks [77]. For imiquimod, five times weekly use for 6 weeks has produced 1-year clearance rates as high as 85% and 5-year clearance rates approaching 80% [78].

Radiotherapy can also be used to eradicate BCCs but is best reserved for patients who cannot undergo treatment with other ablative modalities. Cutaneous atrophy at the treatment site is a common side effect. The overall cure rate approaches 90%.

Treatment of metastatic BCC relies on aggressive surgery, irradiation, and/or palliative chemotherapy with cisplatin, cyclophosphamide, 5-fluorouracil, bleomycin, and vincristine.

Overall, BCC generally carries a good prognosis as the tumors tend to grow slowly and metastasize rarely. Local invasion especially in the head and neck can result in significant morbidity. Routine monitoring every 6 months for the first year following treatment and annually thereafter is essential as one-third of recurrences occur in the first year following treatment, half in the second year, and two-thirds in the third year regardless of the treatment modality [75, 79].

Melanoma

Melanoma is a malignant tumor of epidermal melanocytes. It is the fifth most prevalent cancer among men and the sixth most prevalent cancer among women in the United States. Melanoma represents a significant healthcare problem as its incidence is rising faster than any other cancer [80] despite both the presence of a modifiable risk factor (sun exposure) and its curability when detected in its early stages.

In 2016 an estimate of 91,270 adults (55,150 men and 36,120 women) in the United States were diagnosed with melanoma involving the skin. Melanoma is the fifth most common cancer among men and the sixth most common cancer in women. Before age 50, more women are diagnosed with melanoma than men. However, by age 65, the rate is more than two times higher in men. By age 80, the rate in men is nearly three times higher than in women. The average age of the diagnosis of melanoma is 63 years of age in both men and women. Melanoma accounts for about 1% of all skin cancers diagnosed in the United States, but it causes most of the skin cancer deaths. It is estimated that 9,320 deaths (5,990 men and 3,330 women) from melanoma will occur this year [81].

Chronic sun exposure is the main risk factor particularly in those with fair skin, an inability to tan, and an antecedent blistering sunburn. Pigment is a protective factor, as demonstrated by the relative rarity of melanoma in dark-skinned individuals. Other risk factors include blond or red hair, a family history of melanoma (familial melanoma accounts for approximately 10% of all cases), and congenital giant or atypical nevi.

Melanoma is traditionally classified into five clinicopathologic variants: superficial spreading melanoma, nodular melanoma, lentigo maligna melanoma, acral lentiginous melanoma, and desmoplastic melanoma. Superficial spreading melanoma (Fig. 14) is the most common subtype, comprising 40–50% of all cases in patients over age 65 [82]. It typically presents on the trunk in men and on the legs in women in their fourth to fifth decade. The tumor often begins as a small pigmented lesion that develops irregular features such as marked variations in color involving reds, whites, blues, and blacks, as well as notched borders. The tumor is characterized by a radial

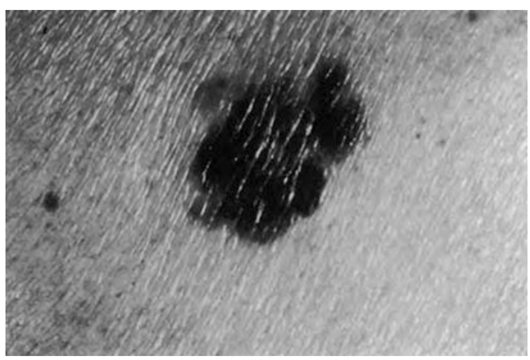

Fig. 14 Melanoma. This example of superficial spreading melanoma has irregular edges and variable coloration. The elderly have an increased incidence of melanoma relative to other age groups, and early diagnosis is the key to cure

growth phase, where malignant cells are localized to the epidermis, followed by a vertical growth phase, which signifies dermal invasion. Elevation, bleeding, and ulceration of the lesion herald the vertical phase.

The second most common type of melanoma in the elderly is the nodular melanoma. These lesions present as elevated, dome-shaped, reddish-brown nodules most commonly localized on the legs or trunk; they arise more frequently in men. They have a short radial growth phase and therefore rarely grow to more than 2 cm in diameter. As they quickly enter their vertical growth phase, nodular melanomas can easily bleed and ulcerate and develop satellite lesions with surrounding inflammation. The tumors begin to develop during the fifth to sixth decade and peak in incidence during the eighth decade, with men more frequently affected than women. Nodular melanomas must be differentiated from seborrheic keratoses, pyogenic granulomas, and pigmented BCCs. Amelanotic melanoma, considered a subtype of nodular melanoma, displays a similar rapid vertical growth phase. These lesions may lack pigment and prove difficult to diagnose.

Lentigo maligna melanoma develops in preexisting lentigo maligna lesions. Although lentigo maligna melanoma represents only 5% of all malignant melanoma cases, it accounts for 10% of melanoma cases in the elderly. Lentigo maligna is, in essence, an in situ melanoma that is in a horizontal growth phase that can last for decades before proceeding to a vertical growth phase. Transformation to lentigo maligna melanoma is defined as invasion of malignant melanocytes into the dermis and is heralded by the formation of an elevated nodule.

Like lentigo maligna melanoma, acral lentiginous melanoma also occurs with disproportionately greater frequency in the geriatric population. Unlike all other subtypes, however, these melanomas most commonly affect Blacks, Asians, and Hispanics. Acral lentiginous melanoma appears as a macular, hyperpigmented area with irregular borders and a blue to black color; it arises on the plantar or palmar surfaces of the hands and feet, on mucous membranes, and in the subungual areas of nails. Subungual variants commonly present as a longitudinal line of pigment extending the length of the nail plate, with the hallmark spread of the pigment to the proximal nail fold referred to as Hutchinson sign. Its location on extremities often leads to the mistaken diagnosis of traumatic hematoma. These tumors are often diagnosed at an advanced stage with an aggressive course compared with the other subtypes.

Finally, desmoplastic melanoma is a relatively uncommon subtype that presents as an unremarkable plaque or nodule which can easily be misdiagnosed at an early stage. It affects older patients most commonly in the head and neck and occurs in men twice as often as in women. Desmoplastic melanoma is frequently associated with nerve invasion and spread along fascial planes and tends to be thicker at the time of diagnosis. They are locally aggressive with a higher rate of local recurrence but exhibit a low incidence of lymph node involvement.

Any pigmented lesion that has undergone changes in size, shape, or color; is inflamed, oozing, bleeding, or itching; or is larger than 5 mm in diameter should be considered malignant until proven otherwise by biopsy. The most frequently occurring colors in melanomas are shades of brown, red, white, or blue and black. Pinks and reds signify inflammation. A blue color arises from light scattering from pigment deep within the dermis (Tyndall effect) and is a poor prognostic indicator.

Full-thickness excisional biopsy with a 1–2 mm margin of normal tissue is the method of choice for suspicious lesions. For large tumors or those that cannot be completely excised because of their anatomic location, an incisional biopsy, such as a punch or elliptical biopsy, is recommended. Histologic characteristics of melanoma obtained from definitive biopsy are powerful independent predictors of 5- and 10-year survival rates.

Clinical subtypes of melanoma vary in aggressiveness. For example, lentigo maligna melanoma has a long horizontal growth phase and is usually recognized prior to the development of metastases. Although prognosis depends on the type of lesion and the presence or absence of lymphatic

Table 1 Clark and Breslow classification of malignant melanoma Clark's level

I Tumor does not invade dermis.		
II Tumor invades only papillary dermis.		
III Tumor expands into papillary dermis but spares reticular dermis.		
IV Tumor invades reticular dermis.		
V Tumor invades subcutaneous tissue.		
Breslow level (mm)	Excision margin	Sentinel node studies
1	1 cm	No
1.0–1.5	1–2 cm	+/–
1.5–4.0	2–3 cm	+
4	3 cm	No

Breslow depth does not correspond precisely to Clark's level. It is used for prognostic purposes and to direct therapy

invasion, the single strongest prognostic factor is the depth of the melanoma measured in millimeters (Breslow depth) (Table 1). Clark's level is sometimes reported but is no longer used as reliably as the Breslow depth.

The American Joint Committee on Cancer has devised a classification system for melanomas that not only takes depth into account but also the extent of regional or distant metastasis. The seventh edition was published in 2010 and is currently the system in use [83]. This clinical staging system is designated the TNM classification. The T component is based on Breslow thickness and histologic evidence of ulceration. Mitotic index was added for small, T1 lesions, less than 1 mm in thickness. The N component is based on the extent of regional lymph node involvement and the tumor burden of the nodes. While the sixth edition allowed the use of microscopic staging of lymph nodes, the seventh edition added the immunohistochemical designation of positive lymph nodes using melanoma-associated markers such as HMB-45 and Melan-A/MART-1. The M component is based on anatomic site of distant metastases and the serum lactate dehydrogenase level. The TNM classification defines five stages based on prognosis: stage 0 (in situ melanoma), stage II (local disease), stage III (regional nodes, in-transit and satellite metastases), and stage IV (distant metastases). The stage groupings and clinical/pathologic criteria are described in Table 2.

Elderly patients tend to present with poor prognostic features and therefore have increased mortality rates. Malignant melanoma in the elderly tends to present later, be thicker, have histologic ulceration, and be of nodular type. Additionally, elderly patients present more frequently with satellite and in-transit metastases and have anatomic localization to areas other than the head and neck [84]. The reasons for this are complex but likely include some combination of decreased vision, increased tolerance for skin lesions, decreased social support, and increased comorbidity.

Most authorities agree that excision based on the thickness of the primary lesion is the mainstay of melanoma treatment. Over the past few decades, however, the guidelines for surgical margins have been redefined by several randomized prospective clinical trials [85–91].

In situ lesions (Clark's level I, TNM stage 0) are by definition noninvasive. The goal for treatment of these lesions is to remove all tumor cells locally. If standard excision is the method of choice, 0.5 cm margins are usually adequate for in situ lesions. However, if the tumor is clinically ill-defined, wider margins may be advisable. The tumor margins should be assessed with a Wood's lamp and marked prior to administration of anesthesia. Lesions that have invaded the dermis and that are up to 1 mm in depth require excisional margins of 1 cm. Margins of 2 cm are recommended for lesions with a Breslow depth of 1.0–4.0 mm. Any lesion more than 4 mm thick should undergo wide excision with margins up to 3–5 cm.

The role of lymphadenectomy in malignant melanoma remains controversial. Prophylactic lymphadenectomy is not indicated for in situ lesions, as they do not show evidence of metastasis. Sentinel lymph node biopsy, a procedure that permits biopsy of the first node that drains a regional lymphatic plexus and is thought to be representative of all nodes in that region, is advocated for all patients with primary melanomas >1 mm thick and for patients with high-risk thin (<1 mm) or stage IB (ulcerated) melanomas. The role of sentinel node biopsy versus clinical observation has recently been addressed by the Multicenter Selective Lymphadenectomy Trial-1

Table 2 American Joint Committee on Cancer classification for malignant melanomas

Stage	Classification			Clinical and pathologic criteria
O	Tis	NO	MO	In situ melanoma
IA	T1a	NO	MO	1.0 mm_2 or less in thickness, no ulceration, mitoses less than 1/mm_2++
IB	T1b	NO	MO	With ulceration or mitotic rate more than 1/mm_2
	T2a	NO	MO	1.01–2.0 mm_2 in thickness
IIA	T2b	NO	MO	1.01–2.0 mm_2 with ulceration
	T3a	NO	MO	2.01–4.0 mm without ulceration
IIB	T3b	NO	MO	2.01–4.0 mm_2 in thickness with ulceration
	T4a	NO	MO	> 4.0 mm_2 in thickness without ulceration
IIIA	T1-4a	N1a	MO	Any invasive T excluding > 4 mm_2 in thickness with ulceration, 1 regional node with micrometastases[a]
	T1-4a	N2a	MO	Any invasive T excluding > 4 mm_2 in thickness with ulceration, 2–3 regional nodes with micrometastases
IIIB	T1-4b	N1a	MO	Any invasive T, 1 regional node with micrometastases
	T1-4b	N2a	MO	Any invasive T, 2–3 regional nodes with micrometastases
	T1-4a	N1b	MO	Any invasive T excluding > 4 mm_2 in thickness with ulceration, 1 regional node with macrometastases
	T1-4a	N2b	MO	Any invasive T excluding > 4 mm_2 in thickness with ulceration, 2–3 regional macrometastases
	T1-a/b	N2c	MO	In-transit or satellite metastases without nodal metastases
IIIC	T1-4b	N1b	MO	Any invasive T, 1 regional node with macrometastases
	T1-4b	N2b	MO	Any invasive T, 2–3 regional macrometastases
	Any T	N3	MO	Any T, >/= 4 regional nodes including in-transit or satellite metastasis with positive metastatic nodes
IV	Any T	Any N	M1	Any lesion with distant skin, subcutaneous, lymph node, or organ metastases

Source: Used with permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer Science + Business Media, LLC, www.springlink.com

[a]Micrometastases now include those seen on standard H&E staining or with melanoma-specific immunohistochemical markers

[92]. This prospective randomized multicenter trial demonstrated that the result of the sentinel node biopsy is the most powerful independent predictor of survival, but it did not demonstrate that the sentinel lymph node biopsy itself leads to a survival advantage. Contrary to previous speculation, the performance of the sentinel lymph node biopsy was not associated with the development of in-transit metastases. Despite the absence of a clear survival benefit, the sentinel node biopsy does provide valuable staging information and can lead to better management of regional disease. Nodal status is the most important prognostic factor in staging malignant melanoma. The revised AJCC staging system for melanoma accounts for the number of positive nodes as well as the overall tumor burden. Patients with only one positive node have a better prognosis than patient with multiple nodes.

Because malignant melanoma is considered a radioresistant tumor, the role of irradiation in metastatic disease is mostly palliative.

In the treatment of advanced metastatic disease, immunotherapeutic strategies are a focus of great interest. Specifically, an increasing number of clinical trials with interleukin-2, interferon, allogeneic whole-cell vaccines, recombinant viral vectors, adoptive immunotherapy combined with lymphodepletion, CTLA-4 blockade, allogeneic cell lysates, and dendritic cell manipulation are advancing our understanding of tumor immunology and potentially extending survival [93, 94]. The prognosis of patients with widely metastatic disease remains poor, but the full development and refinement of these strategies are progressing.

The perception that aggressive systemic therapy may have unacceptable toxicity in the elderly has limited our understanding of the effect of patient age on chemotherapy efficacy and toxicity. In the treatment of melanoma with isolated limb perfusion, patients of increased age demonstrated similar response rates with no increase in local or systemic toxicity [95]. Similarly, in a small group of elderly patients treated with high-dose IL-2 for melanoma and other tumor types, there was no demonstrated increase in adverse events to warrant their exclusion in future studies [96]. Therefore, while chronological age itself may not affect the efficacy or toxicity of any particular therapy, practical considerations necessitate the careful evaluation of comorbid disease, functional and mental status, support network, and patient willingness to tolerate the difficult side effects of treatment.

Patients who have been diagnosed with melanoma need close follow-up because they may be prone to developing a second primary tumor. Most recurrences arise within the first 18 months but can be delayed for many years. Follow-up should occur four times a year for the first year and at least twice a year thereafter [97]. Early recognition of local or regional disease or new primary melanoma lesions in this population can significantly alter the mortality rate from malignant melanoma.

Atypical Fibroxanthoma

Atypical fibroxanthoma is a spindle cell neoplasm of mesenchymal origin that develops on the head and neck of elderly, light-skinned individuals. The tumor presents as an asymptotic, solitary, firm nodule less than 2 cm in diameter which may go on to ulcerate or hemorrhage. Grossly, the lesion can resemble a SCC, BCC, epidermoid cyst, or pyogenic granuloma. Risk factors for tumor development include chronic sun exposure, radiation, local trauma, and male gender.

One of the unique features of this tumor is its malignant-appearing histology. Aside from the well-defined tumor margins and absence of deep tissue invasion, the tumor appears histologically indistinguishable from malignant fibrous histiocytoma [98].

Electrodesiccation and curettage is not considered adequate treatment because it does not remove the deep tissue, which may be invaded by tumor cells. The recurrence rate with tumors treated by wide excision is estimated to be approximately 10% [99]. Mohs surgery, which has the added advantage of conserving more normal tissue than wide excision, is currently the preferred method of treatment with recurrence rates ranging from 0 to 6.9% [100].

Merkel Cell Carcinoma

Merkel cell carcinoma is a rare malignant tumor of the neuroendocrine-derived Merkel cell. This tumor of unknown etiology typically affects persons over the age of 65, though cases of Merkel cell carcinoma developing in individuals as young as 7 years of age have been reported [101].

Merkel cell carcinoma manifests as a rapidly growing, solitary, pink to violet dome-shaped nodule on sun-exposed skin. These tumors are most commonly distributed on the head and neck (50% of cases), extremities (40% of cases), and trunk (10% of cases) of elderly Caucasians. The overlying epidermis may be shiny and intact with fine telangiectasias, or it may be ulcerated. Because of its nonspecific presentation, Merkel cell carcinoma is often not recognized prior to biopsy. It may be misdiagnosed as an SCC or BCC, a desmoplastic or amelanotic melanoma, or a pyogenic granuloma. Light microscopy may not be diagnostic because the tumor mimics other poorly differentiated small cell tumors. Confirmation of the diagnosis may require electron microscopy, which shows the characteristic secretory granules and paranuclear fibrous bodies.

Once the diagnosis of Merkel cell carcinoma is confirmed, a complete physical examination with attention to regional lymphadenopathy and organomegaly, and a thorough work-up including chest radiography and baseline laboratory tests, with liver function tests, should be performed.

Merkel cell carcinoma is an aggressive tumor with local recurrence rates of 40 to 45% following excisional biopsy with 2–3 cm margins [102]. In anatomically complex areas, Mohs surgery should be considered.

Sentinel lymph node biopsy or elective lymph node dissection is also recommended because of early lymphatic spread. Radiation therapy following surgical excision is considered for tumors >2, whereas chemotherapy currently has a very limited role in treatment.

Five-year survival rates for localized disease range from 44% to 68% and for regional or metastatic spread 23% to 42% [103, 104].

Conclusions

Common cutaneous neoplasms that afflict the elderly arise from the epidermis or dermis and can be benign, premalignant, or malignant. Recognizing these lesions is important for providing the appropriate care to a growing geriatric population. A routine, thorough skin examination enables physicians to monitor the elderly patient closely for the development of precancerous and cancerous lesions, which can ultimately be life-threatening. Minimizing the risk of malignant tumor development by avoiding risk factors such as UV radiation should be emphasized in the elderly population.

Case Study

Recurrent Basal Cell Carcinoma on the Nose of a 75-Year-Old Woman

A 75-year-old woman presented with a slowly growing scar-like lesion at the junction of the right nasal ala and cheek. It was present for approximately 3 years. She noted a 1-month history of a nonhealing lesion at the same site. Dermatologic history was significant for a BCC of the right nasal ala that was treated by electrodesiccation and curettage 5 years earlier. There was no history of radiation therapy. Her medical history was significant for insulin-dependent diabetes and hypertension. Social history was significant for loss of her husband 2 years ago. She lives alone.

Examination of the right cheek and right nasal ala demonstrated a 1.5 × 1.5 cm irregular, indurated, smooth-surfaced, shiny plaque with an indistinct border. Within this lesion, on the right ala, was a 3 mm crusted telangiectatic papule with hemorrhagic crust.

Laboratory data, including CBC, LFTs, and renal function tests, were normal. A biopsy from the edge of the plaque demonstrated irregular, narrow, strand-like proliferations of palisading, basaloid tumor islands in a dense fibrous stroma that extended to the base of the biopsy. These histologic features were consistent with BCC, sclerosing or morpheaform subtype. Mohs surgery was selected as the treatment of choice.

The first stage of Mohs surgery revealed a BCC with distinct nodular and morpheaform features. There was a focal area of epidermal ulceration and a nodule of palisading basaloid tumor islands extending from the deep epidermis into the superficial and mid-dermis. In the deeper and lateral sections, there were morpheaform strands of basaloid cells extending to the margins of the specimen. The tumor was cleared after the second stage of Mohs surgery. The postoperative defect extended to the cartilage of the ala and measured 2.5 × 2.3 cm. The wound was repaired under local anesthesia only in the office setting with an auricular cartilage graft and subcutaneous hinge flap. The secondary defect was closed in a linear fashion, and the area over the graft was left to epithelialize by second intention.

Discussion

Morpheaform BCCs and BCCs of mixed type that have morpheaform features are slow-growing and asymptomatic and resemble scars, making them easily neglected by elderly patients. The clinical borders are indistinct, and the histologic tumor often extends far beyond what the clinical appearance would suggest. These cancers have a propensity for invasion and destruction of adjacent tissues, and they have a higher risk of recurrence than other subtypes of BCC.

Superficially destructive procedures such as cryotherapy, electrodesiccation and curettage, topical imiquimod, or elliptical excision have an increased risk of recurrence as demonstrated in this case. Mohs micrographic surgery is the treatment of choice as it offers the most complete margin evaluation and provides for immediate reconstruction if indicated. Mohs surgery is an office procedure performed using local anesthesia and is generally well tolerated. To facilitate the procedure, there should be proper preoperative consultation that addresses mental status issues, medication use, anticoagulants, the need for prophylactic antibiotics, and comorbid conditions. In the perioperative period, elderly patients often require additional support including attention to positional and emotional comfort as well as monitoring for orthostatic hypotension, hypoglycemia, and cardiovascular events. Anxiety can often be allayed with casual conversation.

Because of the large defects that may result from excision of morpheaform lesions, comorbidities such as diabetes, vascular disease, and the generalized slower wound healing in the elderly must be considered. It must be remembered that complex multistage repairs, while technically possible, may not be advisable in the elderly considering longer operative times and prolonged recovery.

In the postoperative period, pain is most often managed with acetaminophen alone. When more potent analgesics are required, slower drug metabolism, decreased glomerular filtration rates, and potential drug interactions from polypharmacy must be considered. Additionally, the postoperative need for complex or prolonged dressing changes with uncommon materials should be avoided. In general, wound care instructions are discussed with the patient as well as any caregiver present. Before discharge, adequate time is provided for patients to ask questions including concerns for cosmesis and recurrence. As follow-up, we advocate same evening and 24 h phone calls with wound check at 1 week.

Pressure Sores in the Elderly

Pressure sores represent localized soft tissue injury from unrelieved pressure over a bony prominence. The most common bony surfaces involved, in order of occurrence, are the sacrum, ischium, and greater trochanter [105]. In these areas, capillary perfusion pressures (30 mmHg) are exceeded when lying supine, sitting, or lying on the side, respectively [106]. Clinical studies have demonstrated that external pressure greater than 60 mmHg for 2 h leads to irreversible tissue damage [107]; More importantly, soft tissue injuries can be prevented when pressures as high as 450 mm Hg are relieved for as little as 5 min [108]. This observation affirms the key preventive role of repositioning.

Pressure sores are a disease of the elderly: two-thirds of pressure sores occur in patients over 70 years of age [109]. Most of the remaining occur in spinal cord injury patients. Fourteen percent to seventeen percent of patients in a US acute care hospital have pressure sores [106]. The majority of pressure sores occurring in the acute care hospital setting develop within the first 2 weeks of admission [110], probably because elderly patients remain bed-bound until their acute issues are diagnosed and stabilized. In the elderly, the presence of multiple comorbidities contributes to the etiology of pressure sores. Although pressure sores are associated with a twofold increase in mortality, they are not usually the immediate cause of death [111]. More commonly, comorbidities that lead to pressure sores such as cardiovascular, neurological, or orthopedic diseases have their own high mortality rates [112].

Aside from the devastating clinical and psychosocial consequences of pressure sores, they represent a burgeoning health economic crisis. Pressure sores cost $9.1–$11.6 billion per year in the United States. The Medicare estimated in 2007 that each pressure ulcer added $43,180 in costs to a hospital stay [113]. In 2008, the Centers for Medicare and Medicaid Services (CMS) discontinued reimbursement for hospital-acquired stage III or IV pressure sore, emphasizing the hospital's responsibility in documenting and preventing pressure sores.

Goals in the prevention and management of pressure sores are identification of the etiological factors, elimination of these factors, debridement, and wound care. Surgical coverage may be considered when benefits of repair outweigh the perioperative risks, including anesthesia, and pressure sore recurrence.

Pathophysiology

Both extrinsic and intrinsic factors contribute to the development of pressure sores. Extrinsic factors include unrelieved pressure as seen in the debilitated elderly patient, in addition to factors that worsen the local wound environment, such as perineal moisture [114], incontinence [115], and shearing forces from patient repositioning [116].

Intrinsic factors that lead to poor wound healing include skin fragility in advanced age secondary to decreased tensile strength [117, 118], edema, malnutrition, diabetes, end-stage renal disease, and low BMI. Edema in the elderly, due to systemic illness, sets up a downward spiral of ischemia-reperfusion soft tissue injury in which dependent edema is worsened by pressure exceeding the capillary venous outflow pressure (Table 3).

Extrinsic pressures can also be exacerbated by positioning, and clinical studies show that some common positions are particularly problematic. For instance, in a semi-recumbent position with the head of the bed elevated, only friction keeps the patient from sliding down. This situation leads to shearing forces on the skin and soft tissue overlying the sacrum [119]. These shearing forces

Table 3 Extrinsic and intrinsic factors contributing to pressure sore formation

Extrinsic	Intrinsic
Limited mobility	Advanced age
Loss of protective sensation	Skin fragility
Abnormal positioning due to spasticity or contracture	Poor nutritional status
Friction and shearing forces	Dependent edema
Chronic moisture	Immunoincompetence
Other mechanical factors that increase pressure	Infection
	Medical conditions

may result in microvascular thrombosis further contributing to tissue ischemia: topographic pressure maps show why certain areas, such as the sacrum, heels, and ischii, are prone to ischemic damage (Fig. 15) [106].

Malnutrition increases the likelihood of developing pressure sores at least twofold. The 2002 Nutritional Screening Initiative estimates the rate of malnutrition among the hospitalized elderly as 40–60%, nursing home residents as 40–85%, and home care elderly patients as 20–60% [120].

The Braden Scale for Predicting Pressure Sore Risk is a widely used nursing assessment tool to help predict a patient's risk of developing pressure sores. Although there is no clear evidence that risk assessment scales decrease the incidence of pressure sores, the Braden Scale has reasonable predictive capacity with high interrater reliability [121]. The Braden Scale accounts for several extrinsic and intrinsic etiologic factors by scoring six subscales: sensory perception, moisture, activity, mobility, nutrition, and friction/shear. The lower the combined Braden score (ranging from 6 to 23), the higher the risk of pressure sore development.

Intrinsically, different tissues can tolerate ischemia at varying levels. Muscle, with its high metabolic requirements, is more sensitive to hypoxia than skin or subcutaneous fat. Studies confirm that ischemic injury of the muscle overlying the bone precedes damage to the skin producing the cone or "iceberg" model of pressure sores [122]. Although most pressure sore severity indices recognize early skin changes as "low-grade," some degree of muscle damage is inevitable by the time the skin shows changes.

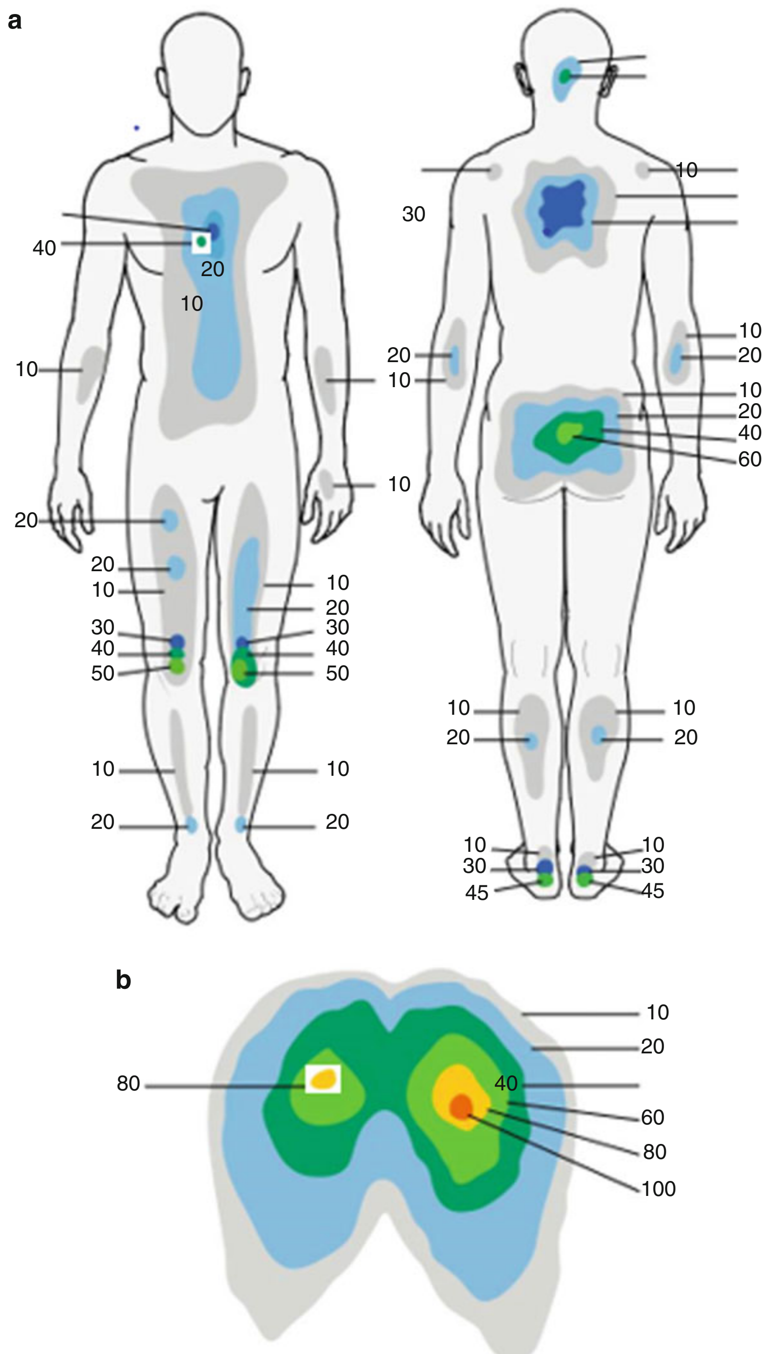

Fig. 15 Topographic pressure maps of the human body in millimeters of mercury. (**a**) Supine (*left*) and prone (*right*) positions. Note that in the prone position, the highest pressures are centered on the sacrum and heels, exceeding 30 mmHg. (**b**) Seated position reveals pressures much greater than 30 mmHg for the ischii. (Reprinted from Lindan O (1961) Etiology of decubitus ulcers: An experimental study. Arch Phys Med Rehabil 42:774, with the permission from Elsevier)

Evaluation

The evaluation of a pressure sore begins with a thorough history and physical examination elucidating the extrinsic and intrinsic factors that contribute to the etiology and chronicity of the wound. Therapeutic efforts, whether nonsurgical or surgical, will fail if these factors are not addressed. For example, a sacral pressure sore in an elderly stroke patient with limited mobility will inevitably recur after surgical coverage if a turning schedule is not planned and implemented.

The most common pressure sore classification system is the National Pressure Sore Advisory Panel consensus development conference scale developed in 1989 and revised in 2007 to include the original four stages and two additional stages allowing identification of clinically suspicious deep tissue injury and unstageable pressure sores: [123].

Stage I: Skin intact but reddened for more than 1 h after relief of pressure. This wound is reversible if extrinsic and intrinsic wound healing factors are controlled.

Stage II: Blister or other break in the dermis with or without infection. Subcutaneous fat is exposed. However, these wounds can generate granulation tissue and heal by secondary intention. The local environment must be monitored for moisture and soiling for healing to progress. Stage I and II pressure sores are the most prevalent [105].

Stage III: Subcutaneous destruction into muscle with or without infection. Theoretically, the soft tissue can heal and contract over the unexposed bony prominence. However, as muscle is sensitive to ischemic necrosis, this is usually a transient stage quickly reaching the final stage of exposed bone.

Stage IV: Involvement of bone or joint with or without infection. This is the stage most commonly prompting a surgical consultation to determine the optimal treatment for providing soft tissue coverage over desiccated, contaminated, and potentially infected bone.

In 2007, the staging system was updated with two new stages: [124].

Suspected deep tissue injury: Purple or maroon localized area of discolored intact skin or blood-filled blister due to damage of underlying soft tissue from pressure and/or shear. This new stage allows clinically suspicious deep tissue injury to be identified.

Unstageable: Full-thickness tissue loss in which the base of the ulcer is covered by slough (yellow, tan, gray, green, or brown) and/or eschar (tan, brown, or black). Eschar or necrosis makes it difficult to determine depth of destruction and frequently represents only the superficial aspect of a deep wound, as seen in Fig. 16.

Osteomyelitis within a pressure sore is definitively diagnosed when bone is excised for biopsy and bacterial culture during surgical debridement. Imaging modalities to diagnose osteomyelitis include tagged white blood cell scans and magnetic resonance imaging (MRI) [125]. However, by the time clinical suspicion is raised by findings such as deep pus not accessible with bedside debridement, surgical exploration is more urgent and appropriate than imaging. As a preoperative adjunct, radiographic imaging may help determine the extent of necrosis in high-risk surgical

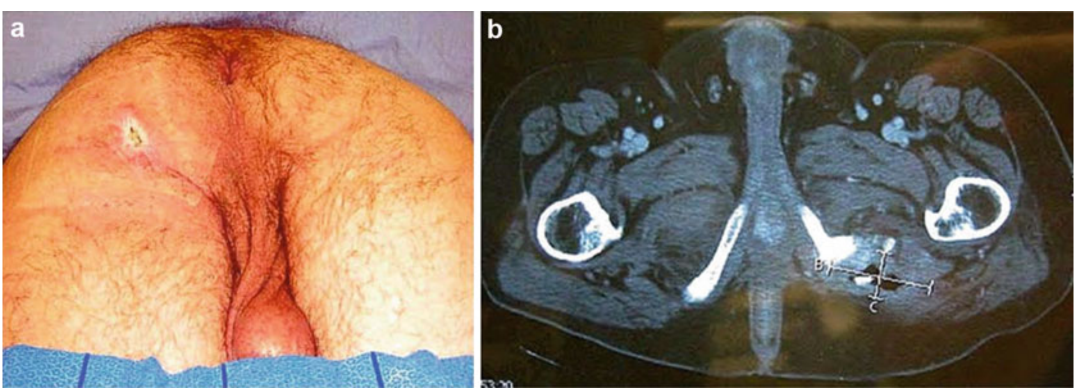

Fig. 16 (below left) Elderly homeless man found sitting on the corner of a street, confused. (**a**) Right ischial pressure sore completely covered with eschar, making it unstageable. (**b**) After bedside debridement of necrotic tissue, the wound extends to the ischial tuberosity

Fig. 17 **(below right)** The patient presented with a chronic left ischial pressure sore with drainage. (**a**) Patient in prone position with open wound on his left ischium. (**b**) Computed tomography scan of patient (the left ischium)

patients or identify the source of infection in atypical pressure sores potentially associated with a perianal fistula or spinal hardware abscesses (Fig. 17).

Infections associated with pressure sores are often polymicrobial due to urine or fecal contamination. Thus, *Proteus*, *Bacteroides*, *Pseudomonas*, and *Escherichia coli* may accompany the more prevalent staphylococcal and streptococcal species. More than half of long-term care patients harbor methicillin-resistant *Staphylococcus aureus* (MRSA) organisms [126]. Whereas swab cultures are invariably positive due to local contamination, intraoperative soft tissue and bone cultures provide more reliable sensitivities.

Pressure sores are always associated with localized inflammation and/or infection. However, unless high-staged or long neglected, they are rarely the cause of sepsis. A urinary tract infection or pneumonia must be suspected and ruled out first as a source of systemic infection in the elderly patient presenting with a pressure sore.

Management

Surgical reconstruction of a pressure sore soft tissue defect is not indicated until unrelieved pressure, local wound environment, and chronic medical illness are stabilized. Otherwise, postoperative recurrence of the pressure sore is inevitable. During preoperative assessment and wound management, there will usually be a period of time in which the pressure sore can be observed and perioperative wound care can be optimized.

Reduction of Pressure and Deleterious Extrinsic Factors

Elderly patients may be acutely obtunded or chronically debilitated and require repositioning every 1–2 h to break the cycle of constant pressure. Meta-analysis suggests that air-fluidized mattresses are better at reducing pressure sores than standard hospital mattresses [127]. Patients who use wheelchairs must learn to shift their weight constantly. Many elderly patients are confined to regular household chairs all day long. Even with intact skin sensation, they remain at risk of developing ischial pressure sores. Bedridden patients must have their lower legs monitored and elevated on foam pillows to prevent heel ulcers.

Elderly patients can demonstrate varying degrees of fecal and urinary incontinence which contribute to the contaminated environment surrounding pressure sores. Urinary incontinence may need to be managed with a sheath or indwelling catheter until the wound begins to heal. For fecal incontinence, a temporary or permanent colostomy may be indicated to increase the likelihood of wound healing or successful surgical repair.

Restoration of Nutrition and Other Wound-Promoting Intrinsic Factors

Elderly patients with pressure sores generally have nutritional intake inadequate to heal their wounds. Dietary intake of nutrients and protein is predictive of pressure sore development [118, 128]. Serum metabolic panels can help with diagnosis and treatment of malnutrition by monitoring markers such as albumin, prealbumin, C-reactive protein, retinol-binding protein, and transferrin. A nutritional analysis of nitrogen exchange and food choices helps determine caloric and protein intake, as well as estimate requirements. Other supplements and treatments to consider include the vitamins A and C which are implicated in wound healing, zinc, protein shakes, pharmacologic enhancement of appetite (megestrol), tube feeding, and parenteral nutrition [121, 129].

Additional intrinsic medical conditions affecting pressure sore healing include anemia, diabetes, HIV, and conditions that lead to edema such as congestive heart failure, renal disease, liver disease, and other causes of hypoalbuminemia.

Wound Care (Active Debridement and Regular Maintenance)

Debridement of devitalized tissue and wound care are the foundation of pressure sore management. Nonviable tissue can appear as dry gangrene or eschar that is not actively infected and may be amenable to mechanical or chemical debridement. Mechanical debridement relies on irrigation, lavage, whirlpool therapy, and sharp excision which can be performed at the bedside or in the operating room. Again, the extent of necrosis may be surprisingly extensive due to the greater sensitivity of muscle to ischemia. For this reason, undermining of the wound beyond the skin edges characterizes pressure sores, and the wound may be substantially larger than the opening in the skin. The use of debriding agents such as proteolytics, fibrinolytics, collagenases, and sterile maggots has been described. Wet gangrene is necrotic tissue that is already superinfected and requires prompt sharp debridement.

In certain areas, such as the heel, pressure sores often are stable and dry. In these wounds, like frostbite injury, local wound care permitting gradual separation of the eschar may be preferable to sharp debridement to maintain as much viable tissue as possible. For heel sores, dry dressings or topical antibacterials such as silver sulfadiazine are useful.

After debridement, several management options are available. The wound can be allowed to heal by secondary intention using a variety of packing materials on a regular basis to allow the wound to heal from the base and to prevent premature skin closure and abscess formation.

Negative pressure therapy with a vacuum-assisted device can be used to facilitate healing by secondary intention. These devices stimulate the formation of granulation tissue and encourage wound contraction, but the wound should be free of infection before sealing it under an occlusive vacuum dressing. Negative pressure therapy may help to downsize the surface area of a wound so that more complex reconstruction options of local or free flap can be replaced with simpler ones such as skin graft or primary closure [130].

Enzymatic debridement ointments have been utilized since the 1950s and continue to be a valuable tool. A recent Cochrane review, however, found that while the data demonstrate a beneficial effect of available dressings including enzymatic debridement, growth factors, and adjunctive therapies such as negative pressure wound therapy, there is no strong evidence to indicate that any given wound care regimen is superior. As a consequence, none has become a dominant or standard form of treatment [131].

Principles of Surgical Treatment

Once nonsurgical management of a pressure sore addresses the etiology and the factors that predispose to pressure sore recurrence, the risk–benefit ratio of surgery versus the perioperative risks for the individual elderly patient can be weighed. Well-recognized flaps have been developed for the most common pressure sores of the sacrum, ischium, and greater trochanter, but management must begin with adequate debridement of non-viable tissue, sinus tracts, and the bursa-like capsule that lines a chronic wound. Pressure sores that come to surgery almost always track to bone, and ostectomy is performed to debride the exposed bone and to obtain biopsies for bacterial culture. Ostectomy also serves to reduce the prominence of bone responsible for the pressure sore.

Pressure sores are rarely repaired by operations on the basic rungs of the reconstructive ladder such as delayed primary closure or a skin graft. Delayed primary closure is prone to dehiscence as it places the surgical suture line directly over the area of pressure.

A skin graft is a thin, fragile coverage option similarly vulnerable to the shearing forces that created the pressure sore in the first place. Skin grafts require a clean, healthy recipient site with a robust blood supply and no exposed bone. Only the most superficial pressure sores meet these requirements.

For full-thickness sores, the guiding surgical principle is provision of vascularized tissue to cover exposed bone, fill the wound completely with adequate padding, and close the surface with durable soft tissue and skin that is under no tension. The ideal flap moves the closure and scar away from the area of pressure.

Flap coverage is a closure option for select patients with the understanding that flap failure and high rates of pressure sore recurrence are inevitable if the multiple factors responsible for pressure sore development are not corrected preoperatively. Unlike a skin graft, a soft tissue flap carries its own blood supply that is preserved, while the flap is transferred into the wound. Flaps are often described by their anatomic makeup. Cutaneous flaps are supplied by direct cutaneous vessels and axially oriented perforating vessels ending in a subdermal plexus. Fasciocutaneous flaps include the skin, subcutaneous fat, and deep fascia. The blood supply originates from septocutaneous vessels that pass up along fascial septae and fan out at the level of the deep fascia to form a plexus from which smaller perforator vessels supply the subcutaneous fat and skin. Musculocutaneous flaps include the muscle, fascia, subcutaneous fat, and skin combined as one unit, based on one or more vascular pedicles.

Previous incisions, whether from trauma or prior surgery, can preclude certain flaps since these incisions and scars are areas where previous blood supply was likely transected. A complete surgical history is mandatory to understand the surgical anatomy when previous flaps were used. A recent large meta-analysis demonstrates the high complication and recurrence rates following surgical reconstruction of pressure sores. Therefore, another important consideration in flap selection is choosing one that preserves blood supply for potential future flaps [132].

Free microvascular flaps are the most complex reconstructive options. They require harvesting a distant flap with its accompanying arteries and veins and transferring it to the recipient bed with microvascular anastomoses to recipient vessels. Elderly patients have comorbidities such as cardiovascular disease and poor general health that often preclude these lengthy microsurgical tissue transfers.

Sacral Pressure Sores

Sacral pressure sores are the most common pressure sore in the elderly who remain bedridden and supine [105]. Given the thinness of soft tissue overlying the sacral prominence, most of these wounds come to the surgeon with exposure of sacral bone. This precludes a skin graft in the sacral area, except in the shallowest of wounds. In general, flap coverage is the better option in elderly patients with intact sensation who will recover mobility. The soft tissues surrounding the sacrum receive their blood supply from perforators from the superior and inferior gluteal arteries supplying the gluteus maximus muscles (see Fig. 18). Cutaneous, fasciocutaneous, musculocutaneous, and muscle flaps can be developed based on these vessels. The gluteus maximus can survive on vascular pedicle alone [132]. Utilizing both pedicles can increase flap reliability and the volume of overlying muscle and soft tissue. However, because the gluteus maximus extends and rotates the thigh laterally

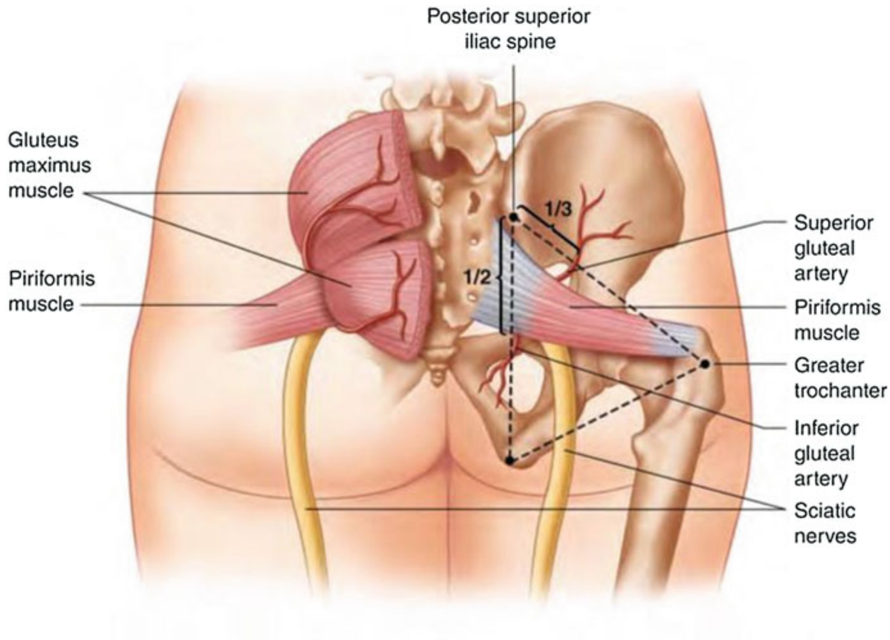

Fig. 18 (Below) The blood supply to the gluteus maximus muscle supplies perforators to the overlying soft tissue surrounding the sacrum. The piriformis muscle marks the midportion of the gluteus maximus muscle, with the superior and inferior gluteal arteries arising above and below the piriformis. The superior gluteal artery can be found one-third of the distance from the posterior superior iliac spine to the greater trochanter. The inferior gluteal artery appears halfway between the posterior superior iliac spine and the ischial tuberosity. (Reprinted from McCarthy J. Current Therapy in plastic surgery. WB Saunders © Elsevier (2005))

and is required for ambulation, this muscle is not considered expendable except in the spinal cord injury patient. If the patient has a chance of recovering ambulation, only the superior or the inferior half of the muscle should be used. For sacral coverage, the superior half of the gluteal muscle is preferred as it is closer to the wound. Alternatively, a cutaneous or fasciocutaneous flap can be used to spare the muscle entirely. The V–Y advancement technique involves creating a triangular-shaped skin island over the gluteus maximus muscle, with one side being the defect and the other two sides forming a "V." The central "V" is shifted into the open wound and the defect is closed in a "Y" configuration. A V–Y advancement flap can be designed in different ways. If not much bulk is needed, a fasciocutaneous flap based on the gluteal perforators can be advanced over the defect without needing to mobilize the muscle. Another way to provide extended coverage of the sacrum is the use of bilateral V–Y advancement flaps, one based on the right gluteal area and one on the left gluteal area (see Fig. 19).

Ischial Pressure Sores

The ischial tuberosities are under high pressure in a seated patient. Unilateral or bilateral ischial sores develop in individuals who are seated for protracted periods of time without adjusting their position and weight distribution. Ischial wounds are challenging for several reasons. The pressure points are bilateral, which means that relieving pressure over one ischium shifts increased pressure onto the contralateral side. Resecting bone on both sides risks shifting weight onto the perineal soft tissues, resulting in scrotal or urethral sores. Chronic and deep ischial pressure sores can develop fistulae involving the rectum or urethra. Control of the fistulae and/or fecal or urinary

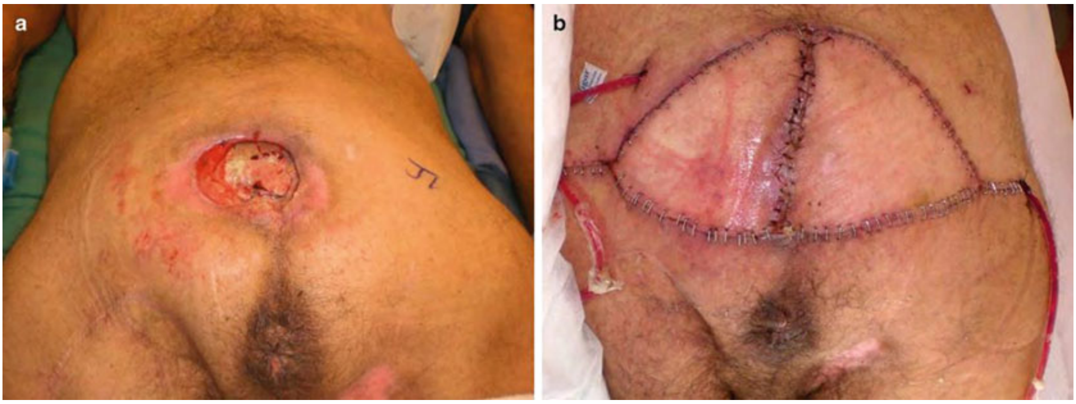

Fig. 19 **(Above)** This male nursing home patient had a stage IV sacral pressure sore with exposed sacrum. (**a**) Preoperative view in the prone position. (**b**) Postoperative view after bilateral gluteus maximusmusculocutaneous V–Y advancement flaps. Note the use of surgical drains under the flap donor sites

diversion must be considered before addressing ischial sores. Finally, because of the strong hip flexors, there can be flexion contractures with varying degrees of deformity which reduce mobility and the capacity for normal weight distribution in either the sitting or the lying position.

Because the ischium has a number of surrounding muscles, a variety of suitable flaps for coverage have been described. These include the inferior gluteal fasciocutaneous thigh flap, inferior gluteus maximus rotational flap, V–Y hamstring advancement flap, gracilis muscle flap, tensor fascia lata rotational flap, and rectus abdominis rotational flap. The first two are considered the most durable flaps and are described in more detail below.

The inferior gluteal fasciocutaneous thigh flap, also called the posterior thigh flap, is a good first choice. This flap is robust and reliable and preserves the gluteus maximus muscle for use in case of future recurrence. The posterior thigh region is supplied by perforators from the descending branch of the inferior gluteal artery. This artery descends deep to the gluteal muscles in a midline axis between the ischium and the greater trochanter and courses toward the popliteal fossa. The distal limit is about 8 cm proximal to the popliteal fossa [133]. The base of the flap should be about 10–12 cm wide, and the point of rotation is 5 cm superior to the ischial tuberosity (see Fig. 20a, b). The descending branch of the inferior gluteal artery is transected distally and preserved proximally as the flap is raised from inferior to superior up to the gluteus maximus muscle and rotated medially to fill an ischial defect (see Fig. 20c, d). If excess length of the flap is available, the distal end can be the de-epithelialized and the subcutaneous tissue tucked into the ischial crater to further eliminate dead space (see Fig. 21).

The other useful flap is the inferior gluteus maximus rotational flap which can be rotated into the ischial wound as a rotational advancement (see Fig. 22) or a rotational island flap. In the latter case, a skin island over the inferior half of the muscle, lateral to the ischial defect, can be elevated with the muscle and rotated medially (see Figs. 23 and 24).

Despite the variety of flaps available to cover an ischial defect, surgical repair is associated with recurrence rates as high as 75 to 77% since patients almost always return to sitting after flap repair [134].

Greater Trochanter Pressure Sores

Given the mobility of the hip, pressure sores over the greater trochanter characteristically have extensive bursa formation with less skin involvement. After resection of the entire defect, obliterate the dead space, and close the ischial pressure sore. Note the two surgical drains: one for the posterior thigh donor site and one for the ischial recipient site.

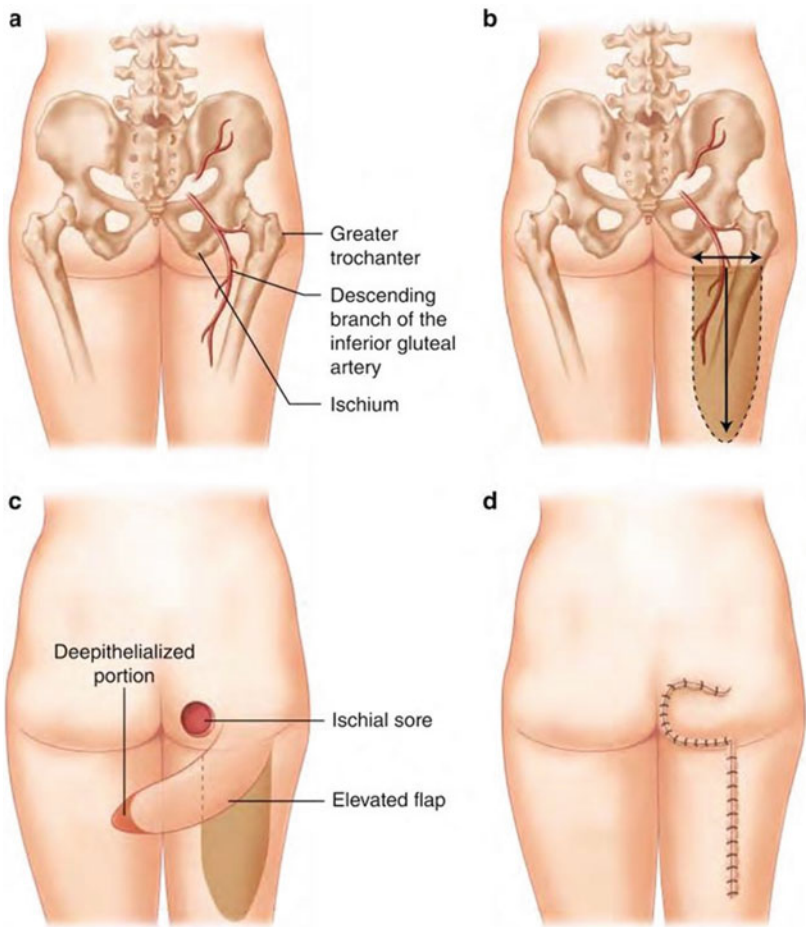

Fig. 20 **(Right)** The inferior gluteal thigh flap. (**a**) The descending branch of the inferior gluteal artery comes off at the midline of the posterior thigh. (**b**) This descending branch supplies the posterior thigh soft tissues, so a flap is designed to allow rotation into the ischial defect and primary closure of the donor site. (**c**) Rotation of the posterior thigh flap medially, inset of the flap into the wound, and primary closure of the donor site. (**d**) Immediate postoperative view after inset of the flap. (Reprinted from McCarthy J. Current therapy in plastic surgery. WB Saunders. © Elsevier (2005))

Foot Pressure Sores

Unlike pressure sores within the pelvic girdle, most pressure sores over the heels, malleoli, and the plantar surfaces of the feet are modest in size and depth. Pressure sores of the feet respond favorably to conservative treatment, particularly in non-weight-bearing areas where less durable soft tissue coverage is required. A scar left by wound contraction and epithelialization may suffice. In larger wounds, debridement and split-thickness skin grafting may expedite closure if the wound bed demonstrates vascularized soft tissue granulation capable of supporting a skin graft. Osteomyelitis of the calcaneus, or any devitalized bone of the foot, must be recognized and debrided if present. Where flap coverage is mandatory, muscle flaps of the abductor digiti minimi, abductor hallucis, and flexor digitorum brevis are described. Fasciocutaneous flaps based on the dorsalis pedis, medial plantar, and lateral plantar arteries can also provide coverage.

Postoperative Care

The postoperative care of surgical flaps includes intravenous antibiotics when indicated for culture-positive osteomyelitis and protection of surgical wounds from urinary and fecal contamination.

Repositioning is critical to protecting a newly transferred flap vulnerable to pressure necrosis in the early postoperative period.

Fig. 21 **(Left)** This man had a chronic left ischial pressure sore that would not heal. (**a**) Preoperative view of ischial pressure with markings for a posterior thigh flap. (**b**) Elevation of the posterior thigh flap, showing it as a fasciocutaneous flap. (**c**) *Inset* of posterior thigh flap to fill the inferior half of the gluteus maximus muscle maintaining the perforators to the overlying soft tissue island. (**d**) Island flap is rotated medially into the defect and the donor site primarily closed. Note the two surgical drains: one in the donor site and one in the ischial wound recipient

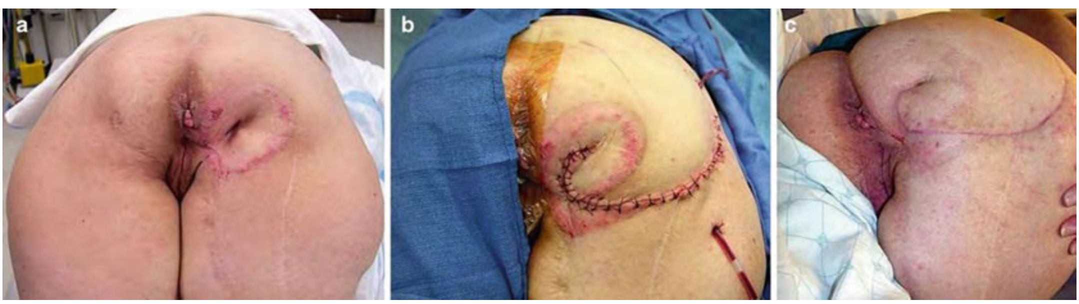

Fig. 22 **(Bottom)** This woman had a recurrent right ischial pressure sore. (**a**) On her preoperative view, note the two vertical scars on her posterior thigh, evidence of a previous hamstring advancement flap. These scars preclude the use of a posterior thigh flap. (**b**) After debridement of the wound and rotational advancement flap of the inferior half of the gluteus maximus muscle with its overlying soft tissues, the flap is *inset*, closing the ischial defect. Note the two surgical drains: one superiorly for the donor site and one inferiorly for the ischial wound recipient site. (**c**) Postoperatively with good healing and intact closure at 3 months

Closed surgical drainage systems are often placed between flaps and the recipient bed to reduce the incidence of postoperative seroma and infection. Drainage should be maintained until the patient has recovered some degree of mobility and fluid output has tapered to a small volume per day.

Spasticity of large muscles, such as the hip flexors, can impede wound healing and compromise surgical flap closure by placing repeated

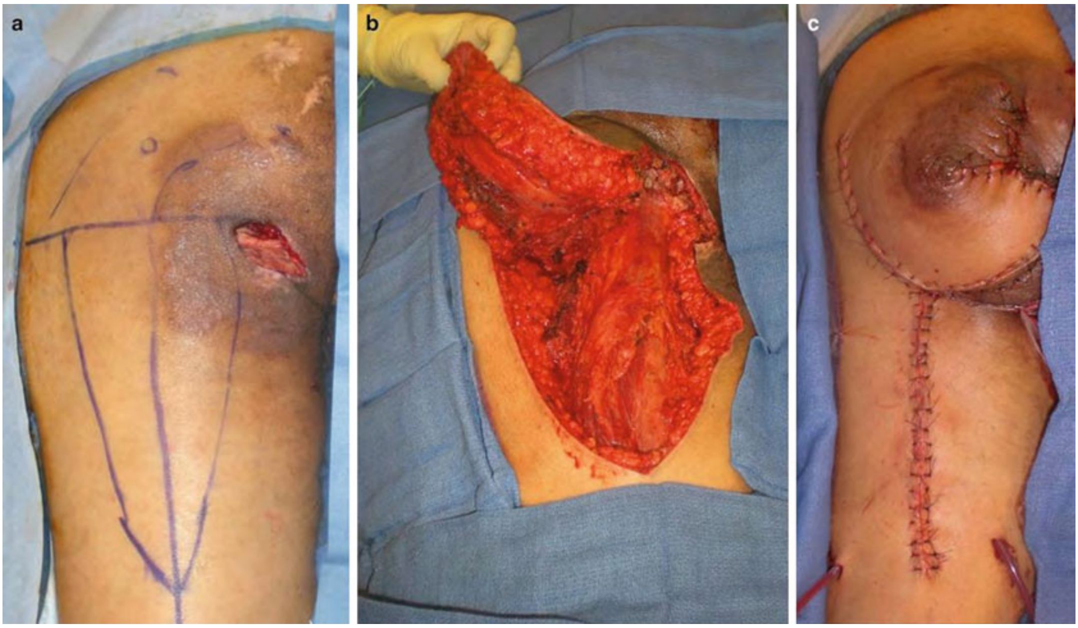

Fig. 23 **(Superior left)** This man had a new-onset right ischial pressure ulcer. (**a**) Preoperative view in the prone position shows stage IV wound that tracks to bone. (**b**) After debridement, the wound is larger, and a musculocutaneous island flap is designed lateral to the wound, overlying the inferior half of the gluteus maximus muscle. (**c**) Elevation of the wound

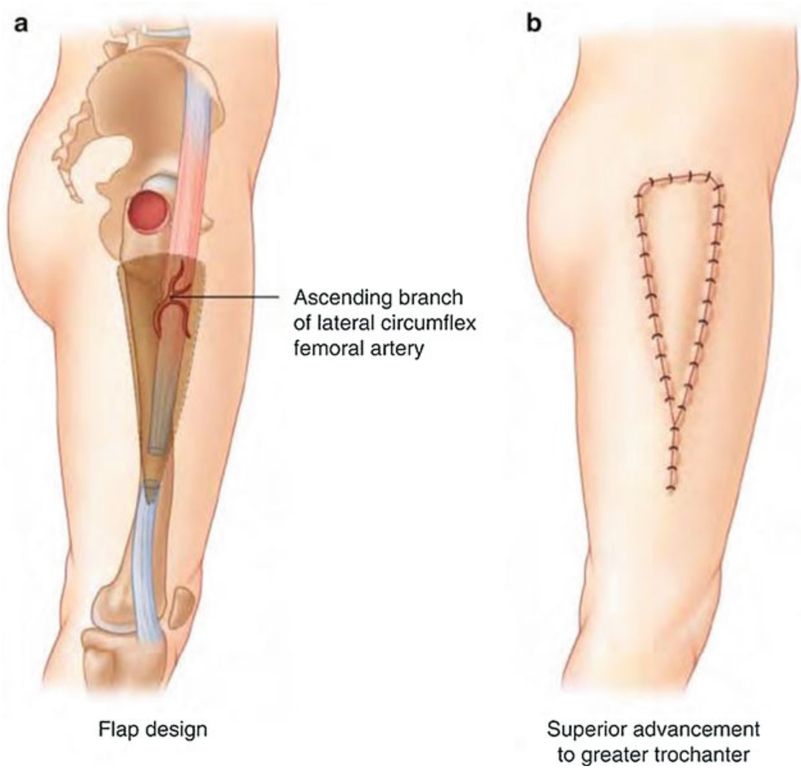

Fig. 24 **(Inferior left)** The tensor fascia late V–Y advancement flap. (**a**) Design of the flap based on the ascending branch of the lateral circumflex femoral artery. (**b**) Closure after flap advancement and inset. (Reprinted permission from Mthes SJ Nahai F (1997) Reconstructive surgery: principles, anatomy and technique. Quality Medical Publishing, St Louis)

tension over incisions and bony prominences. Spasticity can be addressed pharmacologically with muscle relaxants and antispasmodics, such as benzodiazepines, baclofen, and cyclobenzaprine. Refractory spasticity may respond to infusion pumps, nerve blocks, rhizotomies, or epidurals [135]. Physiatry should also be consulted for splinting and physical therapy.

The postoperative protocol is customized depending on the patient, the pressure sore, and the specific flap repair performed.

Air-fluidized mattress can assist in off-loading pressure following sacral or ischial flap closure as these patients will require prone positioning with frequent side-to-side turning. When it is time to begin ambulation or resume sitting in a chair, typically between 3 and 6 weeks, the transition is carefully planned and customized. A common protocol, for example, gradually adds 30 min increments of daily sitting as tolerated [116].

Regardless of immediate postoperative success, pressure sore flap coverage has a high rate of recurrence of about 40% over the long term. Many studies consistently report postoperative pressure sore recurrence within the first 15–22 months [136]. These observations attest to the difficulty of controlling the multiple etiologic factors of this disease including the underlying medical conditions, glucose control, malnutrition, and altered mentation and sensation. Frequent repositioning, vigilant flap monitoring, and daily local wound care are labor-intensive for caregivers and their families. Social issues such as lack of financial resources, inadequate family and/or community support, and drug and alcohol abuse also contribute to the high rate of postoperative pressure sore flap failure and recurrence in the elderly.

Case Study

A 72-year-old man with Alzheimer's dementia is having significant difficulty taking care of himself and performing the activities of daily living (ADLs). He has a history of two myocardial infarctions, congestive heart failure, chronic obstructive pulmonary disease, and insulin-dependent diabetes mellitus and is recovering from a colectomy for stage III cancer, complicated by acute respiratory decompensation requiring ventilatory support. During his convalescence from the colectomy, he developed a 4 cm sacral pressure sore that is fibrinous and foul-smelling and tracks to bone. Discuss the evaluation and management of this pressure sore.

Elderly patients with dementia and those with severe, acute conditions may be deconditioned and debilitated; being bedridden results in chronic pressure over the sacrum and the development of a pressure sore with soft tissue injury deeper than appears on the surface. Correction of the intrinsic and extrinsic factors contributing to the pressure sore is the first step in treatment.

Since the wound is foul-smelling, necrotic tissue harboring infection is present. The first step is excisional debridement, at bedside or in the operating room, with cultures of the deep tissue for both treatment and staging. In addition to serial debridement, enzymatic agents such as collagenase and negative pressure therapy should be considered, while the appropriate lab tests and radiographic imaging is performed.

Intrinsic factors in this patient's case include stabilizing his cardiopulmonary disease, managing his diabetes, and addressing his nutritional status. Obtaining baseline albumin, prealbumin, transferrin, calorie, and protein counts will help determine if wound healing vitamins and protein supplements are needed to maintain caloric intake.

Extrinsic factors: Frequent turning and repositioning on an air-fluidized mattress will eliminate pressure over the sacrum. Prognosis and treatment of the patient's colon cancer should be discussed with his oncologist and colorectal surgeon. If appropriate, a diverting colostomy would eliminate incontinence and soiling of the sacral pressure wound.

If this patient's general condition is deemed unsuitable for surgical closure, a plan for chronic wound care with dressings or negative pressure therapy should be initiated. For positive bone cultures, a schedule for intravenous antibiotics should be developed with an infectious disease specialist. Social services will help determine eligibility either for a long-term care facility or arrangements for home care with the provision of a low-pressure bed and nursing care.

If the patient is a good surgical candidate, debridement followed by flap closure would be planned. After debridement, the wound is 8 cm in diameter. The soft tissues surrounding the sacrum receive their blood supply from the superior and inferior gluteal arteries. Since this patient has no previous surgical scars, either a rotational or V–Y advancement flap may be considered. He will be ambulatory, so sparing the gluteus maximus muscle is desirable. Given the size of the wound, bilateral V–Y fasciocutaneous advancement flaps would be a good choice.

The patient's postoperative care would include the use of surgical drains, protective dressings with routine flap monitoring, bed rest on an air-fluidized mattress, deep vein thrombosis prophylaxis, antibiotic adjustments as dictated by intraoperative cultures, and management of his medical conditions. Provided the wound heals satisfactorily, graduated mobilization could begin at about 3–4 weeks.

Conclusions

Pressure sores are a common problem, with a majority of them affecting the elderly population. The etiology or pressure sores is complex, and multidisciplinary treatment is needed. Extrinsic and intrinsic factors must be addressed before considering surgical flap closure with its anesthetic risks, long healing process, and high recurrence rate. A clean open wound, even with exposed bone and osteitis, can be maintained with consistent wound care and repositioning in elderly patients who are high risk for surgery or pressure sore recurrence.

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Abdominal Wall Hernias in the Elderly

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Abstract

Abdominal wall hernia repair is the most common surgical procedure in the United States. With the US elderly population expected to nearly double in size from 2012 to 2050 (Ortman et al., US Census 1964:1–28, 2014), physicians should expect to see an increasing

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number of elderly patients presenting for evaluation and treatment of abdominal wall hernias. The elderly population deserves special attention as this population often has more comorbidities and shorter life expectancy as compared to a younger population. Thus, it is important for clinicians to discuss goals of care and the risks of treatment options with their elderly patients. Although there is a general paucity of data on outcomes in the elderly hernia population, more data is becoming available for review. Laparoscopic herniorrhaphy appears to be a safe technique for many elderly patients. Watchful waiting has also arisen as a potential option for patients with asymptomatic or minimally symptomatic groin and ventral hernias. This chapter will focus on the preoperative evaluation, repair, and complications of inguinal and incisional/ventral hernias in the elderly. Other hernias will be discussed separately at the end of the chapter.

Keywords
Elderly hernia · Inguinal · Ventral · Incisional · Herniorrhaphy

Case Studies

Case Study #1

Background

A 67-year-old male with a past medical history notable for an asymptomatic right inguinal hernia presents to the emergency room with chief complaint of increasing right groin pain. The patient was first diagnosed with a right inguinal hernia 10 years ago after he noticed it in the shower. After thorough discussion with his physician, he was deemed a candidate for elective repair or watchful waiting. The patient opted for watchful waiting as he was currently the primary caregiver for his ill mother who lived with him at home. Although initially not painful, in the last few weeks he has been experiencing intermittent pain in his right groin. Today, his hernia became "stuck out" and has become progressively more painful. He cannot remember the last time that he had a bowel movement. On exam, he is mildly tachycardic. His right inguinal hernia is incarcerated, and due to some erythema over his groin, there is concern for strangulation.

Management

The patient is taken urgently to the operating room for repair of his right incarcerated inguinal hernia. An open approach is selected by the surgeon, and general anesthesia is administered due to concerns that a local anesthetic will not be effective alone due to the inflammation. During the operation, bowel is found within the hernia sac but appears to be viable, so no bowel resection is performed, and a mesh repair ensues. The patient recovers without incident and is sent home the next day. At his 2-week follow-up appointment, there is no erythema or evidence of recurrence. At his 6-week follow-up appointment there is again no evidence of recurrence, and he is cleared to begin lifting items heavier than 10 pounds.

Case Study #2

Background

A 70-year-old female with a past surgical history notable for an open right hemicolectomy 3 years ago presents to the general surgery clinic with the chief complaint of a painful abdominal bulge. The patient reports that the bulge has been present for 6 months. At first, she did not have pain at the site, but in the last 1 month she has been experiencing daily pain especially when lifting heavy objects. She notes that she can press the bulge back into her abdomen but that as soon as she does, it pushes back out. She denies any changes in her bowel movements. Her past medical history is otherwise notable for well-controlled hypertension and migraines. She has no history of COPD, diabetes mellitus, or falls, and she does not use tobacco products. She lives with her husband who is healthy. On exam, the patient's vital signs are stable, and her BMI is 29. She has a large abdominal bulge at her well-healed laparotomy scar. The bulge is soft and nontender, and there is no overlying edema or erythema. The edges of the rectus fascia are palpated and estimated to be 12 cm apart.

Management

After examining the patient, the surgeon discusses treatment options with the patient including open ventral hernia repair versus watchful waiting. Given the patient's daily pain and overall good health, the general surgeon recommends proceeding with elective open repair with bilateral components separation. Prior to the operation, an abdominal CT scan is recommended to better delineate her anatomy. The general surgeon also discusses involving a plastic surgeon to assist with the components separation. The patient agrees to the plan and meets with the plastic surgeon 1 week later. Her preoperative abdominal CT scan confirms a 12 cm mid-abdominal wall defect. After obtaining her scan, she undergoes an open ventral hernia repair and a bilateral components separation with placement of a bridging mesh in an underlay fashion followed by primary repair of the fascia. During closure, no increase in peak airway pressures is noted. Two subcutaneous drains are placed, and a well-fitted abdominal binder is put on the patient prior to extubation. The patient recovers without complication, and she is discharged from the hospital 2 days later. One week later she is seen by the general surgeon and reports normal bowel movements and minimal pain. One of her surgical drains is removed. Two weeks after this, she is seen by the plastic surgeon and her sutures are removed as well as her final drain. At her 6-week follow-up appointment, she is cleared to begin lifting items greater than 10 pounds and to begin weaning her abdominal binder. At 12 weeks, she is back to her normal activities.

Introduction

Abdominal wall hernia repair is the most common surgical procedure in the United States, with more than 1,000,000 herniorrhaphies being performed annually. Of these, 750,000 are inguinal, 166,000 are umbilical, 97,000 are incisional, and 25,000 are femoral [2]. The incidence of groin hernias in men over age 65 is approximately 13 per 1,000 population [3]. The incidence in women is 12–25% that of men. In a British study of more than 30,000 inguinal hernia repairs, 27% were in an elderly population, 85.5% of repairs on patients aged 65 or older were elective, and the remaining 14.5% were classified as emergency procedures [4]. With the US elderly population expected to nearly double in size from 2012 to 2050 [1], surgeons should expect to see an increasing number of elderly patients presenting for evaluation and treatment of hernias. Given that the majority of all hernias are inguinal and given the great surgical comorbidity that may be associated with incisional/ventral hernia repair, this chapter will focus on the preoperative evaluation, repair options, and complications of inguinal and incisional/ventral hernias in the elderly. Umbilical, Spigelian, and other hernias will be discussed separately at the end of the chapter.

Special Considerations

The elderly population deserves special attention when considering management of abdominal wall hernias as this population often has more comorbidities and shorter life expectancy as compared to a younger population. Additionally, the elderly may suffer from malnutrition, cognitive impairment, and functional dependence. Given this, it is easy to see how an operative complication could lead to prolonged hospital stay, inability to be discharged to home, and overall decreased quality of life in this special population. While several adult surgical risk calculators have been developed to help guide clinicians in discussions with their patients, important risk factors specific to the elderly population have often been left out. Additionally, there is a lack of data regarding the general disease course of hernias in the elderly [5]. Thus, it is imperative that health-care professionals have open and frank conversations with elderly patients before any decision is made regarding treatment of abdominal wall hernias.

For an elderly patient who presents electively for hernia repair, several important considerations must be made after the diagnosis is established. First, the patient must be determined to have decision-making capacity. Second, the provider must assess the patient's overall goals of care. Thirdly, the patient's functional status should be evaluated as this is a strong predictor for surgical outcomes. Next, the provider should discuss the varying treatment options and their risks and benefits for the specific patient. If surgery is considered, all modifiable risk factors should be identified and optimized prior to the procedure [5].

Generally speaking, femoral hernias and groin hernias in females should be surgically repaired due to the high risk for incarceration. Consideration for surgery is given for both symptomatic and asymptomatic groin and ventral hernias. For asymptomatic groin hernias in males, watchful waiting has arisen as option over elective surgery and will be discussed further in detail later in the chapter. Trusses have been historically used to palliate the symptoms of inguinal hernias; however, the data have shown that they are infrequently worn, uncomfortable, improperly fitted, and under the best circumstances, provide appropriate relief in only 31% of patients [6].

When discussing elective hernia repair with an elderly patient, the provider must determine whether or not surgical interventions are in line with the patient's goals of care. Goals of care may include prolongation of life, maintenance of functional independence so as to live at home alone or to not be a burden on family members, and maximizing comfort. Surgical interventions must then be assessed for the ability to decrease the chance of death, cure the hernia without recurrence, improve function, and/or relieve chronic pain. In hernia surgery specifically, the risk of incarceration and strangulation must be weighed against the need for general anesthesia such as in laparoscopic surgery versus the availability of repair under local anesthesia such as in open repairs, the risk for major visceral and vascular injuries, expected length of hospital stay, and rate of recurrence. These details as related to specific hernia type will be discussed further later in this chapter.

As a population ages, the incidence of comorbidities increases while functional status decreases. Functional status may be classified into one of three categories depending on the ability to perform activities of daily living (ADLs): independent, partially dependent, totally dependent. Elderly patients with decreased functional status may report difficulty with ambulating or a history of falls in addition to difficulty bathing or eating. A history of falls or difficulty ambulating is particularly concerning in patients considering an open hernia repair who may have a large incision postoperatively and whose ambulation may be further limited by pain. Poor preoperative functional status has been associated with increased surgical complications and length of stay. In an analysis of over 76,000 patients undergoing ventral hernia repair, totally dependent patients had an increased risk for all adverse short-term outcomes: wound occurrence, pneumonia, pulmonary embolism, deep venous thrombosis, urinary tract infection, myocardial infarction, sepsis, and return to the operating room. Mortality was also increased [7]. In the orthopedic literature, poor preoperative functional status has also been associated with increased risk of discharge to a facility versus home after hip repair [8]. Given this data, physicians may consider nonoperative management in functionally dependent elderly patients. Notably, however, emergent surgery also leads to significant morbidity and mortality in this special population. Thus, physicians must appreciate the added risks in functionally dependent population and counsel these patients carefully.

Prior to elective repair of abdominal hernias, all modifiable risk factors should be optimized. For those with poor functional status, preoperative work with physical and occupational therapists may be beneficial in addition to obtaining home assistive medical equipment and planning for postoperative rehabilitation therapy [9, 10]. Conditions that may cause increased intra-abdominal pressure should also be investigated and corrected, if possible. Increased intra-abdominal pressure puts stress on the repair, interferes with normal wound healing, and may predispose to recurrence. Constipation, symptoms of prostatic hypertrophy, chronic cough, and obesity are common conditions associated with increased tension on the abdominal wall. Managing the first three conditions with medications sufficiently to proceed with operation can often be accomplished in several weeks. Obesity cannot, however, and should not be controlled rapidly. Therefore, significant weight loss should not be used as an absolute prerequisite for repair. Other modifiable risk factors that should be addressed prior to surgery include things such as active smoking, poor control of diabetes or hypertension, anemia, and lack of a support system.

Groin Hernias

The inguinal and femoral canals are anatomically one of the most confusing areas of the human body (Fig. 1). The inguinal canal is bordered anteriorly by the external oblique fascia and posteriorly, also called the floor of the canal, by the transversalis fascia. The superior border is the transversus abdominus and the inferior border is the inguinal ligament, which is itself the inferior edge of the external oblique muscle. The inguinal canal houses the ilioinguinal nerve, the genital branch of the genitofemoral nerve, and the spermatic cord (men) or the round ligament (women). There are two openings to the inguinal canal called the deep inguinal ring and the superficial inguinal ring. The deep inguinal ring is the entrance to the canal and is found above the inguinal ligament at its midpoint, lateral to the epigastric vessels. The deep inguinal ring is made up of an invagination of the transversalis fascia. The superficial inguinal ring is immediately superior to the pubic crest and marks the end of the canal. It is formed by the evagination of the external oblique aponeurosis. The spermatic cord in males or round ligament in females courses through the inguinal canal from the deep inguinal ring to the superficial inguinal ring. The spermatic cord itself is composed of the cremasteric muscle, pampiniform plexus, testicular artery, genital branch of the genitofemoral nerve, vas deferens, cremasteric artery, lymphatics, and the processus vaginalis which may or may not be patent (Fig. 1b). The conjoint tendon, made of the common aponeurosis of the internal oblique and transversus abdominus muscles, inserts onto the pubis immediately behind the superficial inguinal ring and makes up the medial part of the posterior wall of the inguinal canal.

An important concept in groin anatomy is the myopectineal orifice (Fig. 2). Through this

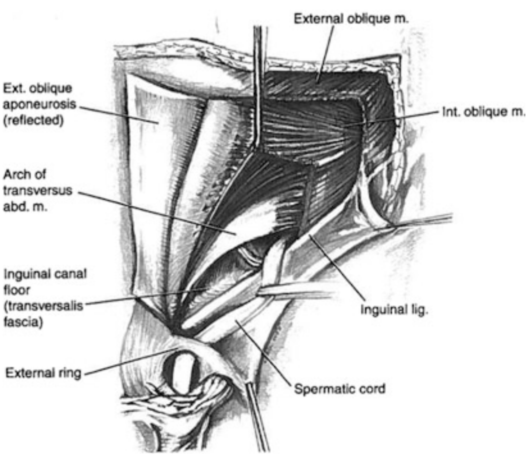

Fig. 1 Anatomy of the inguinal region (reprinted from Mulvihill; Surgery: Basic Science and Clinical Evidence; 2001, with kind permission of Springer Science + Business Media)

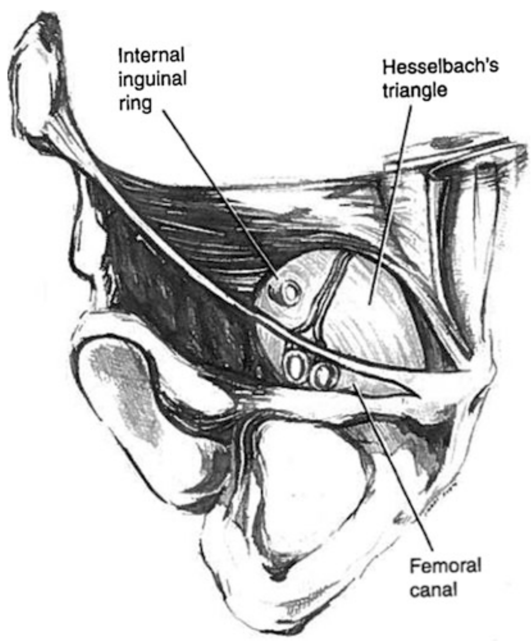

Fig. 2 Myopectineal orifice (reprinted from Mulvihill; Surgery: Basic Science and Clinical Evidence; 2001, with kind permission of Springer Science + Business Media)

anatomic opening, structures traverse from the pelvis to the leg. The myopectineal orifice is bound by the rectus abdominus muscle medially, the iliopsoas muscle laterally, the internal oblique and transversus abdominus muscle superiorly, and the superior pubic ramus with Cooper's ligament inferiorly. The inguinal ligament divides the orifice with the spermatic cord and the femoral vessels passing anterior and deep to the ligament, respectively. The transversalis fascia spans the inner surface. Groin hernias begin as a weakness in the myopectineal orifice when the transversalis fascia attenuates, allowing for a peritoneal bulge [11]. Hernia repair involves fixing the myopectineal orifice or using mesh to replace the attenuated transversalis fascia [12].

The myopectineal orifice can further be divided into three triangles – the medial, lateral, and femoral [13] (Fig. 2). The medial and lateral triangles are separated from the femoral triangle by the inguinal ligament. The inferior epigastric vessels divide the medial and lateral triangles from each other. Groin hernias are either inguinal or femoral. Inguinal hernias occur through the medial or lateral triangles and are termed direct or indirect inguinal hernias, respectively. As such, indirect hernias pass through the deep inguinal ring, lie anterior and medial to the vas deferens within the spermatic cord, and descend through the inguinal canal to the scrotum. These are more commonly congenital and arise from a patent processus vaginalis. Direct hernias pass directly through the floor of the inguinal canal and point anteriorly. This area in the floor of the canal is referred to as Hesselbach's triangle and is bordered by the lateral border of the rectus abdominis muscle, the inferior epigastric vessels, and the inguinal ligament. These are acquired hernias that are due to a weakness of the inguinal floor. A pantaloon hernia has both a direct and indirect component. Femoral hernias occur through the femoral triangle of the myopectineal orifice, medial to the femoral vessels and below the inguinal ligament. Femoral hernias are a variation of direct hernias in which the inguinal ligament prevents the sac from protruding through the inguinal floor. Instead, the sac passes through the femoral canal [14].

Inguinal hernias in elderly persons present very specific challenges. For example, they are frequently long-standing. Many have been present for 10–20 years, although some may have occurred as long as 50–60 years prior to presentation for repair [15–17]. As a result of the chronic nature of these hernias, the surrounding normal anatomic architecture is disrupted and there is loss of appropriate tissue planes to facilitate repair.

Furthermore, with age comes the anticipated loss of muscle mass and tissue strength, making an anatomic repair more difficult. By the age of 80 up to 40% of muscle mass may be lost, with a proportional increase in body fat [18]. Increased comorbidities in this age group can make elective repair challenging, but operative morbidity and mortality is still remarkably low. Prolonged neglect, however, can result in a high incidence of preoperative complications, such as bowel obstruction, incarceration, and strangulation. These conditions frequently necessitate emergency treatment. In a Swedish study, patients undergoing emergent operation for inguinal hernias were on average 12 years older than those undergoing elective repair (70 vs. 58 years old) [19]. However, data suggest that watchful waiting may be a viable option for some in this population [20, 21]. There is also increasing data to suggest that the use of laparoscopy and biologic materials may be of particular interest to this demographic. These issues will be discussed in more detail later in the chapter.

Etiology and Distribution

The etiology of groin hernias differs somewhat in the elderly population. Indirect inguinal hernias, which are often congenital, comprise 90% of the hernias in young men, but account for only 50–60% of hernias in older men. The incidence of direct hernias increases to 35% in men over age 65 years old [16]. Furthermore, the incidence of sliding hernias also increases from 0.5% during the third decade of life to as much as 13% during the sixth to eighth decades of life [22].

There are several reasons for this shift in the incidence of hernia types with age. Acquired hernias are more common with increasing age and are often associated with other physiologic changes or disease processes. In most cases the pathophysiologic mechanism of an acquired hernia is a structural inadequacy of the inguinal floor, which manifests as a direct inguinal hernia. A recent study compared the structure of the rectus sheath in patients undergoing inguinal hernia repair and those undergoing appendectomy and found a significant difference between the patients in terms of alignment and quality of collagen and elastic fibers. In those with inguinal hernias, there was increased disorganization of collagen fibrils, thinning of elastic fibrils, and generalized replacement with ground matter [23]. A similar study showed that these changes were present in the transversalis fascia of both the herniated side as well as the nonherniated side [24].

The inguinal floor may therefore be weakened by any factors that interfere with normal collagen and elastin production. These include congenital connective tissue disorders such as Marfan and Ehler–Danlos syndromes, as well as metabolic defects in collagen formation. Cigarette smoking also plays a significant role in hernia formation. The same proteases and elastases found in the lungs of smokers that lead to emphysema are also found in their serum and can bring about the destruction of elastin and collagen in other tissues. Systemic illnesses with an enhanced leukocyte response can also lead to the release of proteases and antioxidants having a similar effect [25].

Other factors associated with groin hernia formation involve conditions that lead to chronically increased intra-abdominal pressure, such as longstanding constipation and straining, bladder outlet obstruction, chronic cough, obesity, and kyphoscoliosis. Increased intra-abdominal pressure puts tremendous forces on the abdominal wall where there are natural weaknesses, such as the internal inguinal ring and the transversalis fascia. In the elderly patient, it is not uncommon for several of these predisposing conditions to be present simultaneously. Occasionally, this confluence of factors contributes to the development of a giant hernia or one with a large scrotal component. These hernias can become extremely large and may contain a significant portion of the abdominal viscera. When forced reduction of the viscera into the contracted abdominal cavity is attempted, severe respiratory compromise due to increased intra-abdominal pressure and decreased diaphragmatic excursion may occur.

Approximately 15–30% of all herniorrhaphies in the elderly are performed on an emergent basis as a result of incarceration. Overall, 50–60% are indirect and 17–25% are femoral. When separated by gender, 73% of incarcerated hernias in men are indirect and 15% are femoral, whereas femoral hernias account for 50% of incarcerations in women [15, 26, 27]. Although rare, once strangulation has occurred, the hernia changes from a simple mechanical problem to a complex life-threatening systemic illness, and the repair changes from correction of a simple mechanical defect to reversal of a major abdominal catastrophe.

Diagnosis

Up to one-third of patients with groin hernias are asymptomatic [28]. In 70% of patients, complaints typically include the presence of a groin or scrotal mass and pain in the inguinal region. Other symptoms include a heaviness or a dragging sensation in the groin which is often worse at the end of the day. The pain may also wax and wane if the hernia is reducible. In many cases the patient has been aware of, or diagnosed with, a hernia for many years.

Historic factors that contribute to the development of inguinal hernias should always be elicited. Respiratory symptoms with chronic cough, chronic constipation, and symptoms of bladder outlet obstruction are most prevalent in an older population. Examination for the presence of groin hernias should be part of the standard physical exam. Patients should be examined in the erect position, as a reducible hernia is sometimes more difficult to appreciate in the supine position. The only visible abnormality may be groin asymmetry.

Indirect inguinal hernias appear as a small mass in the region of the deep ring, midway between the pubic tubercle and the anterior superior iliac spine. Direct hernias appear more medially, although this distinction is not always clear. Invaginating the skin of the scrotum and introducing the examining finger along the spermatic cord structures into the external inguinal ring will allow for diagnosis. Prolonged standing or increasing intra-abdominal pressure by coughing or with Valsalva maneuver causes the sac and its contents to descend toward the examining finger, where it is felt as a mass or a transmitted impulse. A small hernia defect or a sac that is difficult to reduce presents the greatest risk for future incarceration. In women, inguinal hernias may be difficult to diagnose until they become quite large.

It is not always easy to distinguish an inguinal hernia from a femoral hernia. Femoral hernias more often present with poorly localized pain in the groin area without an obvious, visible bulge. It is important when examining the groin to include an examination of the upper thigh below the inguinal ligament in order to assess for femoral hernias. Most femoral hernias can be felt as a soft mass medial to the femoral vessels. Frequently, hernias in this location are mistaken for inguinal lymph nodes or lipomas. Increased intra-abdominal pressure may transmit an impulse through the sac, but this too can be mistaken for normal transmission of the increased pressure in the femoral vein. Unfortunately, because of these subtle findings, femoral hernias are frequently not diagnosed until they incarcerate. In one review of 83 femoral hernias over 40% were repaired emergently for incarceration [29].

The differential diagnosis of a groin mass is extensive and includes hernias as well as lipomas, lymphadenopathy, abscess, varicocele, hydrocele, testicular mass, testicular torsion, epididymitis, and femoral artery aneurysm [30]. Additionally, some patients with groin hernias may present with typical symptoms but demonstrate no visible bulge on exam. For these reasons, an imaging modality for the diagnosis of groin hernias has been sought for years. Ultrasound has been shown to have an accuracy of 92% for all groin hernias and a 75% accuracy for those without a palpable bulge (Fig. 3) [31]. Therefore, it may be a useful adjunct in qualified hands. Computed

Fig. 3 Ultrasound of inguinal hernia (reprinted from [90], with kind permission of Springer Science + Business Media)

Fig. 4 CT image of inguinal hernia (reprinted with permission from [91]. Copyright © Radiological Society of North America)

tomography and MRI scans may also be beneficial in the evaluation of the difficult groin, with MRI having the highest sensitivity and specificity (Fig. 4) [32, 33].

The diagnosis of an incarcerated hernia is usually not difficult to establish. Most often patients present with a previously recognized hernia that has recently “stuck out.” In the case of a femoral hernia, a painful mass in the groin may be the first indication. Obstructive symptoms such as nausea, vomiting, and obstipation may not be present early in the course but develop if the incarceration goes untreated and progresses to strangulation. Notably, some patients may live with chronic incarceration and experience no symptoms [11]. Strangulation, or ischemia to the incarcerated portion, is indicated by increasing pain and signs of systemic sepsis. On physical examination, a tender, nonreducible mass is present in the groin. Erythema and edema of the overlying skin are suggestive of strangulation of bowel in a hernia sac, as is severe tenderness to palpation. Evidence of strangulation is an indicator for immediate surgical correction.

Numerous studies have shown an association between increasing age and risk for incarceration and strangulation of groin hernias [34–36]. A representative study reports incidence of incarcerated inguinal hernia as 16.8% in patients over age 65, compared to only 4.4% in younger patients [37]. Strangulation has been shown to occur in 1.3–3.0% of all groin hernias, most often in the elderly and children [38]. Indirect inguinal and femoral hernias are the most likely hernias to strangulate although scrotal and recurrent groin hernias have also been associated with increased risk for acute hernia surgery [39]. The probability that an indirect inguinal hernia will strangulate is reported as 2.8% within 3 months of diagnosis and 4.5% after 2 years, compared to 22% at 3 months and 45% at 21 months for femoral hernias [40]. Even among the elderly, older age groups have been shown to be at increased risk for requiring emergent repair, with one study reporting nearly that nonagenarians were three times more likely to present for emergent repair of groin hernias as compared to octogenarians (12% vs. 4.4%) [34].

Kulah et al. examined risk factors for strangulation and bowel resection in elderly patients with acutely incarcerated hernias. In examining 189 patients over 65 years old, it was found that femoral hernias were more frequently strangulated and required bowel resection at presentation. Although males were more likely to present with incarcerated hernias, females were likely to have strangulated hernias, possibly due to the increase in femoral hernias in this population. Late admission was also a significant risk factor for strangulation, bowel resection, and increased hospital stay. Importantly, morbidity increased from 15% to 33% when admission was delayed 48 h after onset of symptoms, and mortality increased from 2% to 9% [19].

Emergency Repair

The approach to an incarcerated hernia in the elderly depends on the nature of the incarceration. Chronic incarcerations pose less of a threat of strangulation and can be treated on an elective basis. Acute incarcerations, on the other hand, require immediate surgical treatment. Forceful attempts at nonoperative reduction may result in an en masse reduction of a compromised loop of intestine within the hernia sac. This ischemic bowel may not produce significant abdominal findings in the older patient until full-thickness necrosis and perforation occur. Any patient with skin changes or systemic symptoms – tachycardia, hypotension, fever, leukocytosis, or lactic acidosis – should raise suspicion for progression to strangulation which requires immediate surgical intervention.

The type of repair for incarcerated hernias depends to some extent on the viability of the contents of the hernia sac. A general or regional anesthetic is usually necessary. In the presence of inflammation, local anesthetic agents are usually not effective. In addition, the muscle relaxation provided by regional or general anesthesia may facilitate reduction of the incarcerated organ. If the incarceration is of short duration and there is no erythema or induration of the overlying skin suggesting strangulation, the choice of approach is less critical. Open anterior repair, which allows careful inspection of the sac contents outside the peritoneal cavity, is usually preferred. Frequently, a recently incarcerated hernia is reduced spontaneously or with minimal force when anesthesia is induced. In this setting, identifying the incarcerated loop of bowel through the hernia defect may be difficult but is usually not impossible.

Skilled laparoscopists may prefer to inspect the bowel and repair the hernia laparoscopically through a transperitoneal approach. A study examining TAPP repair of 28 strangulated inguinal hernias demonstrated a conversion to open rate of 10.7%, for either extensive adhesions or bowel distention. Morbidity was only 4% and there were no deaths or recurrences [41]. The same precautions mentioned previously for laparoscopic herniorrhaphy should be considered here.

If the incarceration is of longer duration or there are signs of local inflammation suggestive of strangulation, an open procedure is safest and most expeditious. Many surgeons prefer a direct anterior approach to the hernia. If ischemic bowel is found in the hernia sac, resection can generally be accomplished through the hernia defect. Open repairs are classified as either synthetic repairs (mesh is used) or suture repairs (tissue-only). If there is minimal contamination and broad-spectrum antibiotics are given, a synthetic mesh repair (Lichtenstein repair) is acceptable [42, 43]. If there is gross contamination or concern for bacterial translocation due to partial obstruction, prosthetic mesh should not be placed, and a suture repair method such as the Shouldice method should be used, accepting a higher risk of recurrence in exchange for a lower chance for infection. Others advise that if there is high suspicion for compromised bowel preoperatively, a small lower midline laparotomy or laparoscopy should be performed for more careful inspection of the bowel and a more controlled resection. After the abdomen is closed, an open anterior repair of the hernia with mesh can be accomplished through a re-prepared field. A detailed description of synthetic and suture repair methods can be found in the "Surgical Treatment" section of this chapter.

The consequences of emergency surgery in the elderly population cannot be understated. There is a threefold increase in morbidity and mortality after emergent operation, regardless of the type of procedure [44]. In addition to age, specific risk factors linked to worse outcomes in emergent groin surgery include a history of COPD or dyspnea [36], delay between onset of symptoms and surgery greater than 12 h, femoral hernia site, nonviable bowel, and American Society of Anesthesiologists (ASA) class 3 and 4 [45]. In a Swedish study looking at over 100,000 patients presenting for groin hernia repair, mortality risk as compared to the general population was increased sevenfold for patients who underwent emergent groin operations and 20-fold for patients that underwent bowel resection [46]. Along with increased morbidity and mortality comes the increased need for intensive care and extended hospital stay in these patients, as well as rehabilitative services. Thus, for elderly patients with multiple comorbidities, emergent surgery could be devastating.

Watchful Waiting Versus Elective Repair

Surgical repair has been the gold standard of care for even asymptomatic hernias for decades. Awareness of complications from hernia repairs in addition to cost concerns and a predicted low annual incident of hernia accident have led surgeons to consider watchful waiting as a viable option for male patients with asymptomatic inguinal hernias. To further evaluate this option, Fitzgibbons et al. randomized over 700 North American patients with asymptomatic groin hernias to either open mesh repair or watchful waiting. Thirty-three percent of patients in each group were over 65 years of age. After 3 years of follow-up, pain and health outcomes were similar in each group. Eighty-five patients crossed over to the repair arm mostly because their hernias became more symptomatic. The rate of hernia accident was only 1.8 per 1,000. There were no deaths associated with hernia accidents [47]. This study seems to support a trial of watchful waiting in all asymptomatic or minimally symptomatic patients. A cost analysis performed as part of the Fitzgibbons study showed that a 2-year watchful waiting was a cost-effective option for such patients [48].

An additional study by O'Dwyer sought to answer a similar question looking at the geriatric population in the United Kingdom. One hundred and sixty patients over the age of 55 were randomized to watchful waiting or operation. Over 12 months, there were 23 patients who crossed over to the repair arm, which is over 20% of those randomized to watchful waiting. This article argues that given longer follow-up there would be more crossover to surgery and that elderly patients' health would only deteriorate over that time, making the risks associated with a hernia accident more severe [49]. In this study, like that of Fitzgibbons, the incidence of hernia accident (strangulation) was rare. There were two patients who crossed over from watchful waiting to repair and experienced significant postoperative complications not related directly to the hernia repair (myocardial infarction and stroke) but presumably to the decrease in the patient's overall health. Clearly as a patient ages, his or her general risks for undergoing any type of procedure increases. Notably, in both study populations, patients had presented to their doctors to discuss their hernias. Thus, the results may not be applicable to those patients with hernias who do not present to their physicians.

In updates to both studies, authors found that with increased follow-up there were increased rates of crossover from watchful waiting to surgery [20, 21]. In the North American trial, 68% of patients crossed over at 10 years; in the UK trial, 72% crossed over at 7.5 years. In both studies, increasing pain was the most common cause for crossover. Only a few patients required emergent hernia repair. A further analysis of the North American data showed that delaying hernia repair did not result in differences in hernia characteristics at time of surgery, degree of difficulty of surgery, or rate of surgical complications [50]. Recurrence rates were also similar between the immediate repair group and the crossover from watchful waiting group. From these studies, the authors concluded that although watchful waiting is a safe option, most patients with painless inguinal hernias will eventually develop symptoms warranting surgery [20, 21]. Thus, elective surgical repair should be considered in medically fit patients [21].

In an effort to optimize patient selection for watchful waiting versus surgical intervention, Sarosi et al. analyzed data collected from the American College of Surgeons Hernia Trial, a trial of 336 patients randomized to watchful waiting versus surgical repair for asymptomatic inguinal hernias. Five risk factors were found to be predictive of crossover to surgery: pain with strenuous activity, chronic constipation, prostatisim, being married, and good health (ASA Class 1 vs. 2). From this data, a crossover risk worksheet was created for clinicians to use when presented with a male patient with asymptomatic hernia. While ~1/3 of Sarosi's study population was patients older than 65 years of age, most were white and ASA I or II, making the generalizability of the results to a larger elderly population unknown [51].

Studies have shown that elderly patients undergoing elective inguinal hernia repair experience similar rates of complications as compared to the younger population [34, 39, 52]. In a retrospective review of NSQIP data on nearly 20,000 patients undergoing inguinal hernia repair (open and laparoscopic), Wu et al. found that overall mortality was extremely low for all ASA classes (<0.2%), even in patients older than 80 years of age. However, the data demonstrated an increase in mortality with emergent repair that was related to age (0.6% with age <65 years of age compared to 10.3% with age >80 years of age). No increase in mortality relating to age was seen in elective repair. Additionally, although an odds ratio analysis showed an increased risk of mortality and morbidity with COPD, dyspnea, smoking, hypertension, and diabetes, the overall risk was still low, leading the authors to conclude that elective hernia repair in elderly patients, even those with comorbid conditions and those older than 80 years of age, is safe [53].

Although surgical repair of groin hernias appears to be safe for elderly patients in general, not all elderly age groups may fare the same. To better assess the risk of increasing age on outcomes, a review of over 2,000 patients aged 80 years or older in the NSQIP database who underwent inguinal hernia repair was performed. Compared to octogenarians, nonagenarians had an increased 30-day overall complication rate as compared to octogenarians (6.1% vs. 3.2%). Mortality was increased tenfold (3 vs. 0.3%). Preoperative variables associated with increased morbidity included totally dependent functional status, congestive heart failure, and emergent nature of the procedure. Preoperative variables associated with increased mortality included older age, emergency repair, and having an open wound. From these results, the authors concluded that elective inguinal hernia repair could be safely performed in octogenarians with low morbidity and mortality but is increased in nonagenarians [34].

Anesthesia

The first step in elective hernia repair is the choice of anesthesia. Avoiding anesthetic techniques that place unnecessary stress on cardiac, pulmonary, and renal reserves may minimize the surgical morbidity and mortality. This is more important in elderly patients who often present with multiple comorbidities. Both general and spinal anesthetic techniques are associated with perioperative complications. Guillen and Aldrete reported that in men over age 70 undergoing elective inguinal hernia repair the incidences of hypotension with spinal and inhaled anesthetic were 43% and 36%, respectively [54]. In a randomized trial of local versus general and regional anesthesia, those patients receiving local anesthesia had less postoperative pain, fewer micturation complications, and shorter hospital stays. These results have been backed up by multiple other studies [55–57]. These data support the concept that local field block is the ideal anesthesia method for elective hernia repair in the geriatric age group. There are, however, a few limitations to this method. Patients with dementia or those who for other reasons are unable to understand commands and lie still on the operative table, as well as those who are unusually anxious, are considered poor candidates for local blocks. The excessive use of sedation necessary to control these patients frequently worsens the confusion and results in respiratory complications, which defeats the whole purpose of using local anesthetic. Further problems are encountered in obese patients for whom adequate local anesthesia may not be achievable because of limitations in dose and absorption.

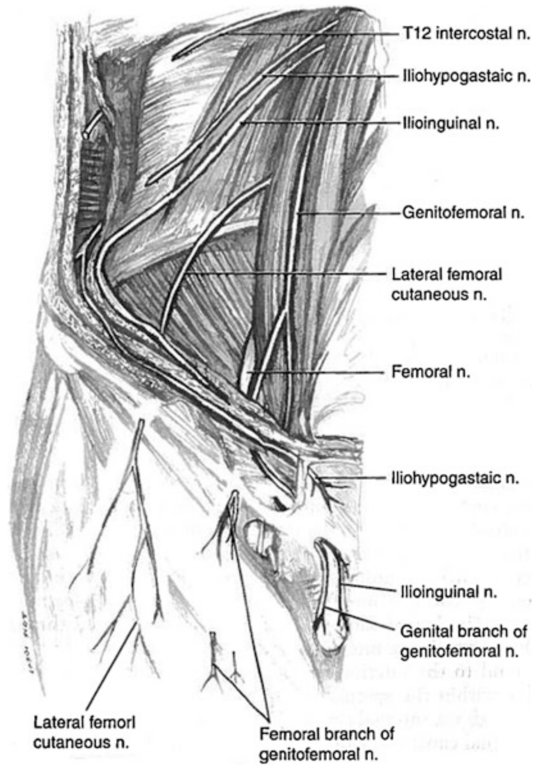

Fig. 5 Nerve supply to the groin (from Mulvihill; Surgery: Basic Science and Clinical Evidence; 2001, reprinted with kind permission of Springer Science + Business Media)

With a detailed understanding of the neuroanatomy of the inguinal region, painless inguinal herniorrhaphy may be accomplished in the elderly patient. The innervation of the inguinal region is complex (Fig. 5). A clear understanding of the intercostal nerve supply is paramount. Following the pattern of dermatome distribution, the tenth thoracic nerve innervates the umbilicus, the first lumbar nerve innervates the inguinal area, and the twelfth thoracic nerve innervates the area in between. The iliohypogastric and ilioinguinal nerves lie deep to the external oblique fascia and lateral to the anterior superior iliac spine. The iliohypogastric originates at the first lumbar nerve and lies under the external oblique aponeurosis after penetrating the internal oblique muscle. This nerve supplies sensory fibers to the suprapubic region. The ilioinguinal nerve follows the same course as the iliohypogastric nerve but lies

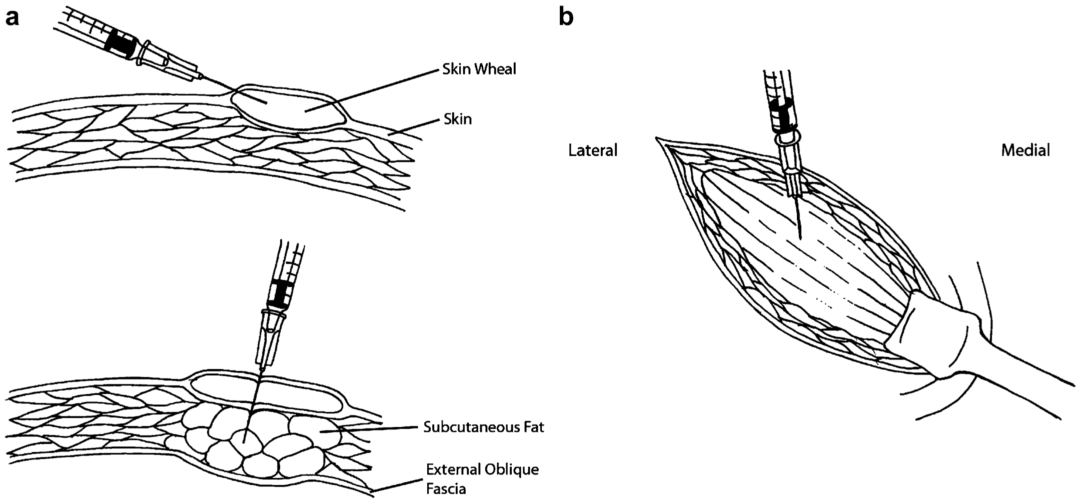

Fig. 6 (**a**) Making the skin wheal. (**b**) Subfascial infiltration

closer to the crest of the ileum and inguinal ligament. The ilioinguinal nerve penetrates the internal oblique muscle approximately 1.0 cm from the anterosuperior iliac spine and supplies sensory innervation to the base of the penis and part of the scrotum (and comparable areas in the female body). The penile skin and a small area of the scrotum are supplied by sensory fibers from the sacral plexus.

When repairing a femoral hernia, more attention must be paid to the ilioinguinal nerve and the femoral branch of the genitofemoral nerve, which supply the upper thigh. The genitofemoral nerve originates from the first and second lumbar nerves to supply sensory fibers to the scrotum and upper thigh and motor fibers to the cremasteric muscle via the genital branch. The genital branch reaches the inguinal canal at the internal abdominal ring. When performing herniorrhaphy under local anesthesia, pain is also felt when traction is applied to the sac or the spermatic cord or when a finger is inserted into the peritoneal cavity. Knowledge of this anatomy is also paramount during the operation to avoid injury to these nerves and thus postoperative inguinodynia.

A simple five-step method has been advocated for the use of local anesthetic during inguinal herniorrhaphy. Appropriate use of this method requires minimal IV sedation with Midazolam and does not necessarily require monitoring or the use of anesthesia staff. A 50:50 mixture of 1% Lidocaine and 0.5% Bupivicaine is used. (1) Approximately, 5 mL of solution is injected subdermally along the entire length of the proposed incision. (2) A skin wheal is then raised using an additional 3 mL along the same path. (3) A total of 10 mL is then injected subcutaneously 2 cm apart. (4) After making the skin incision and beginning to expose the external oblique fascia, 10 mL of solution is injected directly underneath the fascia. This bathes the entire inguinal canal and should anesthetize all three major nerves in this area. (5) Additional injections of a few milliliters of solution may also be injected into the pubic tubercle and the hernia sac and additional solution may be used to bathe the incision prior to closure of the external oblique as well as the skin (Fig. 6a, b) [58]. In this era of cost analysis and health-care economics, inguinal herniorrhaphy is becoming predominantly an outpatient procedure. Even though outpatient general anesthesia is possible, local block facilitates earlier ambulation and is associated with fewer immediate postoperative complications.

Surgical Treatment

Hernia repair may be performed either through an open approach or a laparoscopic approach. Open repairs may be either tissue-only "tension" or suture repairs, or they may be "tension-free" synthetic mesh repairs. Laparoscopic repairs involve two main methods: transabdominal preperitoneal (TAPP) and totally extraperitoneal (TEP).

Suture Repair

Inguinal hernia repair has previously been dominated by an anterior, open approach that uses sutures to reconstruct the inguinal floor with no placement of mesh. This basic tenet of hernia repair has undergone many modifications, with various combinations of suturing the transversalis fascia, conjoint tendon, internal oblique muscle, or transversus abdominis muscle to the inguinal or Cooper's ligament. One of the earliest suture repair techniques was the Bassini technique, first described in 1887 by Edoardo Bassini. In the Bassini technique, the inguinal floor (transversalis fascia) is divided, and the superomedial portion of the fascia along with the conjoint tendon is sutured to the inguinal ligament. Since its first description, the Bassini suture repair has undergone numerous modifications including the Shouldice repair, a technique still used today in select centers. The Shouldice repair, similar to the Bassini repair, opens the inguinal floor; excises redundant, weakened transversalis fascia; and reconstructs the posterior wall using a four-layered suture closure of transversalis fascia flaps [59].

Regarding femoral hernia repairs, one of the classic suture methods described is the Cooper's ligament repair, or the McVay technique. With this technique, the aponeurosis of the transversus abdominus and the transversalis fascia (conjoint tendon) are sewn to Cooper's ligament from the pubic tubercle to the femoral vein. The floor is restored by suturing the femoral sheath to the Cooper's ligament [12].

Synthetic Repair

In 1909, McGavin was the first to use a prosthetic material, a filigree of silver wire, to repair an inguinal hernia [60]. Throckmorton introduced tantalum gauze for use when there was insufficient tissue for adequate primary tissue repair. This material, however, did not prove to be durable. During the 1950s and 1960s, Usher et al. used polypropylene mesh to bolster primary tissue repairs of direct and indirect hernias [61–63]. The premise behind using synthetic materials is to provide a tension-free repair with fewer recurrences and a quicker return to normal activity. It was not until 1986, with the published work of Lichtenstein and Shulman, that synthetic mesh became accepted for primary hernia repair without approximation of the underlying hernia margins (Fig. 7) [64]. With this technique, one single layer piece of mesh is secured over the inguinal floor with a slit to go around the internal ring.

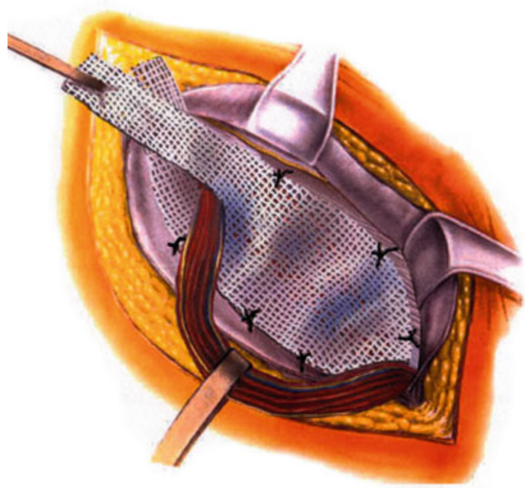

Fig. 7 Lichtenstein repair (from Fitzgibbons RJ, Jr., Abdominal Wall Hernias, Fig. 8. Available at: http://knol.google.com/k/bob/abdominal-wall-hernias/Ilo7ZexB/MyZquQ#What_is_an_abdominal_wall_hernia(3F). Reprinted with kind permission of Springer Science + Business Media)

Data regarding recurrences with a particular hernia repair technique can be difficult to interpret because so much of it comes from specialized hernias center. However, in a recent study comparing the Shouldice (a tissue repair) and the Lichtenstein repair in a general surgery practice, recurrence rates for the mesh repair were 0.7% compared to 4.7% for the tissue repair [65]. A meta-analysis comparing over 11,000 patients from various institutions demonstrated an overall recurrence rate of 2.0% for Lichtenstein mesh repair compared with 4.9% for various tissue repairs and persistent groin pain in 5.1 and 10.1% of patients, respectively [66]. Additionally, a 2002 Cochrane meta-analysis reported a 50–75% decreased risk of hernia recurrence as well as a lower risk for chronic inguinodynia and an earlier return to work with the tension-free approach [67]. Although the Shouldice repair for inguinal hernias has been shown to have a recurrence rate of less than 1% in experienced hands [68], non-specialized centers have been unable to achieve this same low rate [69–71], suggesting that the learning curve is too steep [72]. Suture repairs are typically now used only in cases where mesh may be contraindicated, such as infected or grossly contaminated fields [11].

Since the institution of the Lichtenstein method was first described, a multitude of other methods have attempted to supplant it. The plug-and-patch system was first described in 1993 and utilizes a polypropylene mesh plug to obliterate the defect in the internal ring or the inguinal floor. An additional patch is often used to provide additional support to the inguinal floor (Fig. 8) [73]. Recurrences remain as low as the Lichtenstein method but complications of plug migration and shrinkage have been reported [74].

The Kugel Patch consists of two layers of mesh placed preperitoneally through an anterior approach, thus placing the mesh where it would be placed during a laparoscopic approach. A small muscle splitting incision is used to gain access to the preperitoneal space [73]. Though initial results were very promising showing a recurrence rate of 0.45, these results have never been reproduced and there is a very steep learning curve with recurrence rates as high as 18.2% in the initial learning period and rates as high as 27.8% for recurrent hernias [75, 76].

The Prolene Hernia System (PHS) is another method of prosthetic repair. It consists of two pieces of mesh that serve to overlay and underlay the inguinal floor attached by a mesh connector that is placed either through the internal ring or a defect in the transversalis fascia. The benefits of the PHS are that it touts to repair indirect, direct, and femoral hernias all at once by covering the entire myopectineal orifice preperitoneally [73]. Theoretically, this should reduce hernia recurrence through the lateral triangle of the orifice. As of now, studies demonstrating long-term recurrences with the PHS have not been performed but preliminary results show similar operating times and short-term recurrence rates as both the Lichtenstein and plug-and-patch methods. Some studies have demonstrated less pain with the PHS (Fig. 9) [77, 78].

Currently, there are no studies comparing any of the above techniques specifically in the elderly population. In fact, the majority of studies exclude elderly patients or those with elevated ASA status. It would stand to reason though that any repair amenable to local anesthesia with a relatively

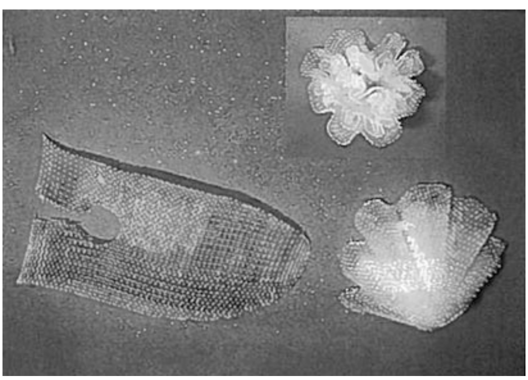

Fig. 8 Plug and patch repair (from Mulvihill; Surgery: Basic Science and Clinical Evidence; 2001, Chap. 43; reprinted with kind permission of Springer Science + Business Media)

Fig. 9 Placement of the Prolene Hernia System

short operating time in the hands of experienced surgeons would suit the elderly population well. Currently, all of the above techniques qualify.

Laparoscopic Repair

Shortly after the success of laparoscopic cholecystectomy became apparent, surgeons began to apply minimal access techniques to a wide variety of other surgical procedures. This approach has become generally accepted for some procedures, whereas for others there is still disagreement. Hernia repair is one of the latter group. Although some skilled laparoscopists prefer the approach for all inguinal hernias, others believe the benefits do not outweigh the risks, particularly in the elderly.

The laparoscopic approach to the inguinal hernia may be performed by either a transabdominal preperitoneal (TAPP) approach or a totally extraperitoneal (TEP) approach. In a TAPP repair, the abdomen is entered in the typical laparoscopic fashion and, once anatomy is appropriately identified, a peritoneal flap is made. The hernia sac is then reduced and dissected free. A piece of mesh is then rolled out over the entire myopectineal orifice and, in most instances, is tacked in place being careful to avoid the bladder and the epigastric vessels. The peritoneal flap is replaced and tacked in place as well (Fig. 10). In the TEP repair, the preperitoneal space is entered. This is most often done with a balloon dissector placed through the umbilical port (Fig. 11). Once the preperitoneal space is insufflated the anatomy of the groin is identified and the hernia sac dissected in a similar fashion as the TAPP repair. Mesh is placed and may be tacked in place. Any defects in the peritoneum are repaired. Previous lower abdominal incisions and radiation are a relative contradiction to the TEP repair, due to the difficulty of dissecting the peritoneum free from the abdominal wall [79].

The difficulty when operating from either the TAPP or the TEP approach is the ability to obtain adequate exposure of the inguinal anatomy. Most recurrences are due to incomplete dissection of the region or inadequate placement of mesh to cover

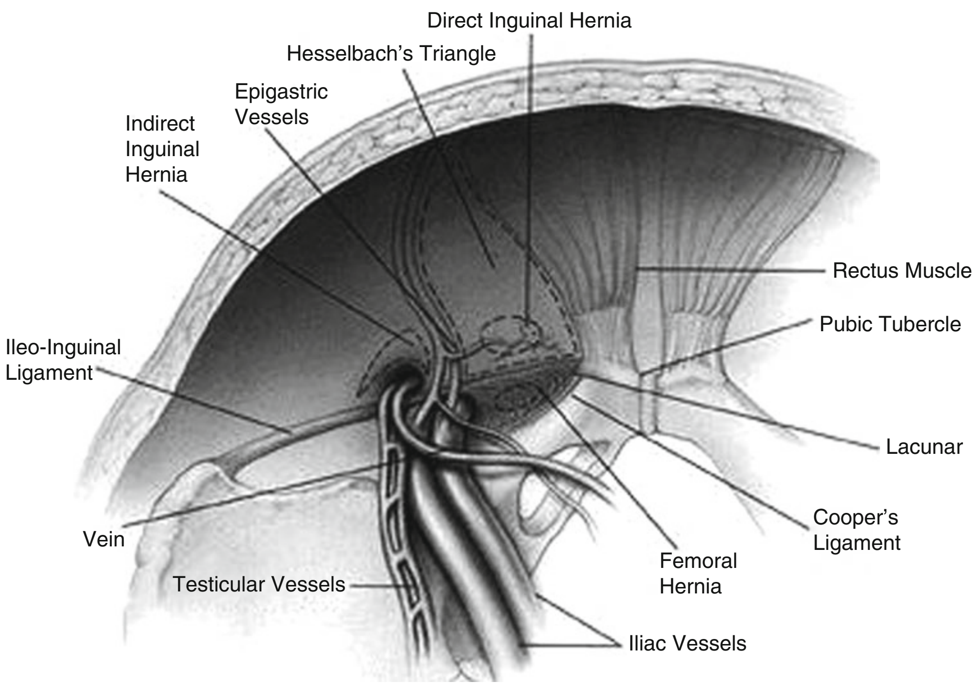

Fig. 10 View of inguinal anatomy (printed with permission from Charles H. Booras, M.D., All about Inguinal Hernias: Symptoms and Causes 5/16/98 http://jaxmed.com/articles/surgery/inguinalhernia.htm)

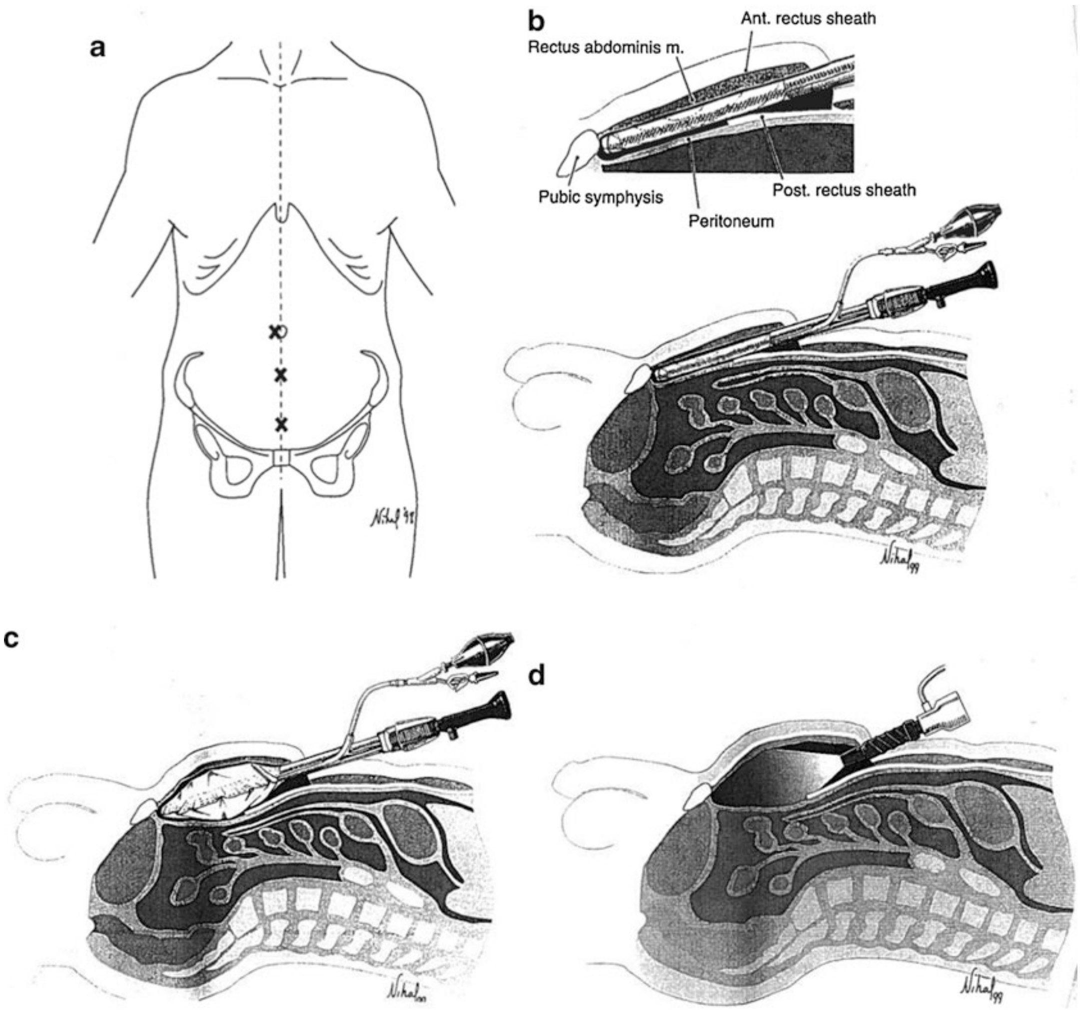

Fig. 11 Use of balloon dissector during TEP repair (from Mulvihill; Surgery: Basic Science and Clinical Evidence; 2001, Chap. 43; Fig. 43.18, reprinted with kind permission of Springer Science + Business Media)

the defect. The TAPP repair provides the largest operating space and the most unobstructed view of the inguinal region and is probably the procedure of choice when learning to perform laparoscopic herniorrhaphy and master the elements of the preperitoneal space. There is no doubt that the more proficient a surgeon is in either of these techniques, the fewer complications they will encounter.

Reported advantages of laparoscopic inguinal herniorrhaphy include less postoperative pain, reduced recovery time and earlier return to full activity, and improved cosmesis. The laparoscopic approach also has the advantage of allowing access to both groins through a single set of incisions, making it the preferred approach for repair of bilateral primary hernias [80–82]. Although the increased time to return to full activity may be an important consideration in a young person, the length of recovery may not be as important in old patients so long as mobility is not significantly compromised. Postoperative pain after the tension-free open approach is rarely severe enough to curtail activity.

There are some significant disadvantages to the laparoscopic approach. Laparoscopic herniorrhaphy requires general anesthesia, is frequently performed by a transperitoneal route, is technically more difficult to understand and learn than open mesh repairs, and in most hands, takes considerably longer. In comparisons of anesthetic techniques for open hernia repair, general anesthesia in the elderly is associated with far higher complication rates than local anesthesia. Therefore, the need for general anesthesia alone could obviate most of the benefits of the laparoscopic approach in some elderly patients. Notably, laparoscopy carries an additional risk for serious vascular and visceral injuries, which in any age group could be devastating (0.9 and 1.8 per 1,000, respectively) [83]. A history of prior pelvic surgery should be weighed carefully when considering laparoscopic repair, as adhesions may make visualization of relevant anatomy very difficult. For those with compromised cardiovascular reserve, laparoscopic repair should be approached cautiously due to the possibility that the patient will not tolerate pneumoperitoneum [84]. Laparoscopic repair has also been shown to be more expensive with some arguing that the increased cost is offset by quicker return to work [85]. In the elderly population where fewer are working, this cost offset may not be as relevant.

Reports of differences in recurrence rates between laparoscopic versus open mesh repairs have been inconsistent. A meta-analysis performed in 2003 compared open versus laparoscopic tension-free herniorrhaphy in over 7,000 patients at 41 facilities and found no significant difference in recurrence between the two repairs. One year later, a multicenter, randomized trial of 2,000 patients found that recurrences were more common in the laparoscopic group 2 years after primary repair (10.1% vs. 4.9%) [86]. In 2015, a large cohort study of more than 125,000 patients reported a reoperation rate of 4.1% in laparoscopic repairs versus 2.1% in open tension-free repairs at 1.5 years after primary herniorrhaphy. Perhaps most notably, the study also found that surgeon case load was strongly inversely related to reoperation after laparoscopic repair of primary inguinal hernia but not after open repair [87]. Because there is a steep learning curve in laparoscopy, some surgeons may prefer to reserve the laparoscopic approach for bilateral and recurrent hernias. Although studies have reported an increasing rate of laparoscopic repairs in the United States and Australia [53, 88], open repair continues to be the most common repair type in many places [89–91].

There is a paucity of studies specifically involving the elderly population and herniorrhaphy techniques. One study evaluated 110 patients over 65 years old with an ASA of either 2 or 3. Laparoscopic operative time was longer than that for open repairs; however, return to work was similar. Fifteen percent of patients experienced complications, the overwhelming majority of which were urinary retention. There was an alarmingly high recurrence rate of 9.7%. Hospital length of stay correlated with ASA status, but recurrences, complications, and return to activities did not [92]. A more recent retrospective review of 104 octogenarians who underwent laparoscopic versus open inguinal hernia repair found no difference in perioperative complications or length of stay between the two repair types. Postoperative urinary retention was more common in the laparoscopic group [93]. A similar study found no significant differences in operating room time, morbidity, or mortality related to the surgery, but found that the length of stay was significantly longer in the open group (1 day vs. 0 days in the laparoscopic group) [94]. Though laparoscopic hernia repair in the elderly appears safe [84, 92, 95–97], its superiority to open repair for primary, unilateral hernias in this population has not yet been determined.

Of note, in addition to a general lack of data regarding specific herniorrhaphy techniques in the elderly, there is even less data regarding female patients. Given the higher frequency of femoral hernias in the female population, the difficulty in diagnosing femoral hernias, and the resultant concern for strangulation, women are often excluded from trials and taken to the operating room faster. If the Lichtenstein approach is used to treat a groin hernia in a female, the entire femoral region may be missed [98], leading experts to recommend that all groin hernias in women be repaired laparoscopically [98–101].

Bilateral Hernias

Numerous authors have recommended that patients with bilateral groin hernias should have both hernias treated at the same time and that the laparoscopic approach should be considered [85, 93, 102–105]. This treatment plan allows for one administration of anesthesia and limits the number of incisions. Bilateral hernias should be managed with a single piece of mesh, large enough to cover both groins, the so-called bikini repair [106]. In patients with multiple comorbidities especially those with decreased cardiopulmonary reserve, the laparoscopic approach may be less ideal due to the need for general anesthesia, the physiologic changes seen with the induction of pneumoperitoneum, and the potential increased length of operating time with inexperienced surgeons. An alternative approach is to first repair the more symptomatic side using an open technique. After the patient recovers from the initial procedure, an open repair of the contralateral side may then be pursued.

Recurrence

When performing hernia repairs, the primary focus of success is determined by the incidence of recurrence. There is a wide variation in the time frame over which recurrences are reported. Hernias recur for one or more reasons: tension on the tissues created by the repair, inherent abnormalities in collagen that predispose to the development of new hernias, an unrecognized second hernia component at the time of the initial repair (usually a small indirect component), and technical error. Hernia recurrences can be classified as early or late. Most early recurrences are due to undue tension on the repair. For instance, when a hernia is due to a defect of the musculofascial abdominal wall, covering the defect with endogenous tissues results in suturing together tissues that are not normally juxtaposed. This then subjects these structures to undue tension [107]. Suture lines under tension exhibit an inadequate fibroblastic response for healing, which results in a weak scar and a subsequent recurrence of the hernia. Furthermore, these suture lines are subject to the same degenerative process that resulted in the initial herniation. The increasing use of tension-free repairs has significantly reduced this type of recurrence.

Late recurrences are usually due to missed components or new hernias at the site of a previous repair or in a new location. This type of recurrence is more appropriately termed reherniation. Following a mesh repair, reherniation occurs because the mesh was not sutured in place or it was not of sufficient size to cover beyond the inguinal floor. Progression of tissue degeneration is of great concern and can be compensated for by placing a large sheet of mesh underneath the external oblique aponeurosis well beyond Hesselbach's triangle. This dissection is extensive but can be necessary, particularly in some patients with severe tissue loss. This is of particular importance when performing a preperitoneal or laparoscopic repair. Appropriate and extensive dissection of the entire myopectineal orifice is necessary to facilitate choosing the right size mesh and performing appropriate fixation. The most common causes of failure are mesh size being too small or inappropriate fixation either inferomedially or inferolaterally [108, 109]. Another study found that the vast majority of recurrences after laparoscopic herniorrhaphy were medial. For this reason, a large piece of mesh should be chosen, sufficient enough to cross the midline with multiple tacks in the pubic tubercle and Cooper's Ligament (Fig. 12).

Patient risk factors for recurrence of hernias are similar to those for the formation of primary hernias. It would stand to reason that the elderly would be more susceptible to recurrence because of an increased risk of those factors already known to cause hernias: obesity, chronic cough, constipation, bladder outlet obstruction, and general degradation of tissue. Age >50 has been shown to be an independent risk factor as well. Those undergoing repair for a recurrent hernia are at greater risk for recurrence than those undergoing a primary repair, as are those with two or more relatives who also suffered from a recurrence [110].

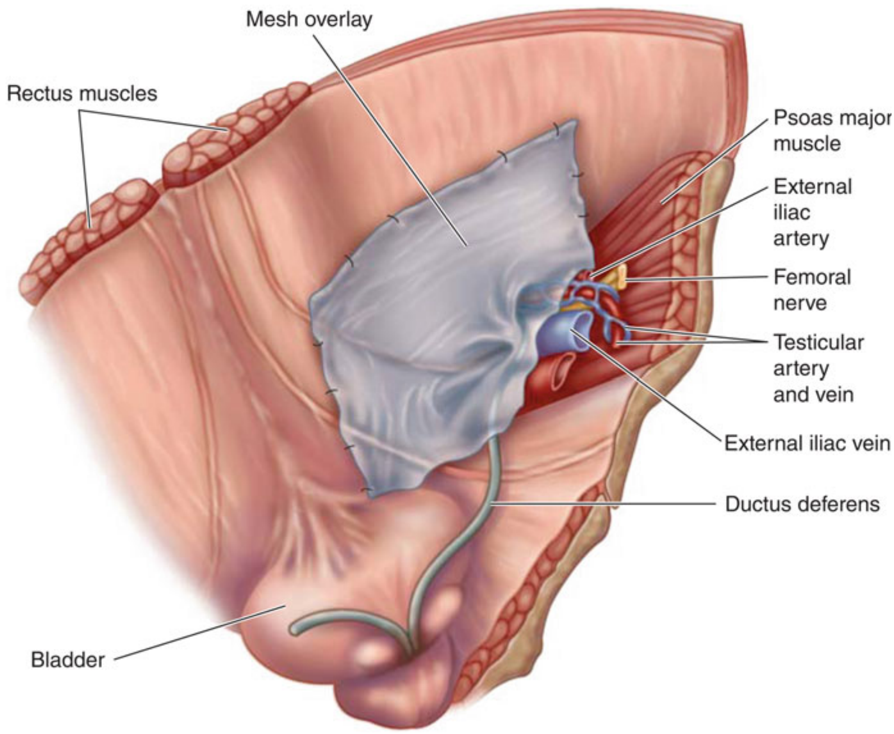

Fig. 12 Appropriate placement of mesh in a laparoscopic hernia repair (from Online Laparoscopic Technical Manual, Laparoscopic Inguinal-Femoral Hernia Repair, Step 5, Deploying and Anchoring the Mesh; http://www.laparoscopy.net/inguinal/ingher11.htm)

For recurrences after open repair, laparoscopic repair is preferred because it allows for dissection through un-operated tissues. For this same reason, the open approach is preferred for hernia recurrences after laparoscopic repair [111]. Notably, in the 2004 large, multicenter, randomized trial previously mentioned, rates of recurrence after repair of recurrent hernias was similar between the laparoscopic and the open tension-free groups (10.0% and 14.1%, respectively) [86]. This finding has been supported by multiple studies [87].

Inguinodynia

As recurrence rates continue to decrease with advances in inguinal hernia repair techniques, a greater emphasis is being placed on other complications of the surgery. One of the most common is inguinodynia or inguinal pain. Although not proven, the potential causes include partial transection or entrapment of a nerve, which eventually leads to neuroma formation and chronic pain. In an open repair, the most common nerves involved are the ilioinguinal, iliohypogastric, and genital branch of the genitofemoral nerve. All three of these nerves supply sensation to the genitals and medial upper thigh. Refer to the previous section on anesthesia for a more in-depth discussion of this anatomy. The nerves most commonly injured during laparoscopic herniorrhaphy are the lateral femoral cutaneous nerve (supplying the upper lateral thigh), and the femoral branch of the genitofemoral nerve (supplying the skin over the femoral triangle), all of which lie near each other. These nerves lie near each other in a space nicknamed the “triangle of pain” (Fig. 13).

A study from the Swedish Hernia register examined 3,000 patients undergoing unilateral primary hernia repair. All techniques (tissue, mesh, laparoscopic) were examined. Overall, 30% of patients were still experiencing pain over

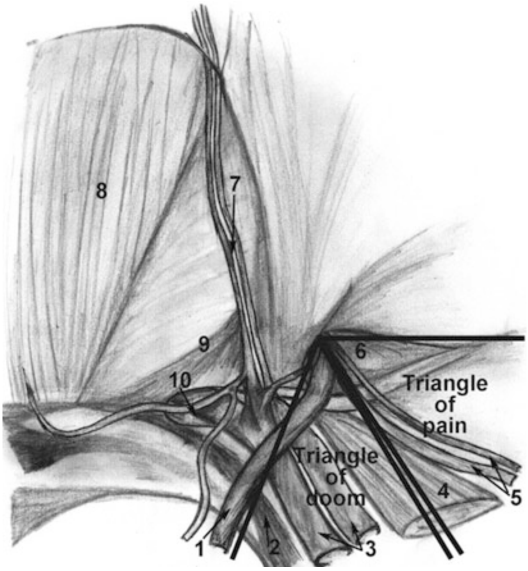

Fig. 13 Triangles of doom and pain – representing where injuries to vessels and nerves occur, respectively, during a laparoscopic inguinal hernia repair (from [92] © Moore and Hasenboehler; licensee BioMed Central Ltd. Available from: http://www.pssjournal.com/content/1/1/3)

a year after surgery and 6% were having significant enough pain to impair their activities of daily life. Risk factors for inguinodynia included age, with those >59 years old having significantly less pain than those younger (21 vs. 33%). Patients having pain prior to their operation were more likely to continue to experience pain afterwards. Operative technique was also important. Anterior approaches, either tissue repair or mesh repair, had the highest incidence (~30%), whereas preperitoneal repair, either open or laparoscopic, had a significantly lower incidence (~20%) [112].

A more recent study looked at chronic pain and numbness in 750 patients up to 5 years after undergoing either laparoscopic TEP repair or open tension-free repair of inguinal hernias. The data demonstrated a higher rate of groin pain in the open group versus the laparoscopic group, although the difference diminished with time – 7.9% difference at 12 months, 5.1% at 24 months, and 2% at 60 months. At all time points, the open group reported groin numbness at rate nearly twice that of the laparoscopic group. There was no difference in thigh numbness between the groups [113].

During an open repair, careful dissection and identification of all the nerves is the best way to avoid injury. If injury is already suspected, complete transection of the nerve is preferable. During laparoscopic repair, careful dissection is also important, as well as judicious tack placement avoiding the "triangle of pain." Some have advocated not securing the mesh, which effectively alleviates this problem [28]. Recent studies have advocated prophylactic ilioinguinal neurectomy during open hernia repair. A double-blind randomized study showed a significant reduction in groin pain in the neurectomy group (8 vs. 28%) without any difference in postoperative numbness [114].

Patients suffering from injury to these nerves typically have pain in the immediate postoperative period, which intensifies over the next few weeks. In most cases, it will regress over 2 months, and in up to one-third of patients it will completely resolve by 6 months [11]. Thus, the initial management consists of injections of local anesthetic and corticosteroids, as well as analgesics and anticonvulsants. In refractory cases, the surgical treatment of choice is a triple neurectomy of the ilioinguinal, iliohypogastric, and genitofemoral nerves. This has shown 85% complete resolution and 15% partial resolution of pain in some case series [115].

Incisional Hernias

Incisional hernias in the elderly are common and often can be challenging to repair. The incidence of hernias in patients with a midline surgical incision is 10–15% [72]. Often, incisional hernias are also referred to as ventral hernias although the term ventral hernias also encompasses epigastric hernias. The etiology of these hernias is often multifactorial. Wound infection, suture failure, malnutrition, increased age, obesity, excessive abdominal straining, smoking, ascites or peritoneal dialysis, chemotherapy, steroids, and tension on the wound closure are factors that have been implicated. Only 60% of these patients will go on to develop symptoms [72]. This typically begins with a noticeable bulge in a previously healed incision. Incarceration is the presenting symptom in 17% of patients leading to a perioperative mortality rate three times higher than that for elective repair [116].

Repair of minimally symptomatic or asymptomatic ventral hernias has remained controversial. Due to concerns for enlargement with time making repair more difficult and due to concerns for incarceration of small bowl obstruction, elective repair of ventral hernias has been recommended [47]. However, primary care physicians may recommend watchful waiting for some of their patients, especially those with multiple comorbidities [117, 118]. More data is needed to better guide recommendations. Recently, a study of 41 patients assigned to watchful waiting for ventral hernia management found a low risk of hernia accidents at 2 years and no change in disease-specific quality of life, leading the authors to suggest that a trial of watchful waiting may be safe for management of minimally symptomatic incisional hernias [47].

There are several special considerations for patients seeking elective incisional/ventral hernia repair. First, patients with a history of falls and difficulty ambulating who may require a large abdominal incision should be approached cautiously as falls in the early postoperative period could lead to dehiscence. Second, patients with breathing difficulties such as those with chronic obstructive pulmonary disease (COPD), asthma, bronchitis, or Pickwickian syndrome may have difficulty with pneumoperitoneum required for laparoscopy, difficulty weaning off of the vent after a large incisional hernia repair, and difficulty wearing a binder postoperatively. Other risk factors for adverse outcomes that have been identified include ASA classes 3 and 4, poor functional status, and COPD among others [119, 120]. Finally, just as in inguinal hernia repair, older elderly patients may fare worse than younger elderly patients. One study of nearly 5,000 patients ≥80 years of age who underwent laparoscopic ventral hernia repair demonstrated a more than threefold increase in mortality as compared to younger adults undergoing repair [121].

Technically, incisional/ventral hernias may be challenging for several reasons. First, it is possible for most of the abdominal contents to become a fixed part of the hernia, which may result in a decrease in the intra-abdominal compartment volume. This in turn complicates complete reduction of the contents at the time of repair. This is known as a loss of domain. Often, a components separation technique is required to reapproximate the abdominal wall when there is loss of domain and/or a large abdominal wall defect. Up to 20 cm of additional medial advancement of the rectus fascia can be obtained in the mid-abdomen with a bilateral components separation [122] either through an open or endoscopic approach. Mesh may be used to reinforce the repair. A second challenge in repairing ventral hernias is that the defects are usually multiple, reflecting failure of wound healing throughout the length of the incision. Identifying all the defects in the "Swiss cheese"-type abdominal wall and freeing all of the underlying adhesions may be tedious and time-consuming. Finally, extreme care must be exercised not to enter the bowel lumen during dissection because most incisional hernias are large and require synthetic materials for repair without tension. Biologic materials mentioned previously are now used to repair these hernia defects, especially in the presence of the contaminated operative field. They may also be used to overlay primary repairs to provide additional stability to weakened tissues, not uncommon to the elderly.

Laparoscopic techniques are being used with increased frequency to repair these large defects. Relative contraindications to laparoscopic approach include loss of domain, abdominal skin grafts, prior surgeries with planned removal of mesh, a small defect with a large sac, incarcerated hernias, active enterocutaneous fistula [123], and large oncological burden with a high chance of needing reoperation. Reported benefits of the laparoscopic approach include shorter length of hospital stay [124–127], decreased rate of wound infection [125, 126, 128], and no difference in recurrence rate as compared to the open technique [125–128]. Additionally, one study found no increase in complications with the use of laparoscopic repair in the elderly as compared to younger adults [129]. New Society of American

Gastrointestinal Endoscopic Surgeons (SAGES) guidelines reflect these findings and point to decreased wound infection rates with the laparoscopic approach but no difference in recurrence or quality of life as compared to the open approach [123]. Further studies specific to the elderly population are still needed.

Umbilical Hernias

The umbilical hernia was first noted in 1 AD by the Hindu physician Charaka, who mistakenly believed it to be an abdominal tumor. Umbilical hernias present as 6% of all abdominal wall hernias. Ninety percent of umbilical hernias are acquired and 10% are congenital [130]. Those less than 2 cm upon birth are likely to close spontaneously. In adults, umbilical hernias occur through an umbilical canal that is bordered by the umbilical fascia posteriorly, the linea alba anteriorly, and the two rectus sheaths laterally [131]. The sac may include omentum, colon, or small bowel. These hernias typically present with complaints of a lump around the umbilicus, pain, or pressure. In adults, prompt repair is recommended after the diagnosis is made due to the increased risk of strangulation.

Umbilical hernias are common in cirrhotic patients and in those with ascites of other etiologies because of the increased intra-abdominal pressure against a thinned umbilical ring and fascia. Umbilical hernia is also an important consideration in patients on peritoneal dialysis. Dialysis must be interrupted and ascites controlled prior to repair to decrease the incidence of recurrence. There are significant difficulties in closing this type of hernia, in order to prevent complications such as ascitic leak, wound infection, and recurrence. Therefore, every effort should be made to avoid strangulation and protect the thin skin over the defect. When necessary, these hernias may be repaired under local or regional anesthesia. Primary repair is optimal, but occasionally a prosthetic or biologic material is needed for tension-free closure.

For years the "vest over pants" method of repair as first described by Mayo was the standard of care. As with inguinal hernias, mesh repairs have begun to supplant primary repairs. There are a variety of meshes available, from simple sheets, to plugs and a combination of the two. A recent study by Shankar et. al. investigated long-term outcomes in patients receiving umbilical hernia repairs. Recurrence rates were noted to be higher in those patients who received a primary repair (9.8% vs. 2.4) with complications between the two being insignificant. Of the factors studied, primary repair, diabetes, and liver disease were noted to be independent risk factors for recurrence. Obesity and ascites were also associated with increased risk of recurrence [132].

Richter's Hernia

A partial enterocele is a form of hernia that bears the name Richter's hernia after August Gottlieb Richter, who first described it in 1785. This hernia is unique because only one side of the bowel wall becomes entrapped in the hernia defect (Fig. 14). Richter's hernias are most often diagnosed in the sixth and seventh decades of life. It requires a small, firm defect for the bowel to partial protrude. The most common sites include femoral ring, inguinal ring, and fascial defects from previous incisions. The terminal ileum is most commonly

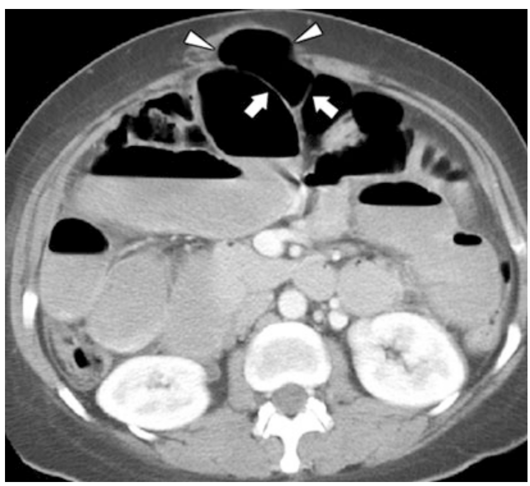

Fig. 14 Richter's hernia (from [93], reprinted with permission of the American Journal of Roentgenology)

implicated. Five to ten percent of these hernias will present as incarcerated and are diagnosed at the time of treatment [133]; however, the first indication of incarceration may not become apparent until strangulation and necrosis occurs. In those diagnosed, there is a notably longer delay to diagnosis and treatment resulting in higher rates of incarceration requiring small bowel resection in up to 50% of patients [134].

There is some concern that the incidence of Richter's hernia may be increasing as laparoscopic surgery becomes more prevalent. Small port-site hernias are the perfect size to involve only a small portion of the bowel. These hernias more commonly present in trocar sites that did not undergo fascial closure [135].

Obturator Hernias

Arnaud de Ronsil first described the obturator hernia in 1724 at the Royal Academy of Science in Paris. This hernia is rare, accounting for 0.05% of all hernias and 0.2% of bowel obstructions [136]. It is usually found in frail, elderly debilitated women, but may also be associated with profound weight loss in other groups. Obturator hernias may be bilateral or associated with hernias through the femoral canal. The obturator foramen, through which the hernia occurs, is the largest foramen in the body. The obturator membrane, however, occludes most of the foramen. The obturator canal consists of a 1–2 cm long and 1 cm wide opening in the superolateral part of the foramen. Usually, this canal is obliterated with fat, which prevents herniation of abdominal contents. In the frail and malnourished, this fat disappears and the potential space is unmasked.

A preoperative diagnosis is difficult because the complaints are not specific and the physical manifestations are minimal. A history of symptoms suggestive of intermittent or partial intestinal obstruction may be elicited. The Howship–Romberg sign – pain radiating down the medial aspect of the leg to the knee due to compression of the obturator nerve – is pathognomonic and is present in up to 50% of cases [29]. However, this sign is often overlooked in the elderly or attributed to other causes. The optimal way to look for an obturator hernia is with the patient supine and the thigh flexed, abducted, and externally rotated. The hernia mass is often concealed underneath the adductor muscles in the thigh. Occasionally, it is possible to feel a small mass on vaginal or rectal examination. The four indicators of obturator hernia – intestinal obstruction, Howship–Romberg sign, prior similar symptoms, a palpable mass on vaginal or rectal examination – are rarely seen together.

Many of the recent studies have looked at ways to decrease time to operative fixation in order to decrease mortality. Most obturator hernias are only correctly diagnosed at the time of operation, with only 30% diagnosed preoperatively. Several studies have looked at algorithms for diagnosis and care of obturator hernias. One should always be suspicious for obturator hernia in elderly patients with signs of bowel obstruction and no previous abdominal operation. Other signs and symptoms are mentioned above and include the Howship–Romberg sign and a palpable groin mass. CT scan should be obtained early in these patients and is the primary diagnostic tool for obturator hernias. CT scan is both sensitive and specific for diagnosis of an obturator hernia and can decrease the diagnostic time by 3 days. The treatment of an obturator hernia found on CT is urgent laparotomy or laparoscopy (Fig. 15). If no hernia is found on CT scan but the patient is exhibiting recurrent symptoms or partial

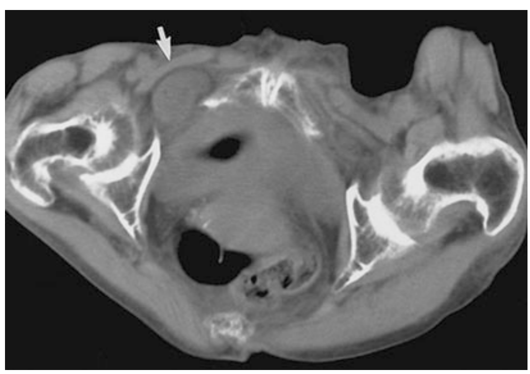

Fig. 15 Preoperative CT showing Spigelian hernia (from [94]. Available at: http://www.rcsed.ac.uk/Journal/vol45_3/4530046.htm)

obstructive symptoms, elective laparoscopy may be performed. It is important to note that one should not delay surgery while attempting to make the definitive diagnosis as these hernias can cause severe morbidity and mortality (up to 70%) [137, 138].

Primary repair of an obturator hernia is impossible because the surrounding tissues are immobile. Some studies have reported using sac ligation alone or flaps of bladder, periosteum, uterine ligament, or rib cartilage to close the defect [139, 140]. These repairs are unsuitable for large or bilateral hernias and may lead to postoperative pain and bladder dysfunction. A synthetic material is usually necessary. A plug system has been described as tension free and easy to perform; however, there is the potential for chronic obturator neuralgia [141]. If the diagnosis has been established preoperatively, the most suitable approach is an open preperitoneal repair, as described by Stoppa et al. [142]. With this repair, a large piece of mesh is placed extraperitoneally to cover both sides of the pelvic floor. If the viability of the incarcerated bowel is questioned once the hernia is reduced, the peritoneum may be opened. In the usual case where the diagnosis is not known preoperatively, an initial transabdominal approach with a preperitoneal mesh repair is optimal. The use of laparoscopic methods has also been described, but there is no current data supporting benefits of this approach.

Spigelian Hernias

The Spigelian hernia, another unusual abdominal wall hernia, is named for Adriaan van den Spiegel, who was the first to describe the semilunar line. The semilunar line is the demarcation from muscle to aponeurosis in the transversus abdominis muscle. Protrusion of a peritoneal sac, organ, or preperitoneal fat from its normal location through this aponeurosis is termed a spigelian hernia. These hernias are usually found at or near the arcuate line. This area is particularly weak due to the anterior position of the transversus abdominis aponeurosis, perforators of the epigastric artery that leave a fascial defect, and the orientation of the fibers of the transverse and internal oblique muscles [143]. Once the hernias enter Hesselbach's triangle, they are termed low Spigelian hernias. These hernias are often located within different aspects of the abdominal wall and may also be termed interparietal, interstitial, intermuscular, intramuscular, or intramural.

Spigelian hernias affect less than 1–2% of the population with hernia defects [144], but some authors have suggested this is an underestimate [145]. Patients most commonly are ages 40–70 years of age. Symptoms of Spigelian hernia include abdominal pain, obstruction, and palpable mass. It is uncommon for these hernias to be visualized directly on the abdominal wall due to the habitus of patients predisposed to them. Factors that may increase the risk of Spigelian hernia include increased abdominal pressure from obesity, rapid weight gain, COPD, multiple pregnancies, chronic constipation, ascites, and previous surgery [143].

The diagnosis is difficult in patients with defects too small to produce overt manifestations on the abdominal wall. It is best to examine patients by having them alternately tense and relax the abdominal wall. Imaging studies are usually necessary to elucidate the source of the localized symptoms. Ultrasonography is a good method for determining a hernia orifice and locating hernia contents. CT scan may also be used to examine the abdominal wall, but the sections must be close together to enable localization of the hernia orifice. Helical CT scans may increase the diagnostic yield. The CT scans may also provide information about the hernia sac and the nature of the abdominal contents in the sac (Fig. 16).

Due to a high risk for incarceration, surgical treatment is recommended. Both open and laparoscopic repairs may be performed [145]. A recent prospective randomized trial comparing open versus extraperitoneal laparoscopic repair showed significant improvement in complications and hospital stay in the laparoscopic group [143]. Regardless of approach, there is often enough laxity in the surrounding tissues to allow for primary closure, although mesh can be used [29].

Fig. 16 CT scan of obturator hernia (reprinted with permission from [91], Copyright © Radiological Society of North America. Available at: http://radiographics.rsnajnls.org/cgi/content-nw/full/21/2/341/F8)

Conclusion

Abdominal wall hernias in the elderly, whether common or unusual, are ultimately surgically correctable disorders. With the increasing number of elderly patients expected to present to general surgeons for evaluation of abdominal hernia, it is important that physicians are knowledgeable about the special considerations for this population. For each elderly patient, the physician should lead an open conversation focused on defining goals of care, assessing functional status, and identifying the specific risks and benefits for each intervention.

Recent studies have shown that watchful waiting may be safe for asymptomatic or minimally symptomatic inguinal hernias. Other hernias wherein the fascial defect is large can also be managed nonoperatively if not symptomatic. Pain is frequently what leads the patient to operative repair.

Elective repair of inguinal hernias, in particular, is safe even in patients with significant comorbidities. With local anesthesia and tension-free repairs, nearly all patients can ambulate immediately, and they can obtain excellent pain control with minimal oral pain medication. Complications are uncommon, and mortality is very low in many large series.

Patients with chronically incarcerated hernias are not at significant risk for strangulation while those with an acute incarceration do have some risk of progressing to strangulation. Therefore, acutely incarcerated hernias present more of an urgent to emergent situation, and surgical consultation early in the patient's course is of utmost importance.

Once strangulation has occurred, a hernia is no longer just a defect in the abdominal wall, and repair is not just patching the hole. The systemic consequences of bowel obstruction and ischemic tissue stress the limited reserves that define the physiologic state of the older patient. Once the inflammatory state is initiated, the cascade of events demands a response that the elderly are frequently unable to mount. Fluid and electrolyte imbalance, dehydration, and systemic sepsis become the major problems, and the mechanical issue of fixing the hernia defect fades in comparison. Morbidity and mortality rates soar.

For those hernias that are rare or the presentation more obscure, an increased level of awareness is necessary to avoid the consequences of incarceration. Although we may have to accept the higher complication rates that accompany the unusual hernia, we should never allow the common hernia to progress from a simple mechanical problem to a deadly systemic illness.

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Benign Esophageal Diseases in the Elderly

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Abstract

Benign conditions of the esophagus and esophagogastric region may have implications in elderly patients that differ from those encountered in younger age groups. Special consideration must be given to the unique presentations as well as to the physiologic impact of treatments and treatment complications in this vulnerable population. Minimally invasive approaches are now preferred for most esophageal diseases that require surgical treatment. Despite these and other improvements in therapy, benign esophageal disorders continue to present great challenges to practitioners treating the geriatric population.

Gastroesophageal Reflux Disease

The full spectrum of gastroesophageal reflux disease (GERD) symptoms and complications are observed in elderly patients and present specific management considerations. Although GERD does not itself present a significant risk for mortality in the elderly, it may impair quality of life and lead to considerable complication-related morbidity. Patient tolerance of severe symptoms is often poor, and complications such as chronic upper aerodigestive manifestations, esophagitis with ulceration, peptic stricture, and Barrett's esophagus may pose significant management challenges in the elderly.

Pathophysiology

The antireflux barrier at the gastroesophageal junction (GEJ) is an anatomically and physiologically complex zone, which consists of (1) the intrinsic lower esophageal sphincter (LES) pressure (10–30 mmHg), (2) intra-abdominal location of the LES (3–4 cm below the diaphragm), (3) extrinsic compression of LES by the crural diaphragmatic sphincter, (4) integrity of the phrenoesophageal ligament, and (5) maintenance of an acute angle of His. Disruption of the antireflux barrier and abnormal clearance of esophageal contents results in increased exposure of the esophageal lumen to gastric refluxate (acidic or alkaline) [1] (Table 1).

Asymptomatic elderly patients differ physiologically from their younger counterparts (Table 2) [2–10]. They may have decreased LES pressure, abnormal esophageal motility and clearance, and an increased pain threshold. Older patients may be more likely to take medications that decrease LES tone and potentiate reflux events. These include nitrates, calcium channel blockers, theophylline, benzodiazepines, anticholinergics, and tricyclic antidepressants. Translocation of the esophagogastric junction and LES into the mediastinum through the esophageal hiatus (type 1, sliding hiatal hernia) (Fig. 1) occurs more frequently with increasing age [11] and is thought to contribute to pathologic reflux by exposing the LES to less extraluminal pressure in the chest as compared to the abdomen. This

Table 1 Pathophysiologic factors contributing to GERD

Increased frequency and duration of transient LES relaxation
Hypotensive LES (0–4 mmHg) leading to free reflux
Disruption of phrenoesophageal ligament and diaphragmatic sphincter (hiatal hernia)
Shortening of intra-abdominal LES
Decreased clearance of esophageal contents due to loss of primary and secondary esophageal peristalsis
Decrease in rate of salivation and salivary bicarbonate
Decreased gastric emptying and increased intragastric pressure

GERD gastroesophageal reflux disease, *LES* lower esophageal sphincter

Table 2 Physiological changes of the esophagus in the elderly

LED
Decreased LES pressure [2]
Decreased LES length [3]
Increase in gastroesophageal reflux events during the postprandial period from pharyngeal stimulation [3]
Esophageal motility
Aperistalsis without any specific etiology [4]
Absent or decreased secondary peristalsis with esophageal distention [5]
Increased tertiary contractions (multiple, simultaneous, nonperistaltic contractions) [6]
Decreased amplitude and velocity of peristaltic waves [2, 7]
Impaired esophageal clearance [8, 9]
Higher pain threshold with esophageal distension [10]

LES lower esophageal sphincter

relatively lower extraluminal pressure permits LES tone to be more easily overcome by intragastric pressure, leading to reflux. Patti et al. have shown that the degree of reflux symptoms, LES dysfunction, and esophagitis increases with hiatal hernia size [12].

Polypharmacy is a relatively unique challenge in geriatric patients, and many common medications can promulgate GERD by impeding esophageal function, delaying gastric emptying, or causing direct esophageal injury. These medications include calcium channel blockers, nitrates, narcotics, alpha-agonists, ferrous sulfate, and nonsteroidal anti-inflammatory drugs [13] A thorough medication reconciliation should be a part of

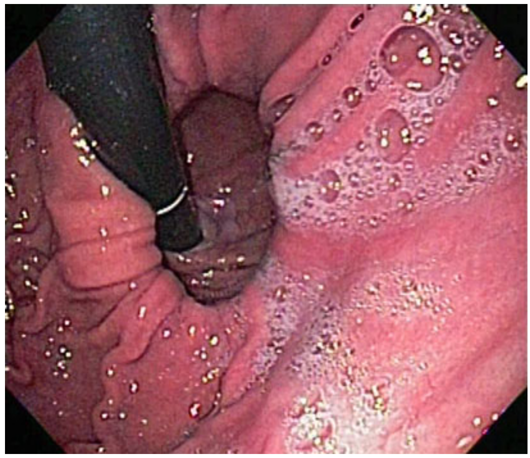

Fig. 1 Retroflexed endoscopic view of type I sliding hiatal hernia. The endoscope is seen emerging from the true esophagogastric junction into the hernia above the muscular ring of the hiatus

the workup of patients presenting with GERD, especially if a simple adjustment will preclude more drastic measures.

Clinical Presentation

A population-based study in Olmsted County, Minnesota, defined the general incidence of GERD symptoms as 19.8% without significant differences with age [14]. Triadafilopoulos and Sharma similarly reported no clear age-related difference in clinical prevalence of GERD above and below age 65 [15]. However, GERD symptom severity may not correlate as well with the severity of pathology in elderly patients. Johnson and Fennerty reported that 34% of patients >70 years old had severe heartburn with a 37% incidence of endoscopically evident severe esophagitis. In contrast, 82% of patients <21 years old with severe heartburn had severe esophagitis only 12% of the time [16]. Furthermore, Collen et al. reported that for a given level of severe reflux symptoms, patients >60 years old had more severe esophagitis compared to younger patients [17]. Zhu et al. reported that 21% of patients >65 years with GERD present with endoscopically severe

Table 3 Symptoms and complications associated with GERD

Typical	
Heartburn	
Regurgitation	
Atypical symptoms	
Chest pain	
Dysphagia	
Dyspepsia	
Anorexia, weight loss	
Dental problems	
Atypical symptoms: respiratory	
Globus sensation	
Laryngitis	
Hoarseness	
Chronic cough	
Asthma	
Bronchitis	
Aspiration pneumonia	
Pulmonary fibrosis	
Complications	
Esophagitis	
Gastrointestinal bleeding	
Peptic strictures	
Barrett's esophagitis	

GERD gastroesophageal reflux disease

esophagitis, while only 3.4% of patients under 65 years have severe esophagitis [18]. Patients with GERD present with symptoms which can be described as typical or atypical or a combination of both (Table 3). Atypical symptoms may be more prevalent in the elderly [14, 19]. Alkaline reflux may also be more frequent and can be associated with respiratory symptoms more often than with heartburn [20]. Pellegrini et al. found that individuals with alkaline reflux have less heartburn, regurgitation, and dysphagia but at least as much esophagitis and stricture risk as those with acid reflux, as well as a higher frequency of pulmonary symptoms [21].

Long-standing GERD can result in complications which may lead to significant morbidity. The incidences of erosive esophagitis (45.4%), esophageal ulcers (6%), and esophageal strictures (8.4%) all increase with age. Furthermore, patients with esophageal ulcers or strictures are generally older than patients with uncomplicated esophagitis [22]. In one report, esophagitis was the cause of upper gastrointestinal bleeding in 21% of patients >80 years [23].

Barrett's esophagus, or columnar metaplasia, is a marker of severe chronic esophageal mucosal injury and has been reported to occur in as many as 10–12% of patients with GERD [24, 25]. The prevalence of Barrett's esophagus increases with age and plateaus by the seventh decade [26]. It occurs more frequently in patients greater than 60 years of age (34 vs. 12%) [17]. Elderly patients with Barrett's esophagus experience less severe symptoms compared to younger patients, which may lead to delayed recognition of the condition [15]. The outcome of Barrett's esophagus which is of utmost concern is its progression to adenocarcinoma, but there are no compelling data that define this risk in the elderly. In a meta-analysis of 41 Barrett's esophagus surveillance studies, the reported cancer incidence was found to be between 6 and 9 per 1000 person-years follow-up [27]. The presence of ulcers, strictures, and nodules was associated with increased cancer incidence. Patients who developed cancer had significantly longer Barrett's segments compared to patients who did not. However, these data did not stratify risk by age, and it is uncertain to what extent age may be an independent risk factor for either dysplasia or cancer.

Treatment for Barrett's esophagus is close surveillance and either medical or surgical control of reflux with the aim to avoid progression of disease. Standard therapy for high-grade dysplasia in Barrett's is esophagectomy. Mucosal ablative therapies (photodynamic therapy, argon plasma coagulation, and cryoablation) for high-grade dysplasia have seen expanded use and could offer benefits to elderly patients, if the morbidity and mortality risk associated with esophagectomy can be avoided. However, uncertain efficacy and potential to undertreat cancer present at the time of the therapy remain a matter of concern.

Diagnosis

Tests to diagnose GERD, GERD complications, and responses to therapy are listed in Table 4. GERD symptoms are frequently under treatment with proton pump inhibitors (PPI) or histamine receptor antagonists (HRA) before any diagnostic

Table 4 Diagnostic studies for GERD

Test	Purpose of study
Cine esophagram	Evaluate anatomical causes for dysphagia; document presence of hiatal or paraesophageal hernia; rule out achalasia, scleroderma, strictures, diverticula, webs, and masses
Endoscopy	Evaluate endoscopy positive vs. negative reflux disease; document healing esophagitis; rule out complications of GERD (esophagitis, stricture, and BE), peptic ulcer disease, and cancer
Esophageal manometry	Evaluate LES function; rule out esophageal dysmotility before proceeding with antireflux surgery
pH monitoring	Document abnormal acid exposure in symptomatic endoscopy-negative patients being evaluated for endoscopic or surgical antireflux therapy; evaluate patients on PPI therapy with persistent typical symptoms; document adequacy of PPI therapy in patients with complications due to GERD
Esophageal impedance testing	Evaluate endoscopy-negative patients with persistent symptoms despite PPI therapy
Bile acid reflux monitoring	Evaluate patients with persistent reflux symptoms with normalization of distal esophageal acid exposure confirmed by pH studies

GERD gastroesophageal reflux disease, *BE* Barrett's esophagus, *PPI* proton pump inhibitor

tests are done. There should be a low threshold to proceed with endoscopy in elderly patients because of the recognized risk of more advanced disease in the face of less severe or atypical symptoms in comparison to younger patients. Endoscopy with biopsy is currently the only study that can effectively identify esophagitis, rule out Barrett's and cancer, as well as document healing of esophagitis with therapy. Cine esophagography can help characterize anatomic and functional features of the esophagus during the passage of ingested barium materials of varying consistencies. Some motility characteristics and disorders (Table 4) as well as esophagogastric junction anatomy can be defined with the study, and it can be particularly useful in evaluating dysphagia.

Complex or suspected reflux disease and persistent or atypical symptoms should be further evaluated using more objective tests, especially when antireflux surgery is being considered. The 2007 American College of Gastroenterology practice guidelines recommend ambulatory pH monitoring to identify pathologic esophageal acid exposure in endoscopy-negative patients being considered for endoscopic or surgical antireflux procedures and patients who are symptomatic on PPI therapy. Symptom correlation index can establish likelihood of causality in the relationship between symptom occurrence and episodes of esophageal acid exposure. Although pH monitoring can also be used to evaluate effectiveness of PPI therapy, a specific threshold value for adequate suppression of esophageal acid exposure has not been defined [28], and no age-specific guidelines for the use of this test are available.

Ambulatory pH monitoring can be performed using a nasopharyngeal catheter system or a wireless pH capsule ("Bravo" probe, Medtronic, Minneapolis, MN) that transmits information to an external receiver. Results from the two systems correlate well, but there may be advantages with wireless pH monitoring. The most important is that the modality is associated with less discomfort, less interference with daily activities, and better patient satisfaction compared to the traditional catheter system. Less interference with daily activities will provide more accurate information about reflux episodes [29]. Furthermore, pH monitoring can be performed for more than 24-h periods, and it may be more feasible to study patients on and off PPI therapy. Disadvantages include the need to place the capsule endoscopically, which adds cost and the potential problems of an invasive procedure. Some patients may have severe chest pain, and the capsule may either dislodge early or not dislodge at all, both of which are problematic situations. Wireless pH monitoring might offer advantages in elderly patients based on improved tolerance, but there are no data that specifically support this assumption.

Esophageal impedance monitoring detects changes in resistance to electrical current across adjacent electrodes with the movement of solids, liquids, and gases. It can detect both acid and alkaline reflux (even very weak patterns of reflux) and evaluate esophageal bolus transit when combined with motility studies. Specific monitoring of bile acid reflux is possible by using a probe that detects bile by spectrophotometry. AGA guidelines suggest that these tests may be useful in patients with reflux symptoms despite PPI therapy and normal pH monitoring studies [28]. They are not widely used at this time because the long-term clinical implications of non-acid reflux are not well studied. It is unclear at this time how recognition of this entity might change management in elderly patients.

Chest pain symptoms in the elderly deserve special mention. The most obvious concern lies in the physician's ability to distinguish cardiac from noncardiac chest pain (NCCP) and to institute the appropriate treatment. Although most patients with GERD-induced chest pain will give a history of antecedent reflux symptoms, the possibility of myocardial ischemia ought to be considered and basic investigations conducted so as not to miss this diagnosis. There is considerable overlap in symptoms attributable to GERD or of cardiac origin. DeMeester et al. performed 24-h pH probe studies in patients with typical angina pectoris symptoms and normal cardiac catheterizations and demonstrated reflux to be present in 46% [30]. A positive correlation between chest pain episodes and acid reflux during the pH probe study can be demonstrated in up to 50% of patients with NCCP [31].

Treatment

Irrespective of patient age, the goals in the treatment of GERD are to ameliorate symptoms, promote healing of esophagitis, maintain remission, and prevent long-term complications. These goals may be achieved using various modalities.

Nonsurgical Treatment

Lifestyle or behavioral modifications can alleviate symptoms in mild reflux disease when employed alone or with medical therapies. These might include the elevation of the head and chest during sleep, avoidance of supine position or sleep less than 3 h after meals, weight loss in overweight patients, smoking cessation, and avoidance of foods associated with reflux (e.g., high-fat foods, chocolate, peppermint, coffee, and alcohol). As mentioned previously, selected medications may decrease LES tone. Caution with these as well as with medications that might predispose to pill esophagitis (potassium tablets, iron sulfate, and alendronate) should be exercised.

Histamine receptor antagonists (cimetidine, ranitidine, famotidine, and nizatidine) may be effective but are used less frequently than proton pump inhibitors (PPIs) as first-line therapy. PPIs (omeprazole, lansoprazole, rabeprazole, pantoprazole, and esomeprazole) inhibit the H+/K+ ATPase proton pump. They have become the mainstay of medical therapy for significant GERD and are now available over the counter (omeprazole). If symptoms are suggestive, empiric treatment is usually started before diagnostic tests are done, and prompt clinical improvement is generally taken as confirmatory of the GERD diagnosis. Historical exceptions to prompt use of PPIs rather than investigations include long-standing GERD and alarm symptoms such as anemia, weight loss, and dysphagia [32]. Since elderly patients may present with more advanced disease and less severe symptoms, an argument can be made for the use of endoscopy prior to starting prolonged acid suppression in order to clearly establish the presence of esophagitis.

Almost 50% of patients with GERD suffer frequent relapses and need some form of maintenance therapy. PPIs are currently regarded as the most effective medications available for acute as well as maintenance therapy for GERD [33], although H2 receptor antagonists may also be effective if PPI treatment cannot be given. Since PPIs are long-acting medications, dosing is convenient for older patients. Added potential advantages include easy administration in older patients with swallowing problems (granules can be mixed in soft food or liquids) and the fact that dose adjustments are not necessary in hepatic and renal insufficiency [34]. Some studies have shown an increased risk for respiratory infections, *Clostridium difficile* colitis, and osteoporosis with PPI use [35].

Cisapride is a prokinetic agent which may be available for use in GERD outside the USA, having been removed from the US market in 2000 due to increased risk for cardiac arrhythmias. Metoclopramide can be problematic in elderly patients due to CNS side effects (sedation and tardive dyskinesia). Other promotility drugs such as tegaserod (serotonin agonist) and baclofen (GABA agonist) may have some efficacy in GERD but are not standard therapies. Singh et al. cross-referenced the interactions of antacids, H_2 blockers, proton pump inhibitors, and sucralfate with common medications for hypertension, diabetes, dyslipidemia, arthritis, and psychiatric conditions. Although the analysis was by no means comprehensive, it found surprisingly few interactions. Notably, omeprazole in combination with diuretics increased the risk of hypomagnesemia, and ranitidine in combination with metformin increased the risk of elevated metformin levels [36]. As noted earlier, a thorough medication reconciliation can prevent complications secondary to polypharmacy.

Surgical Treatment

Indications for surgical treatment of GERD include (1) patient choice in order to discontinue medical therapy, (2) intolerance of medical therapy, (3) persistence of symptoms on medical therapy, and (4) complications of GERD including persistent esophagitis on medication, peptic strictures, and Barrett's esophagus (although the latter indication may be controversial).

The goals of surgery are to repair any associated hiatal hernia, establish an intra-abdominal length of esophagus, and perform a fundoplication as a barrier to reflux. Nissen or 360° fundoplication (Fig. 2) is the most frequently performed antireflux procedure. Toupet or 270° fundoplication has generally been reserved for GERD patients with ineffective esophageal motility, although its efficacy as compared to a loose Nissen fundoplication is controversial [37, 38]. There are numerous other types of antireflux procedure intended for use via transabdominal or transthoracic access methods, but a full discussion of surgical antireflux treatments is beyond the scope of this chapter. It can currently be stated that laparoscopic antireflux procedures represent the surgical standard of care for GERD, and advantages relative to open procedures are well established [39]. Investigations of surgical treatment of GERD in the elderly have generally shown that outcomes are favorable. Table 5 summarizes eight studies that compare surgical outcomes in "older" (>60 years) and "younger" patients (<60 years of age) [40–47]. These have established that postoperative symptom relief is not adversely affected by advancing age with mean follow-up of between 3 months and 5 years. There may be a perception that postoperative complication rates are higher and length of hospital stay are greater for patients >60 years of age, but this has not been consistently observed for antireflux surgery. Although patients >60 years had significantly higher American Society of Anesthesia (ASA) score in four studies and a higher rate of comorbidities in one study, this did not closely correlate with an increase in complication rate and length of stay. The likelihood of mortality with antireflux surgery is very close to zero in both populations.

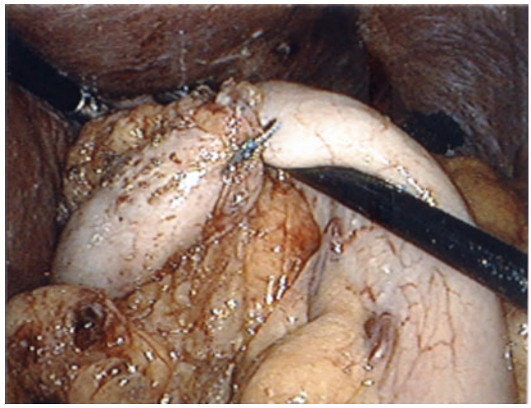

Fig. 2 Laparoscopic Nissen fundoplication. The loose nature of this complete (360°) wrap of gastric fundus around the esophagogastric junction and distal esophagus is demonstrated by the insertion of an instrument below the left-sided fundic component of the wrap

Current data suggest that antireflux surgery can improve formally measured quality of life in elderly patients. Kamolz et al. reported the use of the gastrointestinal quality of life index (GIQLI) to

Table 5 Laparoscopic antireflux surgery outcomes in elderly (>60 years) versus adult (<60 years) patients

Year	Author	Age (years)	*n*	Symptom relief	Complications	LOS (days)	Mortality in elderly
1998	Trus et al. [38]	69 (65–79)	42	=	=	=	None
1999	Brunt et al. [39]	65 (65–82)	36	=	> (13.9% vs. 2.6%)	> (2.3 vs. 1.6)	None
2002	Khajanchee et al. [40]	71 ± 6 (SD)	30	=	=	=	NA
2003	Fernando et al. [41]	68 (60–80)	43	=	=	> (2.9 vs. 1.6)	None
2006	Cowgill et al. [42]	70 (70–90)	108	=	=	> (4.3 vs. 2.6)	One patient
2006	Brehant et al. [43]	70 (65–94)	369	=	> (7.6% vs.4.5%)	> (5.9 vs. 4.6)	None
2006	Tedesco et al. [44]	69 (65–88)	63	=	=	=	None
2008	Wang et al. [45]	73 (70–76)	33	=	> (9% vs. 0.5%)	=	None

SD standard deviation, *n* total number of elderly patients in the study, = similar to adult patients, > greater than adult patients, *LOS* length of stay, *NA* not available

assess postoperative outcomes in 72 patients greater than 65 years of age. Scores were significantly improved 3 months after surgery compared to preoperative values. This improvement persisted 1 and 3 years after surgery and was similar to scores in healthy individuals [48]. Fernando et al. [43] and Wang et al. [47] showed that SF 36 health survey and GIQLI assessments of global and disease-associated quality of life postsurgical outcomes were not significantly different in patients <60 years and >60 years of age. The overwhelming weight of evidence indicates that antireflux surgery is both effective and safe in the elderly and that outcomes are comparable to those achieved in younger patients.

Intraoperative complications of antireflux surgery are uncommon. Esophageal perforation is rare and may result from dissection or bougie injuries. Common causes of intraoperative bleeding are adhesiolysis or injury to the left lobe of liver or the spleen. Bleeding is generally controlled by local measures and rarely requires conversion to an open procedure. Splenic injuries and splenectomy, which were surprisingly common events with open fundoplication (2–5%), are rare occurrences in laparoscopic antireflux surgery. Pneumothorax is also rare and is thought to be due to extensive dissection into the mediastinum. Chest tube placement is rarely required due to the rapid uptake of CO_2. Conversion rates from laparoscopic to open procedures are less than 5%.

Coelho et al. evaluated complications of laparoscopic fundoplication in 77 patients >70 years of age and reported 7.8% gas bloat syndrome, 5.2% dysphagia, and 2.6% gastric ulceration incidences [49]. Although most dysphagia after fundoplication either resolves or responds well to modest dietary measures, severe dysphagia symptoms may on rare occasions require endoscopic dilatation or surgical revision of fundoplication. Technical considerations that minimize the likelihood of postoperative dysphagia include routine division of the gastrosplenic ligament and short gastric vessels and adequate fundic mobilization for a loose wrap. The incidence of anatomic failure of antireflux procedures ranges from 3 to 6%. These cases include fundoplication disruption or slipping or axial herniation of the fundoplication into the mediastinum. Pledgeted suture repair of the hiatus and reinforcement of the defect with a mesh may decrease incidence of some types of anatomic failure [50].

Endoscopic Treatment

Endoscopic therapy for GERD has shown to significantly decrease PPI use, improve symptoms, and decrease but never normalize acid exposure in patients with mild forms of GERD. Proposed exclusion criteria include hiatal hernias greater than 2 cm, esophagitis greater than grade II, and disease refractory to PPI therapy [51]. Currently there are several devices available for GERD endoluminal therapy: (1) LINX (Torax Medical, Inc., Shoreview, MN), (2) Stretta (Mederi Therapeutics, Inc., Norwalk, CT), and (3) EsophyX (EndoGastric Solutions, Inc., Redmond, WA). Many other devices in this area have been discontinued due to poor outcomes. The principles by which these current devices operate are (1) reinforcement of the LES with magnetic beads (LINX), (2) full-thickness serosa-to-serosa plication at the GEJ (EsophyX), and (3) radiofrequency thermal therapy delivered to LES to promote thickening (Stretta). Potential advantages in elderly patients include performance with conscious sedation and relatively short-procedure duration. There may be applications in poor surgical candidates or as a bridge between medical and surgical therapy. However, based on current literature, there are no clear indications based on perceived or measured superiority relative to traditional surgical measures. Published studies have been small and more focused on safety and feasibility than on long-term durability and efficacy. With increasing experience, evolving techniques and hardware, as well as more thorough investigation, endoluminal therapies may become a viable option in the treatment of GERD, with specific applications in the elderly.

Paraesophageal Hernia

Case Study: Part 1

Presentation: A 77-year-old retired policeman with oropharyngeal squamous cell carcinoma s/p radiotherapy was referred to surgical clinic for evaluation of GERD and a right inguinal hernia. His primary symptom was heartburn, but he also suffered from occasional regurgitation, bloating, and chest/epigastric pain. A proton pump inhibitor provided reasonable relief of his heartburn, but he was leery of taking this medication indefinitely. Of note, he already had dysphagia primarily to solids secondary to poor dentition and decreased saliva from his radiotherapy. Regarding his groin, the patient started noticing right groin discomfort several months prior to presentation. Since then the discomfort progressively worsened, and he developed a large bulge extending into his scrotum. He denied obstructive symptoms.

Exam and Workup: On exam the patient was well appearing but clearly underweight. Breath sounds were symmetric. He had a flat abdomen that was soft and nontender. The right groin was remarkable for a large but reducible inguinal hernia. There were no relevant laboratory findings. Additional workup included an upper gastrointestinal fluoroscopic series (UGI), manometry with impedance, and a CT scan of her abdomen and pelvis. The UGI series revealed a large type 3 hiatal hernia with organo-axial rotation and reflux to the midesophagus, new since a comparable study in 2013. High-resolution manometry showed normal lower esophageal sphincter (LES) tone and relaxation, normal peristalsis, and lax upper esophageal sphincter (UES) tone. The CT scan confirmed the presence of the hiatal hernia and showed a right inguinal hernia containing loops of small bowel.

Paraesophageal hernia is primarily a disease of the elderly, and the average age of diagnosis is 60–70 years. The true incidence of hiatal hernias is difficult to determine because majority of patients remain asymptomatic and therefore undiagnosed. There are four types of hiatal hernias. (1) Type I (sliding hiatal hernia): esophagogastric junction migrates through the hiatus and is commonly associated with GERD. (2) Type II: gastric fundus herniates through the hiatus with esophagogastric junction in an intra-abdominal position. This is a true para-esophageal hernia. (3) Type III (combination of Type I and Type II). In this hernia type, gastric fundus and esophagogastric junction herniate into the mediastinum (Fig. 3). (4) Type IV: Type III hernia with herniation of other viscera such as spleen or colon [52]. Type II, III, and IV hiatal hernias are called paraesophageal hernias, and Type III hernia is the most common among

Fig. 3 Barium esophagram of a type III (paraesophageal) hiatal hernia. In this case, there is clear demonstration of the relationship between the axially rotated gastric fundus and the adjacent esophagus, which tapers at the expected location of the diaphragmatic hiatus

them (90%). Type I or sliding hiatal hernias are at least seven times more common than para-esophageal hernias [53].

Pathophysiology

Paraesophageal hernias occur more frequently with advancing age and are believed to result from progression of a sliding hiatal hernia. Prolonged repetitive stretching of the phrenoesophageal membrane due to movement of the esophagus during swallowing, as well as increased intra-abdominal pressure due to conditions such as morbid obesity, COPD, asthma, and chronic constipation, may contribute to more complex patterns of gastric herniation into the chest [53].

Clinical Presentation

Symptoms associated with paraesophageal hernias are primarily related to partial or complete gastric obstruction. Patients present with nausea, bloating, early satiety, chest pain, and fullness relieved with vomiting and dysphagia. Fifteen to thirty percent of patients with paraesophageal hernias complain of GERD symptoms [54, 55]. Patients with larger hernias may suffer from chest pain and shortness of breath. Paraesophageal hernias may be associated with chronic blood loss and anemia due to gastric erosions from prolonged trauma [56]. Gastric volvulus is a possible complication of paraesophageal hernias, with rotation either along the long axis of the stomach (organo-axial) or along a perpendicular axis (mesenteroaxial). Patients with completed volvulus can present emergently with acute gastric obstruction and potentially with gastric strangulation. Symptoms associated with this presentation are epigastric pain, persistent retching and vomiting, bloody vomitus due to gastric ischemia and ulceration, and an acute abdomen and sepsis if a gastric perforation has occurred. Previous studies have reported an acute presentation in 29% of patients with paraesophageal hernias [57, 58]. However, a recent study by Stylopoulos et al. looked at five studies and estimated the probability of developing acute symptoms to be 1.16% per year. The lifetime risk for developing acute symptoms is 18% for 65 years and decreases as patent's age increases [59]. Arguments for mandatory surgical treatment of paraesophageal hernia are generally based on the need to avoid this variably estimated risk, which may be favorably affected by advancing patient age.

Diagnosis

Chest radiograph may demonstrate an air–fluid level in the left chest. Upper gastrointestinal contrast study with barium is the study of choice to diagnose paraesophageal hernias (Fig. 4). Computed tomography can also establish the diagnosis (Fig. 5). Upper endoscopy can aid in recognition of a paraesophageal component of a hiatal hernia and will provide other information such as the presence of esophagitis or ulcerations. Twenty-four hour pH monitoring and esophageal manometry can be considered in patients with GERD symptoms but may not influence surgical planning.

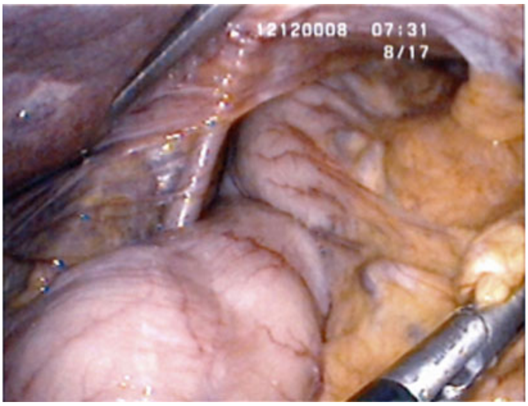

Fig. 4 Laparoscopic view of a type III (paraesophageal) hiatal hernia, with the herniated body and fundus of the stomach above the right crural pillar

Fig. 5 CT chest coronal section of a type III hiatal hernia (paraesophageal), with adjacent contrast-filled esophagus between the distended, herniated stomach, and the thoracic vertebrae. Such studies have become increasingly valuable in more precisely defi ning anatomic relationships in complex hernias of this type. This information can be used to better understand the condition, or as an aid in operative planning

Treatment

Surgical management of symptomatic and asymptomatic paraesophageal hernias has historically represented a mandatory standard of care. This is based largely on reports of a high (28–30%) incidence of acute symptoms necessitating emergency operations, which were associated with high rates of morbidity and mortality [57, 58]. Surgery continues to be the treatment of choice for symptomatic paraesophageal hernias. However, the treatment of asymptomatic and minimally symptomatic hernias has become more controversial. Allen et al. followed 23 patients managed nonoperatively for an average of 78 months and reported that only 4 developed progression of symptoms and that the 2 patients who underwent elective repair did well [54]. Stylopoulos et al. assessed outcomes of elective laparoscopic hernia repair vs. watchful observation in patients with asymptomatic and minimally symptomatic indications based on information from 20 published studies. Using a predictive model, it was determined that less than one in five 65-year-old patients and only one in ten 85-year-old patients will benefit from elective surgical treatment [59].

The goals of operative treatment of paraesophageal hernias are (1) reduction of the herniated stomach (or other viscera), (2) reduction and excision of the hernia sac, (3) hiatal hernia repair with or without prosthetic mesh, and (4) secure subdiaphragmatic positioning of the stomach. Although the use of fundoplication in paraesophageal hernia repair remains controversial, it is frequently used on the assumption that it may reduce recurrent hernia risk as well as reduce postoperative GERD occurrence. As many as 60% of patients with Type III hernias have diminished LES pressures and abnormal esophageal pH monitoring studies [60, 61]. Willekes et al. reported that as many as 30% of patients had preoperative reflux symptoms and that some patients develop postoperative reflux despite the absence of preoperative reflux symptoms. They concluded that GEJ and LES physiology cannot be predicted once it has been surgically disturbed and all phrenoesophageal supporting attachments are divided [55].

Minimally invasive surgery has become the preferred method of management for paraesophageal hernias, with the well-founded expectation of decreased postoperative pain, length of stay, and morbidity and mortality compared to open surgical methods [61–64]. A large series (203 patients) of laparoscopic repair for giant paraesophageal hernia (1/3 or more of stomach herniation into chest) suggests a pattern of disease skewed toward more elderly patients. The mean patient age was 67 years (34–91 years), and median follow-up was 18 months. The median length of hospital stay was 3 days, morbidity was 28%, and mortality was 0.5. Postoperative symptom relief was excellent to good in 92% of patients [63].

Bammer et al. and Grotentuis et al. evaluated outcomes of laparoscopic paraesophageal hernia repair in patients >80 years of age and >70 years of age, respectively. Results were comparable to studies with mixed age groups [65, 66]. Gangopadhyay et al. compared results of laparoscopic paraesophageal hernia repair in three age groups <65 years (Group 1), 65–74 years (Group 2), and >74 years (Group 3). Group 3 had significantly higher ASA scores and hospital length of stay, but their postoperative complication rate, symptom relief, and recurrence rates were comparable to other groups [67]. In a retrospective review of 1005 patients (>80 years of age) who underwent diaphragmatic hernia repair, 43% of procedures were emergent. Emergency operations were more common among older patients, and the concurrent finding of CHF was associated with longer hospital length of stay and mortality (14 ± 1 days and 16%) compared to patients who underwent elective repair (7 ± 1 days and 2.5%) [68]. Laparoscopic paraesophageal hernia repair is a safe and effective option in the elderly, and they should not be denied surgery based on age alone, because emergency surgery in this population is associated with significant mortality. In elderly and debilitated patients with multiple comorbidities, one should consider shorter, less invasive techniques such as anterior gastropexy or placement of percutaneous endoscopic gastrostomy after the reduction of paraesophageal hernias. Agwunobi et al. and Kercher et al. performed these techniques in small series of high-risk patients (13 and 11 patients) with minimal complications and low recurrence rates [69–70].

Case Study: Part 2

Treatment: Based on the patient's constellation of findings and general health, he was offered an elective laparoscopic hiatal hernia repair. The index operation was to include a partial as opposed to full fundoplication in order to minimize the risk of worsening his dysphagia, as well as a possible Collis gastroplasty.

He underwent an uneventful operation with completion esophagogastroduodenoscopy and was subsequently admitted to the surgical ward. There were no medical issues throughout his hospitalization nor did he require anything beyond acetaminophen for pain control. An UGI series on postoperative day 2 showed no obstruction, leak, or malposition of the fundoplication. As such, he was started on a clear liquid diet and ultimately discharged on full liquids with instructions to advance his diet on an outpatient basis. He was symptom-free at his postoperative clinic visit.

Salient Points

1. The hernia sack should be fully reduced and resected.
2. If maximal safe mobilization of the esophagus does not yield adequate intra-abdominal length, a Collis gastroplasty should be performed to mitigate the risk of recurrence. The fundoplication should be wrapped around the neo-esophagus created by the gastroplasty and not below it.

Esophageal Motility Disorders

Esophageal motility may undergo various physiological changes with aging. Among these are decreased secondary esophageal peristalsis, increased ineffective tertiary contractions, and diminished velocity and amplitude of peristaltic waves (Table 2). Esophageal dysmotility may be primary, such as in achalasia, diffuse esophageal spasm (DES), and nutcracker esophagus, or secondary to conditions such as systemic sclerosis, polymyositis, and diabetes mellitus [71].

Achalasia

Achalasia has two incidence peaks: the first between ages 20 and 40 and the second in more elderly patients. Sonnenberg et al. reported an average age of 78 years for patients with achalasia based on hospital admission codes, with a steady increase in hospitalization rates between the ages of 65 and 94 years [72].

Pathophysiology

Achalasia is a primary functional disorder of the esophagus characterized by the absence of peristalsis and incomplete relaxation of the LES during swallowing. These characteristics contribute to a functional obstruction at the GEJ [73]. Although occasional familial clustering of achalasia cases has been reported, most are sporadic and of uncertain etiology [74]. The esophageal manifestations of Chagas disease (*Trypanosoma cruzi*), which is endemic in South America, can be considered a form of achalasia but is accompanied by a host of other infection-related problems. It can be observed in elderly patients and presents particular management challenges largely due to the broader range of systems affected and overall poorer prognosis.

Viral infection has been proposed as a causative factor in achalasia [75, 76]. Reported histologic characteristics are based on resected and autopsy esophageal specimens and most likely reflect advanced disease findings. Wallerian degenerative changes, loss of myenteric ganglion cells, microscopic degeneration of the vagus nerve, and hypertrophy of the muscularis propria of the distal esophagus have been described [77]. A loss of nitric oxide and vasoactive intestinal peptide (VIP)-containing postganglionic inhibitory neurons in the myenteric plexus may be responsible for impairment of LES relaxation due to unopposed cholinergic stimulation [78–80]. Goin et al. have suggested an autoimmune etiology based on the identification of circulating antimuscarinic antibodies in chagasic achalasia [81]. The presence of Lewy bodies in the myenteric plexus and loss of neurons in the dorsal motor nucleus of the vagus in both achalasia and Parkinson's disease suggest a possible link between the two diseases, which appear with high prevalence in the elderly.

Aperistalsis in achalasia is not clearly understood. Inhibitory innervation is believed to be critical to the phasic sequence of esophageal muscular contractions, and it is possible that loss of inhibitory neurons abolishes peristaltic motor function. Long-term aperistalsis and functional GEJ obstruction can eventually result in a massively dilated and tortuous esophagus devoid of any discernible motor function [73].

Clinical Presentation

The most common symptoms of achalasia are dysphagia to solid food, regurgitation of esophageal contents, weight loss, and various patterns of chest pain. Dysphagia is progressive in achalasia and may also interfere with ingestion of liquids. Other clinical complaints may include cervical level dysphagia and difficulty belching. It has been suggested that some symptoms are related to impaired upper esophageal sphincter relaxation [82, 83].

Dysphagia and impaired esophageal emptying in achalasia are due to both impaired LES relaxation and loss of esophageal peristalsis. There is stasis of varying amounts of undigested food proximal to the LES depending on the capacitance of the dilated esophagus and the rate and quantity of food intake. Patients develop techniques to facilitate esophageal emptying, including slow, purposeful swallowing, avoidance of firm foods, postural changes (twisting, stretching), and ingestion of warm liquids with meals. Approximately 40% of patients have chest pain in the xiphoid or substernal areas, which often prompts evaluation for cardiac problems. This pain may be increased by exercise and relieved by rest [84]. Achalasia patients also commonly describe "heartburn," which is most likely related to esophageal stasis [85]. Clouse et al. compared clinical presentations of achalasia in patients greater and lesser than 70 years of age. Although symptom patterns were similar in the two groups, fewer of the older patients complained of chest pain [86].

Patients with achalasia are at risk for developing chronic inflammation, ulceration, perforation, and fistulas as a result of chronic stasis and retention. It has been shown that there is a 33-fold increased risk of esophageal carcinoma in these patients, with a yearly incidence of 3.4/1000. The patients at highest risk are elderly patients with a long-standing history of dysphagia and a markedly dilated esophagus [87].

Diagnosis

A plain chest radiograph may demonstrate a widened mediastinum and an air–fluid level in the posterior mediastinum due to esophageal dilation. A barium esophagram effectively demonstrates the gross esophageal changes, which can include dilation, tortuosity, retention of food and barium, and a symmetric smooth tapering of the esophagus resembling a bird's beak (Fig. 6). The most striking gross feature of achalasia is massive esophageal dilation known as sigmoid esophagus or megaesophagus seen in advanced cases (Fig. 7).

Upper endoscopy should be considered a mandatory study to exclude peptic stricture and malignancy. The latter condition may be associated with clinical changes similar to those of achalasia, particularly in patients over 60 years of age [88, 89]. A diagnosis of pseudoachalasia can be firmly established only by biopsy and histologic demonstration of carcinoma.

Of all currently available studies, esophageal manometry establishes the diagnosis of achalasia most effectively. Although the resting LES pressure is normal in 40% of patients, up to 80% have absent or incomplete LES relaxation with wet swallows. It must be emphasized that the presence of LES relaxation does not exclude achalasia. Post-deglutitive relaxations may appear complete

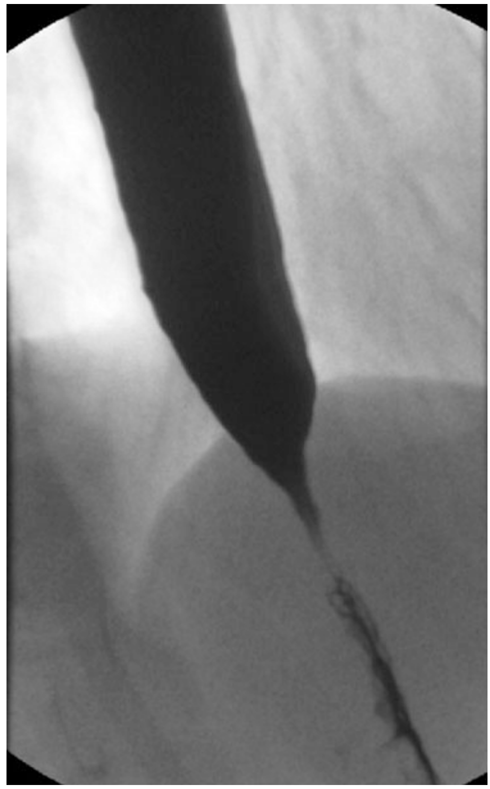

Fig. 6 Bird's beak deformity of the distal esophagus in a patient with achalasia seen on a barium esophagram. This characteristic appearance in a patient with the clinical features of achalasia is strongly suggestive of this condition

Fig. 7 Barium esophagram of a megaesophagus in a patient with advanced achalasia. The barium column may be diluted by retain fluid and food in the enlarged and sometimes tortuous esophagus

but usually are of short duration [90, 91]. Loss of normal esophageal body peristalsis is manifested by simultaneous contractions following wet swallows. Contractile amplitudes are low (10–40 mmHg) with frequent prolonged and repetitive waves. Studies have shown increased basal LES pressure in older patients with achalasia compared to younger patients [92, 93]. Chuah et al. demonstrated a linear correlation between age and LES basal pressure in achalasia patients [93]. Vigorous achalasia is a variant of achalasia characterized by high amplitude (>60 mmHg) simultaneous esophageal contractions, which may be associated with intense chest pain. This form of achalasia may be less frequent in elderly patients.

Treatment

Treatment of achalasia is primarily palliative and is geared toward adequate symptom relief from functional LES obstruction [73]. A variety of nonsurgical and surgical options are available.

Nonsurgical Treatment

Calcium channel blockers and nitrates are the most commonly used pharmacological agents in the treatment of achalasia. Clinical improvement with both sublingual isosorbide dinitrite and nifedipine treatment has been reported; however, symptom relief is variable, 53–87% and 0–75%, respectively [94, 95]. These agents must be taken sublingually immediately prior to meals to achieve the desired result. The major potential side effects that might limit this treatment are headache, hypotension, and tachyphylaxis. However, oral pharmacotherapy has not gained popularity because of its short-lived effects, poor symptom relief, and decreasing efficacy with time. They are definitely an option in patients awaiting definitive therapy and the elderly who have failed botulinum toxin therapy and are poor candidates for pneumatic dilatation and surgery.

Intrasphincteric injection of botulinum toxin type A has shown to effectively reduce LES pressure by inhibiting cholinergic receptors. Pasricha et al. reported a 70% symptomatic relief in patients treated with botulinum toxin with 40% requiring more than one injection [96]. Despite impressive early results, the long-term efficacy of this treatment has been questioned based on high 1-year relapse rates and less successful repeat injection. Older patients and patients with vigorous achalasia have a better response to botulinum therapy [97]. Elderly patients (>60 years) with significant medical problems tolerate this treatment modality well [98, 99].

Pneumatic balloon dilatation has wide acceptance and is a mainstay of treatment for achalasia. This technique employs a rapidly inflated balloon in the distal esophagus to dilate and disrupt the circular smooth muscle fibers of the LES. The procedure is well tolerated with a short hospital stay. The first dilatation results in symptom relief in 50–65% of patients [73]; however, 15–48% of patients require repeat procedures [100–102]. Patients older than 40 years had better 2-year results than patients younger than 40 (67 vs. 29%) [103]. The principal risk of pneumatic dilation is esophageal perforation, which in skilled hands is less than 2%. The risk of perforation is highest with the first dilatation.

Surgical Treatment

Surgical treatment of achalasia consists of longitudinal division of the LES muscle fibers also referred to as *myotomy* or *esophagomyotomy*. This procedure lowers LES pressure and esophageal intraluminal pressure but most importantly eradicates the effects of incomplete LES relaxation. Good to excellent results have been reported in as high as 90% of patients with 1–36 years of follow-up. Follow-up studies have demonstrated an improvement in esophageal emptying, increased LES diameter, and decreased esophageal diameter [104–107]. Although the point in a patient's care at which surgery should be offered is undefined, superior results with laparoscopic myotomy as initial therapy, as compared to pneumatic dilatation and botulinum toxin, have been suggested [108]. Furthermore, Smith et al. reported that complication rates after laparoscopic Heller myotomy were higher among patients who underwent previous endoscopic treatment with GI perforation being the most common complication (9.7 vs. 3.6%) [109].

Laparoscopic esophagomyotomy is currently the most frequently used surgical approach for achalasia, with decreased postoperative pain, length of hospitalization, and technical ease, compared to open and thoracoscopic methods. The peroral endoscopic technique is the latest advance in this field, with efficacy and safety presumably comparable to the laparoscopic approach in skilled hands [110]. Current data indicate that laparoscopic myotomy is a safe and effective option in elderly patients. Kilic et al. reported that in 57 patients >70 years of age who underwent laparoscopic Heller myotomy, there were no perioperative deaths and that there was a 19.3% complication rate and median hospital stay of 3 days. At a mean follow-up of 23.5 months, 96.5% reported improvement in symptoms [111]. Severe preoperative dysphagia, dilated esophagus, and absence of all motility are predictors of poor outcome, and LES pressure >35 mmHg is a predictor of good outcome after laparoscopic Heller myotomy [112, 113]. The overall complication rate for esophagomyotomy is 10%, with GERD being the most common postoperative problem followed by dysphagia from insufficient myotomy [104]. Although partial fundoplication (Dor vs. Toupet) may substantially reduce postoperative reflux with esophagomyotomy, the potential for residual dysphagia has tempered its use.

Diffuse Esophageal Spasm

Diffuse esophageal spasm (DES) is a primary esophageal hypermotility disorder characterized by dysphagia and episodic substernal chest pain. It is a rare condition, the etiology of which is unknown. Although the mean age of occurrence is in the fifth decade, it can occur in elderly patients up to the eighth decade of life. Because the symptom that most often brings DES patients to medical attention is angina-like chest pain, formal workup for a cardiac etiology is almost always undertaken.

Diagnosis

The principal manometric findings in DES are frequent simultaneous and repetitive contractions of abnormally high amplitude or long duration. The finding of 20% or more simultaneous contractions per 10 wet swallows is considered diagnostic of the disorder [114]. LES resting pressures and relaxation with swallows are usually normal. DES activity is intermittent, and ambulatory 24-h manometry allows patients to go about their daily activities and receive whatever typical stimuli are necessary to precipitate an episode [115]. Many patients with DES have an underlying psychiatric history with diagnoses that include depression, psychosomatic complaints, and anxiety. These diagnoses have been reported in 80% of patients with manometric contraction abnormalities [116].

A barium esophagram can help in the characterization of DES. Occasionally, a “corkscrew” esophagus caused by segmental contractions of circular muscle is identified. The finding of an esophageal pulsion diverticulum in a patient with characteristic chest pain is virtually diagnostic of DES. Esophagoscopy should be performed in all patients to exclude the possibility of a tumor, fibrosis, or esophagitis, which might cause esophageal narrowing that may be associated with proximal tertiary esophageal contractions.

Treatment

Treatment of this condition may be difficult. As with achalasia, some patients respond to sublingual nitrates or calcium channel blockers before meals [117, 118]. Esophageal dilation may alleviate symptoms of dysphagia for days to months and can be repeated for continued relief [119]. However, there is an increased risk of perforation with multiple dilations of a hypertrophic, spastic esophagus.

Surgical treatment is generally reserved for medical and endoscopic treatment failures. This consists of a long myotomy aimed at reducing simultaneous contractions and improving compliance at the cost of peristaltic loss and reduced residual muscular contraction amplitude [120]. It can be accomplished thoracoscopically [121], with an 80% rate of diminished symptoms during the early postoperative period. Fundoplication may be performed to avoid reflux but with the same concerns expressed for achalasia. With long durations of follow-up (5.0–10.7 years), surgically treated patients can remain free of chest pain and dysphagia [122].

Other Esophageal Motility Disorders

Nutcracker (hypercontractile) esophagus is another primary esophageal hypermotility disorder that like DES presents as episodic dysphagia and chest pain. It tends to occur later than DES (fifth and sixth decades of life) and can occur in elderly patients as well. It is diagnosed by manometry when average peristaltic pressures are above 180 mmHg and have a prolonged duration. The overall treatment algorithm is similar to DES, except there is no role for dilation, and myotomy may ultimately worsen dysphagia. Secondary esophageal dysmotility disorders occur in conjunction with systemic diseases such as diabetes, hypo- and hyperthyroidism, systemic sclerosis, polymyositis, and amyloidosis. These diseases are prevalent in the elderly and should be kept in mind while working up a patient for a suspected esophageal motility disorder [123].

Benign Tumors of the Esophagus

Benign tumors of the esophagus often go unreported and undiagnosed; their exact incidence is not known. In two large autopsy series, the reported incidences of these tumors were 0.45 and 0.59% [124, 125]. They can be intraluminal, intramural, or extramural. The most common benign tumors of the esophagus are leiomyomas, followed by fibrovascular polyps.

Leiomyomas

Leiomyomas are mesenchymal in origin and account for two-thirds of all benign esophageal tumors. The peak incidence for leiomyomas is between the ages of 30 and 59 but can occur in much older patients [126]. In a review of 838 cases, 56% were found in the lower third of the esophagus, 33% in the middle third, and 11% in the upper third [127]. Majority of leiomyomas are intramural and arise from the muscularis propria, but they can also rise from the muscularis mucosa. Esophageal leiomyomas grow slowly, and 50% of cases are less than 5 cm in size [127] and in some instances maybe as large as 15 cm. They can be single or multiple, spherical well-circumscribed intramural, pedunculated intraluminal, or annular masses.

The most common symptoms are dysphagia (46.9%) and retrosternal or epigastric pain (46.7%). Other symptoms associated with leiomyomas are weight loss, nausea, vomiting, reflux, ulceration, and bleeding [126]. Symptoms do not necessarily correlate with size [126, 128].

Large leiomyomas may present as rounded or lobulated lateral mediastinal growths on chest radiography; this is usually an incidental finding in asymptomatic patients. Barium swallow is the first diagnostic test performed in patients with symptoms suspicious for benign esophageal tumors. Leiomyomas present as a well-circumscribed smooth filling defects with normal overlying mucosa on swallows. Endoscopy confirms the tumor location and further evaluates the mucosa overlying the mass. Mucosa is usually normal and moves freely over the mass in leiomyomas; one may observe luminal narrowing. However, mucosal irregularity, ulceration, and luminal stenosis with obstruction are suspicious for a malignant lesion. Endoscopic ultrasonography is useful in differentiating extrinsic vs. esophageal wall tumors and in delineating their layer of origin. Leiomyomas are well demarcated, uniform, hypoechoic masses, which may arise from the muscularis mucosa or muscularis propria [129, 130]. Identification of leiomyomas that originate in the muscularis mucosa permits consideration of endoscopic removal, while those that originate from the muscularis propria require more invasive surgical enucleation [131]. Computed tomography provides information regarding size, location, and anatomic relationships that may aid in operative planning. Endoscopic biopsy or endoscopic ultrasound-guided fine needle aspiration may provide a definitive tissue diagnosis. This should be reserved for lesions suspicious for malignancy as preoperative endoscopic biopsy is associated with an increased incidence of intraoperative mucosal tears [132].

Indications for surgical treatment are unremitting symptoms, increasing tumor size, mucosal ulceration, to obtain histological diagnosis, and facilitation of other procedures. Although controversial, asymptomatic patients should be managed nonoperatively with periodic radiological follow-up [133]. Symptomatic leiomyomas should be enucleated after performing a longitudinal esophageal myotomy; care should be taken to avoid mucosal injury. Myotomy should be reapproximated to avoid mucosal bulging and postoperative dysphagia. Tumors in the upper and middle third of the esophagus are approached from the right side of the chest, tumors in the lower third are approached from the left, and tumors at the GEJ can be resected through an upper midline abdominal incision. Tumors larger than 8 cm and those that are firmly adherent to the mucosa may necessitate esophageal resection [127, 134]. Resection can be achieved via open and minimally invasive techniques. Thoracoscopic approach has been gaining popularity because of its association with decreased hospital length of stay and postoperative pain in comparison to open procedures [132]. Overall patients tolerate resection well with minimal complications, good symptom relief, and no recurrences [133].

Fibrovascular Polyps

Fibrovascular esophageal polyps are intraluminal polyploid lesions that appear most commonly in the upper esophagus near the cricopharyngeus muscle. These lesions occur predominantly in men during the sixth and seventh decades but are also encountered in much older patients. As a group they include fibromas, fibrolipomas, myomas, myxofibromas, pedunculated lipomas, and fibroepithelial polyps [135, 136]. Early lesions consist of nodular submucosal tissue that may over time elongate into a pedunculated polyp. The geometric forces of peristalsis eventually cause the tip of the polyp to reach the distal esophagus.

Fibrovascular polyps come to medical attention when large enough to cause intermittent dysphagia, substernal fullness, or regurgitation of recently ingested material. The presentation may be more acute if a pedunculated polyp obstructs the esophagogastric junction or becomes ulcerated and bleeds. Although rare, regurgitation of the tumor and asphyxiation secondary to acute glottic obstruction are an additional concern [137]. A barium esophagram demonstrates the smooth polyploid intraluminal filling defect. Upper endoscopy can also be used to visualize the polyp and permits the stalk to be traced to its level of attachment [138].

Fibrovascular polyps are resected to relieve symptoms and prevent aspiration and asphyxiation. The greatest polyp size that might be amenable to endoscopic excision is dictated by the polyp's architecture and location and by the endoscopist's skill. Surgical treatment is undertaken when endoscopic removal is unfeasible. The standard approach is through a cervical incision on the side of the neck opposite the stalk attachment. An esophagomyotomy is performed below the cricopharyngeal muscle, and the polyp is delivered into the wound and amputated at the stalk base. If the base is a significant distance below the cricopharyngeus, a right transthoracic approach can be used.

Esophageal (Zenker's) Diverticula

Diverticula can arise in the cervical, thoracic, and epiphrenic portions of the esophagus as a result of internal (pulsion type) or external forces (traction type). As elsewhere, a true diverticulum contains all layers of the esophagus, whereas a false diverticulum contains merely the mucosa and/or submucosa.

Pharyngoesophageal and epiphrenic diverticula are false pulsion diverticula. One example is Zenker's diverticulum (ZD) which arises in an area of muscular weakness in Killian's triangle proximal to the UES. In contrast, midesophageal diverticula are typically true traction diverticula resulting from an inflammatory process in the mediastinum [139].

Esophageal diverticula are ostensibly rare. Since asymptomatic cases are often unaccounted for, the true prevalence is unknown. Zenker's diverticula are usually discovered between the seventh and eighth decades of life, predominantly in men. The prevalence is estimated to be between 0.01% and 0.11% [140].

Clinical Presentation and Diagnosis

Patients with Zenker's diverticula present with dysphagia (98%), aspiration (33%), regurgitation of undigested food, cough, weight loss, noisy deglutition, halitosis, and voice changes. Although patients with midesophageal and epiphrenic diverticula may present similarly to those with ZD, they are more apt to be asymptomatic and their anomalies discovered incidentally. On rare occasions these patients may also present with chest pain, hematemesis from ulceration, or cardiac arrhythmias from atrial pressure [139, 141]. The risk of malignancy arising within a diverticulum is between 0.3% and 1.5% without relation to size or chronicity [142].

A barium esophogram is often sufficient to diagnose the diverticulum and screen for an associated motility disorder. The radiologist should be forewarned of the risk for aspiration in these patients. Based on the findings of cine esophagography, additional evaluation with endoscopy, manometry, and/or cross-sectional imaging may be appropriate. Specifically, endoscopy is useful in the presence of alarm signs and symptoms to rule out malignancy; manometry is useful to characterize an underlying motility disorder that would affect plans for myotomy; and cross-sectional imaging provides details on associated processes, such as inflammation.

Treatment of Zenker's Diverticula

Diverticula causing mild manageable symptoms can be followed. Treatment is indicated for respiratory compromise (e.g., aspiration), weight loss, and unmanageable symptoms.

Surgical Treatment

Surgical treatment of ZD is approached through a neck incision, usually along the anterior border of the sternocleidomastoid muscle on the left owing to the propensity for left-sided pouches. Once the diverticulum is exposed and dissected free from surrounding tissue, a myotomy is performed approximately 2 cm proximally onto inferior pharyngeal constrictor and 5 cm distally through the cricopharyngeus and along the esophagus. There are three options for addressing the pouch itself: -pexy, resection, or inversion (rare). Small pouches (<2 cm) can be treated with suspension or myotomy alone. Medium-sized pouches (2–5 cm) can be treated with a combination of suspension and myotomy. Larger pouches (>5 cm) are typically excised at the base with a linear stapler [140].

Yuan et al. analyzed 93 studies with over 6000 patients to compare various treatment modalities for esophageal diverticula. In the surgical group, overall mortality and morbidity were 0.6% and 10.5%, respectively. The most common complications were recurrent laryngeal nerve injury (3.3%), leak (3.3%), and cervical infection (1.8%) [143]. Resolution of symptoms ranges from 88% to 95% of patients, with a mean recurrence rate of 3.5% [141].

Endoscopic Treatment

Endoscopic treatment of ZD is carried out using either rigid or flexible endoscopy. Suitable anatomy – adequate neck length, sufficient hypomental distance, cervical flexibility, and modest BMI – is required for the rigid endoscope, whereas most patients are accommodating of the flexible endoscope. Regardless of the approach, the goal is to divide the cricopharyngeus muscle separating the esophagus and the pouch. The optimal pouch size for endoscopic treatment is 3–6 cm as smaller diverticula are difficult to intervene upon and larger ones are likely to have persistent symptoms from the new common channel [141]. The most common methods for dividing the common wall are electrocautery, CO_2 laser, stapling, and various energy devices. There is no conclusive data on a single best cutting technique. Discussion of each technique is beyond the scope of this chapter.

In Yuan's endoscopic group, overall mortality and morbidity were 0.2% and 8.7%, respectively. The most common complications varied by technique, but overall these included cervical/mediastinal emphysema (2.2%) and/or perforation (1.4%) [143]. Endoscopic treatment requires conversion to surgery in 15–68% of cases [140]. Success and recurrence rates in the literature vary from 63% to 100% and 0% to 35%, respectively [143].

	Open surgery	Rigid endoscopic	Flexible endoscopic
Complication rate	Higher	Lower	Unclear
Hospital charge	More	Less	Less
Cervical scar	Yes	No	No
Conversion	Never	Occasional	Rare
General anesthesia	Mandatory	Usual	Optional
Neck extension	No	Mandatory	No
Recurrence	A few	Unclear	Unclear
Treatment sessions	Most 1	Most 1	Most >1
Anatomic limitations, stiff neck, poor mouth opening, etc.	No	Yes	No
Small diverticulum	Suitable	Unsuitable	Unsuitable
Large diverticulum	Suitable	Unsuitable	Unsuitable
Reoperation	Hard, risky	Easy, safe	Easy, safe
Special technique	No	Yes	Yes
Dental injury	No	Occasional	Rare
Recurrent nerve injury	Yes	Rare	Rare

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Elderly Transplant Recipients

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Contents

Abstract

There is a proven benefit of transplantation for the elderly in terms of quality of life and survival advantage over alternative therapies like dialysis. Frailty, comorbidity, access to transplantation, increasing wait time, and delayed allograft function negatively affect transplant outcomes for the elderly. Age-related comorbidities increase the risk of early mortality for seniors undergoing transplant. Pretransplantation activity and baseline

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cognitive function may impact suitability for transplantation and should carefully be considered during the selection process. The aging immune system, age-associated alterations in drug pharmacokinetics, and the risk associated with over-immunosuppression can make immunosuppression management a challenge in this population. Lack of adequate social support and finances can account for noncompliance leading to a poor outcome. When all these factors are taken into consideration, selective geriatric candidates can experience comparable benefits from transplantation as younger candidates. This chapter provides a concise review of factors that can make transplantation a success in the geriatric population.

Keywords
Geriatric · Transplantation · Risk · Frailty · Selection · Outcomes

Introduction

It is now well recognized that elderly patients undergoing transplantation for end-stage organ failure experience improved quality of life similar to their younger counterparts [1]. The number of transplants performed in the elderly has steadily increased over the last decade [2, 3]. Similarly, elderly patients now account for a significant percentage of the transplant wait lists. As of 2015, 22% of patients on the kidney wait list and 20% on the liver wait list were above the age of 65 years [2, 3]. Projections from the Scientific Registry of Transplant Recipients (SRTR) annual report 2015 show that in the coming years there will be an increase in the number of transplants performed in this age bracket. Once considered a relative contraindication in the elderly, transplantation in this age group now forms a sizable population in any transplant program. Identifying features related to transplant outcomes that are unique to this transplant cohort is crucial for ensuring good results since older patients tend to have decreased patient and graft survival after transplantation when compared to younger recipients [4]. However, transplantation is pursued in the elderly population as it confers a definite survival advantage over remaining on the wait list [3].

The main challenges to transplantation faced in this population are complex medical comorbidities, frailty, and managing immunosuppression. The main reason for graft loss in this population is death with a functioning graft. Therefore, as newer organ allocation systems look to optimize utilization of organs, it is likely that the elderly may be disadvantaged. Approaches to counter this may be found in the use of organs from expanded criteria deceased donors or from living donors. Both have shown to be good strategies to increase patient and graft survival in the elderly [5]. Besides the challenges that transplant centers face when considering transplantation in the geriatric population, these patients also face various dilemmas with the onset of organ failure:

1. What treatment options do I have at this age for organ failure?
2. Should I remain on dialysis or will I be able to tolerate a transplant?
3. Which organ is suitable for me, younger kidney with a longer wait time or marginal kidney with a relatively shorter wait time?
4. Should I be looking for a living donor (either related or nonrelated)?
5. Will I be able to afford the posttransplantation care and medications?

The Elderly: Is It Age or Frailty or Both?

Aging is associated with functional and phenotypic changes in the immune system that presents unique challenges regarding immunosuppression management. Aging is also associated with functional decline in other organs systems and that increase the potential of morbidity and mortality from complications after transplantation. Cognitive decline with age may interfere with medication compliance and competence in understanding transplantation in general. It is widely accepted that there is a gap between chronological and biologic age of an individual. Frailty has a significant role to play in defining this gap.

The prevalence of frailty over the age of 65 years has been estimated to be 7–12% [6]. The concept of frailty has been defined as the increased vulnerability of an individual to stressors accompanied by a decline in reserves and functioning of several physiologic systems [6]. Frailty has a negative impact on the outcome after transplantation over and above that can be accounted for by aging alone. Even though the exact mechanisms are incompletely understood, frailty has been found to be associated with dysregulation of energy metabolism, immunosenescence, inflammatory responses, and a deleterious effect on all physiologic systems [6]. It would therefore be of clinical relevance to identify potentially “frail” recipients early in the evaluation process to assure a survival benefit subsequent to transplantation.

Frailty has been associated with an increased risk for adverse postoperative outcomes across various surgical specialties and has been shown to predict prolonged hospitalization, early hospital readmissions, and 30-day postoperative complications independent of age [7–10]. With regard to transplantation, frailty has been identified as an independent risk factor linked to a twofold risk of delayed graft function and mortality following kidney transplantation [11, 12]. Frailty has also been shown to be an age-independent risk factor for early hospital readmissions, with a 1.5-fold adjusted risk for early readmissions in kidney transplant recipients [13]. Sarcopenia or muscle loss, which is often prevalent in the older population, is associated with an increased risk for infectious complications and mortality following liver transplantation [14, 15].

Given these findings, screening for frailty is highly relevant for determining if transplantation in the geriatric population would be truly beneficial. Even though visual assessment is usually adequate to identify frailty, objective diagnostic tools have been developed to improve accurately and consistency in assigning this descriptor. The two widely used tests include the 5-point questionnaire developed by Fried et al. [12] that asks about unintentional weight loss (10 lbs in the past year), self-reported exhaustion, muscle weakness (grip strength), slow walking speed, and low physical activity and the Frailty index which is based on clearly identifiable deficits (measured by clinical symptoms, functional impairments, and laboratory findings) that are compared to age-expected deficits [12, 16].

What Can Be Done to Address Frailty?

In the presence of old age and frailty, physical rehabilitation in the form of exercise training enables patients to effectively participate in activities of daily living and lessens the morbidity caused by chronic illness. Multiple interventions have been proposed that aimed at increasing aerobic capacity by maximizing oxygen uptake (VO2 peak), improving muscle and bone strength, maintaining body composition, and preserving quality of life by reducing fatigue [17]. Exercise and physical activity also have the ability to mitigate posttransplant complications and long-term side effects of immunosuppression such as hypertension, diabetes, and weight gain. Over 30 randomized controlled trials (RCTs) have been conducted to examine the effectiveness of exercise training on outcomes in solid organ transplant recipients [18]. The combination of frailty and old age on a background of chronic illness is associated with poor nutrition, which promotes anemia and hypoalbuminemia. Improving nutrition in this population, with focus on increased protein intake, prevents progression of sarcopenia [19].

Transplantation in Elderly Patients: Criteria for Selection

A diversity of outcomes has been reported in the literature regarding the outcomes of elderly recipients following liver transplantation [20–22]. There is now a greater understanding that physiological age is far more relevant than chronological age when considering suitability for a liver transplant recipient. For example, the presence of preexisting coronary artery disease and arrhythmia is an independent predictor of poor long-term outcomes following transplantation, and cardiac disease is one of the most common causes of mortality among the elderly transplant recipients [23]. Physiological age or general health in the elderly is usually assessed by a thorough geriatric assessment. There are several well-validated tools available for a geriatric assessment, most of which incorporate comorbidity measurement, functional status, nutrition, social support, and other health-related domains like urinary/fecal continence, etc. [24]. Biologic age has been the term used to represent the true chronologic age, while the concept of physiological age has usually been used to describe someone who is in better health than expected for his age. The concept of frailty on the other hand describes someone whose health status is worse. Both these concepts are crucial in deciding candidacy for transplantation as they have an impact on outcomes [6, 24].

Justification of Transplant in Elderly End-Stage Renal Disease Patients

The last decade has seen an alarming growth of the kidney transplant wait list in the United States from 30,000 to more than 100,000 candidates [25]. Among the population with ESRD, patients over 65 years of age are the fastest growing age group worldwide. It is therefore not surprising that elderly individuals are more likely than ever to receive a kidney transplant [26]. The proportion of kidney transplant recipients $\geq$65 years of age alone has increased from about 10–15% in 1997 to 20–30% in 2014 [27].

The survival benefit of kidney transplantation over dialysis was first demonstrated in 1999 by Wolfe et al. [28] Studies previous to then reported equivalent survival for dialysis and transplantation in patient ages 65–70 years and worse survival outcomes after renal transplantation in comparison to remaining on dialysis [26, 29]. Over time, the transplant survival benefit has extended to various patient subgroups including the elderly patients aging 60–74 years old at the time of transplant [30].

There is no absolute age cutoff for kidney transplant candidacy, however; overall health of the patient, with regard to frailty and coexisting comorbid illness, is an important consideration when selecting elderly candidates for transplantation. The UK Renal Association guidelines state that "age is not a contraindication to transplantation, but age-related comorbidity is an important limiting factor," while the American Society of Transplantation guidelines maintain "there should be no absolute upper age limit for excluding patients whose overall health and life situation suggest that transplantation will be beneficial" [31, 32]. In general, instead of applying definitive age limits, a careful assessment of patient's physiological age rather than chronological age should be considered when determining candidacy for transplant. Several studies have shown that despite age, elderly patients receiving renal transplants fair better than their counterparts on chronic dialysis in terms of general physical health, social functioning and independence, and mental health [33, 34].

Access to Transplantation for Seniors: The UNOS New Allocation Policy

Although it can be assumed that wait-listing of elderly patients is mainly determined by coexisting comorbidities, it has been reported that wait-listing is often not even considered in the absence of any formal contraindications [35]. Reasons for non-consideration for transplantation in the elderly are multifold including lack of referral by treating nephrologists, misconceptions regarding candidacy or criteria for transplantation in dialysis centers, patient uncertainty as potential candidates, physician's belief of "displacing" a kidney from a younger potential recipient, and lack of dissemination of education related to transplantation [36]. In Europe and the United States, only about 10% of ESRD patients aged 65 years or older will be wait-listed and/or transplanted within the first 4 years of ESRD therapy, while in those below 65 years of age, this figure is as high as 60% [37, 38]. It has been shown that the wait time for a deceased donor renal transplant (DDRT) has exceeded the life expectancy for subgroups of the elderly candidates who were non-white, blood type B or O, highly sensitized, 70 or older, diabetic, female, with excessively low or high BMI, or on dialysis [39]. Although access to transplantation for older patients has improved in the recent years, the cumulative probability of transplantation from any donor source (deceased or living) at 3 years after initiating dialysis was only 7.3% [40].

The original national kidney allocation system was based on accumulated time since wait listing. Kidneys were dichotomized into standard criteria donor (SCD) or extended criteria donor (ECD) classification based on the donor organ quality. This classification disadvantaged placement of ECD kidneys, leading to high discard rates of many otherwise transplantable organs. Allocation seemed inefficient with placement of kidneys with long projected posttransplant graft survival in recipients with short posttransplant life expectancy and vice versa. One of the first large-scale initiatives for efficient organ allocation is the old-to-old approach launched by the Eurotransplant Senior Program (ESP) in 1999 [41]. Kidneys from donors age 65 years or older were allocated to recipients age 65 years or older within a narrow geographic area without considering donor HLA matching in order to minimize cold ischemia time with acceptable 5-year patient and allograft survival. In the United States, a new allocation system was implemented in 2014 to overcome shortcomings of the older allocation with several prominent changes including replacement of the SCD/ECD designation to KDPI (kidney donor profile index), which more accurately expresses quality of the donor kidneys. This index uses ten donor parameters and allows calculation of estimated post-transplant survival (EPTS), to enable 20% of candidates with the highest EPTS to receive priority for the top 20% of kidneys and offer efficient combined local and regional placement of kidneys with KDPI >85%. This system enhances utilization of these organs and minimizes the discard of the 15% of kidneys with the shortest estimated potential length of function to [42]. With this allocation in practice, senior recipients are faced with two challenges, a proportional shift of deceased donor kidneys toward younger recipients resulting in increasing wait times and increased availability of marginal or higher KDPI kidneys for transplantation with high perioperative morbidity which could compromise graft and patient survival.

Due to the long waiting list, allocation of kidneys for transplantation needs to be optimized to maximize the utility of kidney allografts. This is relevant when transplanting elderly patients where the lifespan of the kidney can be limited by age-related illness and mortality. In an otherwise healthy recipient 60 or older, this risk is more than double that of a younger adult recipient (9.2% versus 3.5%, respectively) [43]. The risk of mortality in the first year after a DDRT is higher for older transplant recipients compared to those remaining on the wait list, and this further worsens in the presence of age-related comorbidity or other factors such as delayed graft function (DGF) or receiving an ECD kidney. The survival advantage of transplantation markedly decreases along with increasing costs as wait time increases for a deceased donor in older patients. Hence, some transplant centers advocate DDRT for relatively healthy senior patients up to ages 65–70 with wait times up to 2 years and living donor transplantation in other situations or in patients up to age 80 years [44].

Selecting the Right Candidate: Evaluation Issues in the Elderly

Overall, the health status of an elderly individual impacts their chance of being transplanted. An extensive pretransplant evaluation and risk stratification are therefore warranted to avoid transplanting frail patients with comorbidities and maintain the balance between benefits and harms of transplantation. Certain surrogate markers of frailty or poorer general condition includes a prolonged time between start of dialysis and placement on the waiting list since longer dialysis period tends to exacerbate complications and comorbidities. Similarly, period of “inactive status” on the wait list could also indicate poor health. There are varying recommendations for exclusion of elderly patients for transplantation. Patients with an anticipated post-transplant 5-year survival of less than 80% or an anticipated overall survival of less than 2 years, patients predicted to experience worsening quality of life, or those who had a low probability of surviving beyond current waiting times should be preferably excluded from listing [31, 45–48].

There are no clear-cut selection guidelines for transplant candidacy in elderly patients. Most transplant programs adopt their own listing policies depending on wait times for availability of deceased organs, existing comorbid conditions of the potential recipient, and other criteria deemed suitable per the center's policies. Several factors to be considered when determining transplant candidacy in an elderly patient include overall health status; comorbidity from cardiovascular disease and malignancy; "geriatric syndromes" such as delirium, falls, and frailty; functional and cognitive impairment; and adequacy of social and financial support. Due to large geographic variations in the wait times within the 58 donor service areas, local waiting times are equally important [49]. Since waiting time also depends on the blood type, patients with O and B blood types have the longest waiting times, whereas A and AB blood types get transplanted sooner [50]. Hence, an elderly patient with an unfavorable blood type, in an OPO with long waiting times, will have a better chance at survival with a living donor. In the absence of reliable tools to accurately estimate duration of survival posttransplant, pretransplant physical function is highly predictive of posttransplant outcomes [51]. Frailty is highly prevalent in individuals with ESRD, and hence simple evaluation of frailty scores prior to listing can help identify candidates at risk of poor performance posttransplant [52, 53]. In older patients, frailty is independently associated with postoperative complications, length of stay, discharge to a skilled or assisted-living facility, and mortality [7, 9, 54]. A single-center study of kidney transplant recipients found a 25% prevalence of frailty, threefold higher than community-dwelling older adults. Frailty was found to be a strong independent risk factor for DGF and mortality. Frailty is associated with a 94% increased risk of delayed graft function, a 61% increased risk of early hospital readmission, and a 2.2-fold increased risk of mortality compared to non-frail recipients [55]. In liver transplant recipients, sarcopenia, estimated by core muscle size and considered as an effective objective surrogate of frailty, is associated with higher risk of posttransplant infections and mortality [14, 15].

Elderly patients are more likely to have coexisting comorbid conditions; therefore, careful screening of cardiovascular disease and cancer is mandatory to assess perioperative and long-term mortality risk. According to the American Heart Association and the American College of Cardiology Foundation, noninvasive stress testing may be considered in patients $\geq$60 years without any active cardiac conditions but presence of two of the following coronary artery disease risk factors including diabetes, hypertension, dyslipidemia, prior cardiovascular disease, left ventricular hypertrophy, smoking, and more than 1 year on dialysis [56]. On the other hand, the ERA-EDTA guidelines recommend performing a standard exercise tolerance test and cardiac ultrasound such as asymptomatic high-risk patients and restricting noninvasive stress imaging (dobutamine stress echocardiography or myocardial perfusion scintigraphy) only for candidates with a positive or inconclusive exercise tolerance test. Patients with a positive stress test need further evaluation with coronary angiography to assess ischemia [57]. Evaluation for cancer includes colonoscopy, mammogram, Pap smear, prostate-specific antigen, and skin examination as indicated. Atherosclerotic vasculature and lack of appropriate sites for implantation often rule out candidacy in older patients, and hence suitable imaging studies, such as a CT scan of the abdomen and pelvis without intravenous contrast, are necessary part of the evaluation process. Aging is associated with increasing incidence of depression, cognitive impairment, and dementia which is poorly recognized in the ESRD population [58].

Even subtle cognitive deficits may impair a candidate's ability to follow the complex posttransplant medical regimens necessary for successful outcomes. Despite the high prevalence, testing for cognitive impairment is not routinely performed. High-risk elderly candidates should undergo neuropsychologic testing to identify those who are at increased risk of functional decline, repeated hospitalizations, and eventually death. Validated screening tools for detection of cognitive defects in this population are the Montreal Cognitive Assessment tool, Mini-Mental State Examination, and the St. Louis University Mental Test to name a few [58]. Lack of adequate social support and finances may be another impediment in this population. The elderly often face social isolation due to depression, loss of a spouse or partner, financial restraints, visual or functional impairment, and cognitive deficits. Most patients 65 years or older qualify for Medicare that will cover 80% of the cost of transplantation; however, additional supplementary insurance is required to cover medication costs. Absence of social and financial support often leads to noncompliance and poor outcomes [33].

Organ Selection for the Elderly Transplant Candidate

Liver Transplantation

Livers from donors aged over 70 years are much more likely to be discarded than livers from younger donors [59]. However, use of such livers has shown to have acceptable outcomes and, in several cases, results equivalent to those obtained using livers from donors younger than 70 years of age [60, 61]. Important to the success of using older organs is minimizing cold times (<8 h) and the extent of macroscopic steatosis and restricting use of such organs to recipients without acute liver failure or hepatitis C, first transplants, age less than 45 years, and with body mass index below 35 kg/m^2 [62, 63].

Kidney Transplantation

Organ options for kidney transplantation in the elderly include kidneys from a living donor or a deceased donor, i.e., donation after brain death (DBD) or cardiac death (DCD). Living donor offers the least risk of perioperative mortality due to immediate function and the best long-term outcomes in elderly transplant recipients [64]. Even the use of an older living donor in this population has shown acceptable outcomes [65, 66]. Survival advantage over dialysis is now well established with the use of low or high KDPI grafts (>85%, expanded criteria donor per older terminology). However, the survival benefit with DCD donors is unclear. This is due to the risk of perioperative morbidity and mortality from the 40% rate of delayed graft function (in comparison to the 20% rate otherwise), which can further have a negative impact in an elderly recipient [67]. In general, for most elderly patients the choice of an organ will largely depend on local waiting time, recipient age, race/ethnicity, cause of renal failure, and projected survival on dialysis.

The Older Living Donor: Should There Be an Upper Age Limit?

Liver Transplantation

Living donor liver transplantation provides an alternative organ resource to deceased donor livers. Although usually used for pediatric and lower MELD adult liver failure patients in the United States, this is the main resource for liver transplantation in several Asian countries due to the scarcity of deceased donors [68, 69]. The use of older living donors has increased over time, but the number of donors aged over 60 years remains very limited [70, 71].

Though not a common practice, isolated reports of live liver donors over 70 years of age have been cited [72]. The use of elderly living liver donors is controversial not only due to the increased risk of complications to the donor but also due to the risk of primary nonfunction and lower graft survival in such cases. Hence in the United States, age for a liver living donor is limited to less than 60 years [73, 74].

Kidney Transplantation

Living donor renal transplantation is the best option for ESRD not only in terms of a valuable resource for organ shortage but also offers the best outcomes for patients, in terms of graft and patient survival. As the rate of living donor kidney transplantation has gradually increased, the selection of older living donors (>60–65 years) has also increased. Several large cohort studies including older living kidney donors have found no significant differences in perioperative surgical morbidity and mortality for these donors compared with younger donors and similar risk of death and end-stage renal disease (ESRD) to that of matched controls from the general population [75–78]. Older donors not only scored higher than their younger counterparts in post donation quality of life surveys but also reported higher satisfaction with cosmetic outcomes of the surgery [79, 80]. Overall, there is no current evidence precluding kidney donation over the age of 60 or even 70 years.

Age of the donor has a direct impact on the transplant outcome. With regard to graft and recipient survival, outcomes of kidneys from older living donors are inferior to those from younger living donors; however, this difference dissipates over time [65]. Death adjusted and unadjusted allograft survival is comparable between kidney transplantations from old and young living donors [81]. When compared with deceased donors, graft survival with older living donors was still better than that of kidneys from deceased older donors and comparable to that of kidneys from deceased younger donors. Hence, a carefully selected older living donor should never be excluded especially when this may be the best option for a sensitized patient or when it is the only living donor option for a patient.

Immunosuppressive Strategies in Older Recipients

Graft loss in the elderly most often reflects death with a functioning graft, death resulting from existing cardiovascular risk which is further aggravated by immunosuppression in addition to associated infections and malignancies. Hence understanding the structural and functional changes of the immune system in the elderly population is prudent for selecting the best immunosuppressive strategy for this age group.

Immunosenescence and Immunological Characteristics of the Elderly Recipient

Older patients have an age-associated progressive decline in immune functions defined as "immunosenescence." With advancing age, the ability to respond to an immunological challenge decreases. Increased morbidity and mortality associated with aging result from multiple mechanisms altering the innate and adaptive immune system. Senescence affects the innate immune system, which serves as a major barrier against infections, by increasing pro-inflammatory cytokines [82]. This effectively exacerbates ongoing chronic allograft damage by increasing the inflammatory response. Dysregulation and alteration of the receptor-driven functions of neutrophils, such as apoptosis, chemotaxis, and superoxide anion production, in older patients increase the risk of mortality from infectious complications. Natural killer (NK) cells participate in immune response against solid organ grafts through allograft rejection and tolerance and may predict morbidity and mortality in older people through an essential role concerning risk of infections and cancers [83]. Older patients have been shown to have a decreased proliferative response of NK cells when stimulated with IL-2 [84].

Old age-related thymic involution affects adaptive immunity with reduction of the number of circulatory naïve T cells and a compensatory increase in memory T cells [85]. This reduction in naïve T cells has thought to be a reason for lower rates of acute rejection in the elderly. However, this has not translated to successful withdrawal of immune suppression [86]. Humoral response is also altered with reduced number of naïve B cells in comparison to the memory B cells [85]. Overall, this increases morbidity associated with the individual's vulnerability to infection from reduced antibody formation, tendency to form autoantibodies, and enhanced release of inflammatory mediators [85].

Risk and Challenges for Immunosuppression Considerations

In terms of the effect of aging on rejection and infection, patients >65 years of age experience a much lower (20%) risk of acute rejection in comparison to the 37% risk in younger patients and a fivefold increased risk of death due to infection [87, 88]. Risk of acute rejection increases with the use of kidney from an older donor, and this may affect long-term graft survival due to critical nephron loss in an already marginal kidney [89]. Early acute rejection within 90 days of transplantation adversely impacts both patient survival and death-censored graft survival [90]. Immunosuppressed elderly patients with an already compromised immune system are at an increased risk for developing severe infections with an exponential increase in death related to infectious complications [91].

Use of immunosuppressive agents in the elderly is associated with increased rates of post-transplant morbidity. Immunosuppression causes a 30% increase in the risk of new-onset diabetes after transplant per decade of age [92]. Compared to younger kidney transplant recipients (20–29 years old), the relative risk of immunosuppression-associated cancer in elderly recipients is 8.92 for recipients between 60 and 69 years old and 11.6 in recipients >70 years old [93]. Kidneys from older donors are more susceptible to ischemia/reperfusion injury and associated risk of delayed graft function and acute rejection due to vascular and glomerular senescence. As a result, nephrotoxicity from calcineurin inhibitors (CNI) can be exacerbated in aging kidneys, further increasing risk of chronic allograft nephropathy and graft loss [94]. Other aspects that need to be considered when formulating immunosuppression strategies for the elderly include adverse drug reactions, drug-drug interactions, and medication non-adherence that has a strong inverse relationship with the number of drugs prescribed [95].

General Considerations for an Optimal Immunosuppressive Regimen

There is a limited evidence for age-adapted immunosuppressive regimens due to the underrepresentation of this age group in clinical trials. In general, elderly transplant recipients receive the same immunosuppression regimens as their younger counterparts. However, old age is a risk factor for many drug-related adverse effects. Age can affect responses to medication with increased organ susceptibility for drug-related toxicity or drug-drug interactions. Age-related changes in drug pharmacokinetics include decrease in drug absorption, reduced hepatic metabolism due to age-related decrease in hepatic mass and blood flow, and increase in the volume of distribution for lipophilic drugs due to increase in the percentage of body fat compared to body water [96]. Elderly recipients are at higher risk for early acute rejection in the presence of an older allograft, and long-term immunosuppression is associated with an increased risk of infections and malignancies. Hence adequate initial and finely tuned maintenance immunosuppression is the key for optimal long-term allograft outcomes in this group. Despite the absence of randomized trials, CNI and steroid minimization or early steroid withdrawal have been recommended in this population due to the deleterious effects of these medications on blood pressure along with lipid and glucose metabolism [97, 98].

Use of induction immunosuppression in the elderly has been popularized in the United States in the last few years to enable CNI minimization and early steroid taper or withdrawal. More than two-thirds of the recipients over 60 years old receive induction with either anti-thymocyte globulin (ATG) or interleukin-2 receptor antagonists (IL2RA) [99]. Use of ATG in in this situation has shown a reduction of the risk of acute rejection with improved graft survival [99]. However, the use of ATG increases the risk of morbidity and mortality from infections, especially when the cumulative dose exceeds 6 mg/kg [100]. Monitoring of lymphocyte depletion by measuring CD3/CD4 counts can help guide ATG therapy. As such, recipients with high immunological risk benefit with induction therapy using ATG, whereas IL2RA is a safer option for low or intermediate risk [99].

The increased frequency and severity of steroid associated complications including infections, impaired wound healing, fractures, diabetes, and cardiovascular events provides a good rationale for steroid avoidance or early taper in older population. In comparison to standard steroid therapy, steroid avoidance or early withdrawal has been shown to be associated with higher 3-year patient survival (83.6 vs 86.3, $p = 0.004$) despite a modest increase in the rate of rejection (14.3% versus 12.3%, $p = 0.002$) [98]. Attempt at steroid minimization is thus justified in older patients with low immunological risk. CNI minimization also helps reduce early as well as delayed nephrotoxicity. The latter in addition to the cardiovascular side effects of CNIs can result in graft loss [101]. Belatacept is a new costimulatory blockade molecule, targeting the CD80-CD86/CD28 pathway, which has been proposed as an alternative to CNIs [102]. Its use led to comparable rates of DGF and acute rejection but resulted in lesser toxicity in terms of better renal function, better blood pressure control, and better lipid profile and lesser incidence of NODAT at 5-year post-transplantation [102]. As it is administered by scheduled monthly injections, it also has an added benefit of better long-term medication compliance and adherence [103].

There is limited information about long-term immunosuppression management in the elderly. Therapy is usually individualized with modifications made in the face of serious complications of drug-related side effects, life-threatening infections, or cancer.

Outcomes

Transplantation for elderly with end-stage organ failure has a definite survival benefit over other treatment modalities currently available. Elderly individuals who receive kidney transplants benefit from a substantial reduction in mortality with a nearly 4-year increase in their projected lifespan compared to those who stayed on dialysis [28]. This benefit was dependent on the quality of the graft, as patients who received grafts from living donors had a higher probability of survival at 5 years [3]. Also, among elderly recipients of deceased organ donors, those from younger donors have better survival than those from older donors. The 5-year patient survival for kidney transplant recipients above 65 years of age receiving a deceased donor organ was 75.2% while for those who received living donors was 83.9%. For the same age group, 5-year allograft survival for recipients of a kidney from a deceased donor was above 70% while for those with a living donor was 79% [3]. As mentioned above, the main reason for graft loss in this population is death with a functioning graft. Death-censored graft survival on the other hand is no worse in the elderly than it is in their younger counterparts [3].

Mortality for end-stage liver disease in the elderly is significantly higher than mortality in younger patients, resulting in higher wait list mortality in this age group. For patients aged above 65 years, the wait list mortality was the highest of all age groups at 13 per 100 patient years [2]. In comparison, wait list mortality for patients aged 18–34, 35–49, and 50–64 is 8, 11, and 11, respectively, per 100 patient years [2]. In patients aged above 65 years, 5-year graft survival is 63% while patient survival at 5 years is 68% [2]. This was markedly lesser than their younger counterparts. Having said this, another rationale used to justify transplantation in the elderly is the transplant-related survival benefit. It is representative of the difference between life expectancy with and without transplant. Despite lower 5-year survival, the elderly demonstrated a transplant-related survival benefit similar to younger patients [104]. The main reasons for graft loss in this age group were also death with a functioning graft. Overall, graft failure was not an important cause of death, and death-censored graft loss rates were not higher for older recipients when compared to this age bracket [105].

In recent years, outcomes after transplantation have moved beyond morbidity and mortality to incorporate quality of life. Transplantation has a positive impact on the quality of life of the elderly. Data from studies performed by several groups across the country demonstrate QOL metrics at 1 year from transplant are similar to or even higher than age-matched values from the general population. Also, in the case of kidney transplantation, another benefit of transplantation in the elderly is its cost-effectiveness over remaining on renal replacement therapy such as hemodialysis or peritoneal dialysis. However, if wait times for transplantation increased to over 2–4 years for the elderly patient, the cost benefits to be gained from transplant appear to diminish [106]. Strategies to counter the compounding effect of waiting are the early use of living donors or the use of donors from increased risk population and marginal deceased donor kidneys with KDPI >85%.

Conclusion

The recent era has seen an increase in the percent of elderly transplant candidates because of the demographic changes resulting from increased longevity of the population. While there are no absolute age cutoffs for consideration to receive a transplant, frailty and comorbidities in an elderly transplant recipient can reverse the survival benefit offered by transplantation. Frailty, baseline cognitive function, physical impairment, lack of mobility, history of infections or malignancy, and cardiovascular comorbidity assessment during transplant evaluation are critical in the elderly to better predict their suitability for transplantation. The new kidney allocation system, implemented in 2014, made provisions to better age-match donors and recipients as well as directed the best quality of organs to the recipients among the top 20% of wait list candidates with the longest estimated posttransplant survival. This is likely to adversely impact the senior population by decreasing the proportion as well as quality of deceased donor organs available for transplantation. It may also lead to increasing the wait times to transplant for the elderly. Since the survival advantage of transplantation markedly decreases with increasing wait time, increased utilization of increased risk donors, marginal deceased donor kidneys with KDPI >85% (analogous to previous extended criteria allocation) and living donor kidneys have emerged as realistic options for timely transplantation of the elderly recipients. The concept of "old for old" allocation should be judiciously applied taking into consideration the deleterious effects of delayed graft function particularly in this population and the increased risk of first-year mortality. Implementation of measures to reduce the incidence of DGF by quicker allocation of such marginal kidneys to older recipients locally or over a narrow geographic area will help minimize the cold ischemic times. Immunosuppressive protocols should be individualized based on the clinical course and immune monitoring taking into consideration the decreased alloresponse of an older recipient and the increased immunogenicity of older organs. Nonetheless, the 5-year patient and graft survival for elderly recipients are comparable to the younger population with proper candidate selection. By carefully balancing the benefits and risks associated with organ transplantation in elderly recipients, we can offer them improved physical and mental health leading to improved vitality in the elderly.

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44 Benign and Malignant Tumors of the Liver

Rebekah R. White and Vijay G. Menon

Contents

Abstract

As the population ages, mortality from cancer has increased, and increasingly cancers of the liver are being encountered in an older population both in the USA and worldwide. The most commonly encountered primary tumor is hepatocellular carcinoma, and the most commonly encountered metastatic tumor is of colorectal origin. Evaluating elderly patients for surgical management involves assessment of their preoperative function, both with overall physiology and evaluation of the liver itself. Prehabilitation regimens to optimize the patient are being promoted, and assessment of the aging liver for cirrhosis and regenerative

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capability needs to be assessed or even augmented. Benign tumors in otherwise asymptomatic patients rarely require intervention and are usually observed. Malignant tumors are managed with multiple modalities including surgical resection or transplantation, liver-directed therapies such as ablation or hepatic artery embolization, as well as chemotherapy or biologic therapy targeting the relevant tumor type. Data is conflicted, regarding outcomes of performing complex hepatobiliary surgery in the elderly, but overall advancing age in a patient with appropriate physiological and liver reserve should not preclude surgery.

Keywords
Hepatocellular carcinoma · Cholangiocarcinoma · Liver metastases · Benign liver tumors · Liver resection · Cirrhosis · Liver disease · Liver transplantation · Prehabilitation · Liver regeneration

Introduction

Over the last two decades, the field of hepatobiliary surgery has evolved and continues to push limits with improving outcomes. Multiple studies have shown that major resections can safely be undertaken with good outcomes, but only a small percentage of these studies have specifically looked at surgery in the older population. The purpose of this chapter and this textbook is to evaluate disease processes and their management in the elderly, and to that end we review the existing data as well describe our experiences in managing liver tumors in the elderly.

Case Study

Background

A 78-year-old male with morbid obesity and insulin-requiring diabetes mellitus who presented with RUQ pain and liver function test (LFT) abnormalities. Ultrasound demonstrated

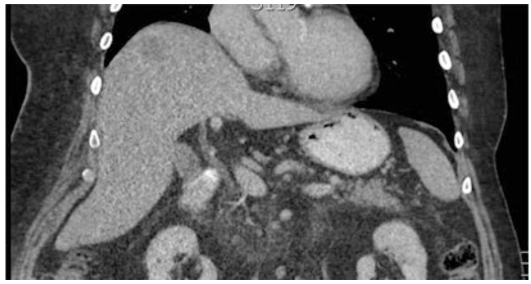

Fig. 1 Triphasic CT with irregularly shaped mass

choledocholithiasis as well as a mass in the dome of the liver. Subsequent triphasic CT demonstrated an irregularly shaped 5 cm mass with slight arterial enhancement but most clearly seen in the venous phase (Fig. 1). The patient underwent ERCP with successful clearance of the common bile duct and resolution of his symptoms. He was transferred to our center for further management. Lab work was remarkable for a mildly elevated CA19-9 (66), a normal AFP and CEA, and normal LFTs except for low albumin (3.1) and mildly elevated transaminases. PET/CT demonstrated mild uptake (SUV3.9) in the mass and no extrahepatic disease.

Management

The patient was taken to the OR for laparoscopic (hand-assisted) wedge resection and cholecystectomy. A thoracic epidural was placed preoperatively for postoperative pain control. His postoperative course was remarkable for an acute increase in his creatinine to a high of 1.9 on POD#2 that was attributed to relative hypotension associated with epidural and which improved after discontinuation. He was discharged to a SNF on POD#5 then subsequently returned to living independently at home. Pathology revealed moderately differentiated hepatocellular carcinoma with negative margins in a background of steatohepatitis. He was doing well without evidence of recurrent disease at his 3 month follow-up visit. This case highlights the challenges of managing liver tumors in elderly patients who often have multiple comorbidities. Minimally invasive approaches may help to shorten hospital stays and are particularly useful in obese patients who are at risk for significant wound complications. The use of epidural anesthesia remains controversial, and – while avoidance of systemic narcotics is certainly beneficial in elderly patients – the risks of associated relative hypotension need to be recognized.

Epidemiology of Liver Neoplasms

With an aging population, cancer diagnosis and mortality from cancer have increased, nearly matching "traditional" causes of death such as cardiovascular disease (Fig. 2) [1]. Recent CDC data from 2014 ranks heart disease, *malignant neoplasms*, chronic low respiratory disease, cerebrovascular disease, and Alzheimer's disease as the five leading causes of death in the population older than 65 years [1]. It is estimated that there will be approximately 600,000 cancer-related American deaths in 2016.

SEER data [3] show that primary liver cancer – hepatocellular cancer (HCC) and intrahepatic bile duct cancer/cholangiocarcinoma (ICC), together – is currently the 13th most common cancer in the USA. However, with an annual increase in incidence of 3.7% and 3.0% in males and females, respectively, primary liver cancer is estimated to become the 11th most common cancer by 2030 [4].

Although there are several more common cancers than HCC and ICC, the mortality rates from these cancers are high with overall 5 year survival of 17.5% in the USA [3]. Currently, HCC and ICC are the fifth leading cause of death in the USA with estimates suggesting that by 2030, these cancers will become the third leading cause of cancer death in the USA [4]. Of note WHO data shows that after lung cancer, liver cancer is already the leading cause of cancer-related death worldwide with 788,000 deaths in 2015 [5].

SEER data show that the median age at diagnosis of liver and intrahepatic bile duct cancer is 63 years (Fig. 3) [3] suggesting that there is a large patient population over 65 years of age who could potentially undergo surgery, although localized disease is seen overall in only 43% [3].

The most common malignant liver tumors in the USA, however, are secondary (metastatic) tumors, with the most common primary origin being colorectal cancer (CRC). The overall

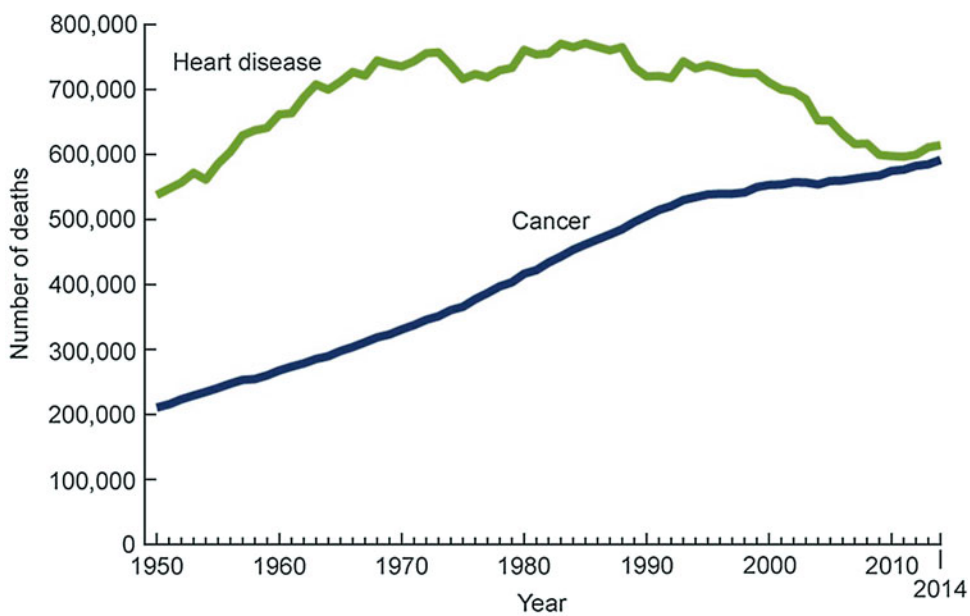

Fig. 2 Number of deaths due to heart disease and cancer [1]

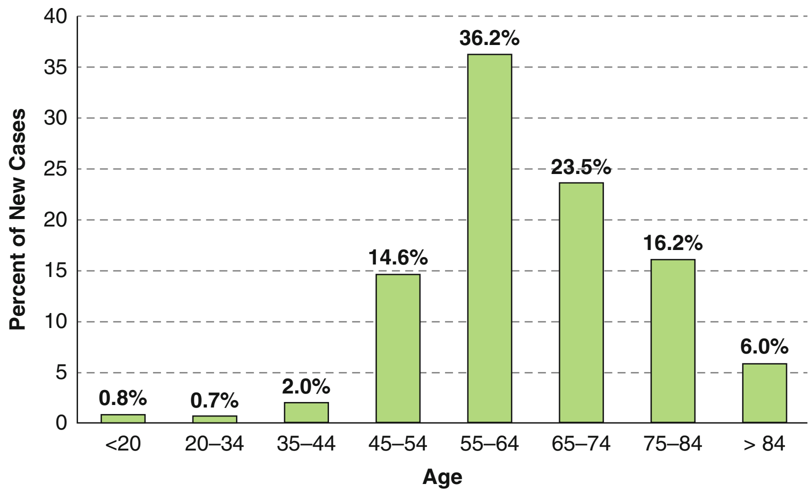

Fig. 3 Percent of new cases by age group: liver and intrahepatic bile duct cancer [3]

incidence of CRC is 41.0 per 100,000, with an overall lifetime risk of 4.4% of persons being diagnosed with CRC. Most cases occur in patients older than 65, with a median age of diagnosis of 68 years, and approximately half of patients diagnosed with CRC will present with or develop liver metastases.

Benign liver tumors are much more common than malignant tumors and are often noted incidentally on ultrasound. They are more commonly seen in patients under 50 years of age, with recent data supporting hemangiomas as being more prevalent (3.6%) than focal nodular hyperplasia (0.18%) and hepatic adenomas (0.04%) [2].

Liver Surgery in the Elderly

Operating in the elderly population is more common and less avoided than in the past. Defining the age for the elderly population itself is variable, with studies making comparisons in patients younger or older than 65 years of age all the way up to a nonagenarian population.

A review of ACS NSQIP data in 2006 [6] showed expectedly that age was significantly associated with morbidity and mortality. However, their focus was specifically on patients older than 80 years of age. Even when ASA scores and cardiac and other comorbidity scores have been controlled for, given their association with elderly populations, studies invariably show worse surgical outcomes in elderly compared to younger populations. However, these outcomes have to be gauged against those of nonsurgical management in the same elderly population.

Hepatobiliary surgery in any population, whether cirrhotic or non-cirrhotic or young or elderly, is not a minor procedure. Perioperative management and decision-making at the pre-, intra-, and post-op stages have improved and advanced over the years, allowing more aggressive approaches to resection with acceptable outcomes [7, 8]. Several studies have reported nearly equivalent outcomes in elderly and younger populations [9–11] or worse but acceptable outcomes in older patients [12–16] with liver resection. A few studies have even shown better outcomes in the elderly after liver resection compared to the young [17, 18], although multiple variables including type of tumor and other factors greatly influence outcomes of these studies. Several studies have also shown better outcomes with surgery compared with ablative or medical management [19, 20] in the elderly, though surgery produces overall higher improved survival in the younger population.

One of the great benefits of minimally invasive surgery is the reduced length of stay, earlier recovery, and less need for opioid pain control with smaller incisions. Multiple studies have shown excellent oncological and survival outcomes with laparoscopic hepatic surgery. A recent large multi-institutional study comparing open and laparoscopic surgery in patients older than 70 showed comparable R0 resection rates, recurrence-free and overall survival, and significantly lower blood loss, overall morbidity, and shorter high dependency unit stay in the laparoscopic group [21]. Of note, however, patients aged 70–74 were more likely to benefit from laparoscopic surgery, with gradual loss of these advantages with increasing age. In the next few sections, we will look more closely at the unique characteristics of an aging liver as well as preoperative evaluation and optimization.

The Aging Liver

Aging decreases volume of the liver, with several studies showing decreases of 20–40% as one gets older [22–25]. Blood flow is also decreased, with an approximately 35% reduction in those over 65 years old compared to a younger population [26]. The liver cells themselves have reduced mass with aging as seen in radioisotope studies [27]. In addition there is polyploidy, decreased smooth endoplasmic reticulum, accumulation of dense bodies, and declining and dysfunctional mitochondria. The biochemical and metabolic effects of an aging liver include a slightly reduced serum albumin concentration, elevated serum gamma glutamyltransferase and alkaline phosphatase levels, reduced serum bilirubin levels, and stable serum aminotransferase levels [28].

Most pertinent to hepatic surgery is the ability of the liver to regenerate. With aging there is a decrease in the regenerative ability with subsequent delay in the restoration of liver function. It is thought that fewer hepatocytes enter S-phase in the elderly after partial hepatectomy and that they enter at a slower rate [25]. Animal studies have suggested that cell growth may be impaired by increased reactive oxidative species in the hepatocytes of aged mice and that ablation of the promoter gene reduced this post-hepatectomy oxidative stress [29, 30]. Investigators have also suggested that reduced cell proliferation in the elderly may be due to loss of hepatocyte telomere length [31, 32], although other studies have countered that other pathways allow for appropriate regeneration [33].

Cirrhosis is the end result of fibrosis resulting in destruction of normal liver architecture and loss of hepatocytes. Histologically, it is characterized by nodular regeneration with dense fibrotic septa and distortion of hepatic vascular architecture. The clinical manifestations of cirrhosis arise from portal hypertension and loss of hepatic synthetic function. Cirrhosis is the 8th leading cause of death in the USA and 13th leading cause of death worldwide [1]. The major causes of cirrhosis are chronic hepatitis B and C virus infection, alcohol, and nonalcoholic steatohepatitis.

Nonalcoholic fatty liver disease and its subtype nonalcoholic steatohepatitis (NASH) have emerged as a leading cause of cirrhosis. The causes of this entity are thought to be obesity with most of the consequences a result of insulin resistance (Fig. 4) [34]. The mortality risk in compensated cirrhosis is 4.7-fold and decompensated cirrhosis is 9.7-fold higher than the general population [35]. Delving into the pathophysiology and management of cirrhosis is beyond the scope of this chapter, but two interesting aspects of cirrhosis should be addressed. Cirrhosis generally takes several years to develop and as a result is more commonly seen in an elderly population. HCC principally occurs in the setting of cirrhosis, and, as discussed earlier, the median age of diagnosis is in the seventh decade of life [3]. Although not as strongly associated with cirrhosis, the risk of ICC is also increased in patients with liver disease [36, 37]. Operating on the elderly should take into consideration whether there is underlying liver disease, even if compensated, as the ability of the liver to regenerate is compromised in the older patient.

Pre-op Evaluation and Prehabilitation

There are relatively few absolute contraindications to liver surgery in general, but certainly there are comorbidities that make surgery and/or the expected recovery more difficult [38, 39]. Several indices and algorithms have been created to estimate the risk of adverse outcomes after

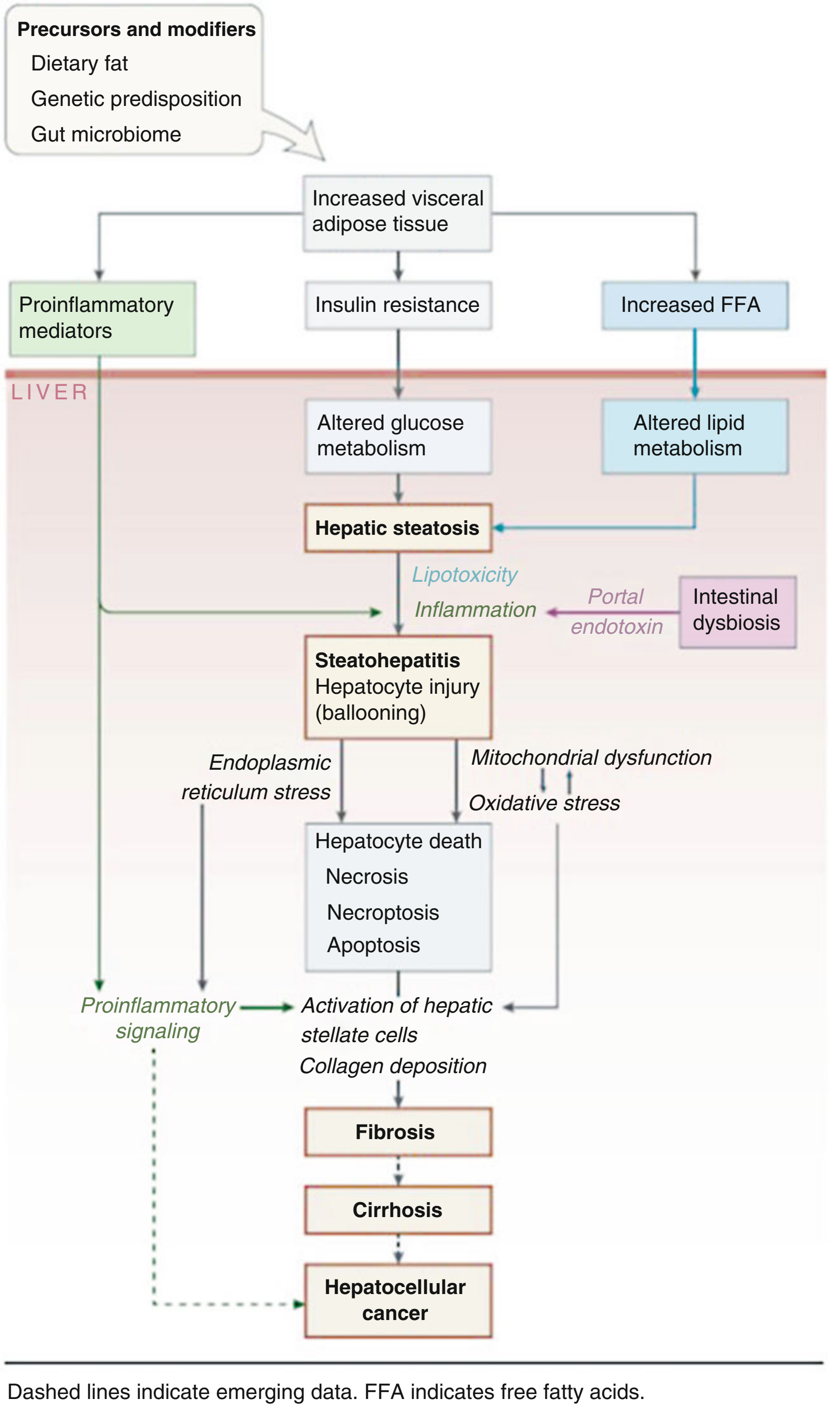

Fig. 4 Mechanisms involved in the pathophysiology of NAFLD [34]

surgery [40–43], and these are likely to be focused on in other chapters of the textbook. Of note, there was an excellent collaboration between the American College of Surgeons and the American Geriatric Society optimal preoperative assessment of the geriatric surgical patient (Table 1) [44].

Several studies have focused on risk factors for cardiac and pulmonary complications after surgery. However, one of the most important predictors of outcomes after liver surgery stems from the liver itself, specifically the presence and degree of cirrhosis with two major scoring systems, Child-Turcotte-Pugh (CTP) and Model for End-Stage Liver Disease (MELD) score, used to stratify mortality.

A study from Duke University [45] analyzed the ability of ASA class, Charlson Index, and CTP and MELD scores to predict mortality and morbidity. They found that only ASA and CTP were predictive, suggesting that MELD – which was originally created for assessing outcomes of transjugular intrahepatic portosystemic shunt and used for liver transplant listing – may not be as useful for hepatic resections, which generally occur in patients with CTP B or less. Other studies have suggested that MELD may be used as surrogate for CTP C, although the C-equivalent MELD score has ranged from 9 to 17 in these studies [46, 47]. Most surgeons perform liver resections only in CTP A and select B patients. In fact, surgery, other than liver transplantation, is generally avoided in CTP C patients unless there is backup of liver transplant for any potential decompensation.

Table 1 Checklist for the optimal preoperative assessment of the geriatric surgical patient [44]

Assess the patient's **cognitive ability** and **capacity** to understand the anticipated surgery
Screen the patient for **depression**
Identify the patient's risk factors for developing postoperative **delirium**
Screen for **alcohol** and other **substance abuse/ dependence**
Perform a preoperative **cardiac** evaluation according to the American College of Cardiology/American Heart Association algorithm for patients undergoing noncardiac surgery
Identify the patient's risk factors for postoperative **pulmonary** complications and implement appropriate strategies for prevention
Document **functional status** and history of **falls**
Determine baseline **frailty** score
Assess patient's **nutritional status** and consider preoperative interventions if the patient is at severe nutritional risk
Take an accurate and detailed **medication history** and consider appropriate perioperative adjustments. Monitor for **polypharmacy**
Determine the patient's **treatment goals** and **expectations** in the context of the possible treatment outcomes
Determine patient's **family** and **social support system**
Order appropriate preoperative **diagnostic tests** focused on elderly patients

Most studies have acknowledged that chronological age itself should not deter surgical therapy. There have been several studies focusing instead on "physiological age," reporting on the use of frailty index or sarcopenia as an aid in surgical decision-making. A study from Johns Hopkins [43] incorporated weakness, weight loss, exhaustion, low physical activity, and slowed walking speed into a five-point scale for frailty and found that frailty independently predicts morbidity in surgical patients older than 65 years of age. A modified frailty index was used by investigators from Emory [48] to assess home discharge rates in elective vascular surgery patients and found that frail patients were significantly less likely to return home, regardless of whether a post-op complication occurred. There are several frailty indices or geriatric assessments available, and overall they correlate well with morbidity in cardiac [49–51], minimally invasive surgery [52, 53], colorectal surgery [54], and overall GI surgeries including liver resection [55, 56].

Sarcopenia is the loss of skeletal muscle mass and can be used independently or as an adjunct with frailty. Several studies have used total psoas area or total psoas volume to measure sarcopenia and have shown adverse outcomes after liver resection or liver transplant [57–60] with a Johns Hopkins study [61] in 2015 reporting a significant difference of 40% vs. 18% complication rate in sarcopenic vs. non-sarcopenic patients with Clavien grade >= 3 occurring in the former group only, although overall survival was not significantly different between the groups.

Assessment of frailty and sarcopenia preoperatively allows for a frank discussion of risks and benefits of surgery but also allows for possible optimization. "Prehabilitation" regimens have been used to improve functional and physiological reserve to potentially negate the effects of "aging" on operative outcomes. A recent systematic review analyzed outcomes in nine studies and overall found no difference in postoperative complication rate in the control groups and the prehabilitation groups, but two studies showed improvement in health-related quality of life [62]. Contrary to this review, another meta-analysis [63] suggested that prehabilitation, consisting of inspiratory muscle training, aerobic exercise, and resistance training, appeared to decrease incidence of post-op complications in patients undergoing intra-abdominal operations. However, the authors caution that the grade of evidence is very low. Studies specifically looking at prehabilitation in liver surgery have not shown significant differences in morbidity or mortality with these regimens despite improvements in cardiopulmonary function [64, 65].

One of the significant drawbacks to these studies in cancer patients is the short duration with which to implement the prehabilitation, as long delays in oncologic surgery are usually not appropriate. Another issue is the lack of uniformity of various regimens. Most regimens include measures to improve physical exercise, but they rarely involve nutritional support and psychosocial support – the trifecta that make up the so-called "trimodal" prehabilitation program.

The liver's ability to regenerate allows major hepatectomy, but this is compromised with aging and cirrhosis, as discussed above. Multiple studies [66–70] over the last decade have shown a minimum future liver remnant (FLR) of greater than 20–30% is essential to preserve post-op liver function and reduce chances of liver failure. In patients who have received extensive chemotherapy or have cirrhosis, FLR of greater than 30–40% is necessary.

However, there are procedures that stimulate liver regeneration and lower the risk of liver failure in patients with small predicted FLR. The two widely reported methods are portal vein embolization (PVE) and associating liver partition and portal vein ligation (ALPPS). Both of these techniques increase the volume of the future liver remnant (FLR), allowing for a potentially better oncologic procedure with lower risk of liver failure. In portal vein embolization, the portal vein supplying the lobe or segment of liver with tumor is embolized, which has the effect of causing hypertrophy to the other lobe. Given the size discrepancy between the right and left liver, PVE is usually used to increase left liver FLR to allow a right hepatectomy or extended right hepatectomy. Studies have showed that, after this treatment, the augmented FLR allows for previously "unresectable" lesions to now become resectable since there is less fear of liver failure post-op [70–72]. The risks of PVE include PV thrombosis, bleeding, and increasing inflammation in the hilum. A more accelerated hypertrophy can be seen with ALPPS. In this procedure, the right portal vein is ligated surgically, and there is in situ transection between the lobes. Within days, the left lobe hypertrophies and the right lobe can be resected along with its right artery and hepatic duct branches [73–75].

Benign Liver Tumors

Benign liver "tumors" can generally be classified as epithelial or mesenchymal. The major mesenchymal "tumor" is hemangioma, and common epithelial "tumors" include adenoma and focal nodular hyperplasia (FNH). Of these, only adenomas are actually neoplasms, but they all present as mass lesions which can sometimes be difficult to distinguish from tumors.

Hemangiomas can be either solitary or present as multiple lesions, with the majority being less than 5 cm. Hemangiomas are more common in the younger population and are more frequent in females. Most hemangiomas are found incidentally during unrelated abdominal surgery or on imaging. Symptoms generally occur in patients with lesions greater than 5 cm and usually consist of pain or fullness. Hemangiomas in children have more serious consequences including high-output cardiac failure and consumptive coagulopathy.

General consensus [76] is that hemangiomas do not need resection and do not even need follow-up imaging. Symptomatic hemangiomas may benefit from surgical resection, which typically consists of enucleation since wide margins are unnecessary.

Hepatocellular adenoma (HCA) is also rarely seen in the elderly population and normally seen in young women of child bearing, with a history of oral contraceptive use. The majority of HCA are solitary and in the right lobe. Similar to hemangiomas, they can vary in size with large lesions more likely to cause symptoms. HCA can occasionally present with acute onset of hemorrhage, necrosis, or infarction [76], and there is a small risk of malignant transformation to HCC [77]. Initial management includes avoidance of oral contraceptives and hormone-containing intrauterine devices. For lesions greater than 5 cm, intervention through surgical or nonsurgical modalities is recommended due to risk of rupture and malignancy, although surveillance can also be utilized in high-risk patients to assess growth pattern and stability of the lesion [76, 78].

Focal nodular hyperplasia (FNH) is also rarely seen in the elderly population and is thought to be a hyperplastic response to hyperperfusion by anomalous arteries in the center of the nodule. FNH is usually solitary and rarely larger than 5 cm. FNH can be usually diagnosed on the basis of imaging characteristics and, once diagnosed, rarely requires further intervention or even surveillance [76].

Overall benign tumors are usually incidental findings in the elderly, and aggressive surgical management is rarely warranted unless there is diagnostic uncertainty.

Malignant Liver Tumors

Malignant tumors are generally classified as primary or metastatic, with the latter being far more common in the liver. Over the course of the next section, we will discuss in more detail the two most common primary tumors, HCC and ICC, as well as the two most commonly resected metastatic tumors, colorectal cancer (CRC), and neuroendocrine tumors (NET). Surgical resectability is based on achieving complete resection while leaving an adequate amount of parenchyma with adequate blood flow and biliary drainage. Detailed operative method of liver resection can be found in specialized textbooks [79–81].

Most patients with malignant liver tumors have unresectable disease and are unable to undergo resection. In patients with disease confined to the liver, other liver-directed therapies, such as thermal ablation (radio-frequency ablation (RFA), microwave ablation, cryoablation), hepatic arterial therapy (transarterial embolization (TAE), chemoembolization (TACE), radioembolization (TARE)), or stereotactic body radiation therapy (SBRT), may be an option.

Hepatocellular Carcinoma

Over 80% of patients diagnosed with HCC have cirrhosis, with a 5 year cumulative risk of development of HCC in cirrhotics ranging from 5% to 30% [82]. Although HCV is more commonly associated with HCC in the USA, chronic HBV infection is more common worldwide. HCC usually occurs in the setting of cirrhosis, but it can occur in patients with chronic HBV without cirrhosis, with factors such as elevated viral loads, infection with HBV genotype C, coinfection with HCV or hepatitis delta virus, family history of HCC, exposure to mycotoxin aflatoxin, alcohol, and tobacco use [83, 84]. HCV risk factors for HCC include older age at time of infection, coinfection with HIV or HBV, and heavy alcohol use. Whereas in HBV HCC can occur in non-cirrhotics, HCV almost always occurs in cirrhotics or in those with advanced fibrosis [85]. Heavy alcohol use, obesity, and metabolic syndrome have been shown to be risk factors for HCC irrespective of chronic viral hepatitis status [86].

The presentation of HCC can be similar to benign tumors, either being asymptomatic or causing abdominal pain due to size. However, unlike benign tumors that rarely occur in the setting or cirrhosis, HCC may present with hepatic decompensation, ascites, Budd-Chiari syndrome,

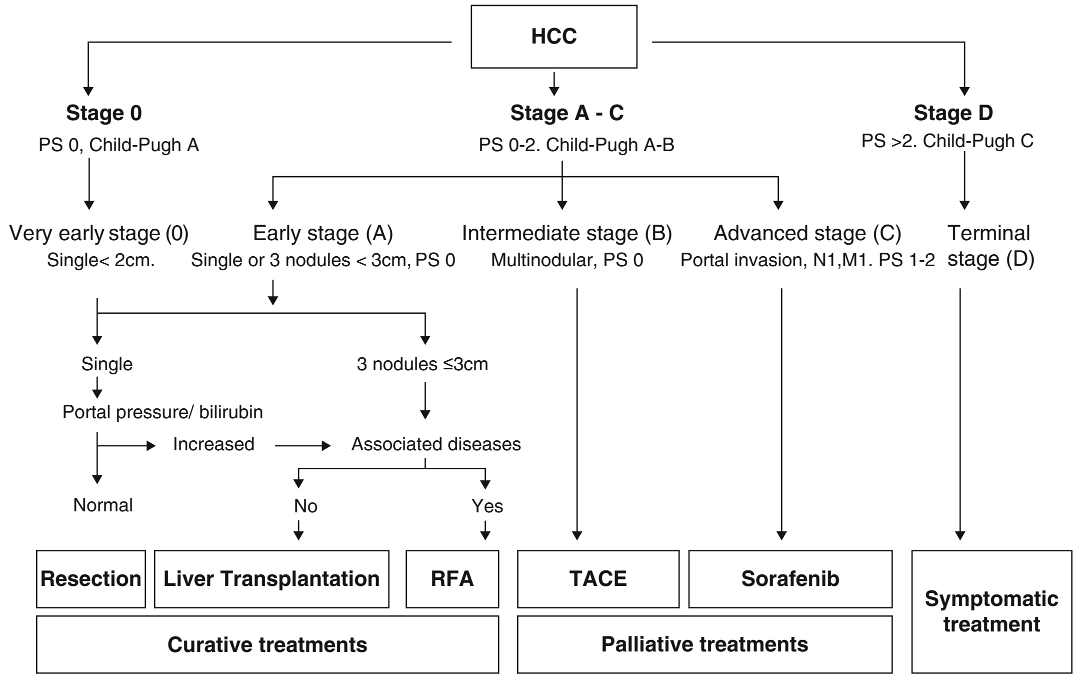

Fig. 5 BCLC staging system for HCC [87]

variceal bleeding, jaundice, or encephalopathy. Also, nonspecific symptoms such as weight loss, anorexia, or fatigue may be present.

The most important component of HCC diagnosis is imaging, supplemented by tumor markers, specifically alpha fetoprotein (AFP). Initial imaging diagnosis may occur in the setting of surveillance studies. Association guidelines recommend surveillance ultrasound screening every 6 months in HBV carriers and those with chronic hepatitis with concurrent measurement of AFP [87, 88]. Nodules less than 1 cm can be reassessed at three to six monthly cycles with ultrasound, but those greater than 1 cm should undergo a multiphase contrast-enhanced CT or MRI. The feeding of the tumor by the hepatic artery and its branches produces very classical imaging findings of early arterial enhancement and delayed washout in the venous phase (see image). Atypical features warrant a tissue biopsy for diagnosis, but otherwise, imaging findings typical for HCC in a patient with liver disease do not require biopsy prior to treatment.

There are multiple staging systems for HCC, but the Barcelona Clinic Liver Cancer (BCLC) staging system is the most widely accepted staging system (Fig. 5) [87].

In HCC, multiple studies have showed a 5 year survival of 60–75% with resection [89–93]. In non-cirrhotic patients, multiple centers have mortality rates less than 5%, and blood transfusion requirement is also becoming less necessary. As mentioned previously, methods to increase the FLR also greatly aid in allowing larger resections. In patients with cirrhosis, resection is often not possible given the prohibitive perioperative risks. Liver resection for HCC in the elderly has been reported by several Asian studies with conflicting outcomes. A large nationwide Japanese database study suggested that increasing age was significantly associated with mortality [94], whereas another study found similar morbidity and recurrence-free and overall survival in patients aged either side of 70 years [95].

Liver transplantation (LT) is an excellent modality for treatment of patients with HCC with or without cirrhosis, although often LT is reserved for high MELD cirrhotics as they would not be able to safely undergo a liver resection. A seminal article from investigators from

Milan detailed outcomes in HCC patients undergoing transplant, by using characteristics of the tumors on explant to determine acceptable outcomes [96]. The United Network for Organ Sharing (UNOS) used these Milan criteria to determine eligibility for liver transplantation. The patient may have a single 5 cm tumor or three 3 cm tumors, overall not totaling more than 8 cm, no evidence of vascular invasion, and no evidence of extrahepatic disease, with the original Milan data reporting 5 year actuarial survival of 74%. LT is rarely indicated or part of the treatment paradigm for non-HCC malignancies, and as such most transplant studies feature HCC. Several studies in the elderly in this population have shown conflicting results with equivalent or worse outcomes [97–100]. Overall, however, due to comorbidities and donor pool shortages, LT is uncommon in patients older than 65 years of age. A UNOS database study [101] analyzed outcomes of transplant in patients with age less than or greater than 70, with or without HCC, and the results unsurprisingly showed that overall 5 year survival was higher in the younger population at 72% vs. 55%. When the young and older populations are separated into HCC or non-HCC subgroups, however, the 5 year survival for the older age group was nearly identical at 54% with HCC vs. 55% without HCC, whereas in the younger population, the 5 year survival was significantly lower at 67.8% with HCC vs. 73.8% without HCC. Overall this suggests that liver transplant survival is not affected by HCC at an advanced age.

The SHARP trial was a landmark study looking at the overall survival and time to symptomatic progression with use of the multikinase inhibitor, sorafenib, in patients with advanced HCC in a primarily western population [102]. Investigators found significantly improved overall survival of 10.7 vs. 7.9 months in the group receiving sorafenib vs. placebo group, though median time to symptomatic progression was similar at 4.1 vs. 4.9 months, respectively. With his study and the near-equivalent results produced from a randomized controlled Asian study [103], sorafenib is now commonly used for advanced HCC with modest benefit and the occasional anecdotal isolated case reports showing occasionally curative responses [104]. Sorafenib was studied for use as adjuvant therapy after resection or ablation, but the STORM trial concluded that sorafenib was an ineffective intervention [105].

RFA, TACE, and TARE have been used to downstage tumors to transplant eligibility but have also been used as stand-alone treatments. RFA has been shown to be safe and effective with 5 year survivals of up to 76% reported in early-stage disease in patients with well-preserved liver function [106]. TACE and TARE are rarely curative and are used most often as a bridging to transplant, with local tumor control up to 70% [107, 108]. The NCCN guidelines [109] recommend the use of liver-directed therapy in patients with disease that is not eligible for resection or transplant, and this may be an appealing option for elderly patients deemed too high risk for liver resection.

Intrahepatic Cholangiocarcinoma

Overall, ICC makes up around 10% of all cholangiocarcinoma and 10–20% of primary liver tumors. It arises in the peripheral bile ducts within the liver parenchyma. The majority of patients are over 65 years at diagnosis, with a slight male preponderance. Risk factors include conditions causing biliary inflammation and fibrosis, such as primary sclerosing cholangitis and primary biliary cirrhosis; congenital malformations such as choledochal cysts and hepatolithiasis; cirrhosis risk factors such as HBV, HCV, and alcohol; as well as parasitic infections of *Clonorchis sinensis* and *Opisthorchis viverrini* [36, 37].

The presentation of ICC is often with nonspecific symptoms of abdominal pain, weight loss, and occasionally painless jaundice when the mass nears the biliary confluence. Diagnosis is typically made with imaging. CT imaging shows a hypodense mass in the unenhanced phase with irregular margins, with peripheral rim enhancement in the arterial phase and progressive hyperattenuation on venous and delayed phases.

Tumor markers are less specific for ICC than HCC, with CA 19-9 levels showing limited sensitivity and specificity.

There are fewer staging systems present for ICC than HCC, and, although no strict consensus, the 7th edition of AJCC/UICCA is favored by most [110]. Stage I and II disease is resectable, and when combined, these stages encompass 30–40% of cases. Hepatic resection is indicated in ICC without evidence of distance metastases, with 5 year survival of 20–40% [111–113]. Recurrence rates are high at approximately 70%. Although the Mayo protocol of neoadjuvant chemoradiation prior to LT was developed for hilar cholangiocarcinoma [114], there is no role for liver transplantation in ICC.

Stages III and IV are considered unresectable, and these patients have options of gemcitabine/cisplatin combination chemotherapy, fluropyrimidine-based therapy, or liver-directed therapy such as SBRT, TACE, or RFA per NCCN guidelines [109]. A recent study from Memorial Sloan-Kettering [115] compared patients with locally advanced, unresectable disease receiving a hepatic artery infusion pump with floxuridine combined with systemic chemotherapy vs. those with systemic chemotherapy alone and found a significantly increased median overall survival of 30.8 vs. 18.4 months, respectively, and 5 year survival of 20% vs. 5%, respectively.

The overall survival for ICC is dismal with SEER data [3] suggesting a localized vs. regional vs. distant stage 5 year survival of 15% vs. 6% vs. 2%, with local and regional disease having significantly lower survival than local and regional extrahepatic bile duct cancer (30% and 24%, respectively).

Colorectal Cancer Metastasis

Colorectal cancer (CRC) is the fourth most common cancer in the USA and has the second highest overall mortality. The liver is the most common site of metastasis, nearly fourfold more than the lung, and occurs synchronously in 15–20% and developing in another 60% of patients during the course of the disease. Unfortunately, only 15–25% of patients with colorectal liver metastases (CLM) are considered to have resectable disease.

Both CT and MRI are important imaging modalities, given their ability to asses at least two phases of vascular enhancement. CLM in general appear as hypoattenuating masses, best visualized during portal venous enhancement. NCCN guidelines [116] recommend a repeat colonoscopy if greater than 6 months since previous colonoscopy or curative colon surgery to assess for a metachronous colon lesion or recurrence at primary site.

CLM usually occur in non-cirrhotic patients, and therefore even large liver resections can be undertaken with lower risk of liver failure than in primary liver cancers, in general. Multiple large series have shown acceptable 5 year survival rates of up to 58% [117–119], with a large SEER database study reporting 32.8% [19]. Historical non-operative patients have had 5 year survival rates of less than 5%. The risk of recurrence is high with up to 60% of patients having recurrence, but repeat resection is sometimes an option for these patients. A Clinical Risk Score developed at Memorial Sloan-Kettering [120] is widely used to predict outcomes after resection. The score takes into consideration five clinical criteria – nodal status of primary, disease-free interval from primary to discovery of liver metastases of <12 months, number of tumors >1, preoperative CEA level >200 ng/ml, and the size of the largest tumor >5 cm with the study that developed this score identifying a 5 year survival of 60% with a score of 0 compared to 14% with a score of 5.

The most controversial issue in the management of CLM is the role of neoadjuvant chemotherapy. 5-Fluorouracil (5-FU) is the cornerstone of therapy, but the addition of oxaliplatin or irinotecan (along with 5-FU and leucovorin known as "FOLFOX" and "FOLFIRI," respectively) dramatically improves response rates and survival over 5-FU alone. The addition of biologic agents targeting VEGF (bevacizumab) or EGFR (panitumumab, cetuximab) to chemotherapy further improves outcomes [121–123]. For patients with unresectable CLM, chemotherapy with or without biologic therapy is used with reevaluation of resectability every 2 months. A large study of 1,104 patients with unresectable CLM [124] treated with neoadjuvant chemotherapy reported that 12.5% became resectable after therapy. A randomized trial in Europe compared "perioperative" (pre- and post-op) chemotherapy to no chemotherapy in patients with resectable CLM and demonstrated improved progression-free survival with chemotherapy but no difference in overall survival [125]. The issue therefore remains controversial, particularly since both oxaliplatin and irinotecan have been associated with liver toxicity that can increase complications after liver resection [126]. The benefits of modern chemotherapy appear to extend to elderly patients with advanced disease [127], but elderly patients are also at increased risk of toxicity due to underlying organ dysfunction and less predictable pharmacokinetics. The potential benefits of neoadjuvant chemotherapy in the elderly population may therefore be small relative to the risks.

The management of synchronous CLM is even more complicated by decision-making around the management of the primary tumor. A large multi-institutional study [117] showed that simultaneous and staged resections for synchronous liver metastases can be performed with comparable morbidity, mortality, and long-term outcomes, although staged procedures were more commonly used for larger hepatic resections. Overall, outcomes for metastatic CRC have improved substantially over the last several years, due to improvements in both medical and surgical management. There are now so many different treatment options that there is little consensus regarding the components and sequence of therapy.

Neuroendocrine Metastasis

Neuroendocrine tumors (NETs) are rare tumors that arise from Kulchitsky's enterochromaffin cells and that are characterized by positivity for chromogranin A and synaptophysin by immunohistochemistry. NETs of the gastrointestinal tract (also known as carcinoid tumors) or pancreas spread to the liver hematogenously in 40–85% of patients. Approximately 75% of liver metastases are synchronous with the primary NET [128]. Neuroendocrine liver metastases (NELM) are considered the most powerful prognosticator of survival of patients with NET regardless of primary site [129, 130]. NETs can occur at all ages but are more commonly seen after the fifth decade, with the exception being appendiceal NET that occurs closer to 40 years of age. Symptoms of disease vary based on the origin of the tumor and whether it is biochemically "functional." The diagnosis of NELM is easier to make if there is a known primary, although often the liver metastasis may be the first manifestation of NET. These are highly vascular lesions, and often it is the hepatic arterial phase that provides the best phase for detection of NELM when using either CT or MRI. Somatostatin receptor scintigraphy is able to identify patients with NET expressing the somatostatin receptor subtype 2 and is specific for NETs but not very sensitive for small tumors. Given the poor outcomes with high-grade tumors, tissue acquisition is often indicated when a primary is not found or previously resected, and markers of proliferation such as Ki-67 and mitotic index are used to guide management.

Because NETs are relatively rare, there are very few randomized studies. In general, liver resection is considered reasonable when all visible disease can be removed but should only be attempted in those with well-differentiated tumors [131]. Subtotal resection of NELM (debulking or cytoreduction of greater than 80% of the tumor) has also been associated with longer survival than with nonsurgical management. The Mayo Clinic [132] reported a large experience of hepatic resection and cytoreductive therapy, achieving a 5 year survival of 61% and 10 year survival of 35%. More recent studies including a large multinational study have shown 5 and 10 year survivals of up to 74% and 51%, respectively [133]. In patients with disease not amenable to surgery, liver-directed therapy has also been associated with prolonged survival [134], as has systemic therapy with somatostatin analogues [135] or peptide receptor radionuclide therapy [136].

The behavior of well-differentiated NETs is so indolent, that risks of treatment have to be weighed carefully against the risks of tumor progression. Many elderly patients will be more likely to die from comorbid conditions than from their NET, and aggressive surgical therapy may not be warranted unless symptoms cannot be controlled by other modalities.

Conclusion

Advancing age should not preclude the use of liver resection for appropriate indications. Chronological age should carry less weight than frailty or sarcopenia, and in older patients comorbidities need to be balanced with the possible benefits of quality and duration of life afforded by complex hepatobiliary surgery. Surgery itself is evolving. Techniques to augment the future liver remnant have allowed us to perform more extensive resections safely. Advances in minimally invasive surgery may allow for liver resection to be performed with reduced length of hospitalization and opioid use. Overall, as the average life expectancy increases, and the incidence of liver tumors increases, further work is needed to not only risk stratify elderly patients but also optimize them prior to surgery.

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Benign and Malignant Neoplasms of the Exocrine Pancreas

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Abstract

The incidence of most benign and malignant tumors of the pancreas increases with age. A multidisciplinary approach is necessary to ensure appropriate treatment and optimize patient outcomes. Unfortunately, treatment disparities persist when compared with the general population as many patients are denied appropriate therapy based on advanced chronological age. Furthermore, elderly patients are often excluded from clinical trials despite the fact that they are more likely to be affected by these groups of tumors. There is growing evidence to suggest that age alone is not a reason to withhold potentially curative surgery or standard of care chemotherapy. However, several studies have reported increased risk of surgical complications and chemotherapeutic toxicity, which may be explained by the presence of additional comorbidities, frailty, poor functional status, and altered drug metabolism. Various tools, such as the comprehensive geriatric assessment, have been developed to guide clinicians in the management of these complex patients. In the following chapter, we discuss the multidisciplinary approach for diagnosis and management of benign and malignant pancreatic tumors with a focus on the role of surgical resection.

Introduction

Pancreatic neoplasms represent a major healthcare problem for the aging population. The elderly are at risk for the entire spectrum of benign and malignant pancreatic tumors. Pancreatic adenocarcinoma is the most frequent and clinically significant. It is the fourth leading cause of cancer death in the United States, and its incidence increases with age. The diagnosis and treatment of pancreatic cancer often represent a significant clinical challenge in the elderly, as there is a significant bias against aggressive surgical treatment in this population. In recent years, however, advances in diagnostic techniques, improved outcomes with regionalization of care, and a deeper understanding of prognostic factors have improved our ability to treat this challenging disease. However, significant treatment disparities persist and elderly patients are often inappropriately denied potentially beneficial, and sometimes curative, therapy. In addition to pancreatic adenocarcinoma, the recognition and diagnosis of benign and premalignant pancreatic tumors has become more common in the elderly. These tumors require a thorough understanding of their clinical behavior as one weighs these risks with the risk of surgery in the elderly population. Fortunately, many of these tumors are amenable to less invasive therapeutic procedures with lessened perioperative morbidity and mortality.

Epidemiology

According to the National Cancer Institute, the incidence of pancreatic cancer is approximately 53,670 new cases per year, with 43,090 deaths per year from the disease [1]. Pancreatic adenocarcinoma is among the most lethal cancers, with a 5-year survival rate of only 8.2% for 2007–2013. It is most frequently diagnosed in patients aged 65–74, with a median age at diagnosis of 70 years. A total of 97.5% of cases are diagnosed in patients above the age of 45, 66.5% above the age of 65, and 13.6% above the age of 84 (Fig. 1).

Cystic neoplasms of the pancreas are much more common than was once thought. The increased reliance on axial imaging has led to

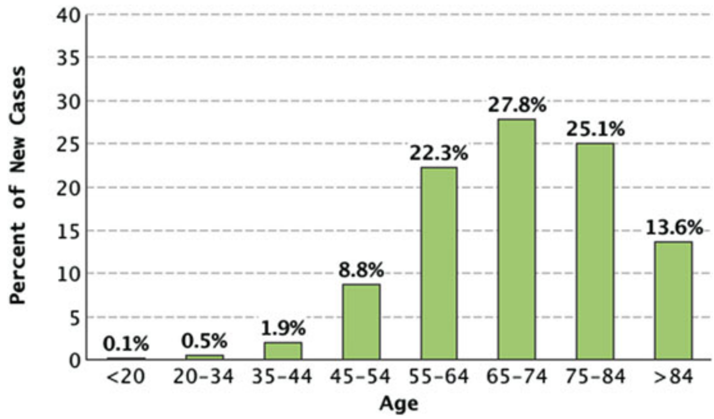

Fig. 1 Pancreatic cancer incidence by age. https://seer.cancer.gov/statfacts/html/pancreas.html. SEER 18 2010–2014, All Races, Both Sexes

the incidental identification of a wide spectrum of asymptomatic benign and malignant disease. Pancreatic cysts are rare in patients younger than 40 years of age. Studies based on axial imaging and autopsies have estimated prevalence rates as high as 19–25% in patients age 70–79 years and 30–37% in patients over 80 years old [2].

Risk Factors

Environmental and genetic factors have been implicated as risk factors for pancreatic cancer. As noted above, advanced age is a significant risk factor for both pancreatic cancer and pancreatic cysts. Male gender and African American race are also associated with higher rates of pancreatic cancer. Among many potential environmental risk factors, cigarette smoking has been confirmed as a major contributor, with a two-fold greater risk of developing pancreatic cancer among smokers compared with non-smokers. Patients with obesity, diabetes, and chronic pancreatitis are also at increased risk.

Percent of New Cases by Age Group

Genetic factors often play a role in the development of pancreatic cancer. There are multiple inherited familial cancer syndromes that increase the risk of pancreatic cancer, including Peutz–Jeghers, hereditary pancreatitis, hereditary nonpolyposis colon cancer (HNPCC), ataxia-telangiectasia, familial atypical mole and multiple melanoma (FAMMM) syndrome, familial breast cancer 2, and familial adenomatous polyposis. There is also a significantly increased risk of developing pancreatic cancer in patients with a family history of the disease without association with a specific syndrome. Patients who have two first-degree relatives with pancreatic cancer have a 6-fold increase in risk, while patients with three affected first-degree relatives have a 32-fold higher risk of developing pancreatic cancer [3]. It is also important to note that age becomes a significant factor in these kindreds, as the age of cancer diagnosis in subsequent generations actually becomes progressively younger.

While the genetic significance in these cancer syndromes is apparent, advances in molecular genetics have led to the identification of frequent genetic mutations even among sporadic pancreatic cancers. These include inactivated tumor-suppressor genes such as p53, p16, and DPC4, each of which are found in >50% of sporadic pancreatic cancers. Mutations in K-ras, an oncogene involved in signal transduction, are found in over 90% of pancreatic cancer.

Perhaps the most increasingly identified risk factor for pancreatic cancer is the presence of a precancerous lesion, such as IPMNs or other mucinous cystic neoplasms. The increasingly frequent identification of these tumors, primarily in asymptomatic patients, has led to the development of management algorithms for the management of precancerous lesions and surveillance for disease progression. The optimal techniques and interval for follow-up may vary based on patient-specific characteristics including age. Nevertheless, for IPMNs, both the incidence of malignancy and invasiveness increases with age.

Pathology

Solid Tumors

Solid tumors of the exocrine pancreas are classified according to their cell of origin, which may include the pancreatic ductal epithelium or the acinar cell. Solid tumors can be either malignant, premalignant, or benign. Ductal adenocarcinoma is the most common neoplasm of the exocrine pancreas, accounting for more than 75% of all malignant pancreatic tumors. Ductal adenocarcinoma arises most commonly in the pancreatic head (65%) but may also be present in the body or tail (15%) or diffusely involve the whole pancreas (20%). Tumors of the head tend to be smaller at diagnosis, as they are more likely to cause obstructive jaundice earlier in their development. Adenocarcinomas arise from pancreatic ductal tissue, often obstructing ductal branches and causing a desmoplastic reaction with associated fibrosis and chronic pancreatitis. They often infiltrate into vascular, lymphatic, and perineural spaces, leading to early local and metastatic spread. Common sites of local invasion are duodenum, stomach, transverse mesocolon, colon, spleen, and adrenal glands. Pancreatic cancer typically metastasizes to regional lymph nodes and then liver, peritoneum, lungs, and adrenal glands. Pathologic examination of resected specimens often reveals the presence of precursor lesions (see below) in close proximity to the cancer. The recognition of these lesions has broadened our understanding of the development of adenocarcinoma.

Pancreatic adenocarcinoma is staged based on the tumor characteristics, node involvement, and metastatic disease (TNM) classification system, as outlined by the American Joint Commission on Cancer (AJCC). This system has considerable prognostic significance, with Stages I and II representing resectable, and therefore potentially curable, disease.

In addition to ductal adenocarcinoma, a very small percentage of solid exocrine tumors is comprised of adenosquamous carcinoma, acinar cell carcinoma, giant cell carcinoma, and pancreatoblastoma. Pancreatoblastoma should rarely be considered in the differential in an elderly patient, however, as it is found almost exclusively in children less than 15 years of age.

Cystic Tumors

Although once considered rare, increased use of axial imaging techniques has led to a surge in the identification of cystic tumors of the pancreas, such that 10% of patients over the age of 70 are diagnosed with a pancreatic cyst. However, great controversy exists as to precisely which patients will benefit from additional work-up, intervention, and follow-up [4]. Inflammatory pseudocysts are commonly diagnosed in association with pancreatitis and their management is well described. Cystic tumors of the pancreas include serous cystic neoplasms, mucin-producing cystic neoplasms (MCN and IPMN), solid pseudopapillary or Hamoudi tumors, and lymphoepithelial cysts.

Serous cystadenomas are relatively common among cystic tumors of the pancreas (Fig. 2). They are benign, slow growing tumors that are most common in elderly women and can manifest anywhere in the pancreas. Typically, the lesion consists of many tiny cysts lined by a cuboidal epithelium that has a honeycomb appearance. Oligo- or macrocystic variants are also possible and represent about 10% of cases. Serous cystadenocarcinoma is an exceedingly rare malignant variant that may be difficult to distinguish histologically from its benign relative. Finally, although almost always benign, these tumors can grow to massive size and compress or occlude visceral vessels, giving the appearance of being "locally unresectable." This is most commonly seen in the elderly population.

Unlike serous neoplasms, which are almost always benign, mucin-producing cystic tumors

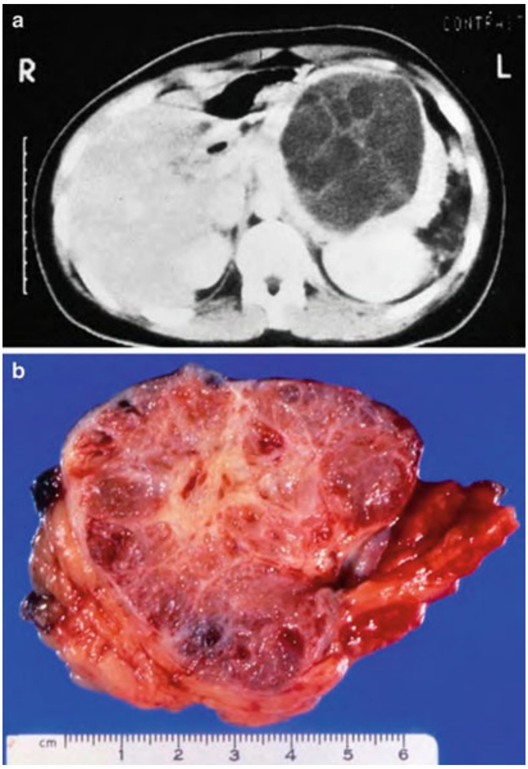

Fig. 2 Serous cystadenoma seen in (**a**) cross-sectional imaging and (**b**) histologic section

of the pancreas have considerable malignant potential. There are two distinct types of mucin-producing pancreatic tumors, mucinous cystic neoplasms (MCNs, or mucinous cystadenomas), and intraductal papillary mucinous neoplasms (IPMNs). Both types are characterized by abnormal growth of mucin-producing epithelial cells, but IPMNs involve the main pancreatic duct or ductal branches, while MCNs do not. MCNs occur almost exclusively in women and are most common between age 40 and 50. They are typically found in the body or tail and contain a distinctive subepithelial ovarian-type stroma (Fig. 3). The degree of dysplasia of MCNs can vary from benign to malignant, with up to one-third containing an invasive component. In contrast to MCNs, IPMNs are slightly more common in males, do not contain ovarian stroma and are more common in the pancreatic head, neck, and uncinate process, but can occur anywhere within the gland (Fig. 4 and Table 1).

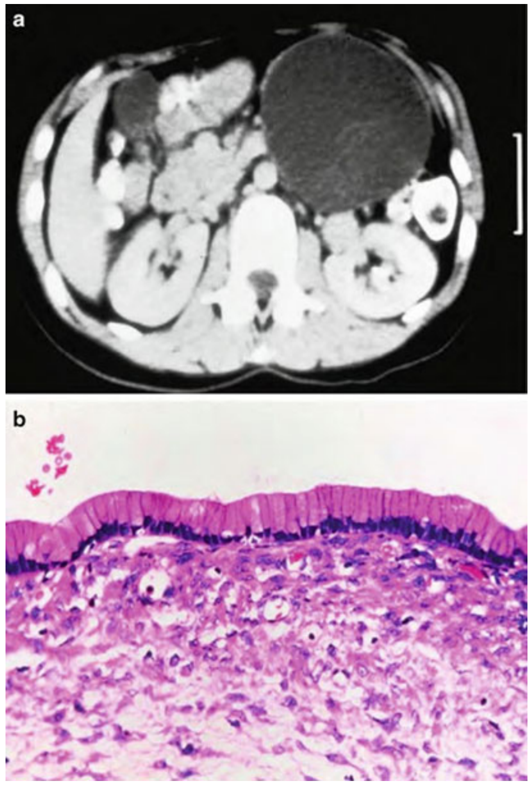

Fig. 3 Mucinous cystic neoplasm seen in (**a**) cross-sectional imaging and (**b**) histologic section showing typical histologic feature of “ovarian stroma”

Fig. 4 Multidetector CT (MDCT) scan with IV contrast showing main-duct type IPMN

IPMNs are classified into 3 types: main duct, branch duct, and mixed type. All subtypes may be benign, but all are also at risk for malignant transformation. The risk is greatest with main-duct

Table 1 Comparison between MCN and IPMN

	MCN	IPMN
Age (years)	40–50	60–80
Gender	F>M	M>F
Location	Body/tail	Head
Pancreatic duct involvement	No	Yes
Mucin found at ampulla	No	Yes
Ovarian-like stroma	Yes	No

Table 2 Likelihood of malignancy in main duct IPMN [5] (*Source*: Data from Salvia et al. [5])

	Benign	Malignant	Total	*P* (benign vs. malignant)
n	57	83	140	–
Gender (M/F)	31/26	40/43	71/69	NS
Median age	60.9	67.3	64.8	0.042
Smoking history (%)	35 (61%)	43 (52%)	78 (56%)	NS
Abdominal pain (%)	43 (76%)	47 (57%)	90 (65%)	0.038
Jaundice (%)	2 (3.5%)	21 (26%)	23 (16.5%)	0.001
Weight loss (%)	23 (40%)	39 (47%)	62 (44%)	NS

IPMN with 20% of tumors harboring high grade dysplasia and 45% with invasive carcinoma at the time of resection (Table 2). The epithelial lining of most main duct IPMNs has an intestinal phenotype and expresses intestinal lineage markers, such as CDX-2 and MUC-2.

Branch duct IPMNs are the most common cystic tumor of the pancreas. They typically display a gastric type epithelium, though oncocytic, intestinal, and pancreaticobiliary subtypes also exist. They are associated with a field defect within the pancreas and can occur throughout the gland, with 24–41% of patients presenting with multifocal disease [6]. Pathologic features associated with increased likelihood of malignancy include the presence of mural nodules, ductal dilatation and, the size of the cyst. The average rate of malignancy within a surgically resected branch-duct IPMN is approximately 25% [7]. In addition, there is an increased risk of concomitant pancreatic ductal adenocarcinoma in the entire pancreas.

Much less common, the solid pseudopapillary tumor, also known as Hamoudi tumor, or solid cystic neoplasm, is found predominantly in young women. This tumor is considered to be malignant but with very low metastatic potential.

Precancerous Lesions

The recent increase in identification and understanding of premalignant lesions of the pancreas has elucidated the processes associated with the progression from benign to malignant disease. Multiple precursors to adenocarcinoma exist, including pancreatic intraepithelial neoplasia (PanIN), and the cystic precursors IPMN and MCN. PanIN is divided into three grades of increasing dysplasia. PanIN-1 is characterized as a proliferative lesion without nuclear atypia; PanIN-2 is associated with a moderate degree of architectural and cytonuclear abnormalities; PanIN-3 has severe nuclear abnormalities with abnormal mitoses, but without invasion through the basement membrane. PanIN-3 is also referred to as carcinoma in situ and is almost always found in close proximity to an invasive cancer [8]. The prevalence of PanIN lesions increases with age. 33% of patients greater than 60 years old and with no known pancreatic disease have a PanIN-1 lesion. It is proposed that advanced age, in addition to other factors, must be present for a PanIN-1 lesion to progress to PanIN-3 and then to invasive cancer. These factors include genetic events such as telomere shortening, K-ras and p16 mutations, and clonal expansion [9].

IPMNs are macroscopic precursor lesions, which can also progress from benign to malignant histologically. About half the resulting invasive neoplasms are actually colloid (mucinous) carcinomas, with the remainder being the typical tubular adenocarcinoma. The progression to malignant IPMN is directly related to age, with multiple clinical studies demonstrating an increased percentage of malignant lesions in patients of increasing age [5, 10].

Clinical Presentation

History and Physical

Tumors of the exocrine pancreas in their early stage are often asymptomatic or present with the insidious onset of nonspecific symptoms. Tumors in the head of the pancreas typically lead to obstructive jaundice (80%), which is often the only specific symptom pointing to the diagnosis. In an elderly patient, the development of jaundice, with dark urine, acholic stools, and pruritus, should lead to prompt diagnostic workup with a high index of suspicion for malignancy. Abdominal and/or back pain (72–87%) and weight loss (90–100%) are common presenting symptoms and often signify locally advanced disease. New-onset diabetes or the development of "acute pancreatitis"-like symptoms should also raise concern. Nonspecific gastrointestinal symptoms may also exist. Fatty stools may signify pancreatic exocrine insufficiency.

Physical examination may reveal jaundice, and in some cases a palpable gallbladder. Signs suggestive of advanced cancer, such as cachexia, ascites, abdominal mass, migrating thrombophlebitis, palpable supraclavicular lymphadenopathy (Virchow's node), periumbilical lymphadenopathy (Sister Mary Joseph's Node), and pelvic drop metastases (Blumer's shelf), are obvious evidence of advanced disease with a poor prognosis. Among elderly patients, the presenting signs and symptoms of pancreatic cancer are not significantly different compared with younger patients [11, 12].

Laboratory Studies

There is no screening test or definitive laboratory test for pancreatic cancer. In patients with cancer in the body or tail of the pancreas, laboratory values are typically normal. In patients presenting with jaundice, laboratory studies will reveal an increase in total bilirubin and alkaline phosphatase, with occasional mildly elevated transaminases. Biliary obstruction can also lead to malabsorption of fat-soluble nutrients, which can lead to malnutrition and subsequent decreases in albumin, iron, hemoglobin, and vitamin-K-dependent clotting factors.

The most widely used tumor marker to aid in the diagnosis of pancreatic cancer is CA 19–9, a Lewis blood-group-related mucin glycoprotein. CA 19–9 is present at low levels (<38 U/ml) in most healthy patients, but often elevated in pancreatic cancer and has been shown to correlate with the stage of disease and survival in patients with resectable disease [13]. CA 19–9, however, may be falsely elevated in patients with obstructive jaundice, cirrhosis, pancreatitis, and other malignancies. CA19–9 has an overall sensitivity of 83% and specificity of 82%, but by raising the cutoff value to 200 U/ml and combining it with other testing modalities, the accuracy increases to 95–100% [14].

Management of Malignant Neoplasms

Diagnosis and Staging

When clinical symptoms or laboratory abnormalities are suspicious for a malignant pancreatic neoplasm, the first step toward diagnosis is noninvasive imaging. Computed tomography (CT) scan or magnetic resonance imaging (MRI) with or without cholangiopancreatography (MRCP) are useful noninvasive imaging studies. Transabdominal ultrasound can confirm obstructive jaundice by demonstrating a dilated biliary tree but lacks the sensitivity of CT and MRI in actually defining a pancreatic mass. Most clinicians regard pancreatic protocol CT scan with multiphase intravenous (IV) contrast enhancement as the initial imaging modality of choice. In recent decades, the development of multidetector CT (MDCT) has reduced acquisition time and dramatically enhanced image resolution [15] (Fig. 5). In addition, when dual phases of IV contrast are used, both arterial and venous structures can be well visualized to determine local involvement by the tumor and resectability (Fig. 6). The inclusion of a “pancreatic phase” of IV contrast often leads to improved pancreas-to-lesion distinction. As well as visualizing the lesion and any associated blood vessels, CT is able to detect extrapancreatic disease, including liver, lung, and peritoneal metastases, to further optimize preoperative staging [16]. In spite of these advantages, clinicians may be hesitant to expose elderly patients to the potential toxicity of IV contrast. The effect of patient age on contrast enhancement during CT scans of the pancreatobiliary region has been evaluated, and the ideal dose of IV contrast in the elderly may be about 10% less than the general population, or 0.07 mL/kg instead of 0.08 mL/kg. This dose, which takes into account changes in cardiac output and blood volume in the elderly, optimizes tumor enhancement and lessens the risk of nephrotoxicity [17].

Fig. 5 Multidetector CT (MDCT) scan with IV contrast revealing a 1 cm tumor in the head of the pancreas (*arrow*)

Fig. 6 Dual-phase contrast MDCT allows clear delineation of peripancreatic vessels, showing a detailed angiographic reconstruction. Note the tumor encroachment of the superior mesenteric vein

Most studies have found no advantage of MRI over MDCT, with the exception of possible improved visualization of small liver metastases and peritoneal implants [16]. MRCP has the added benefit of 3D visualization of both the bile and pancreatic ducts, often revealing the “double duct” pattern of obstruction and can eliminate the need for invasive cholangiography. Another potential modality for the diagnosis and staging of pancreatic cancer is the positron emission tomography (PET) scan. Although PET scanning shows increased uptake of the glucose tracer by both the primary tumor and metastases in other cancers, it has not been shown to reliably provide useful diagnostic information in patients with pancreatic cancer [18].

When noninvasive studies raise concern for a malignant pancreatic lesion, or when noninvasive studies are inconclusive, invasive studies may be indicated to confirm the diagnosis. Endoscopic retrograde cholangiopancreatography (ERCP) provides an endoscopic view of the ampulla and visualizes the biliary and pancreatic ductal systems (Fig. 7). ERCP can also be used to obtain cytologic brushings of suspicious areas in the pancreatic ductal system. While cytology results approach 99% specificity, the sensitivity is <50% due to a high false-negative rate [19, 20]. ERCP has been shown to be safe and well tolerated in elderly patients [21]. Rodriguez-Gonzalez et al.

reported 159 ERCPs performed on patients 90 years of age or older. Complication rate (2.5%) and procedure-related mortality (0.7%) were low, and therapeutic interventions were able to be performed in 96% of indicated cases [22]. Although ERCP is a safe and valuable tool, its role in the diagnostic work-up pancreatic cancer has diminished with the use of MRCP. ERCP is now currently used predominantly for endoscopic stent placement, for both palliative and preoperative biliary decompression.

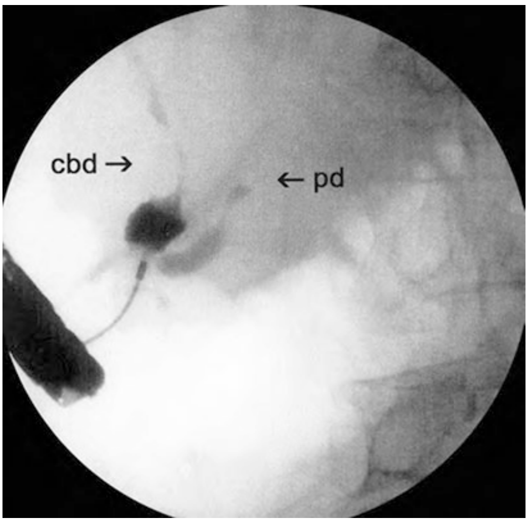

Fig. 7 ERCP of patient with adenocarcinoma of the pancreatic head. Note the involvement of both the common bile duct (cbd) and pancreatic duct (pd)

Endoscopic ultrasound (EUS) has gained acceptance as a critical tool in both the diagnosis and staging of pancreatic cancer. EUS sensitivity and specificity in detecting pancreatic cancer are 85–100 and 80–100%, respectively (Fig. 8). Multiple studies have demonstrated greater diagnostic accuracy of EUS compared to MDCT, particularly in the detection of small tumors less than 2 cm in size [23–26]. EUS can also be used to obtain a cytologic diagnosis via fine needle aspiration (FNA). This technique is typically more accurate than ERCP with brushings. Sensitivity with EUS-guided FNA ranges from 75 to 90%, and specificity approaches 100%. Complications of EUS are uncommon, even in the elderly.

A preoperative histologic or cytologic diagnosis of pancreatic cancer is not necessary in patients with a clearly defined presentation – obstructive jaundice and a pancreatic mass on CT – in a patient who is considered to be a candidate for surgical resection, regardless of age. When a tissue diagnosis is indicated, EUS-guided FNA has become the preferred method. Yet, even in the elderly patient, a high level of clinical suspicion should override a negative cytologic diagnosis. EUS offers the advantage of the close proximity to the tumor, and for cancers of the pancreatic head, the needle traverses the duodenum, which

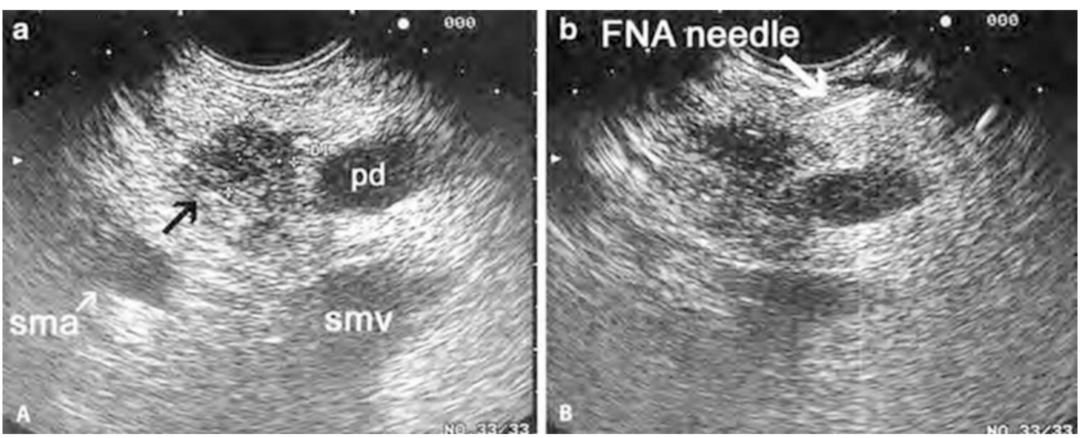

Fig. 8 Endoscopic Ultrasound. (**a**) The tumor (*black arrow*) is clearly visualized, as well as its relationship to the superior mesenteric artery (sma) and vein (smv). (**b**) Fine-needle aspiration of the tumor for cytologic examination

will be resected. Conversely, percutaneous fine needle aspiration has fallen out of favor both due to the fact that the distance of the pancreatic tumor from the skin surface leads to a higher incidence of false-negative aspirations, as well as the risk of seeding of the tumor along the needle tract, leading to intra peritoneal spread of the tumor.

Surgical resectability of a pancreatic cancer requires that the tumor both shows no evidence of metastatic disease (liver, peritoneal cavity) or local invasion of key adjacent structures. For most surgeons, direct extension of tumor into adjacent organs, encasement of the celiac or superior mesenteric arteries, significant encasement or occlusion of the portal – superior mesenteric vein (SMV) complex, involvement of distant lymph nodes, or obvious metastatic disease will preclude resection of a pancreatic head cancer [27–29]. For tumors of the pancreatic body and tail, extensive involvement of the celiac axis or SMA, the SMV/portal vein, adjacent organs, or the presence of distant metastasis typically renders the tumor unresectable. Isolated splenic vein or splenic artery involvement does not preclude resection. Most surgeons find CT scan to be the most useful tool in predicting resectability, but some studies indicate that EUS may be more accurate in determining local invasion of surrounding vasculature [16, 23, 26].

Unfortunately, neither MDCT nor EUS is able to detect small peritoneal or liver metastases, which are common with pancreatic cancer. This is best assessed with diagnostic laparoscopy. The role of routine laparoscopy has become less clear as the sensitivity of CT scanning has increased. Several reports have shown that routine laparoscopy for pancreatic head cancer would spare very few patients from a laparotomy (5–15%) [30, 31]. The value of laparoscopy is increased in evaluating cancers of the body and tail, however, as these patients are found to have occult metastatic disease at operation 50% of the time [32]. Diagnostic laparoscopy in the management of pancreatic cancer must be used on an individualized basis, taking into account the age and comorbidities of the patient, as well as the likelihood of finding occult metastatic disease. It would seem appropriate, however, if suspicion exists in an elderly patient that laparoscopy, to spare the patient an unnecessary laparotomy, might be in order. The degree of CA 19–9 elevation may also be taken into consideration [33]. Finally, the need for surgical palliation of biliary and duodenal obstruction must also be taken into account, as patients who require palliative bypass will not benefit from laparoscopy. On the other hand, as the endoscopic and laparoscopic technical ability has advanced, many palliative procedures can be performed using these techniques, avoiding the need for open surgical procedures.

Preparation for Operation

If the decision is to proceed with an operation for pancreatic cancer in an elderly patient, proper preoperative preparation is required. Thorough multidisciplinary assessment of cardiopulmonary status, renal and hepatic function, the state of hydration, nutrition, anemia, and coagulation abnormalities is necessary. All efforts should be made to optimize the patient's overall health prior to proceeding with operation for resection or palliation. Nutritional status can have a major impact on surgical outcomes after major abdominal surgery, including pancreatectomy [34, 35]. The importance of optimal preoperative nutritional status is further amplified in elderly patients. A team-based approach can help ensure that patients have the necessary resources to ensure appropriate preoperative nutrition. Referral to a nutritionist may be helpful to optimize oral intake in patients that are able to take food by mouth. In patients that are unable to tolerate an oral diet because of gastric outlet obstruction, gastroparesis, or delayed gastric emptying, the available data support placement of a nasojejunal feeding tube, which allows for enteral nutrition with less risk than percutaneous feeding tubes. Parenteral nutrition, once used routinely in the preoperative period, is now generally discouraged and reserved for patients that are unable to tolerate any form of enteral feeding [36].

The role of preoperative biliary decompression with ERCP and stenting should be discussed in a multidisciplinary fashion with the patients surgeon and gastroenterologist. Biliary decompression can be performed by percutaneous transhepatic drainage or by placement of an endoscopic stent at the time of ERCP. Endoscopic stent placement has become the preferred method, as it is usually accomplished with less pain and complications and is better tolerated by patients. The benefit of routine preoperative biliary drainage is questionable, however, with multiple series suggesting that the use of preoperative stenting increases the incidence of perioperative complications, especially wound infection [37]. Therefore, preoperative biliary drainage is indicated only in selected patients, with advanced malnutrition, sepsis, or correctable medical conditions. Preoperative biliary drainage may be useful in allowing time for improvement of the patient's overall health status, particularly in an elderly patient. Furthermore, if surgery is to be delayed to facilitate referral of the patient to a high-volume center, endoscopic biliary stenting can be advantageous. Finally, if preoperative neoadjuvant therapy is considered, biliary drainage is often necessary before such therapy can be initiated.

In more recent years, there has been a focus on standardization of perioperative care and creation of care pathways, which may apply to or be specific for elderly patients. In particular, geriatrics evaluation and a frank preoperative discussion concerning the possibility of prolonged hospitalization and recovery are mandatory. Care-givers for the postoperative setting should be identified and the possibility of inpatient rehabilitation after hospital discharge should be discussed so that appropriate plans are made in advance. Furthermore, careful discussion regarding the patient's goals and values is necessary and should occur prior to surgery. Although clinicians typically focus on postoperative mortality and discrete complications such as pancreatic leak, sepsis, bleeding, and pneumonia, the higher than average risk of postoperative functional and cognitive decline should be addressed explicitly as for many elderly patients the effect on quality of life can be significant [38]. Existing tools such as the comprehensive geriatric assessment (CGA) and the preoperative assessment of cancer in the elderly (PACE) have been shown to be effective in identifying modifiable risk factors and predicting complications and death [39, 40].

Resection of Lesions of the Pancreatic Head

Pancreaticoduodenectomy (Whipple procedure) is the appropriate procedure for resectable cancers of the head of the pancreas, regardless of the age of the patient (Fig. 9) [41]. While many clinicians have regarded advanced age as a relative contraindication for major surgery, there is clear evidence that age alone should not preclude surgery for pancreatic cancer. Prior to 1980, when the morbidity and mortality for pancreatic resection were substantially higher in all age groups, several studies found that elderly populations fared worse than their younger counterparts. For example, Herter et al. observed that operative deaths rose from 7.7% in patients in the 41- to 50-year age group to 25% in patients 61–70 years of age [42].

Lerut and colleagues also noted a significant increase in mortality, 41% versus 5% ($p < 0.001$), and morbidity, 58.8% versus 16.3% ($p < 0.01$), in patients undergoing pancreaticoduodenectomy over the age of 65 when compared to that in younger patients [43]. Finally, Obertop et al. reported 33% mortality following pancreaticoduodenectomy in patients over age 70 compared to 4% in younger patients [44].

Since these early studies, countless authors have challenged the view that pancreaticoduodenectomy is unsafe in elderly patients. One of the first series to show equivalent outcomes in elderly patients was from The Johns Hopkins Hospital, which reported 145 consecutive pancreaticoduodenectomies performed without mortality. Subgroup analysis, which separated patients by age (≤ 70, $n = 37$; <70, $n = 108$), revealed no significant difference in the incidence of postoperative complications. No specific complication was significantly more frequent in the older group, and the incidence of many serious complications seemed to be lower in patients older than 70 years. Operating time, blood loss, and length of stay were also without significant

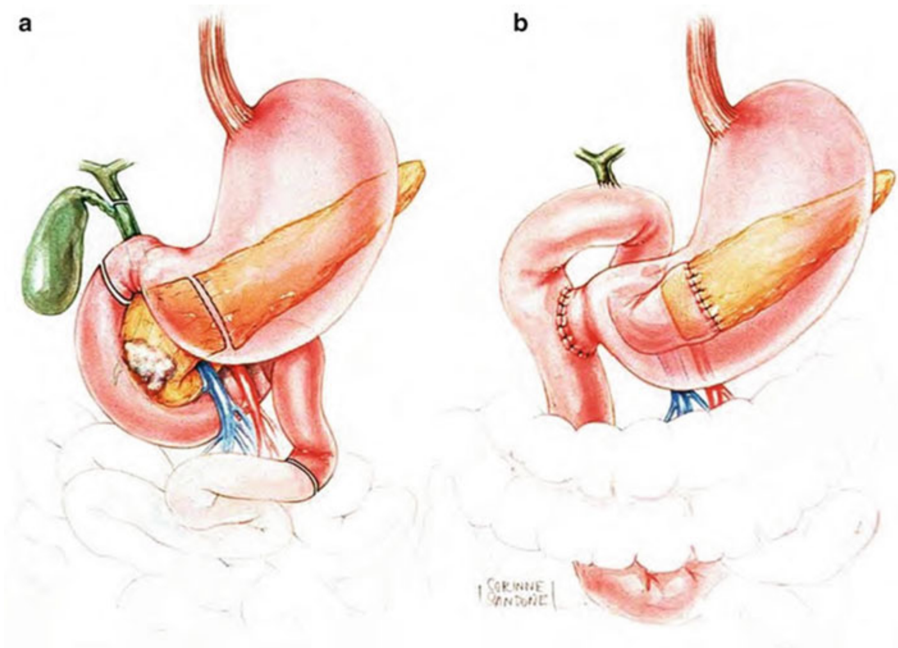

Fig. 9 Pylorus preserving pancreaticoduodenectomy (**a**) Depicts the extent of resection for a pylorus-preserving pancreaticoduodenectomy for cancer of the head of the pancreas. (**b**) Depicts reconstruction with an end-to-end pancreaticojejunostomy, end-to-side hepaticojejunostomy, and a retrocolic duodenojejunostomy (Reprinted with permission from Cameron [41])

difference between the two groups, and no deaths occurred in either group [45].

Since 1990, numerous single-center series have reported the perioperative outcome of pancreatic resection in the elderly [46–65]. Most of these studies found equivalent or acceptable morbidity and mortality rates in elderly patients compared with younger cohorts, suggesting that chronologic age alone should not be seen as a contraindication to surgery.

In one such study, Delcore et al. reported a series of 42 patients between age 70 and 80 who underwent pancreaticoduodenectomy. The incidence of major complications was 14%, with 2 operative deaths (5%) [66]. Hannoun and colleagues reported perioperative morbidity and mortality in 223 patients undergoing pancreaticoduodenectomy, with 44 patients who were of age 70 and over. Perioperative morbidity was similar in the two groups (35%), while mortality was actually decreased in the older patients (4.5% vs. 10%) [49]. In a large series from Memorial Sloan Kettering Cancer Center, Fong et al. analyzed the results of 138 elderly patients (≥70 who underwent major pancreatic resection compared to 350 patients under age 70) [50]. Length of stay (20 days vs. 20 days), frequency of complications (39% vs. 45%), and perioperative mortality (4% vs. 6%) were no different in the younger versus older groups. In fact, there were no deaths among the 24 patients aged over 80 years who underwent pancreatic resection. Analysis of the complications in this study identified that a history of cardiopulmonary disease, abnormal preoperative ECG or chest radiograph, and operative blood loss of >2000 ml were the most powerful predictors of a complication [50].

Ultimately, experienced groups of surgeons have extended the operative indications for resection to patients over 80 years of age and several groups have reported outcomes in this age group (Table 3). A series of 46 patients aged 80 and over, undergoing pancreaticoduodenectomy over a 10-year period at Johns Hopkins, were compared to 681 patients under 80 who underwent the procedure during the same time period [51]. The two

Table 3 Summary of publications comparing perioperative outcome between octogenarians and younger patients

Reference	Number of patients by age	Perioperative mortality	Perioperative complications	Median overall survival (months)	Comments
Sohn et al. 1998 [51]	46 ≥ 80 years 681 < 80 years	4.3% 1.6%	57% 41% ($p = 0.05$)	18 m 17 m	Survival is 3-year. No significant differences
Makary et al. 2006 [52]	10 ≥ 90 years 197 = 80–89 years 2491 < 80 years	0% 4.1% 1.7%*	50% 52.8% 41.6%*	–	*p, 0.05, but after controlling for comorbidities complications and mortality rate NOT significant between age groups Includes benign disease
Khan et al. 2010 [53]	53 ≥ 80 years 567 < 80 years	2% 1%	51% 37% $p = 0.004$	13.5 m 18.9 m	Elderly less likely to get adjuvant therapy
Lee et al. 2010 [59]	74 ≥ 80 years 703 < 80 years	5% 4%	47% 51%	11.6 m 18.1 m	No significant differences
Hatzaras et al. 2012 [60]	27 ≥ 80 years 490 < 80 years	3.7% 3.7%	52% 59%	33.3 m 21.9 m	No significant differences
Sukharamwala et al. 2012 [54]	333 ≥ 80 years 4226 < 80 years	Or 2.14 (ci 1.15–3.98); ($p < 0.02$)	Or 1.62 (ci 1.3–2.03); ($p < 0.0001$)	–	Meta-analysis (no difference in wound infection, delayed gastric emptying, or pancreatic fistula; increased cardiopulmonary complications)
Melis et al. 2012 [58]	25 ≥ 80 years 175 < 80 years	4% 0.6%	68% 44%	17.3 m 13.1 m	Octagenarian with increased length of stay (20 vs. 14 days, $p = 0.01$)
Belyaev et al. 2013 [57]	76 ≥ 80 years 1629 < 80 years	11.8% 2.5% ($p = 0.0001$)	Medical: 57% vs. 18% (p 0.0001) Surgical: 26% vs. 36% (p 0.75)	–	Includes benign disease. Elderly with increased medical comorbidity and delayed gastric emptying
Lee et al. 2014 [61]	475 ≥ 80 years 4102 < 80 years	6% 2% ($p < 0.0001$)	Increased pulmonary complication, stroke, sepsis, and wound disruption in patients older than 80 years	NR	
Frakes et al. 2015 [62]	26 ≥ 80 years 26 = 76–80 years 35 = 70–75 years 106 < 70 years	0% 11.5% 0% 2.8%	No difference in leak, wound infection, fistula, or medical complications	18.7 16.1 23.4 m 23 m	No significant differences in complications, mortality, and long-term survival. Elderly less likely to receive adjuvant therapy

groups were similar with respect to gender, race, intraoperative blood loss, transfusions, and type of resection performed. The older patients had a shorter mean operative time (6.3 ± 1.3 vs. 7.1 ± 4.0 h, $p < 0.05$) but a longer postoperative length of stay (median 15.0 vs. 13.0 days,

$p < 0.05$) than their younger counterparts. A higher incidence of overall complications was seen in the older patients (57% vs. 41%, $p = 0.05$), with a statistically significant increase in delayed gastric emptying among the elderly (33% vs. 18% $p = 0.03$). Perioperative mortality was slightly higher among the elderly patients (4.3% vs. 1.6%), but this was not statistically significant. Another study several years later by the same group examined the outcomes of pancreaticoduodenectomy in the very elderly, which included patients aged 90 and older [52]. Three groups that underwent pancreaticoduodenectomy between 1970 and 2005 were compared: under age 80 ($n = 2491$), age 80–89 ($n = 197$), and age greater than 90 ($n = 10$). While the patients aged 80–89 did have a higher mortality rate (4.1% vs. 1.7%, $p < 0.05$) and complication rate (52.8% vs. 41.6%, $p < 0.05$) than their younger counterparts, these differences were not significant after adjusting for preoperative comorbidities. Multivariate analysis found that coronary artery disease and COPD were independent risk factors for mortality after pancreaticoduodenectomy, but age alone was not.

Over the last decade, several other groups have reported increased, but still acceptable morbidity and mortality in very elderly patients [52–58], while others have found no difference in major complications or mortality in patients above the age of 80 years [59, 60] (Table 3). The very elderly are more likely to have increased lengths of stay and although the majority can be discharged home, there is increased utilization of inpatient transitional care facilities in this population. Despite a slightly higher rate of perioperative complications in the very elderly, most studies report no difference in overall or disease free survival.

In addition to the numerous studies that looked specifically at patient age, several large series examined all patients after major pancreatic resection to elucidate overall prognostic indicators for outcome. One such study came from the Massachusetts General Hospital, in which 733 consecutive pancreatic resections performed from 1990 to 2000 were reviewed. The authors found that mean age of patients increased significantly over that time period, from 57 to 65 years of age. Multivariate analysis of this series of patients did not identify age as a significant prognostic indicator of poor outcome [67].

In recent years, the fundamental question has shifted from whether elderly patients with pancreatic cancer can be treated safely with surgical resection, but how to optimize patient selection and streamline care to improve outcomes. Pancreatic cancer is more prevalent in the elderly, and given the aging population, it is now commonplace to operate on patients well into their 80s and beyond. It is clear that chronologic age alone should not be a contraindication to resection with curative intent. Whenever possible, we recommend utilization of high-volume centers for these complicated patients [68–70]. Diligence is required in the postoperative setting to appropriately identify and rescue patients with complications.

Finally, in recent years, series of minimally invasive pancreaticoduodenectomy either by standard laparoscopic [71] or robotic techniques [72] have been reported with comparable short-term outcomes to traditional open resection. It might be hoped that as these techniques are more widely applied, elderly patients might benefit from a less morbid incision.

Resection of Lesions of the Body and Tail

The opportunity to resect cancers of the body and tail of the pancreas is typically more limited than that of the pancreatic head, due to high frequency of advanced disease at diagnosis. If an elderly patient appears to have resectable disease based on available imaging, many surgeons favor diagnostic laparoscopy to look for occult metastatic disease before proceeding with resection. In the absence of metastatic disease, distal pancreatectomy with splenectomy is the operation of choice. Although less well studied than outcomes after pancreatic head resection in the elderly, available data indicate that elderly patients tolerate distal pancreatectomy well. In a study of the risk factors predicting outcome after distal pancreatectomy, multivariate analysis found that age was not an independent predictor of outcome [73].

Even more than with patients undergoing pancreatic head resection, minimally invasive distal pancreatectomy has been applied with multiple series reporting advantageous short-term outcomes [74]. It would again appear that elderly patients may benefit from such techniques in the appropriate setting.

Palliation

The vast majority of pancreatic cancers are unresectable at the time of diagnosis. Thus, optimal palliation of symptoms to maximize quality of life, and possibly allow for systemic chemotherapy, is of great importance. The three primary symptoms warranting palliation are obstructive jaundice, gastric outlet obstruction, and pain. Palliation in patients with unresectable pancreatic carcinoma has evolved with the increased use of endoscopic biliary and duodenal stenting. Endoscopic stent placement is associated with decreased procedural morbidity and mortality, but is not always feasible and lacks the durability of surgical bypass [75]. Most surgical series report mortality rates of less than 5% and a much lower incidence of late jaundice when compared to endoscopic palliation [76]. Nuzzo and colleagues compared the outcomes of elderly patients (over age 70) undergoing surgical versus endoscopic palliation, surgical palliation resulted in better long-term outcomes with similar morbidity [77]. Mean survival after surgery was significantly higher than that after stent placement (13.2 months vs. 7.29, $p < 0.001$), and total readmissions were fewer after surgery than stenting (1 vs. 25, $p = 0.001$) (Table 5).

Although the role of endoscopic palliation in patients found to be unresectable during preoperative evaluation has been well defined, many surgeons still favor surgical biliary bypass, should the tumor be unresectable at the time of laparotomy. This is best accomplished by an anastomosis of the bile duct to the small intestine as a hepaticojejunostomy. If patients have duodenal obstruction, a gastrojejunostomy is also performed. (Fig. 10) [41].

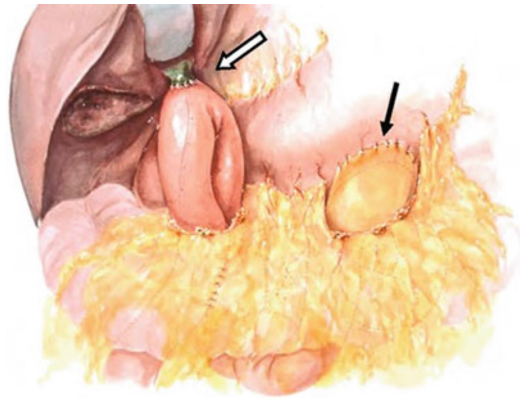

Fig. 10 Roux-en-Y hepaticojejunostomy (*white arrow*) is performed for biliary decompression, and a retrocolic gastrojejunostomy (*black arrow*) relieves gastric outlet obstruction (Reprinted with permission from Cameron [41])

The role of prophylactic gastrojejunostomy for palliation in patients found to have unresectable pancreatic cancer intraoperatively has been addressed by two prospective randomized trials. The first randomized 87 patients with unresectable periampullary cancer at the time of laparotomy to either prophylactic retrocolic gastrojejunostomy or no gastrojejunostomy. None of the patients who underwent gastrojejunostomy developed late gastric outlet obstruction, whereas the patients without gastrojejunostomy had a 19% rate of late gastric outlet obstruction requiring intervention ($p < 0.01$). Length of stay, morbidity, mortality, and long-term survival were comparable between the two groups [78]. In a second prospective, randomized multicenter trial, patients with unresectable cancer at the time of laparotomy underwent either a biliary bypass alone (single bypass) with hepaticojejunostomy or a double bypass with both a hepaticojejunostomy and a retrocolic gastrojejunostomy [79]. The group who underwent double bypass had significantly decreased incidence of late gastric outlet obstruction without any increase in complication rate, providing evidence that prophylactic double bypass should be strongly considered in these patients.

A recently reported series from the ACS NSQIP database evaluated perioperative morbidity and 30-day mortality in patients that underwent surgery for unresectable pancreatic cancer [75]. This series included patients determined to have locally advanced and/or metastatic disease at the time of planned resection, as well as those with known unresectable disease taken to the operating room specifically for palliative purposes. Not surprisingly, patients that underwent biliary and/or gastrojejunal bypass experienced increased morbidity (12 vs. 20%, $p < 0.001$), but equivalent mortality rates (5 vs. 6.5%, $p = 0.21$). On multivariate analysis, age greater than 70, emergent operation, disseminated cancer, albumin less than 3 g/dl, and renal insufficiency were independent risk factors for death. Dependent functional status, diabetes, and preoperative leukocytosis were independently associated with serious morbidity [75]. This underscores the point that in patients with multiple risk factors, the risks of surgical palliation must be carefully considered.

Laparoscopic gastrojejunostomy and metallic stent placement are less invasive alternatives that may be better tolerated. A number of series have shown excellent results with laparoscopic gastrojejunostomy [80, 81]. In addition, the role of endoscopic stenting for duodenal obstruction has quickly expanded (Fig. 11). Several retrospective studies have compared outcome after duodenal stent placement versus surgical bypass. In one study, 42 patients who underwent gastrojejunostomy were compared with 53 patients who underwent stent placement [82]. There were no differences between the groups as far as minor complications, early major complications, and long-term survival, although the surgical group had fewer late complications (22% vs. 60%), and the stented group had a shorter length of hospital stay (6 days vs. 18 days, $p < 0.001$). For patients with advanced unresectable disease or elderly patients with poor performance status, duodenal stent placement has become the procedure of choice.

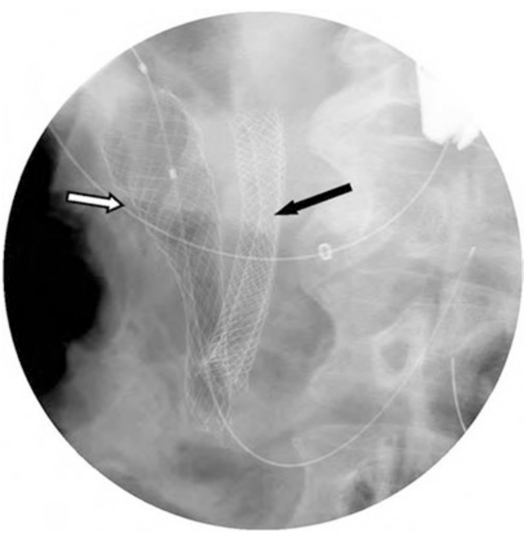

Fig. 11 Enteric palliation using an endoscopically placed duodenal stent (*white arrow*) and relief of biliary obstruction with biliary stent (*black arrow*)

The management of pain in patients with advanced pancreatic adenocarcinoma is one of the most important aspects of care, and multiple complementary treatment strategies are available. Most patients can be successfully managed with a combination of short- and long-acting oral opiates, often combined with topical sustained-release opiates. However, appropriate dosing of opioids in the elderly must be considered. Inadequate treatment of pain in elderly cancer patients has been well documented [83]. Unrelieved cancer pain in the elderly can lead to disturbances in mood, sleep, appetite, and cognition. Many health-care providers have misconceptions about pain perception in the elderly, tolerance and addiction, and increased potency of medications.

When pancreatic cancer pain is intractable despite appropriate opioid analgesics, local procedures that target either the celiac plexus or the splanchnic nerves are recommended. Two methods exist for absolute alcohol neurolysis of the celiac plexus: standard needle placement through the midback (with CT or fluoroscopic guidance) or endoscopic ultrasound (EUS)-guided needle placement. Both methods have been shown to significantly reduce pain for sustained periods of time, with the EUS-guided approach having fewer complications [84–86]. When a pancreatic cancer is determined to be unresectable at laparotomy, intraoperative chemical splanchnicectomy can be performed with direct injection into the area of the celiac axis (Fig. 12) [41] Lillemoe and colleagues performed a prospective, randomized, double-

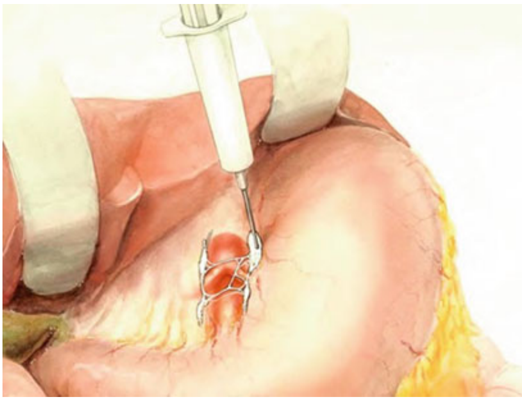

Fig. 12 Chemical Splanchnicectomy. After identification of the celiac axis in the lesser sac, 50% ethanol is injected into the celiac plexus for pain control (Reprinted with permission from Cameron [41])

blind, placebo-controlled trial comparing chemical splanchnicectomy with 50% alcohol to a sham saline injection [87]. The patients who received alcohol injections had significantly improved pain scores compared to those who received saline at 2-, 4-, and 6-month follow-up assessments, as well as at the final assessment ($p < 0.05$). This procedure can also be performed during laparoscopic staging for pancreatic cancer. Neurolytic celiac plexus block also improved multiple quality-of-life measures in those patients. In the elderly population, EUS-guided neurolytic celiac plexus block likely delivers the least invasive, most effective option for intractable pancreatic cancer pain.

Postop Care and Complications

Frailty and comorbidities are common in the elderly. Attention to detail is required in the postoperative setting to insure early identification of complications and appropriate management. Adequate fluid and electrolyte maintenance, glucose regulation, pulmonary toilet, and pharmacologic prophylaxis for deep venous thrombosis are routine. Unfortunately, complications are common in all age groups after pancreaticoduodenectomy, with typical rates of 30–40%. The difference in complication rates between elderly and younger patients has been addressed by multiple retrospective comparisons [46–65]. Although numerous studies have found no difference in complication rates between these two groups, others have reported higher rates of delayed gastric emptying [51, 57], cardiopulmonary morbidity [54], stroke [61], or sepsis [61]. Several studies report that elderly patients with comorbidities have increased complication rates compared to younger patients with the same comorbidities [52]. This suggests that careful preoperative patient selection and increased postoperative diligence are warranted in elderly patients who undergo major pancreatic resection.

Chemotherapy/Radiation Therapy

The multimodal approach to pancreatic cancer has realized significant advances over the last decade. Treatment approach varies considerably based on local characteristics of the tumor at presentation. Patients with localized, clearly resectable pancreatic cancer should undergo surgery with curative intent. The role of neoadjuvant therapy in these patients is a matter of debate and best considered in the context of a clinical trial, which is often not an option for the elderly. There are several theoretical advantages to a neoadjuvant approach, including enhanced patient selection for a morbid operation, earlier treatment of micrometastatic disease, and the opportunity to monitor response to systemic therapy in vivo that make this approach appealing [88–90].

Patients with borderline resectable and locally advanced pancreatic cancer have a high risk of positive margins if surgical resection were to be pursued. Several criteria have been offered to better define these terms and are based on the involvement of surrounding vascular structures [91–93] (Table 4). In patients with borderline resectable and locally advanced disease, there is general consensus that the initial approach should be neoadjuvant chemotherapy and chemoradiation with the goal of downstaging the tumor such that resection is possible. Stereotactic body radiation therapy (SBRT) is an important recent advance in radiation therapy and is frequently used in borderline resectable or locally

Table 4 Common definitions of borderline resectable pancreatic cancer

Blood vessel	NCCN [91]	AHPBA/Consensus [93]	MD Anderson [92]
Celiac axis	Distortion or narrowing of the vessel wall, and/or reconstructible occlusion	Uninvolved	Short segment occlusion/ reconstructible
Superior mesenteric artery	Tumor-vessel interface ≥180 degrees of the circumference of the vessel wall	Abutment	Abutment
Hepatic artery	Reconstructible short segment interface between tumor and vessel	Abutment or short segment encasement	Abutment or short segment encasement
Superior mesenteric vein/ portal vein	Distortion of narrowing of the vessel wall, and/or reconstructible occlusion	Abutment, impingement, encasement of the SMV/ PV or short segment occlusion	Short segment occlusion/ reconstructible

Table 5 Palliative biliary bypass versus biliary stenting in patients >70 years of age with unresectable pancreatic cancer [77] (*Source*: Data from Nuzzo et al. [77])

	Surgery ($n = 24$)	Stent ($n = 35$)	p Value
Mortality (%)	1	3	NS
Morbidity (%)	6	10	NS
Patients readmitted	1	15	0.006
Number of readmissions	1	25	0.001
Mean survival (months)	13.2 ± 8.06	7.29 ± 2.25	<0.001

advanced pancreatic cancer. Follow-up imaging is planned to assess treatment response and suitability for resection. It should, however, be noted that radiographic changes on CT may not adequately reflect tumor response to therapy [94, 95]. A more aggressive surgical approach involving exploration and serial biopsies along potentially involved vascular structures has been recommended. Although operative times and blood loss appear to be increased after neoadjuvant therapy, decreased postoperative morbidity has been reported [95]. The optimal neoadjuvant approach is yet to be determined and regimens are typically extrapolated from the metastatic setting.

A recent series from the Medical College of Wisconsin reported outcomes of 246 patients, including 36 (15%) patients age ≥ 75, with pancreatic cancer treated with moderate course (2–4 months) neoadjuvant therapy [96]. Patients older than 75 years were equally likely to undergo successful surgical resection. Failure to complete neoadjuvant therapy and surgical resection was increased with borderline resectable versus resectable disease at presentation, increased posttreatment/preoperative CA 19–9, and Charlson Comorbidity index ≥6. Overall survival in this series was 24 months for all comers and 37 months in patients that completed surgical resection. Older patients in this series were more likely to be discharged to a transitional care facility, but there was no significant difference in perioperative morbidity, mortality, or overall survival [96].

A modest, though significant, benefit of adjuvant chemotherapy therapy has been demonstrated after resection of pancreatic cancer and is thus the recommended by the NCCN. 5-FU was considered standard of care until the landmark CONKO-001 trial published in 2007 demonstrated improved 5-year and median survival with adjuvant gemcitabine compared with resection alone [97].

The landscape of systemic therapy for metastatic pancreatic cancer shifted dramatically in 2011 with the ACCORD-11 trial [98]. This trial demonstrated that overall survival with fluorouracil, leucovorin, oxaliplatin, and irinotecan (FOLFIRINOX) was significantly improved compared with previous standard of care gemcitabine for patients with metastatic pancreatic cancer (6.8 vs. 11.1 months, $p < 0.001$). However, this can be a toxic regimen and patients with performance status >1 and age $\geq$ 75 were excluded from the trial. Furthermore, only 29% of patients were older than 65 years. Age was an independent predictor of poor survival, but patients older than 65 years did benefit from FOLFIRINOX (HR = 0.48). Studies are ongoing to assess the tolerability and efficacy of dose-adjusted FOLFIRINOX in the elderly.

The MPACT trial also demonstrated improved survival with combination gemcitabine and nab-paclitaxel compared with gemcitabine monotherapy [99]. Elderly patients and those with poor performance status were included in this trial and 10% of the patients were above the age of 75 years. Given the available data, it is reasonable to consider FOLFIRINOX in fit patients age 65–75, and gemcitabine combination chemotherapy for patients older than 75 or those with poor functional status. Palliative gemcitabine monotherapy may be considered for the very elderly or frail. Adjuvant chemoradiotherapy has also been used for many years, but its benefit has not been definitively established and is an area of active investigation. Additional experimental strategies including immunotherapy, molecular targeted therapy, and vaccine-based therapy are also of great interest, particularly in the adjuvant and metastatic setting.

Long-Term Outcomes and Quality of Life

Despite improvements in surgical management and perioperative mortality, long-term survival remains poor following resection for pancreatic adenocarcinoma. Despite advances in multimodal therapy, 5-year actuarial survival rates after pancreaticoduodenectomy rarely exceed 20%. A large study of a statewide database of 2230 patients diagnosed with pancreatic cancer found that advanced age at diagnosis was an independent risk factor for decreased survival (hazard ratio 1.23, CI 1.18–1.29). However, this is likely explained by underutilization of surgery in the elderly [100]. When the elderly are treated with appropriate surgery and adjuvant therapy, several series have shown that age is not an independent prognostic factor for long-term survival. Most analyses find tumor characteristics, such as tumor size, nodal status, margin status, and tumor differentiation, stage, CA 19–9 and treatment approach to be the most influential prognostic factors for survival [101, 102].

Numerous studies have examined long-term outcome after pancreatic resection in the elderly compared to younger patients (Table 3). The majority of series report similar 5-year survival rates in elderly patients as those in younger patients [51, 53, 58, 59, 60, 62, 103].

As with short-term outcomes, hospital volume is an important determining factor in long-term outcome after pancreatic resection. High-volume, single-institution series report postresection 5-year survival rates as high as 29%, while population-based studies report rates of 15–16% [68, 69, 104]. A study by Birkmeyer and colleagues investigated the relationship between hospital volume and 5-year survival after major cancer surgery. This study showed that for pancreatic cancer resection, there was a difference in long-term survival between low- and high-volume hospitals (10.8% vs. 15.9%) [105]. These data, like those regarding perioperative outcome, suggest that elderly patients are best served at high-volume institutions.

Data with respect to quality of life after resection for elderly patients with pancreatic adenocarcinoma are lacking. One study compared subjective quality of life scores in patients older than 70 years after pancreaticoduodenectomy with matched individuals that underwent laparoscopic cholecystectomy. Three months postoperatively, patients that underwent pancreaticoduodenectomy reported more fatigue, nausea, vomiting, diarrhea, weight loss, pain, and loss of efficiency. However, by 6 months there were no significant differences between the cohorts [106]. Additional data are needed to further address quality of life after pancreatic resection in the elderly.

Treatment Disparities in the Elderly

Unfortunately, most patients with pancreatic cancer (52%) are found to have distant disease at the time of diagnosis.

A dismal prognosis has led to an overall pessimism for the aggressive treatment of this disease. According to the SEER National Cancer Registry database, 7% of patients have localized disease, and 26% present with regional disease. When these 33% of patients with locoregional disease have been studied, only about half of them underwent any form of surgical or radiation treatment [107, 108]. Even among Stage I patients, who are potentially curable with resection, Bilimoria et al. found that 71% did not undergo surgery. Analysis of these patients showed that 6.4% were excluded due to comorbidities, 4.2% refused, 9.1% were excluded due to age alone, and 38.2% were not offered surgery for undetermined reasons [107]. In addition to the 9.1% who were excluded due to age, the average age of patients who were not offered surgery was significantly higher, 71.7 versus 62.1 ($p < 0.0001$). This study suggests that age has a major influence in the management options that are offered to patients, including referral to a surgeon (Fig. 13). Gawron et al. found similar differences, with a much higher percentage of older patients treated nonoperatively [109]. This unfortunate trend is true for cancer-directed surgery in other diseases as well, with underutilization in elderly populations [110]. This disparity has continued over time [111]. A more recent analysis of the SEER database reported similar findings: 10,505 patients older than 65 years with locoregional pancreatic adenocarcinoma, only 51% received treatment (chemotherapy and/or surgery). Of these patients, only 11.1% received multimodal therapy [112].

Management of Benign and Premalignant Neoplasms

Diagnosis

The diagnosis and management of benign pancreatic neoplasms has become an increasingly frequent problem in recent years. This is in part due to the increased detection of asymptomatic lesions due to the widespread use of cross-sectional imaging studies. The challenge is determining which lesions are malignant, benign but premalignant, or benign with no malignant potential. Most asymptomatic lesions are cystic and include mucinous cystic neoplasm (MCN), intraductal papillary, mucinous neoplasm (IPMN), and serous cystadenoma (SCA). Cross-sectional imaging (with or without pancreatography), endoscopic ultrasound, and cyst fluid analysis are the

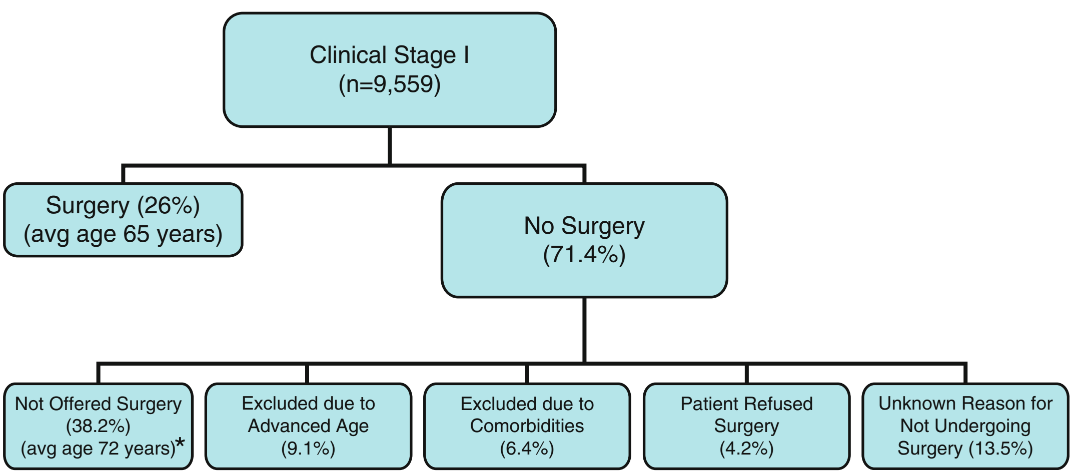

Fig. 13 Failure to operate on stage I pancreatic cancer. Note the role of age in the chances that a patient will be offered surgery. *$p < 0.0001$ compared to age of patients who underwent surgery (Data from Bilimoria et al. [107])

principal methods for evaluating cystic lesions of the pancreas.

Multidetector CT scan is generally the first technique used, whether it reveals an incidental, asymptomatic lesion, or has been obtained in the workup of abdominal symptoms. CT can often help discern between several types of cysts, based on specific characteristics. For example, the presence of multiple small-diameter microcysts, stellate scar, and sunburst calcifications is characteristic of SCAs and distinguishes these lesions from mucinous cystic tumors (Fig. 2). In addition to aiding in classification of cysts, several findings on cross-sectional imaging can predict the likelihood of malignancy of a cystic pancreatic lesion: peripheral calcification, dilated pancreatic duct, and presence of a solid component [113]. A noninvasive alternative to CT is MRCP, as this technique can determine if the lesion communicates with the pancreatic ductal system. IPMNs typically communicate with the pancreatic ductal system, whereas MCNs do not. MRCP or ERCP, as an invasive procedure, can classify IPMN into main duct type, branch duct type, or mixed type IPMN, which has important management implications [114]. Endoscopic ultrasound with fine-needle aspiration (EUS-FNA) is useful in differentiating between cyst types. The viscosity of aspirated fluid is the first clue to diagnosis, as mucinous neoplasms have a higher fluid viscosity than serous ones. Fluid analysis revealing a high mucin content and high carcinoembryonic antigen (CEA) is diagnostic of a mucinous neoplasm, with an accuracy of 79% [10]. This differentiation between mucinous and nonmucinous is essential, as serous tumors are very rarely malignant and in most cases can be managed without surgery.

Estimating the Malignant Potential

When a pancreatic cystic lesion has been classified as mucinous, whether it be MCN or IPMN, the clinician must then determine the likelihood of malignancy. Management of asymptomatic pancreatic cysts can be challenging and optimal treatment approach remains an area of controversy. The American Gastroenteroligal Association (AGA) [115] and International Association of Pancreatology (Fukuoka) [116] have provided recommendation to better delineate criteria for EUS and surgery. Surgery is recommended for high risk features, which include mucinous cysts $\geq$3 cm associated with main duct dilation and/or a definitive mural nodule. *KRAS* and or *GNAS* mutations with *TP53* and *PIK3CA* or *PTEN* mutations are also worrisome. Cytology that raises concern for malignancy is an indication for surgery. In patients with IPMN, a main-duct subtype, side branch tumors with a dilated main pancreatic duct, elevated serum CEA or CA19–9, presence of jaundice, and new-onset diabetes have all been shown to be predictors of malignancy [117]. In addition, cyst fluid analysis revealing markedly elevated levels of CEA is associated with malignancy [103, 104]. Cytology of the cyst aspirate may also be used, which has a specificity of 83%, but the high false-negative rate creates a low sensitivity (34.5%) [118]. Finally, advanced age is also associated with increased likelihood of malignancy, as most series find the average age of patients with malignant lesions to be 5–6 years older than patients with benign tumors [119].

Indications for Resection

In elderly patients, the decision to proceed with surgical resection must take into account the patients symptoms, the likelihood of malignancy, the patient’s general medical condition, and the expected morbidity and mortality of the procedure. In patients with serous cystadenoma, the likelihood of malignancy is less than 1%, so surgery should only be offered to symptomatic patients in relatively good heath or for tumors demonstrating significant growth. In the case of mucinous cystic neoplasms (MCNs), resection is indicated in symptomatic patients and in cases with a high suspicion of malignancy. Because it is impossible to determine malignancy preoperatively with absolute certainty, many surgeons advocate surgical resection for all patients with MCN who are suitable operative candidates. For patients with branch duct IPMN, malignancy is extremely rare in asymptomatic patients with lesions less than 3 cm. Therefore, only those patients who are symptomatic or have large (>3 cm) lesions should undergo resection. In contrast, main duct IPMN has a malignancy rate of 60–92%, leading to most authors recommending resection for all patients [120].

Resection

When the decision is made to resect a benign or premalignant tumor of the pancreas, most resections are performed using traditional pancreaticoduodenectomy or distal pancreatectomy. However, in recent years, multiple new minimally invasive and/or pancreas-sparing techniques have become popular options for surgical management. These include laparoscopic distal pancreatectomy with or without splenic preservation, and central pancreatectomy. For lesions of the body and tail of the gland, laparoscopic distal pancreatectomy, with or without the spleen-preserving procedure, has gained favor with many surgeons [121, 122]. The laparoscopic technique has become widely applied for benign tumors or small tumors of undetermined malignant status. In patients considered to have a high probability of malignancy, splenectomy should be considered. For benign small lesions in the mid-pancreas, a central pancreatectomy may be an appropriate choice, as it preserves as much pancreatic tissue as possible to ensure maintenance of endocrine and exocrine function. An even less invasive option for benign neoplasms is enucleation, in which the lesion is essentially "cored" out from the pancreatic parenchyma. This procedure is most appropriate for lesions that are not in communication with the main pancreatic duct [123].

Outcomes

Theoretically, the long-term survival after resection of a benign or premalignant pancreatic tumor should be comparable to age-matched controls. However, patients with IPMNs are at risk for recurrent disease in the remnant gland after partial pancreatectomy. The extent of surgical resection of IPMNs should be determined by the extent of disease (especially the presence of multifocal lesions) and intraoperative frozen section of resection margins. After resection, patients with even benign or noninvasive IPMNs require careful follow-up for recurrent disease, which has been reported in approximately 10% of patients [5]. Survival for patients with resected invasive IPMNs is substantially better than for pancreatic ductal carcinoma and in some series approaches 50% at 5 years [10]. The role of postoperative adjuvant therapy for invasive IPMN has not been specifically determined but in general has been applied similarly to ductal carcinoma.

Conclusions

Tumors of the exocrine pancreas are a significant issue in the elderly. In general, older patients should be treated aggressively with similar indications for surgery and similar procedures as in younger patients. The morbidity and mortality of major pancreatic resection have decreased among all age groups over time, making safer surgery an option. Great care should be taken, however, in assessing an older patient's preoperative risk factors, potential for increased life expectancy, and hospital volume before proceeding with major surgical resection. In patients with pancreatic malignancy, multidisciplinary management is mandatory, and resection, which offers the only chance of cure, should not be withheld based on chronological age alone.

Case Study

Mr. Smith is an 80-year-old man who presented with painless jaundice, dark urine, clay-colored stools, and pruritus. His workup at an outside hospital consisted of a CT scan, which showed a potentially resectable 2.5 cm mass in the head of the pancreas, and an ERCP, which demonstrated pancreatic and biliary ductal obstruction. A biliary endostent was placed. Finally, an endoscopic ultrasound was performed, which showed a pancreatic mass with no evidence of visceral vessel invasion. Fine-needle aspirate performed at the time of EUS was positive for pancreatic cancer. The patient was referred for surgical evaluation.

The patient's past medical history is significant for a 40-year smoking history, although he stopped smoking 20 years ago. He has long-standing atrial fibrillation and has been on anti-coagulation with warfarin. The patient has an internal cardiac defibrillator in place. He has type II diabetes managed with oral medications. He has a history of prostate cancer treated with radiation therapy, which has resulted with neuropathic bladder, which requires self-catheterization. He also has a history of a left hip replacement.

After determining that the patient was indeed a potential candidate for surgical management, follow-up with his cardiologist was obtained where echocardiogram revealed an ejection fraction of 20–25%, likely due to a nonischemic cardiomyopathy. His medications included avandia, corgard, glucosamine, iron, lasix, metformin, and norvasc. On review of systems, he denied chest pain, but exercise tolerance was limited with shortness of breath at one block or one flight of stairs. He had no history of cerebral vascular accident or stroke. He had lost a total of 10 pounds since the presentation. He denied nausea, vomiting, or blood in his stool.

The patient was evaluated preoperatively by cardiology as well as in our preoperative assessment and testing center and was brought to the operating room for a planned pancreaticoduodenectomy. His warfarin was stopped 5 days before surgery and on the morning of admission, he had a normal INR. General anesthesia was induced following placement of an epidural catheter for intraoperative anesthesia and perioperative pain control. After general anesthesia was obtained, the patient underwent a diagnostic laparoscopy, which showed no evidence of metastatic disease. A classic pancreaticoduodenectomy was then performed with an estimated blood loss of 400 ml and no intraoperative complications. After the reconstruction, a feeding jejunostomy was placed. At completion of the surgical procedure, the patient was extubated and transferred to the ICU. He was maintained in the ICU overnight and then transferred to a progressive care unit in the morning following surgery. On postoperative day two, tube feeds were initiated, and on postoperative day 3, the patient was started on a clear liquid diet. The patient was maintained with perioperative prophylaxis with lovenox, and on postoperative day four, with no evidence of bleeding in the drains, the patient was started on therapeutic heparin for the remainder of his hospitalization. On postoperative day 3, he developed an episode of atrial fibrillation with rapid ventricular response, and cardiology follow-up was obtained. His heart rate was eventually controlled with digoxin and beta blockers which were not associated with hemodynamic instability. Perioperatively, he had some confusion, thought to be due to intervenous narcotic PCA, but this cleared, and his pain was eventually well controlled with tylenol. He was able to tolerate a diet although oral intake was only marginal, and he was, therefore, maintained on cycled tube feeds throughout the remainder of his hospitalization. The patient was discharged to a rehab center on postoperative day 10 with drains removed and on therapeutic lovenox until his anticoagulation was adequate on oral warfarin.

The patient was seen in follow-up on 1 month after discharge. He has recently been returned to his home where he lives independently with family nearby. He tolerates a diet although we are still using the feeding jejunostomy for daily boluses of tube feeds but felt that his oral intake was adequate. He had no new cardiac events and was therapeutically anticoagulated with warfarin. His feeding tube jejunostomy was removed. His incision was well healed.

Final pathology revealed a $2.7 \times 2.2 \times 1.6$ cm ductal carcinoma of the pancreas. All margins were negative. One of 13 pancreatic lymph nodes showed direct invasion by the cancer, but all other lymph nodes were negative. (AJCC Stage pT3, N1, M0). After consultation with the patient and his family, it was felt that his recovery was adequate for referral to medical oncology for consideration of postoperative adjuvant chemotherapy.

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Colorectal Cancer in Elderly Patients: Considerations in Treatment and Management

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Abstract

America's population is aging, and the number over the age of 80 will double by the year 2050. This, combined with the fact that colorectal cancer is a common malignancy, with an increasing incidence with age, explains why treating the elderly patient with colorectal cancer is becoming increasingly commonplace. This chapter focuses on how the disease may present differently in elderly patients; how the risks of treatment and surgery can be assessed and used to guide treatment decisions; how various aspects of colorectal cancer treatment may be different, or the same, for geriatric patients; and finally, how outcomes in the perioperative period can be optimized by choices in surgical technique and perioperative care. Caring for these elderly patients requires considerable skill and judgment that takes into consideration their comorbidities, the various options for treatment, and a global understanding of how the risk and benefit equation works for the various treatments such that appropriate care is rendered to optimize short-term outcomes balanced with the desire to achieve good long-term cancer control.

Introduction

Colorectal cancer is common and the risk of developing this malignancy increases with age. An aging population further compounds this: by the year 2050, 84 million Americans will be over the age of 65, nearly double the 43 million who were that age in 2012, and accounting for over 20% of the population [1]. Furthermore, the number of those who are considered the "Oldest of the Old," those over the age of 80 years, will double by 2050 [1]. Treating the elderly colorectal cancer patient is becoming increasingly commonplace, and since surgery forms the basis of colorectal cancer treatment, surgeons often find themselves on the front line, maneuvering around the elderly patient's co-morbidities, trying to avoid early morbidity and mortality, while balancing concerns over quality of life and advantageous short-term outcomes, with the desire to achieve good long-term cancer control.

This is a population of patients that is incredibly heterogeneous, not only in terms of comorbidities, but also in terms of daily activities and social functioning. Caring for these patients requires considerable thought and skill to manage and treat their ailments. A more global picture of each individual may be what is best suited for optimal outcomes. Unfortunately, little is clearly understood as to how well elderly patients tolerate any number of treatments as they are often excluded from clinical trials due to multiple comorbidities and other confounding factors.

The aim of this chapter is not a thorough review of colorectal cancer and its treatments, to which we would refer you to any number of excellently written chapters, articles, and guidelines on the subject that provide an extensive explanation [2–5]. Rather, this chapter will focus on how aspects of the disease and its treatments may be different, or the same, for geriatric patients. We aim to provide the clinician with an improved understanding of items and options to consider when caring for elderly colorectal cancer patients. Specifically, we will address how the disease may present differently in elderly patients, how the risks of treatment and surgery can be assessed and used to guide treatment decisions, how outcomes in the perioperative period can be optimized by choices in surgical technique and perioperative care, and how neoadjuvant and adjuvant treatments may be differently utilized in geriatric patients. Furthermore, we will focus the discussion on adenocarcinoma of the colon and rectum as this represents the vast majority of colorectal cancer seen in this patient population.

Case Study #1

An 80-year-old female with a history of chronic kidney disease, atrial fibrillation, congestive heart failure, pulmonary hypertension, and previous transient ischemic attacks on oral anticoagulation presented to the emergency department with gastrointestinal bleeding and anemia. She required several transfusions of packed red blood cells and colonoscopy demonstrated a large ascending colon mass, which was biopsied and confirmed to be moderately differentiated adenocarcinoma. Additional staging evaluation was negative and her carcinoembryonic antigen level was normal. On questioning, she was very physically active prior to struggling with symptoms of anemia, participating in aerobics and weight training at her local gym. She had an active social life and lived independently with her husband. She denied any significant weight loss in the months prior to her admission. Her exam was remarkable for a petite, alert, vibrant elderly woman in no acute distress with good cognitive functioning and an unremarkable abdominal exam with no previous abdominal surgery. She was taken for a laparoscopic right hemicolectomy once her oral anticoagulation was reversed, which was well tolerated and proceeded without complication. The operation took slightly longer than 2 h and the estimated blood loss was less than 100 mL. Postoperatively, she was treated according to our postoperative enhanced recovery pathway with early ambulation, early advancement of diet on the first postoperative day, and minimization of narcotics using transversus abdominis blocks and intravenous acetaminophen. She was evaluated by physical and occupational therapy and met criteria for discharge to home, which occurred on postoperative day five. Her pathologic assessment revealed a Stage IIIB (pT3 N1b M0) moderately differentiated ascending colon cancer with 2 of 28 nodes positive, no lymphovascular or perineural invasion, and negative margins. She was evaluated for adjuvant chemotherapy and elected to forgo this to avoid the impact of medication-related side effects and to maximize her quality of life. She did well for 34 months after her surgery, returning to her previous level of activity, without any evidence of recurrence on imaging or serum markers, at which time she succumbed to her cardiac disease with an acute event.

This case highlights several principles of caring for geriatric colorectal cancer patients. First is a thorough understanding of the patient beyond their acute cancer diagnosis. The woman in this case study clearly functioned at a level above most of her peers, demonstrating high-level physical and mental functioning as well as good nutrition despite symptoms of anemia that had crept in over a few months. Furthermore, she had an ample social support system of family and friends to help in her recovery. While using metrics to objectively assess frailty, such as the CGA and the Fried criteria, can give an objective "definition" to a patient's frailty, inquiring about these issues during history taking is also quite valuable, as often an accurate assessment can be made and a rough categorization of frailty and risk-assessment can be obtained without an excess of time spent in the effort.

Secondly, the use of a minimally invasive surgery and an enhanced recovery pathway was helpful in speeding recovery and minimizing the impact of surgery. While the operation likely took longer to complete than a typical open right colectomy, the laparoscopic approach offers minimal incisions, and therefore, a reduction in postoperative pain and minimization of narcotic use, which is especially helpful in geriatric patients. She used minimal narcotics, she was able to ambulate soon after her operation, and she was able to avoid any issues with postoperative delirium, which is so common in geriatric surgery patients. Our practice is to also include our patients on a predefined enhanced recovery pathway for all nonemergent surgery, regardless of disease process, age, or comorbidities.

In addition to the use of a minimally invasive operation, a care path that includes strategies to minimize narcotic use in the postoperative period with preference given to nonnarcotic options for pain control and use of regional anesthetics such as epidurals and blocks can be very helpful in the geriatric population. Patients are also allowed clear liquids after surgery and advanced to low fiber soft diet as tolerated, often by the first or second postoperative day. Furthermore, standard activity instructions ensure that patients are ambulating the night of surgery, in many cases, with the help of a dedicated and well-trained nursing staff. Another component of the care path is setting the expectation of the surgical recovery plan prior to surgery so patients are aware of what to expect and the time-line at which milestones often occur. Such management of expectations sets up what is "normal" for the patient and allows them to feel comfortable in their recovery.

Lastly, this case also emphasizes the impact competing comorbidities can have on overall survival in the geriatric patient population. Certainly, this patient had a number of significant comorbidities, one of which ultimately ended her life. From all available evidence, her cancer had not recurred and she continued to have a durable benefit of surgery at the time of her death. By intervening and treating her colon cancer, we were able to allow her to enjoy nearly another 3 years with an excellent quality of life that she would not have had otherwise.

Case Study #2

An 86-year-old woman presented to the emergency department with abdominal pain, constipation, and distension. Her radiographic imaging suggested a mass in the rectosigmoid colon and she underwent a flexible sigmoidoscopy that showed and obstructing mass at 30 cm. A biopsy was taken that demonstrated poorly differentiated adenocarcinoma. She also underwent a stent placement to relieve the obstruction. She lived with her husband, and her regular activities including caring for him, as he suffered from dementia, and caring for their home. She had several adult children and grandchildren who lived nearby and helped her and her husband. Her comorbidities were limited to hypertension and diabetes, controlled on oral medications. After completing a slow bowel prep over several days, she underwent a completion colonoscopy which demonstrated only the known mass at 30 cm.

Subsequently, she underwent a hand-assisted laparoscopic sigmoid resection. On abdominal exploration, a small area of peritoneal metastases was noted at the left side of the anterior peritoneal reflection near her primary tumor in the rectosigmoid colon. She underwent a sigmoid resection with mobilization of the splenic flexure, followed by a pelvic peritonectomy. Her recovery was unremarkable and she was discharged home on postoperative day number four in the care of her family with home physical therapy. Her pathologic report documented a moderately differentiated adenocarcinoma with mucinous features, pT3 N2a, M1b, with 5 of 28 lymph nodes positive for adenocarcinoma along with peritoneal metastases, negative colonic margins, and evidence of lymphovascular and perineural invasion. She was evaluated by her medical oncologist, who repeated her cross-sectional imaging after surgery. She was noted to have evidence of pelvic peritoneal recurrence at 2 months after surgery in the location of the previous peritonectomy. Therefore, she was treated with oral capecitabine and bevacizumab for 6 months. Repeat imaging has shown stability of her pelvic disease and she has continued to do well in the 16 months since her surgery.

This case highlights several other considerations when caring for geriatric patients. In the emergency setting, several options are available to manage large bowel obstruction, including proximal diversion and gastrointestinal stenting. The authors' practice is to use stents primarily as a bridge to surgery, as illustrated in this case, or in situations where they can be used for palliative symptom relief. The stent, in this case, allowed for preparation of her colon for a full colonoscopy as well as a colon resection. Perhaps the greatest benefit, especially for elderly patients, is the ability to turn an emergent operation into an elective operation. In addition, avoidance of a colostomy is primary goal of therapy, as a stoma can be very difficult for a geriatric patient to manage, especially if there are dexterity issues. A stoma can mean a loss of the ability to live independently. Stent placement in the upper rectum and sigmoid colon is overall well tolerated but does entail risks of perforation, recurrent obstruction, and migration.

This case study demonstrates the use of chemotherapeutic agents that have been shown to be well tolerated in the geriatric population, such as capecitabine and bevacizumab. For this patient, this regimen was chosen to avoid the toxicities associated with oxaliplatin and irinotecan use, which can be debilitating in the geriatric population. Additionally, while this patient could potentially be a candidate for intraperitoneal chemotherapy and cytoreduction, the morbidity of such an operation is much higher than elective resections, which is not congruent with her goals of care given her current excellent quality of life and lack of symptoms. Balancing toxicities, morbidities, and disease symptoms is paramount in approaching the care of elderly cancer patients, and thorough discussion with patients and their family members should be encouraged to allow for shared decision making and identification of a treatment plan with which all are comfortable.

Epidemiology

Incidence in Geriatric Patients

Colorectal cancer is the fourth most common cancer and the second leading cause of cancer-related mortality in the USA, behind lung cancer [6]. In 2017, an estimated 135,000 new cases of colorectal cancer were diagnosed with over 70% occurring in patients over the age of 65 and more than 10% occurring in patients over age 80 [4, 7]. Age is a well-known and established risk factor for colorectal cancer with the vast majority of cases occurring in patients over the age of 50. The incidence of colorectal cancer continues to increase each decade thereafter without any indication of downtrends or plateaus [8].

While colorectal cancer rates in patients over age 50 are generally decreasing, most likely due to increased utilization of screening tests, the growing population of elderly patients as a whole ensures no shortage of patients with colorectal cancer [7]. In Italy, there was an increase in patients over age 74 having treatment for colorectal cancer during a three-decade span and the number of patients over 80 years old who had treatment doubled [9]. It is encouraging to note that during that time, more elderly patients were being offered resection without changes in palliative or emergency surgeries [9]. This suggests physicians were offering standard of care surgery to more elderly patients than ever before, though they still are behind the curve compared to younger patients.

While elderly patients can have heritable colorectal cancer syndromes, the likelihood of this is small. Familial Adenomatous Polyposis typically presents in the first three decades of life and the average age of presentation of Lynch syndrome, also known as Hereditary Non-polyposis Colorectal Cancer (HNPCC), is under 50 years old. What is important to know is that patients with Lynch Syndrome have five to seven times the risk of metachronous tumors [10]. Thus, elderly patients with a personal history of colorectal cancer and appropriate previous treatment, perhaps before genetic evaluations were routine or well understood, could be presenting with a metachronous cancer that may be associated with a heritable condition. The other main relevance for elderly patients is to inform younger family members of their diagnosis as changes in screening recommendations may be appropriate for those younger family members.

Inflammatory bowel disease (IBD) is another well-known risk factor for colorectal cancer development. Traditionally, duration of inflammation and the extent of inflammatory disease are both predictors of cancer risk [11]. However, IBD is increasingly more often diagnosed in older patients and may be associated with an earlier development of colitis-associated colorectal cancer [12]. Elderly patients with a previous history of colitis should be assessed and followed closely, even if the colitis is quiescent.

Survival in Geriatric Patients

Despite significant advances in the treatment of colorectal cancer in the last few decades, including surgical techniques and systemic medical therapies, it is unclear if older adults are reaping the same benefit as younger patients. While some studies report that long-term survival of very old patients is comparable to that of younger patients, other studies demonstrate that survival in older adults after colorectal cancer is decreased [13–15]. The reason for these discrepancies is unclear, though likely multifactorial. Aside from tumor related features, elderly patients less often undergo screening procedures, and when cancer is found, less frequently have surgery [13, 16]. Regarding adjuvant treatment after surgery, older adults are less likely to be referred to medical oncology, are less likely to receive chemotherapy, or be given the standard of care regimen, and their treatment is likely to be discontinued early compared to younger adults [4, 16, 17].

Competing causes of mortality may be another cause for discrepancies in survival; elderly patients are more likely to have significant comorbidities that are risk factors for poor outcomes after surgery [17, 18]. In a systematic review of surgery for colorectal cancer in elderly patients, the primary finding was that overall survival was reduced for elderly patients; however, for cancer specific survival, age-related differences were much less striking, suggesting that the difference in overall survival between elderly and younger patients cannot be explained in terms of cancer deaths alone and the impact of other noncancer causes of mortality is significant [19]. In one Japanese study evaluating age and comorbidities on colorectal cancer survival, the authors found that diseases other than colorectal cancer influence overall survival more for patients over age 75 who had curative surgery [17]. This was again shown in a Dutch study of colorectal cancer patients that demonstrated conditional relative survival, which reduces the impact of age-related differences in survival, was similar in all age groups and that postoperative complications were a more probable cause of mortality [15]. When 90-day mortality was excluded, long-term disease-free survival up to 10 years after colorectal cancer treatment was unchanged in a cohort of elderly German patients, yet they continued to show decreased overall survival [14]. Interestingly, when considering disease-specific survival or recurrence rates, the authors found no relationship to age, suggesting that the increased mortality of geriatric patients is related to concerns other than their colorectal cancer [14].

These studies suggest that for elderly patients, the first year after colorectal cancer surgery and treatment may be the most critical as the stress of surgery and impact from competing comorbidities is significant. Essentially, the patients have the lowest physiologic reserves and are at their most vulnerable during this time. In a study utilizing the California Cancer Registry, patients 80 years or older had high in-hospital mortality, twice the readmission rate of younger cohorts, and high one-year mortality; medical complications, increasing co-morbidities, and cancer stage were predictive of increased mortality [20]. In a study evaluating readmissions after colectomy for colon cancer using the Surveillance, Epidemiology, and End Results (SEER)-Medicare database, age was not found to be predictive of 30-day readmissions but was significantly predictive of one-year mortality (OR 2.70, 95%CI 2.36–3.08) [21]. Dekker et al. (2011) also noted that those factors that predicted 30-mortality, such as comorbidities, emergent surgery, and prolonged hospitalizations, also predicted an increased 1-year mortality [15]. Postoperative pneumonia and cardiovascular complications have been highly associated with increases in postoperative morbidity and mortality in elderly patients [18].

These confounding issues cloud the consideration of long-term outcomes and survival in elderly patients as it becomes incredibly difficult to tease out and isolate any single key contributing factor. These studies suggest that the delayed consequences of surgery continue beyond the time of discharge and significantly affect morbidity and mortality, especially in vulnerable elderly patients. One way to improve outcomes for elderly patients is to identify problems and comorbidities and intervene early to allow the opportunity to control some of these confounding variables and improve overall survival. The data do seem to indicate that when appropriately treated, and when comorbidities are managed and complications are avoided, elderly patients obtain similar oncologic benefit from treatment and experience similar cancer-related outcomes. This suggests that there should be no age cut-off for appropriate treatments and consideration should be given to a more global assessment of these complicated patients.

Screening in Elderly Patients

Screening for colorectal cancer has clearly been demonstrated to have efficacy in reducing the incidence of colorectal cancer as well as cancer-related mortality. There has been controversy, however, related to which screening and surveillance methods are optimal, how frequently the tests should be done, who should undergo testing, and the cost-effectiveness of the various strategies. Thusly, a number of acceptable options are available each with their own benefits and drawbacks. The recommendations of available screening tests and intervals are summarized in Table 1. Fecal Occult Blood Test (FOBT) has been used for decades and has several advantages including cost-effectiveness, ease of administration, and lack of any invasive component. However, blood in the stool can be from any number of alternative causes; it is rather nonspecific for cancer. The positive predictive value of FOBT has been reported to increase with age from 1.6% for those under 60 years of age to 3.6% for those over 70 years of age [22]. Stool DNA screening tests that detect cellular genetic changes associated with colorectal cancer have been recently introduced. These have shown variation in specificity with regard to patient age; for patients younger than 65 years, specificity was 94.0%, compared to 87.1% for those older than 65 [23]. Regardless of age, any positive stool test needs to be followed

Table 1 Summary of colorectal cancer screening recommendations for each major society [24, 122–124]

Screening Test	Interval	US Preventative Services Task Force (2016)	National Comprehensive Cancer Network (2015)	Multi-Society Task Force[a] (2008)	American College of Gastroenterology (2009)
Sensitive guaiac Fecal Occult Blood Test (FOBT)	Every 1 years	Recommended	Recommended	Recommended	Recommended
Fecal Immunogenicity Test (FIT)	Every 1 or 3 years	Recommended	Recommended	Recommended annually	Recommended annually
Stool DNA test	Unknown; Every 1–3 years	Recommended	Recommended	Recommended, interval unknown	Recommended every 3 years
Flexible Sigmoidoscopy	Every 5 years	Recommended	Recommended with or without stool based testing every 5–10 years	Recommended	Recommended
Flexible Sigmoidoscopy plus FIT	Every 10 years with FIT or FOBT every 1 years	Recommended	Recommended with FIT or stool DNA at year 3; repeat 5–10 years	Not recommended	Not recommended
Colonoscopy	Every 10 years	Recommended	Recommended	Recommended	Recommended
CT colonoscopy	Every 5 years	Recommended	Recommended	Recommended	Recommended
Circulating methylated *SEPT9* DNA	Unknown	Not specified	Unavailable for guideline	Unavailable for guideline	Unavailable for guideline

[a]The Multi-Society Task Force included the American Gastroenterological Association, the American Society for Gastrointestinal Endoscopy, the American College of Gastroenterology, the American Cancer society, and the American College of Radiology

with a colonoscopy for localization and biopsy to be sure of the diagnosis [24].

In 2008, the US Preventative Services Task Force first issued age cutoffs for colorectal cancer screening, stating those between 50 and 75 years of age should undergo screening, while the decision to screen adults age 76–85 should be tailored to the individual patient [24]. The USPSTF recommends against screening adults older than 85 years [24]. Elderly patients are more likely to have complications from screening procedures, such as perforation, that can significantly impact the positive benefit of the procedure, especially in the setting of competing comorbidities and limited life expectancies. Approaching screening in elderly patients, or even in those with significant comorbidities, is a matter of balancing risk and benefit and including the patient in the decision-making process.

Clinical Presentation and General Treatment Considerations in Elderly Patients

Often, patients present after having a positive screening test and a colonoscopy that demonstrated a mass, and a biopsy of this confirms the diagnosis. As with any surgical evaluation, a complete history and physical should be performed, with specific attention to obstructive symptoms and subtle signs of anemia [5]. Additional symptoms of colorectal cancer are detailed in Table 2. Global symptoms such as weight loss, anorexia, and pain are often suggestive of advanced disease. Basic evaluation for colorectal cancer patients includes a baseline serum carcinoembryonic antigen (CEA) level, which can be used for prognosis and during the surveillance period to detect recurrence [25]. Preoperative staging should include a computed tomography scan of the chest abdomen and pelvis with intravenous contrast to evaluate for any distant metastases [5, 26]. For rectal cancer, local staging of the pelvis should be performed with a pelvic MRI or endorectal ultrasound [3]. Currently, the 7th Edition of the American Joint Commission on Cancer (AJCC) Cancer Staging Manual is the accepted standard for staging tumors [26]. The 8th edition, which contains additional information on the molecular staging of tumors, is expected to be released in early 2018 [27].

Table 2 Symptoms associated with colorectal cancer. (Adapted from the following: Oliver et al. [125], Hyman [126])

Global symptoms	Right-sided cancers	Left-sided cancers	Rectal cancer
Weight loss	Occult blood mixed in stool	Change in bowel habits, obstruction	Fresh blood
Anorexia	Anemia	Red blood in stool	Mucus discharge
Streptococcus bovis infection			Perineal pain, tenesmus
			Palpable mass

Most patients with colorectal cancer present with nonmetastatic disease (Stage I-III) where surgery is the cornerstone of treatment. Elective surgery for colorectal cancer entails removal of at least a 5 cm margin of bowel proximal and distal to the tumor, removal of any nonviable or compromised bowel, and *en bloc* complete removal of the draining lymph nodes that are located along the vascular supply. Therefore, the location of the tumor (i.e., right, left, rectum) dictates the type of operation needed (i.e., right hemicolectomy, left hemicolectomy, proctectomy) and the vascular supply that is divided as seen Fig. 1. A minimum of 12 lymph nodes has been established as the minimum required to have adequate sensitivity and specificity for determining the pathologic nodal stage of the tumor [5].

Emergency Surgery

Occasionally, patients present more urgently, often with obstructive symptoms due to the tumor decreasing the luminal diameter of the bowel. When this occurs, it is an emergency and can be managed in several ways depending on the location and the extent of the disease. If the tumor

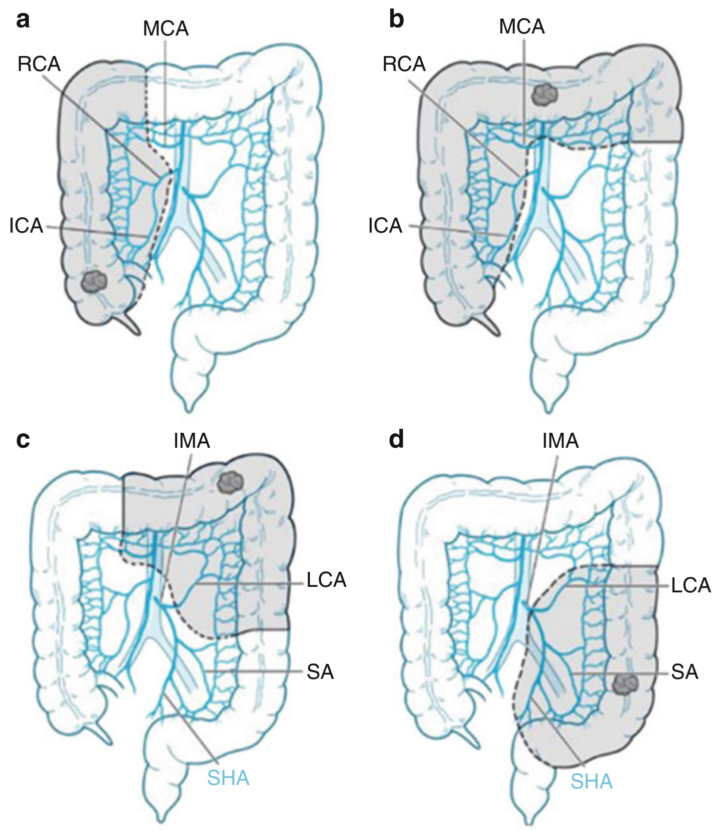

Fig. 1 Schematic drawing of various segmental colon resections, demonstrating the vascular pedicle and mesocolic excision that is performed *en bloc* with colectomy. (**a**) Right hemicolectomy with ligation of Ileocolic Artery (ICA) at its origin and Right Colic Artery (RCA), if present. (**b**) Extended right or transverse colectomy with ligation of ICA, RCA and Middle Colic Artery (MCA). (**c**) Left hemicolectomy with Left Colic Artery (LCA) ligation at its origin off the trunk of the Inferior Mesenteric Artery (IMA). (**d**) Sigmoid colectomy with high ligation of the IMA at its origin off the Aorta. (From Rosenberg and Morris [127])

is in the abdomen without extensive extra-intestinal involvement, then primary resection is indicated to both relieve the obstruction and obtain a diagnosis and staging [5]. If the tumor is in the pelvis or there is significant extra-intestinal involvement or the patient is especially ill, consideration should be given to a proximal diverting ostomy to relieve the obstruction and allow medical optimization prior to any additional treatment. In patients presenting with perforation, either at the tumor site or distant, they should be treated immediately with resection of the perforated area and tumor, if possible, as this is a life-threatening situation [5]. Bleeding from the tumor is another emergency that can occur, though is less common. After appropriate resuscitation, reversal of coagulopathies, and localization of the site of bleeding, surgery is indicated if ongoing control of the bleeding is not obtained. Surgical resection of the primary tumor for either perforation or bleeding should proceed along the same oncologic principles as for elective resection [5]. If the patient is hemodynamically unstable or the tumor cannot be localized, a subtotal colectomy should be considered according to standard oncologic principles described above.

Elderly patients have been noted to present with more advanced disease than their younger cohort, are more likely to have significant co-morbidities, and are more likely to have emergency surgery than their younger cohorts [19, 20, 28]. In a study of colorectal cancer patients over age 80, over 10% required an emergency operation, compared to 5% in those who are younger [18]. Unfortunately, the complication rate of those elderly patients was also elevated at 50% compared to 34% for younger patients [18]. Early mortality in geriatric patients having emergency surgery is also elevated, 36% for those over 80 years in another Germany retrospective review compared to 16% for those under age 80 ($p = 0.03$) [14]. Emergency surgery has also been associated with more advanced tumor stage, another factor that can impact long-term survival [14].

The high rate of emergency surgery among geriatric patients correlates with comorbidities and poor outcomes and is another factor that raises the postoperative mortality rate and lowers the overall survival for these patients [29]. It remains to be seen if more aggressive screening measures in appropriately fit elderly patients might have an impact on reducing the morbidity related to emergency surgery in the oldest of the old. Future studies should be aimed to examine questions such as these.

Metastatic Colorectal Cancer

Elderly patients are just as likely as their younger cohorts to present with metastatic disease, which is found in a fifth of patients at the time of diagnosis. There are many options available for treatment, but the most commonly seen scenario involves colorectal liver metastases. In general, for those patients who are candidates for surgical resection, there is a small survival benefit and chance at durable cure [30]. Encouragingly, there appears to be similar rates of resection for appropriately selected patients. In a German retrospective review, there was no difference between elderly and younger patients in the rates of synchronous resections for the primary tumor and distant metastases (20% vs. 22%, respectively) and no difference in the number of palliative procedures performed in the two age groups either [14]. In a retrospective review of 13 years of experience with surgical treatment of colorectal liver metastases, there was noted to be no difference in postoperative complications between those over age 75 (10% of patients) and those under age 75, though increased preoperative comorbidities were associated with increased complications [31]. It must be noted that these are highly selected patients who had excellent functional status and were good surgical candidates, so limited conclusions should be drawn about the generalizability of these results to the geriatric population as a whole. However, it does appear that for metastasectomy and synchronous primary resection, elderly patients can have good outcomes with surgery, even for metastatic disease.

When patients are not good surgical candidates or their disease is oligometastatic, there are other options available for patients that are significantly less invasive including percutaneous ablative techniques or embolization techniques that can be performed for liver metastases and provide considerable survival benefits for patients. In a randomized trial comparing radiofrequency ablation (RFA) plus systemic chemotherapy to systemic treatment alone, median survival times were comparable between the two groups, but progression-free survival was longer in the RFA plus chemotherapy arm [32]. However, local recurrence after RFA was found to be comparable to surgical resection in two European randomized trials [33]. It is unknown how such treatments are tolerated by elderly patients, though the lower complication rate supports that this may be a useful technique to consider in elderly patients when quality of life would be significantly impaired with surgical treatments [4].

Palliative chemotherapy can give a significant survival benefit, with current optimal therapy resulting in the 1-year relative survival rates more than 50% and median survival nearing 2 years with optimal treatment [7, 30]. The first-line treatment is a combination regimen including 5-flourouricil, leucovorin, and oxaliplatin, known as FOLFOX. Yet little research is available to understand the benefit and tolerability in elderly patients with limited reserves and comorbidities. In a Korean study of well-functioning patients over age 80 with either metastatic colorectal or gastric cancer, dose reductions or delays in FOLFOX regimens were necessary in 7 of 28 patients (25%) due to treatment-related toxicities, primarily hematologic complications [34]. In 50% of the colorectal cancer patients, a partial response was noted and median progression-free survival was 7.3 months (95%CI 0.9–13.7 months) with 1-year survival rates of 43% [34]. Capecitabine, an oral 5-FU prodrug, has similar survival benefit to 5-FU with leucovorin and has been proposed to be preferred and better tolerated than infusional 5-FU [35–37]. The FOCUS2 study evaluated patients who were not candidates for full-dose FOLFOX chemotherapy who then received either 5-FU with leucovorin or capecitabine alone or in combination with a reduced dose of oxaliplatin [38]. Toxicity was greater in the capecitabine arm and survival outcomes were not different for those who received oxaliplatin [38]. Taken together, both studies suggest that when elderly patients are appropriate for oxaliplatin, its use may have benefit, but lower doses for less fit patients may not offer any advantage. Another alternative is 5-FU with leucovorin and irinotecan, known as FOLFIRI, a regimen that is often used for those younger who cannot tolerate oxaliplatin. In patients over age 75 with metastatic disease, FOLFIRI was found to have an increased rate of severe toxicities compared to 5-FU with leucovorin alone, without any improvements in progression-free survival [39].

There are other alternatives that have shown improvements in the tolerability of systemic chemotherapy, including intermittent dosing of oxaliplatin and an infusion rather than bolus administration of 5-FU [4]. Furthermore, targeted agents such as antibodies against the vascular endothelial growth factor (VEGF) receptor and epidermal growth factor receptor (EGFR) antibodies can be reasonably tolerated in older adults. Bevacizumab, a VEGF monoclonal antibody, does have an increased rate of arterial thrombotic events in elderly patients, limiting its use in those over age 75 [4, 40]. Cetuximab and panitumumab are EGFR agents that are well tolerated in older adults without increases in side effects and they offer a survival benefit even when given as monotherapy [4]. Therefore, these are both ideal choices for elderly frail patients with metastatic disease who are candidates.

Concerns for Elective Colorectal Cancer Treatment in Geriatric Patients

For patients presenting with nonmetastatic disease, the primary treatment for colon cancer is surgical, with resection of the involved segment of colon and the corresponding mesentery that contains the draining lymph nodes, regardless of age at the time of presentation [2, 41]. For rectal cancer, standard therapy incudes neoadjuvant chemoradiation for improved local control of the disease, followed by surgical resection following the principles of total mesorectal excision [3, 42]. A flow chart of the treatment algorithms is presented in Fig. 2. We will focus the remainder of this chapter on the discussion of topics that are specific and highly relevant for physicians caring

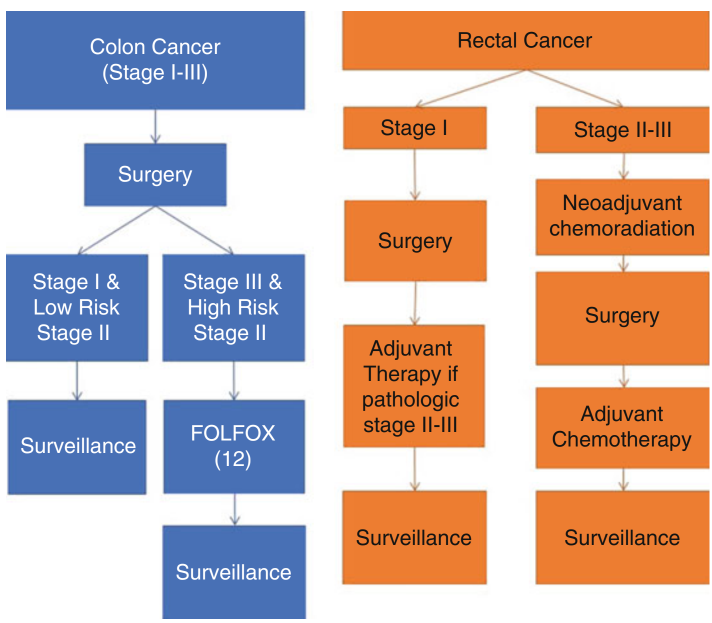

Fig. 2 Schematic diagram of the standard treatment sequencing for colon compared to rectal cancers

for geriatric patients with colorectal cancer, including surgical risk assessment, surgical techniques, and postoperative care. Furthermore, the remainder of the discussion will focus on those patients having elective surgery for colorectal cancer.

Geriatric Surgical Risk Assessment

As patients age, there is a correlational decrease in physiologic and functional reserves that can be markedly pronounced in geriatric patients. These changes leave patients vulnerable when new stressors, such as cancer and surgery, are undertaken. Close consideration of each patient's physiologic standing and comorbidities prior to surgery can allow physicians to intervene with treatment in advance. This might significantly improve outcomes and the trick is learning to identify these patients.

"Frailty" has been proposed as a key feature in some elderly patients that is a risk factor for poor outcomes after surgery [43]. There are several metrics designed to identify frail patients, including the frail phenotype Fried-criteria and the frailty index [44–46]. Regardless of the tool, frailty has been associated with a risk at least three to four times higher for severe complications after surgery [43]. Furthermore, frail patients have lower survival after treatment for colorectal cancer, with five-year survival of 25% for frail patients compared to 66% or normal nonfrail elderly patients [47].

Frailty screening tools use criteria such as weight loss, walking speed, and self-reported exhaustion along with assessment of impairments, such as diseases and disabilities, when evaluating patients. These tools are widely used in research, but little used clinically, given the added time and resources needed to execute them properly (see Table 3). Additionally, these metrics do not identify specific disease processes that would allow interventions to occur before surgery; they are useful for screening and prognosis only. A two-stage approach includes using these metrics to identify frail patients, who then undergo further assessments using the Comprehensive Geriatric Assessment, a multidisciplinary assessment of an individual's functional status, physical performance, comorbidity, medications, cognitive and emotional functioning, nutrition, and social support network [48]. The CGA aims to identify specific issues that may be treated prior to surgery and has been recommended by the International Society of Geriatric Oncology (SIOG) [49]. The National Comprehensive Cancer Network has also issued guidelines on caring for older adults with cancer and has outlined a number of aspects consistent with a comprehensive assessment [50]. Interestingly, in a recently published randomized Norwegian study, such a strategy did not result in improved postoperative complications despite employing rigorous screening and assessments, possibly due to low recruitment goals and an inconsistent application of prehabilitation therapies [51]. Additional studies are in recruitment to understand how such a comprehensive evaluation can identify needs and specific programs to prepare elderly patients prior to surgery [48].

A thorough history and physical exam, performed by any physician, can go a long way to meeting many of the goals of a standard focused geriatric assessment. Such an examination can identify subtle signs and symptoms of diseases, such as cardiac disease and pulmonary

Table 3 Frailty screening tests [44–46]. (ADL = activities of daily living; MI = myocardial infarction; CHF = congestive heart failure; CVA = cerebral vascular accident; DM = diabetes mellitus)

Frailty Phenotype Metrics	Frailty Index Metrics
Grip strength	Help with ADLs (bathing, dressing, eating, grooming, toileting, stairs, shopping, housework, cooking, finances, medications)
Walking time	Weight loss
Weight loss	Self-rating health; change in last year
Physical activity	Activities (walking outside, lifting >10 pounds, perceived effort, grip strength, walking pace)
Exhaustion	Emotional state (depression, happiness, loneliness)
	Comorbidities (MI, CHF, CVA, cancer, DM, hypertension, arthritis, lung disease, obesity)

insufficiency that can be optimized prior to surgery. Particular attention should be paid to examining the heart and cardiac function, including evaluation for signs and symptoms of congestive heart failure, as this is a leading predictor of mortality and nearly 85% of patients over age 80 have some type of cardiac risk factor [18]. For those rare patients who are not taking beta-blockers already and are found to have some evidence of cardiac ischemia, administration of beta-blockers for 1–2 weeks prior to surgery should be considered as this is associated with reductions in cardiac perioperative mortality [52]. Consideration should be given to functional cardiac assessments, including dobutamine stress echocardiography, for those patients with cardiac risk factors or symptoms. The management of cardiac ischemia in the perioperative setting is a topic of significant controversy with much variability in recommendations for types of cardiac stenting used as well as duration and type of antiplatelet therapy. Close collaboration with your interventional cardiologists can help significantly in coordinating the most prudent treatment options for these complex patients to avoid not only an excessive bleeding risk during colorectal surgery but an increased risk of cardiac events in the perioperative period. As of yet, there are limited consensus guidelines as to perioperative management to help guide clinicians [53].

Pulmonary assessment is also of paramount importance in this patient population. After abdominal surgery, there is an expected 15–30% reduction in functional residual capacity [54]. Older patients are more than twice as likely as younger patients to have respiratory complications in the postoperative period [19]. This can have considerable consequences for patients who already have reduced pulmonary function due to comorbidities. Identifying obstructive disease in the preoperative setting allows administration of bronchodilators, mucolytic agents, and possibly antibiotics for acute exacerbations. Furthermore, pulmonary rehabilitation programs can offer considerable benefits in mortality and morbidity reduction [55].

Identifying patients with malnutrition can also be critically important in preoperative risk assessment. Over 5% of patients age 70–80 years old are undernourished, and this may be even higher for patients with an underlying malignancy due to cancer-related cachexia worsening aging-related sarcopenia and anorexia [18, 56]. Malnutrition is a known prognostic indicator for poor outcomes, including anastomotic leak and perioperative mortality [56–58]. Clinical markers of malnutrition can be somewhat misleading. Body Mass Index (BMI) is a well-established metric in the general population, yet is less accurate in elderly patients due to age-related sarcopenia; serum albumin and prealbumin levels are other often used clinical metrics for identifying those at risk. Objective measures, such as the Malnutrition Universal Screening Tool (MUST) or Patient-Generated Subjective Global Assessment (PG-SGA), have more sensitivity and specificity for identifying patients with cancer who are at risk for malnutrition [56, 59]. These objective tests can be difficult to administer and are often timely, limiting their use in clinical practice.

Managing patients clinically who present with significant malnutrition can be difficult clinically as well, even when there is little question of the extent of the nutritional deficit. For those patients with significant malnutrition or critically ill patients, parenteral nutrition before surgery may be beneficial in reducing complications after surgery, yet the optimal duration and type (i.e., immunomodulating diets) of nutritional optimization is unclear [60–62]. Unfortunately, patients with such severe malnutrition are seldom in a situation where surgical care can be significantly delayed and often require emergency procedures that do not allow time for nutritional optimization. However, if delaying surgery is possible in severely malnourished patients, administration of parenteral nutrition for at least 7 days has been shown to reduce postoperative complications [60, 62].

Enhanced Recovery Pathways

Fast-track programs, otherwise known as enhanced recovery after surgery (ERAS), have become an idea that is very much in vogue and can be beneficial to elderly patients. Enhanced recovery programs originated in Denmark and

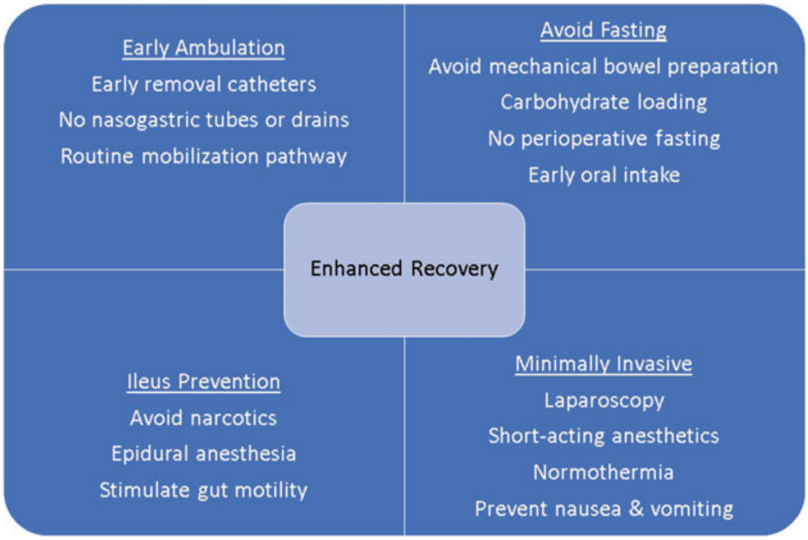

Fig. 3 Diagram outlining possible elements that can be included into an enhanced recovery after surgery (ERAS) pathway

are designed to minimize the stress response of surgery and promote the rapid return of function for the patient [63, 64]. Often, these programs contain many specific strategies, but no two programs are the same as each is tailored to the specific patient population at that institution. Common strategies include avoidance of bowel preparation and minimal fasting, ileus prevention, preference for minimally invasive procedures, early mobilization, and early oral intake after surgery (see Fig. 3) [65]. Such pathways have been shown to reduce complications and the length of hospital stays, without increasing readmissions or mortality after colorectal surgery [66, 67].

For elderly patients, similar benefits may be achieved, though it is not completely understood how well elderly patients with limited mobility might participate in such programs. One study found that only 55% of patients over age 80 were out of bed the day after surgery, compared to 70% for younger patients [68]. Participation in enhanced recovery is important and benefits are noted when patients adhere to at least 70% of the programs elements, with increasing benefits for increasing participation; for those patients who are the highest participators (>90% adherence to protocol), a 25% reduction in morbidity and 50% reduction in mortality was noted [69]. Geriatric patients could stand to gain considerably from these benefits if participation can be encouraged and supported with adequate resources.

Two randomized control studies specifically evaluated ERAS pathways in elderly patients and demonstrated that they did indeed gain benefit from these strategies [70, 71]. Included only patients with colorectal cancer having open surgery who were older than age 70; those following the ERAS protocol received a thoracic epidural with no narcotics, oral liquid diet starting 6 h after surgery, catheter removal by postoperative day 2, normal meals and a carbohydrate drink prior to surgery [71]. Those patients in the ERAS group had faster return of bowel function by 3 days (78 h vs. 49 h, $p < 0.01$), shorter hospital stays by 4 days (9 vs. 13, $p < 0.01$), and 54% fewer complications than the traditional group, significantly in pulmonary and urinary infections as well as heart failure [71]. Furthermore, the ERAS group had significantly fewer episodes of delirium in the postoperative setting (3% vs. 13%, $p < 0.01$), which was associated with a lower level of serum IL-6, a proinflammatory cytokine suspected in the development of postoperative delirium [71, 72]. Wang and colleagues (2012) specifically evaluated patients older than age 65 having laparoscopic surgery for colorectal cancer randomized to either ERAS pathways or traditional care and found similar results with shorter hospital stays by 1 day (6 vs. 7, $p < 0.01$) and fewer complications (5% vs. 21%, $p < 0.01$) [70].

Additional cohort studies have reported mixed results on the rate of overall morbidity and mortality in elderly patients participating in ERAS protocols, though none reported differences in pulmonary complications, suggesting that the risk of aspiration due to early oral intake may be limited [73]. Unfortunately, many of the reports evaluating the utility of ERAS pathways in elderly patients are of only moderate quality, including the randomized studies discussed above, and fail to report on compliance to ERAS elements or confounding comorbidities and frailty that could significantly impact outcomes, especially in elderly patients [73].

Avoidance of narcotics is a central tenant of enhanced recovery pathways. Epidural anesthesia in elderly patients who require a laparotomy can be particularly beneficial as it can minimize or avoid entirely the need for narcotic medications in the postoperative period, which can reduce the risk of respiratory depression and delirium in vulnerable patients. In a randomized controlled trial of patients over age 70 years having major abdominal surgery, those who received a patient-controlled epidural after surgery, rather than patient-controlled intravenous analgesic, had better pain control, improved bowel recovery, and improved mental status during the postoperative period [74]. This is in congruence with many studies from patients of all ages on the benefits of thoracic epidural in the postoperative setting after abdominal surgery summarized in a Cochrane Review, demonstrating that the use of local anesthetic in a thoracic epidural with or without opioids is associated with improvements in bowel recovery, reduced pain scores, and reduced lengths of stay for open surgery [75]. Not only is pain control improved, but respiratory function is not depressed with epidural anesthesia as it often is with narcotic pain medications. Other strategies, such as nonsteroidal anti-inflammatory medications, are another option to minimizing narcotic use; however, the side effects and possible toxicities may limit their use in a population of patients with significant comorbidities.

Use of a mechanical bowel preparation on prolonged fasting prior to colorectal surgery remains an area of ongoing debate without a clear answer. ERAS protocols support the avoidance of mechanical bowel preparations to avoid significant dehydration prior to surgery, and the American Society of Gastroenterology also recommends against the use of magnesium citrate or combination agents for elderly patients and those with renal failure due to risks of dehydration [76]. Concerns of operating on unprepped bowel include spillage and difficulty manipulating the heavy bowel, especially during laparoscopy as well as an inability to perform intraoperative colonoscopy if needed. Mechanical bowel preparation in elderly patients necessitates increased intraoperative fluid requirements that have been independently associated with postoperative complications – for each liter of fluid given, there was a 32% increase in the probability of postoperative complications in one prospective study [69]. Specific studies evaluating the efficacy of mechanical bowel preparation in elderly patients have yet to be conducted, but prudent use of aggressive mechanical bowel regimens is warranted in this vulnerable patient population.

Furthermore, use of a preoperative carbohydrate drink prior to surgery was found to be protective and associated with reductions in postoperative symptoms of 44% – particularly risk of nausea, vomiting, pain, diarrhea, and dizziness [69]. Ultimately, the lack of these inciting symptoms leads to reductions in the rate of wound dehiscence when carbohydrate drinks were given (OR 0.16, 95%CI 0.05–0.50) [69]. While this study is not randomized, there is some significance suggesting that consideration be given to close monitoring and compliance to protocols for these factors. Balancing the risks of a mechanical bowel preparation and carbohydrate loading in this population with the benefits and needs is key to balancing these patients' postoperative complications.

While some have advocated for an Intensive Care Unit (ICU) stay in the immediate postoperative setting for all elderly patients, there are little data regarding this practice. The most frequent complication in the immediate postoperative period is cardiac with 96% of perioperative infarcts detected on electrocardiogram in the first 2 days after surgery, and it is thought that a short, but not too long, stay in the ICU could help detect and treat these complications when they arise [18]. On the contrary, ICU stays, especially for geriatric patients, are associated with reduced mobility and increased delirium and may lead to longer overall hospital stays [77–79]. It has not been our practice to routinely admit geriatric patients to the ICU following elective surgery without a clear indication (i.e., inability to extubate, vasopressor requirement). We would advocate using remote telemetry monitoring for those with cardiac risk factors in an intermediate-care unit or regular hospital ward where patients will be encouraged to participate in ERAS elements.

Minimally Invasive Surgery

The benefits of minimally invasive surgery are extensive and well accepted. Patients are expected to have less pain, shorter hospital stays, quicker recoveries, and fewer complications when colectomy and proctectomy are performed laparoscopically [80]. For colectomy, many studies have demonstrated that the oncologic benefit is the same as open surgery in regards to completeness of resection and lymph node harvest [81–83]. The data on laparoscopic proctectomy for rectal cancer are less clear, and initial studies demonstrated concerns for appropriate circumferential margins, though this did not translate into differences in local recurrence or survival [82]. Robotic surgery, which facilitates surgery in the pelvis and generally has a lower learning curve than laparoscopic proctectomy, has gained considerable enthusiasm in recent years. There is currently a randomized trial exploring the outcomes of laparoscopic and robotic surgery to better understand the differences between the two techniques and the final results have yet to be published [84].

Despite these benefits in outcomes and improvements in recovery, minimally invasive surgery remains underutilized in colorectal resections, with only 29% of colectomies done laparoscopically in 2009 [80]. Not only are elderly patients not offered surgical resection as often as younger patients, they are less likely to have minimally invasive surgery performed when surgery is done [80, 85]. There can be several reasons that surgeons may be reluctant to offer minimally invasive surgery to elderly patients, including longer operative times, risks of pneumoperitoneum in the setting of severe pulmonary and cardiac comorbidities, advanced or bulky disease, and an emergency setting [86]. Despite these, many observational studies have explored the benefit of minimally invasive surgery in the geriatric patient population and reported that for elective surgeries, the risks are acceptable.

In a single-institution study from Italy, patients older than 75 were matched to a younger cohort of patients having elective, nonpalliative surgery for colorectal cancer [87]. There were no differences in rates of conversion to open surgery, use of diverting ileostomies, lymph nodes removed, or operative times between the two groups [87]. The elderly patients had a higher postoperative morbidity rate, 24% compared to 8% in the younger cohort; however, the rates of anastomotic leak were similar in the two groups (2% each) [87]. The elderly patients did have more medical comorbidities (i.e., atrial fibrillation and renal failure) as well as wound infections (6% vs. 2%), likely reflecting underlying poor nutrition and other competing comorbidities that affect outcomes [87]. Noteworthy is that there were no differences in mortality in the study [87]. Again, these results point to comorbidity management as key to having good outcomes in this complex patient population.

Robotic-assisted surgery can have similar benefits for elderly patients, though may be less attractive as the operative time is generally longer than laparoscopic surgery and often patients are positioned in steep Trendelenburg, especially for pelvic surgeries. In a retrospective analysis of patients undergoing elective colectomy using propensity score matching in the National Inpatient Sample (NIS), Juo and colleagues (2014) demonstrated that robotic colectomies were not associated with any additional in-hospital complication rates, mortalities, conversions to open procedures, or decreased routine discharge rates when compared to patients having laparoscopic colectomy [86]. Robotic colectomy did incur a higher overall hospitalization cost than laparoscopic colectomy by nearly US$3000 [86]. The future utility of robotic colectomy and proctectomy will need to be further explored in prospective trials to determine the potential benefit for colon and rectal surgeries, especially in regard to geriatric patients.

Minimally invasive surgery in elderly patients can have concrete benefits, but it is not fully understood how these surgeries affect patient-reported outcomes and quality of life in this population. In another study of elderly patients' health-related quality of life (QOL) following surgery for colorectal cancer, elderly patients over age 70 had a more significant decrease in global QOL at 1 month after surgery when compared to their younger counterparts, most notably in fatigue, sleep disturbances, appetite loss, and dyspnea [88]. These changes can significantly impact elderly patients and their ability to be independent and thus significantly impact their quality of life. Another study found that the use of laparoscopic surgery in elderly patients having colectomy for cancer was associated with maintaining patients' independent living status after surgery more often than when patients had laparotomies [89]. In most cases when treating patients with colorectal cancer, cure of the disease is the ultimate goal, but in elderly patients, quality of life may take precedence over quantity. Understanding how surgical technique impacts patients with multiple comorbidities is important. While laparoscopic and robotic colectomy and proctectomy are complicated procedures, elderly patients should be offered these types of minimally invasive surgery whenever possible, as there are no data to suggest they are harmed and much to support considerable gains from minimally invasive surgery.

The Volume–Outcome Relationship

Much has been made in recent years regarding the association of high volume centers that perform a larger volume of highly specialized and technical procedures [90]. This relationship is true for both colon as well as rectal resections with high volume hospitals having lower 30-day readmissions and 1-year mortality [21]. In an exploration of the Nationwide Inpatient Sample (NIS) database in 1997, patients having surgery for colorectal cancer at a low volume center were more likely to be healthy with no significant comorbidities, have had emergency surgery, and had a higher in-hospital mortality rate (3.7% vs. 2.5%, $p = 0.006$) compared to those patients who had surgery at high volume centers [91]. This difference in mortality was primarily due to differences in age; for patients over age 80, the mortality rate at the highest volume centers was 4.6% compared to 7.3% ($p = 0.04$) at the lowest volume centers [91]. While the absolute difference may seem small, 27 elderly patients would need to be referred to a high-volume center to prevent one death, a manageable number that does not put undue stress on either end of the health-care spectrum and could promote regionalization of care and optimization of outcomes [91]. Interestingly, the relationship of hospital volume did not hold true in the Veterans Affairs (VA) system [16]. The authors were not able to find an association with low volume centers and high-volume centers within the VA system, though it is likely that alternate definitions of volume could alter the reported effect [16].

These findings may be reflective of the complex needs required to care for elderly patients with considerable comorbidities where the advantages of a high-functioning system and network can have considerable advantages. Such a strategy of selective regionalization for elderly patients capitalizes on the available resources at high volume centers to help manage complex comorbidities in the immediate postoperative setting.

Sphincter Sparing Surgery for Rectal Cancer

It is unclear if the anastomotic leak rate in elderly patients is elevated compared to younger patients, or if this is a reflection of more profound underlying diseases and risk factors, such as malnutrition. Marusch et al. (2005) found that in those patients having colorectal surgery for cancer, in patients over age 80, the rate of anastomotic leak that required surgery was not elevated compared to younger patients (2.2% vs. 2.8%), but the rate of anastomotic insufficiency that did not warrant an operation was elevated (0.6% vs. 1.9%) [18]. A large meta-analysis of studies published evaluating outcomes in elderly patients after colorectal surgery did not find evidence of an elevated anastomotic leak rate among elderly patients, even when only rectal cancer studies were included alone [19]. In elderly patients having laparoscopic surgery, no difference in anastomotic leak was noted compared to younger patients [87]. Interestingly, in a retrospective study of patients over age 65 having colorectal surgery utilizing the American College of Surgeon's National Surgical Quality Improvement Program (ACS-NSQIP), increasing age alone was not a risk factor for anastomotic leak [92]. The authors did identify a number of risk factors for anastomotic leak in elderly patients and developed a nomogram to help predict the risk in individual patients and guide clinical decision making [92].

While the anastomotic leak rate is not necessarily elevated in elderly patients due to age alone and patients should be considered for primary anastomosis when appropriate, it is prudent to consider the negative impact on quality of life should a low anastomosis be created in patients who are less mobile [93, 94]. It is well understood that bowel dysfunction after low colorectal anastomoses can severely impact quality of life for patients [95]. Consideration of a permanent ostomy is prudent in these patients, though care of an ostomy can also have an impact, particularly in patients who are partially dependent or have limited dexterity.

While total mesorectal excision and reconstruction after neoadjuvant chemoradiation is the standard of care, in elderly patients with significant comorbidities who are not candidates for a major abdominal operation, local excision of the rectal tumor can be considered. Local transanal excision of early rectal cancers is best considered for those with low tumors (<8 cm from the anal verge), favorable histology, T1 or T2 and N0 status, and lesions of smaller size [96]. Local techniques such as transanal excision or transanal excisional microsurgery have excellent outcomes with morbidity between 4 and 30% and mortality less than 0.5% after surgery, though local recurrence rates of 15% are higher than when standard mesorectal excision is undertaken [97].

Another potential way to minimize the impact of rectal cancer surgery on elderly patients is to consider total neoadjuvant treatment and give all medical treatment up-front prior to surgery, including systemic chemotherapy and standard combined chemoradiation therapy. When induction systemic chemotherapy is given first, followed by combined chemoradiation therapy, 36% of patients were found to have either no evidence of residual tumor on imaging or examination (complete clinical response) or no residual tumor on final pathology after surgery (complete pathologic response) [98]. Such results raise the question of whether patients who have a complete clinical response even need to have surgery to remove the offending organ and this is currently an active area of study and debate. For the appropriately selected patient who is willing to undergo close follow-up and is averse to either a low anastomosis or ostomy, such a strategy can have reasonable outcomes long-term comparable with standard therapy [99].

Colorectal Cancer and Inflammatory Bowel Disease

Inflammatory bowel disease (IBD), both Crohn's Disease (CD) and Ulcerative Colitis (UC), raises the risk of developing colorectal malignancies in subjected patients, though UC is thought to have a higher malignancy risk at 60% greater than the risk of the general population, increasing with severity and duration of UC among other factors [11, 100]. The current standard of care for patients with UC and a new colorectal adenocarcinoma includes a total proctocolectomy (TPC) either with or without an ileal-pouch anal anastomosis (IPAA), a reconstruction to maintain bowel continuity and avoid a permanent ostomy [101]. IPAA can be difficult as patients often have numerous liquid bowel movements every day and continence can be compromised, two factors that become even more concerning when patients' mobility is reduced as they age [102]. Ileostomy is also associated with risks, including dehydration, and can be difficult for older patients with limited dexterity to manage well.

As such, some patients elect to undergo a more limited partial resection of the segment containing malignancy, understanding the future risk of metachronous lesions is unknown, and little data exist outside of single-institution case series to support this practice. Khan et al. (2017) performed a review of patients with UC and colorectal cancer who had surgery using the VA database, which encompasses all 50 states and has long-term outcomes data [103]. The authors identified 59 patients that underwent surgery, of which 25 had partial resection (PR) and 34 had total proctocolectomy [103]. The group that had PR was older with a shorter length of UC, less severe and less extensive UC than those whom had TPC; they also had earlier stage cancers with 24% having no residual disease in the resected specimen after finding adenocarcinoma in the resected polyp and only 5% of the TPC group had such findings [103]. While both groups recovered well after surgery, the majority of those in PR group required additional medical therapy for UC following resection. No patients were diagnosed with metachronous colorectal cancer during the follow-up (median 7 years), though an equal number of patients in each group developed distant recurrence (4% vs. 6%) [103].

As with many decisions about treatment choices for geriatric patients, a balance is warranted when considering the extent of resection for those with UC and colorectal cancer. Data suggest that partial resection is a reasonable alternative for those who have less severe, less extensive UC or might have significant issues related to ileostomy or IPAA. Patients who are candidates for partial resection should also be counseled about the need for close follow-up and the likely need for ongoing treatment of colitis along with additional endoscopic surveillance.

Neoadjuvant and Adjuvant Therapy in the Elderly

While surgical resection remains the cornerstone of colorectal cancer treatments, in many cases additional treatments are given to improve outcomes. Specifically, radiation therapy with radiosensitizing chemotherapy is given for Stage II and Stage III rectal cancer prior to surgery, which has been shown to decrease local recurrence rates in a notoriously difficult to treat disease [2, 104]. Adjuvant systemic cytotoxic chemotherapy is then given after rectal resection surgery. It is also given for colon cancer after colectomy when patients are found to have Stage III disease or Stage II disease with certain high-risk features [3, 5].

Geriatric patients more often do not receive standard treatment than their younger cohorts and are less likely to be given adjuvant and neoadjuvant treatments. In Japan, patients with Stage III colon cancer, only 35% of those over age 75 received adjuvant therapy, in contrast to 70% of those under age 75 [17]. The same trend holds true in the United States, where only 43% of octogenarians with Stage III colon cancer who were eligible for adjuvant chemotherapy after surgery actually received it [105]. Fears of severe side effects and poor tolerance to treatment dominate the decision-making process. The prevailing rationale is that elderly patients have less reserve to tolerate the side effects of neoadjuvant or adjuvant treatments and that the expected benefits are more limited in these patients due to their decreased overall survival from competing comorbidities. Unfortunately, there are little high-quality data to help guide physicians as few geriatric patients are included in clinical trials.

Neoadjuvant Chemoradiation Therapy for Rectal Cancer and Geriatric Patients

Neoadjuvant combined chemoradiation therapy is considered standard treatment for Stage II and Stage III rectal cancer. This should include a 5-FU based agent in radio-sensitizing doses given concurrently with external beam radiation [2].

This strategy has been shown to reduce local recurrence after rectal cancer surgery [104]. Furthermore, these treatments also allow the tumor to regress prior to surgery, known as tumor downstaging, and can potentially impact the type of operation offered to patients [106]. For example, a low rectal cancer that is directly adjacent to the sphincter complex might require an abdominoperineal resection and permanent ostomy, but if tumor regression occurs due to neoadjuvant therapy, then the patient may be a candidate for sphincter-preserving low colorectal anastomosis.

The rate of use of neoadjuvant chemotherapy for rectal cancer in geriatric patients is particularly dismal, despite its well-accepted benefit of reducing local recurrence after surgery and potential for downstaging and sphincter preservation. In one German review, only 14% of eligible rectal cancer patients received neoadjuvant treatment according to guidelines, in comparison to 73% of those under age 80 ($p < 0.01$) [14]. This may be due to issues with elderly patients' ability to tolerate neoadjuvant chemoradiation therapy. In a review of patients age 75 or older having chemoradiation for rectal cancer, 25% required a radiation treatment break and 33% had a dose-reduction, break or discontinuation of concurrent chemotherapy, with only 17% completing therapy without any deviations [107]. Interestingly, these results were consistent whether patients had preoperative or postoperative chemoradiation therapy. This contrasts with an Italian study that found elderly patients who were considered vulnerable were still able to tolerate neoadjuvant chemoradiation at rates similar to fit elderly patients [108]. Therefore, elderly patients should be offered neoadjuvant chemoradiation unless significant contraindications to treatment are noted as they can gain considerable benefit as per younger patients in reducing local recurrence and tumor downstaging.

Adjuvant Chemotherapy and Geriatric Patients

Adjuvant 5-flourouricil (5-FU) chemotherapy has a demonstrated overall survival benefit for Stage III colon and rectal cancer following oncologic resection [109]. It also has been shown beneficial in decreasing recurrence and improving survival for patients with Stage II rectal cancer, even when treated with neoadjuvant therapy and surgical resection [110]. For young patients, oxaliplatin is given in conjunction with 5-FU & leucovorin, known as FOLFOX, as the first line therapy, but oxaliplatin has not shown a survival benefit for elderly patients in previous studies [111, 112].

In a recent large review of octogenarians with Stage III colon cancer using the National Cancer Database in the United States, those who received adjuvant chemotherapy of any kind were younger, more often male, had fewer comorbidities, and in a higher income bracket than those patients who did not receive adjuvant chemotherapy [105]. Furthermore, they were also more likely to have more nodal involvement (N2 disease) [105]. On multivariate analysis, young age, N2 node status, income over US$46,000, and treatment not at comprehensive community care program were independent predictors of receiving adjuvant chemotherapy, and adjuvant therapy was associated with increases in overall survival for octogenarians compared to those who had surgery alone, from 35 months to 62 months median [105]. Even those who were offered chemotherapy but refused, amounting to 28% of those who had surgery alone and representative of physiologically fit patients with minimal comorbidities, had a decreased overall survival at 43 months median [105]. This retrospective review demonstrates that overall five-year survival was improved by 20% with the use of adjuvant chemotherapy in Stage III disease in octogenarians, even though this group had more advanced disease. What is interesting is this study did not account for type of chemotherapy nor any dose-reductions or early cessation and yet significant benefit was still noted [105]. As mentioned above, only half of eligible patients received chemotherapy and considerable improvements in survival could be anticipated if more elderly patients were offered adjuvant therapy.

Oxaliplatin can also be given with capecitabine, an oral prodrug of 5-FU, and offers a survival benefit above 5-FU and leucovorin alone [37, 113]. Oxaliplatin can have significant side effects, the most significant of which is neuropathy, primarily in the hands and feet and can persist for years after finishing treatment and elderly patients have been shown to be more susceptible to this neuropathy than younger patients [114, 115]. When this occurs in elderly patients, it can significantly impact their ability to perform daily tasks, such as self-dressing, and is a risk factor for falls that might warrant institutionalization and negatively impact quality of life [116, 117]. As the benefit of oxaliplatin in elderly patients overall is not well understood, it is not recommended in the routine oncologic adjuvant therapy for patients over age 70 and this decision should be made on an individual basis [50]. It is also no known whether oxaliplatin may be better tolerated in fit, healthy elderly patients, or if 5-FU alone offers a benefit for unfit, less health elderly patients. A randomized controlled trial is currently enrolling patients age 75 or older with Stage III completely resected colon cancer in France to help understand the disease-free survival benefit of various chemotherapy regimens in elderly patients [118].

The utility of adjuvant chemotherapy for rectal cancer, after neoadjuvant therapy and complete surgical resection, is also poorly understood for similar reasons. In retrospective review of patients having treatment for colorectal cancer in Japan, for those over age 75, adjuvant therapy was found to be independently associated with improved DFS for both colon and rectal cancer patients [17]. However, when elderly patients who received FOLFOX were compared to those who received 5-FU with leucovorin alone, adding oxaliplatin did not improve survival for patients over age 73, regardless of nodal status [112]. These studies suggest that there is limited benefit to adding oxaliplatin in older patients, though they do benefit from other adjuvant regimens.

The Comprehensive Geriatric Assessment (CGA), advocated initially for perioperative clinical assessments, can also be applied in the postoperative setting to help risk stratify patients for adjuvant chemotherapy. In a prospective study, patients 75 years or older were administered the CGA and stratified into fit, medium-fit, and unfit categories to receive either standard adjuvant chemotherapy, an adjusted regimen, or best supportive care according to fitness [119]. The authors found that classification into these categories not only correlated with 5-year survival, but those classified as unfit had a significantly greater risk of noncancer related death. This study demonstrated the CGA can help discriminate elderly patients with competing comorbidities who may gain little benefit from adjuvant therapies.

Posttreatment Surveillance

Surveillance after treatment for curative colorectal cancer is multifactorial, including frequent examinations to evaluate for symptoms suggestive of recurrence, blood tests to detect changes in serum biomarkers, cross-sectional imaging to detect asymptomatic recurrences, and repeat endoscopy to look for metachronous polyps or lesions. These recommendations are summarized in Table 4.

For patients with Stage II or Stage III colon or rectal cancer, or for those whom had curative resection of Stage IV disease, ongoing surveillance is indicated. This should include an office visit and examination and serum CEA level every 3–6 months for 2 years, then every 6 months for 5 years. Imaging should include a Computed Tomography scan of chest, abdomen, and pelvis annually for 5 years. Those patients enrolled in high intensity surveillance programs had higher

Table 4 Surveillance after curative treatment for colorectal cancer [2, 3, 120]

Office visit and examination	Every 3–6 months for 2 years Then every 6 months until 5 years
Serum carcinoembryonic antigen (CEA)	Every 3–6 months for 2 years Then every 6 months until 5 years
Computed tomography (CT) Chest, abdomen, and pelvis	Annually for 5 years
Colonoscopy	1 year after preoperative colonoscopy (or 3–6 months after surgery if previous colonoscopy was not complete)

rates of detection of asymptomatic recurrences and underwent curative resections for often [120]. What is not clearly understood is the frequency of liver imaging, which can allow earlier detection of potentially curable metastases, and could be considered for very-high risk patients such as those with N2 disease, prior liver resection, or prior indeterminate liver lesions. For patients with Stage I colorectal cancer, surveillance may be indicated for those with higher-risk features, such as poor histology, lymphovascular invasion, positive margins, transanal excision, or T2 disease [120]. The literature exploring the benefit in Stage I disease is limited and more heterogeneous. Overall, the risk of recurrence in Stage I colon cancer is <5% and the benefit of high-intensity surveillance may be limited, though the rates of salvage are excellent [120]. The National Comprehensive Cancer Network Guidelines do not recommend additional surveillance beyond close interval colonoscopy as described below for either Stage I colon cancer or Stage I rectal cancer patients who underwent oncologically appropriate mesorectal excision and full surgical staging [2, 3].

Colonoscopy is indicated after curative treatment and surgery for colorectal cancer to evaluate for metachronous or local recurrence. The first colonoscopy should be 1 year after surgery or 1 year after the diagnostic complete colonoscopy [121]. Subsequent colonoscopies should be in 3 years and then 5 years, if no additional high-risk lesions are found. Following this, colonoscopy should be at 5-year intervals. For patients with rectal cancer, which has a higher rate of local recurrence, closer surveillance may be indicated. For those patients who did not receive standard of care treatment (i.e., transanal excision of early rectal cancer, no neoadjuvant chemoradiation therapy for Stage II or III, surgery that was not total mesorectal excision), flexible sigmoidoscopy to evaluate the pelvis and anastomosis should be performed every 3–6 months for the first 23 years after surgery in addition to the colonoscopy recommended above for metachronous surveillance as these patients have higher risk of local recurrence [3, 121]. For those patients with rectal cancer who did receive neoadjuvant chemoradiation and appropriate surgical resection, the risk of local recurrence is <5% and the likelihood of detecting curable disease is minimal; therefore, the benefit of more frequent proctoscopy may be more limited and is not in the most recent NCCN guidelines [3].

In all guidelines, surveillance after curative treatment is recommended to continue for 5 years. How this timeline effects elderly patients remains unclear. In elderly patients, this may entail less time as the risks of ongoing interventions (i.e., colonoscopies) should be balanced against the expected survival benefits of detecting recurrences. Furthermore, it should be discussed in advance with elderly patients what their goals would be should recurrence be found. Again, a candid discussion with the patient about expected benefits versus risks should be undertaken.

Conclusions

The outcomes of treatment for colorectal cancer in elderly patients could be similar to that of younger patients if careful selection and appropriate attention to detail is maintained. These patients require special considerations and a thoughtful discussion of the balance between risks and benefits with any treatment options, especially in the setting of significant comorbidities. The impact on quality of life and the possibility of losing independence due to complications or side effects from medications or surgery should be carefully considered.

When surgery is offered, minimally invasive strategies should be utilized to minimize the recovery and morbidity for elderly patients. Enhanced recovery programs should be strongly considered to reduce the stress of surgery and optimize outcomes during the perioperative period. Following surgery, if adjuvant chemotherapy is indicated, it should be strongly considered and many options are available that can offer benefit without long-term consequences. Approaching the management of elderly patients from multiple perspectives, perhaps with the help of a geriatrician, can appropriately frame the problem and help the surgeon and patient understand competing comorbidities.

There does not appear to be any such thing as "too old" for standard treatment, especially surgery, and age alone should not be a criterion for surgery or other treatments. Rather, a global assessment of the patient, including medical comorbidities, functional status, and support system, should be undertaking to understand not only the medical risks of treatment, but the impact complications and poor outcomes may have on a patients' quality of life. Including the patient and family members in the discussion will lead to optimal decision making and a clear understanding of what is in store.

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47 Gastric Cancer in the Elderly

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Abstract

Gastric cancer is the fourth most common cancer worldwide and the second leading cause of cancer death, representing a major contributor to the global health cancer burden. In the Western world, gastric cancer has been on the decline overall but remains a significant risk factor in the elderly population. This chapter will review the epidemiology, diagnosis, and treatment of gastric cancer in the elderly. Emphasis will be placed on landmark clinical trials which guide current surgical management and perioperative therapy decision-making. Up-to-date management recommendations from the National Comprehensive Cancer Network (NCCN) and European Society for Medical Oncology (ESMO) will be integrated in the discussion. Special focus will be given to issues relating to advanced age and how these issues impact decision-making for oncologists managing this growing patient population.

Keywords

Gastric cancer · Geriatric surgery · Total gastrectomy · Partial gastrectomy · Subtotal gastrectomy · Frailty · Elderly · Gastric adenocarcinoma

Introduction

Cancer is the second leading cause of death worldwide. In 2015, it is estimated that there were 17.5 million cancer cases worldwide and 8.7 million deaths [1]. During the preceding decade, cancer incidence increased by 33%, with population aging contributing 16% to this incidence [1]. Worldwide, gastric cancer is the fourth most common cancer by incidence and second leading cause of cancer death [2]. In the Western world, gastric cancer has been on the decline overall, but its incidence in the elderly population is increasing [3, 4]. Given its incidence worldwide and its association with aging, gastric cancer is a significant contributor to the global cancer burden and a disease that is critical to understand in the elderly patient population. In this chapter, the focus will be primarily on gastric cancer in the Western patient population, addressing issues specific to the geriatric surgical patient.

Epidemiology

Gastric cancer demonstrates significant global variation. Highest incidences are found in Eastern Asia, Eastern Europe, and South America, with lower rates in the United States and Western

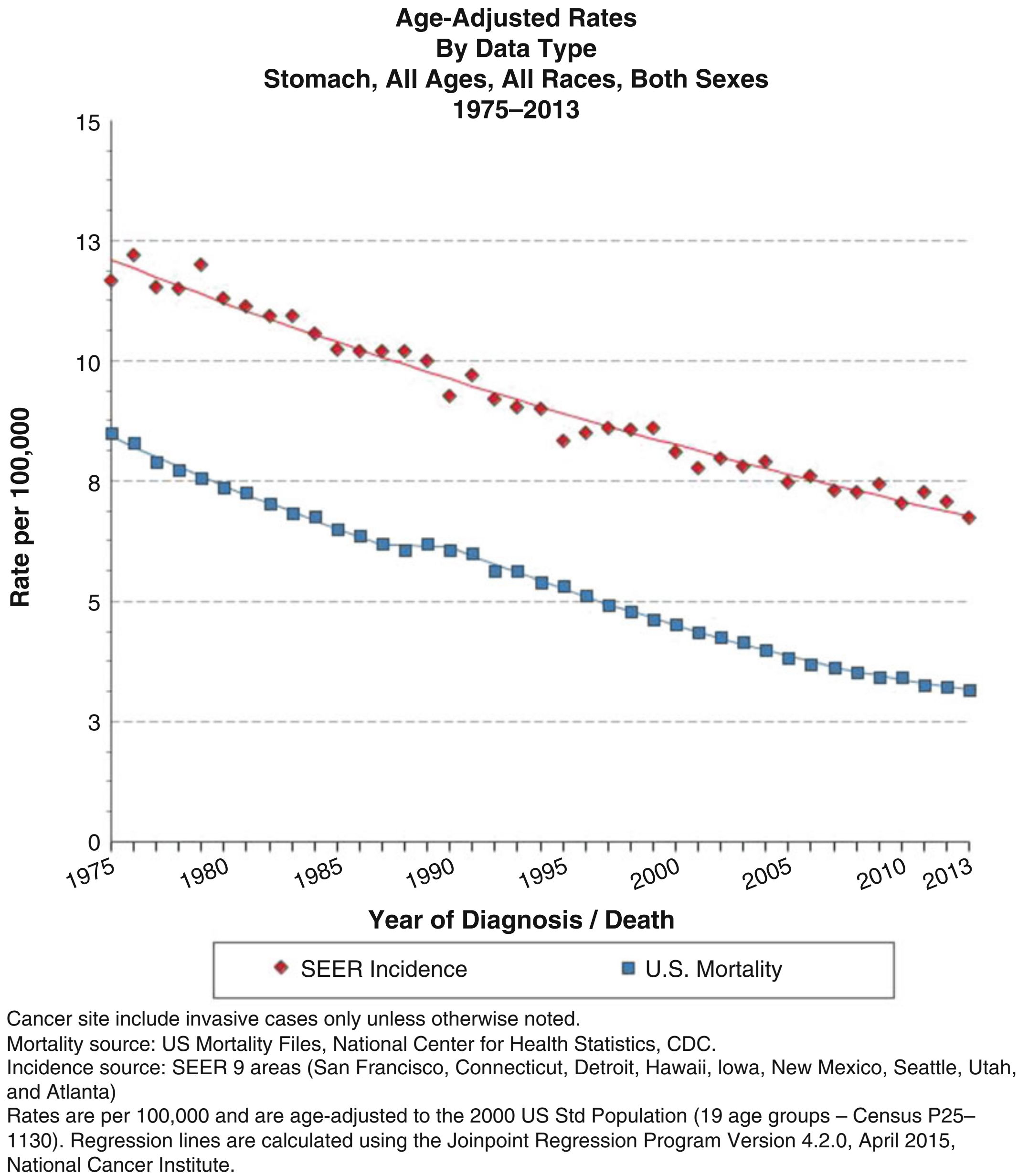

Fig. 1 Age-adjusted rates of gastric cancer incidence and mortality (1975–2013) (https://seer.cancer.gov/faststats/selections.php?#Output)

Europe [5]. Gastric cancer in the United States has seen an overall decline in both incidence and mortality over the past several decades (Fig. 1) [4]. This decline stands in contrast to the early twentieth century, when gastric cancer was the leading cause of cancer mortality in the United States and Europe until the late 1930s. This decline has been attributed in part to the decrease in incidence of infection with *Helicobacter pylori* [6], a known risk factor for more distal gastric cancers. The decline may also be related to the increased use of refrigeration for food storage (and subsequent decreased used of salted and smoked foods).

Though the overall incidence of gastric cancer in the United States has decreased over the past several decades, the relative incidence of proximal gastric cancers has increased. A SEER analysis in the early 1990s demonstrated the rising incidence of adenocarcinoma of the esophagus and gastric cardia [7]. This increase affected white men disproportionately as compared to women and other races, and, ultimately, cardia tumors represented half of all gastric cancer incidence in this group. This change has been attributed in part to the increases in obesity and gastroesophageal reflux disease.

In 2016, it is estimated that the incidence of gastric cancer in the United States will reach 26,370 people, and about 10,730 people will die from this disease [3, 8]. The median age of gastric cancer patients in the United States is 69 years [4]. It is a cancer clearly associated with advancing age (Fig. 2): approximately, six out of ten patients diagnosed with gastric cancer in the United States are at least 65 years of age. While gastric cancer is not in the top 10 cancers in the United States by incidence, it carries a low rate of survival. The overall 5-year survival rate of patients with gastric cancer in the United States is about 29% [9]. Survival also declines with increasing age of incidence (Fig. 3).

Gastric cancer overall affects men more frequently than women, and this predominance persists in the elderly population. In 2016, men will comprise 16,480 of cases and women about 9980 of the projected 26,370 cases of newly diagnosed gastric cancer in the United States [3]. Some have suggested this imbalance is due to differential exposure to environmental carcinogens, while others postulate hormonal causes [10].

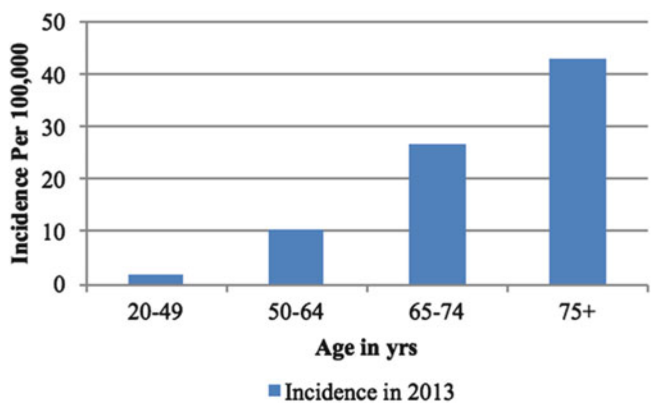

Fig. 2 Increasing incidence of gastric cancer by age in 2013 (https://seer.cancer.gov/faststats/selections.php?#Output)

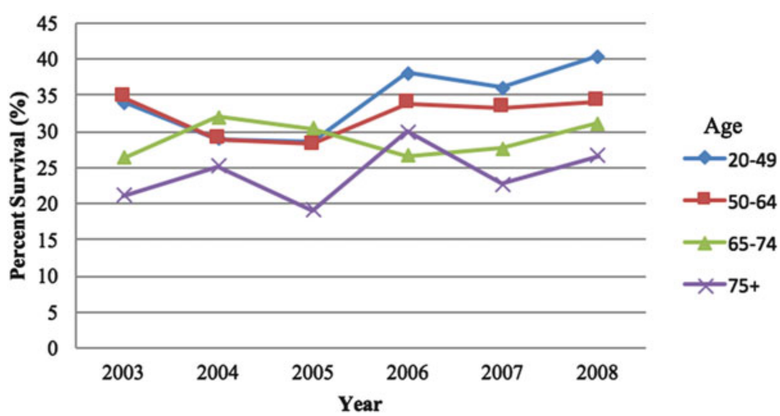

Fig. 3 A 5-year survival by age cohorts (2003–2008) (https://seer.cancer.gov/faststats/selections.php?#Output)

Risk Factors

H. pylori infection is one of the most important known causes of gastric cancer, primarily associated with more distal gastric cancers. According to Herrero et al., up to 90% of non-cardia gastric cancer is attributed to *H. pylori* [6]. These gram-negative bacteria have many virulence factors that induce pro-inflammatory, pro-proliferative cell signaling and epithelial damage. Host genetics that produce a heightened pro-inflammatory response in the presence of this bacterium add to the increased risk of transition to gastric cancer [11]. The effects of these pathological phenomena increase the risk of developing gastric adenocarcinoma over time, which makes *H. pylori* a critical risk factor for elderly patients [12]. As the recognition of the role of *H. pylori* in the pathogenesis of peptic ulcer disease and gastric cancer has grown, so too have aggressive efforts to eradicate this pathogen. The decrease of these diseases over the last few decades can likely be attributed to these efforts.

The majority of gastric cancers are considered sporadic. However, approximately 5–10% of gastric cancers are considered to have a familial component, and 3–5% are associated with cancer predisposition syndromes. Gastric cancer is increased in hereditary diffuse gastric cancer, Lynch syndrome, juvenile polyposis syndrome, Peutz-Jeghers syndrome, and familial polyposis syndrome. Because these syndromes are generally associated with early onset of gastric cancer, they are less commonly encountered in the elderly patient and thus are not a focus of this chapter.

Other important risk factors for gastric cancer are obesity and gastroesophageal reflux disease (GERD). In the United States, one in three adults is obese, comprising nearly 78 million adults, as well as 13 million children. Clearly associated with numerous health issues such as hypertension, diabetes, and heart disease, there is a growing recognition of the role of obesity in cancer. Elderly patients are no different: data from the National Health and Nutrition Examination Survey from 2007 to 2010 demonstrated that more than one-third of the adults over the age of 65 were obese [13]. By 2050, the number of elderly patients is expected to double to 88.5 million. Obesity and GERD have been primarily associated with proximal gastric cancers, and this rise in obesity may offset some of the decreases in gastric cancer seen over the past few decades.

Environmental risk factors have also been associated with gastric cancer. Low consumption of fruits and vegetables and high intake of salts, nitrates, and pickled foods have all been implicated [2]. Heavy alcohol use may also be a risk factor for more distal gastric cancers [14]. And, as with many solid tumors, smoking appears to increase the risk for gastric cancer.

Anatomic Classification

Gastric cancers are primarily divided into cardia and non-cardia locations. Non-cardia tumors are sometimes called true gastric tumors, whereas cardia tumors are called gastroesophageal (GE) tumors. The most common classification of gastroesophageal tumors is the Siewert classification [15]. This classification identifies three types:

Type I: center of the tumor located within 1–5 cm above the anatomic GE junction

Type II: center within 1 cm above and 2 cm below the GEJ

Type III: center between 2 and 5 cm below GEJ (may infiltrate the GEJ from below)

All gastric cancers involving the GE junction should be classified by Siewert tumor type. Anatomic classification is important due to significant differences in risk factors, incidence, disease course, and treatment regimens. Consistent with National Comprehensive Cancer Network guidelines, this chapter will focus on the management principles of true gastric cancers, including Siewert type III [16]. Siewert type I and II tumors are more commonly treated according to esophageal cancer guidelines.

In elderly patients, lower or distal third tumors predominate (42–63%), whereas younger patients' incidence ranges from 31 to 44% and middle and upper third tumors predominate [10]. In addition, multiple synchronous gastric cancers are more prevalent in the elderly (8–15%) [10]. These multiple tumors arise predominantly in the distal third of the stomach.

Some have suggested this pattern is related to the higher prevalence of intestinal-type gastric cancer in this age group.

Histologic Classification

Gastric adenocarcinomas are histologically diverse. This diversity has led to a number of classification schemes, including the Lauren and WHO [17, 18]. According to the Lauren classification, gastric carcinomas are characterized as diffuse, intestinal, mixed, or indeterminate types. Diffuse carcinomas are poorly differentiated with the absence of gland formation, whereas intestinal carcinomas are mostly well to moderately differentiated and form glandular structures [2]. Diffuse type tends to spread transmurally, or via lymphatics, whereas intestinal type is more commonly associated with hematogenous spread of metastases.

The intestinal subtype is more common in high-risk and elderly patient populations, and the diffuse type is more common in women and younger patients. Prognosis tends to be less favorable for patients with diffuse-type carcinomas. This subclassification as intestinal or diffuse also has implications for systemic therapy, as intestinal type cancers more frequently overexpress HER2-neu. This implication for therapy has led the NCCN to recommend reporting this histologic subtype in pathologic evaluations [16].

The WHO classification, on the other hand, divides gastric carcinomas into five types: tubular, papillary, mucinous, poorly cohesive, and rare variants. This classification aligns these cancers with classification of other gastrointestinal malignancies [2]. In general, tubular and papillary carcinomas roughly correspond to intestinal type in the Lauren classification, and poorly cohesive (including signet ring types) correspond to diffuse-type carcinomas.

Molecular Classification

Recent significant molecular subtyping work has begun to emerge in the literature [19]. Utilizing The Cancer Genome Atlas, investigators analyzed 295 primary gastric adenocarcinomas and identified four molecular subtypes: EBV-positive tumors, microsatellite instability (MSI), genomically stable, and chromosomal instability. Currently, such subtyping is not part of consensus guidelines for pathologic review from either the National Comprehensive Cancer Network (NCCN) or European Society for Medical Oncology (ESMO) guidelines [5, 16]. However, these efforts hold great promise to better characterize prognosis and target systemic therapies in the future.

NCCN and ESMO guidelines do recommend pathologic evaluation for HER2 positivity [5, 16]. Overexpression of HER2-neu is observed in 10–15% of gastric cancers [5]. Currently, the NCCN recommends assessment of HER2-neu overexpression in patients with inoperable locally advanced, recurrent, or metastatic disease. ESMO guidelines currently recommend assessment of HER2-neu overexpression in patients with metastatic disease (level 1 recommendation).

Presentation and Diagnosis

Gastric cancer remains a challenge clinically. Most patients with early-stage gastric cancer are asymptomatic and therefore remain undiagnosed until a later stage. In countries where the incidence of gastric cancer is high – such as Japan and Korea – screening programs have enabled early detection and overall more favorable outcomes. However, in the United States, due to the low incidence of gastric cancer, widespread endoscopic screening programs have low positive predictive value, and therefore disease is most commonly detected at later symptomatic stages of disease.

Efforts at early detection in Western countries have primarily focused on high-risk patient populations, especially in those with hereditary cancer syndromes associated with an increased risk of gastric cancer. This difficulty in detecting gastric cancer early in Western countries is even more profound in the elderly patient population, where frailty and malnutrition further complicate management decisions.

The most common presenting symptoms may be fairly nonspecific. In a study of 1172 patients with resectable gastric cancer at Memorial Sloan Kettering Cancer Center, the most common presenting symptoms were anorexia, weight loss, pain, and vomiting [20]. These symptoms can also be frequently seen with a number of gastrointestinal conditions, and patients are often treated for presumed benign etiologies before suspicion for underlying malignancy arises. With more advanced disease, other symptoms may occur. Dysphagia may be associated with tumors at the GE junction. Abdominal distention, nausea, and vomiting may also occur secondary to obstructing masses at the distal stomach.

Diagnosis may also follow abnormal laboratory values suspicious for underlying gastric malignancy. Positive fecal occult blood tests or iron deficiency anemia can spur a workup for gastrointestinal bleeding. Though colorectal malignancy is a more common etiology for these abnormalities, frequently an upper endoscopy is often pursued with a lower endoscopy, resulting in a reasonably timely diagnosis of gastric cancer.

Physical examination findings are also often unremarkable, except in very advanced disease. Findings such as Sister Mary Joseph sign (palpable periumbilical node), Virchow's node (palpable left supraclavicular node), and Blumer's shelf (palpable mass on rectal exam) are rarely seen in the modern era.

Endoscopy is the examination of choice for confirming the diagnosis of gastric cancer. Historically, upper GI series with barium was an important component of the initial workup. Barium studies can demonstrate intraluminal mass and irregular rugae, but its sensitivity is low. Currently, upper GI series are primarily used in advanced cancers to assess significance of obstruction. This modality may also be useful for linitis plastica, where a contrast study may show nondistensibility of the stomach. In general, though, upper endoscopy has largely supplanted contrast studies in the initial workup of gastric cancer.

Upper endoscopy has the benefit of direct visualization of the upper digestive tract. Suspicious masses or ulcerations can be directly biopsied. Sensitivity of upper endoscopy for making the diagnosis of gastric cancer has been reported to be as high as 90–96% [21]. Typically, six to eight biopsy specimens with standard-size endoscopy forceps are sufficient to obtain the diagnosis. Cytologic brushings or washings are much less frequently used in the initial workup of a gastric mass.

Workup

Once the diagnosis is made, clinical staging is critical as over 50% of patients will have advanced disease at the time of diagnosis [16]. For these patients, curative resection is not indicated.

Both endoscopic ultrasonography (EUS) and CT imaging of the chest and abdomen are essential modalities for proper preoperative staging; both are recommended by ESMO and NCCN [5, 16]. EUS provides the more accurate tumor (T) and lymph node (N) staging and maybe the proximal extent of disease. EUS discriminates T1–T2 lesions versus T3–T4 at approximately 86% sensitivity according to a recent Cochrane review [22]. Lymph node positivity was 83% sensitive. As nearly 70%–80% of the patients with resectable disease will have involvement of regional lymph nodes, this clinical assessment is critical for applying appropriate treatment modalities and sequencing.

For assessment of distant disease, CT imaging of the chest and abdomen/pelvis is the diagnostic modality of choice. Its sensitivity for T staging is limited (43% to 82%), and its utility in lymph node staging is variable [16]. However, given the high incidence of advanced disease at the time of diagnosis, investigation of distant metastatic disease is mandatory.

PET-CT and MRI are less commonly used for the workup of gastric cancer. Though PET-CT plays an important role in the preoperative management of esophageal and GE junction cancers, its utility is less established for true gastric cancers, given the availability of EUS and high quality CT imaging. In addition, PET-CT has a low detection rate in diffuse and mucinous tumor types due to low tracer accumulation. MRI has been advocated for its ability to detect occult peritoneal disease, but that ability appears to depend on the administering institution.

Currently, it is not recommended by ESMO or NCCN guidelines.

Because of this difficulty in detecting peritoneal disease with conventional imaging methods, diagnostic laparoscopy with cytology has been advocated by some but remains controversial in the workup of gastric cancer. Currently, laparoscopy +/− peritoneal washings carry a level III recommendation (supported by prospective cohort studies) in the current ESMO guidelines for patients with stage IB–III gastric cancer [5], i.e., patients with potentially resectable disease and at least T2 by localized staging. NCCN guidelines recommend laparoscopy with cytology for patients with clinical stage T1b (tumor invades the submucosa) or greater who are considered surgically resectable and who are undergoing preoperative therapy (2B recommendation) [16].

Positive peritoneal cytology, even in the absence of macroscopic peritoneal disease, is classified as M1 disease and carries a poor prognosis. It is also common. In a study of 657 patients at Memorial Sloan Kettering Cancer Center with preoperative assessment of surgically resectable disease, laparoscopy revealed M1 disease in 31% of patients [23]. The strongest preoperative predictors for occult metastatic disease in this study included GE junction/whole stomach tumors and lymphadenopathy. Typically, in patients with macroscopic disease, surgical resection is contraindicated. In patients with positive cytology only, up-front surgical resection should not be pursued except in palliative circumstances. However, in the subset of patients who respond to systemic therapy, the role of surgery is controversial. These patients should be treated in the context of a clinical trial.

Once clinical stage is established, appropriate decisions can then be made for need for or intent of surgical intervention.

Geriatric Assessment

In the elderly patient with locoregional disease being considered for surgical resection, another critical element of the preoperative assessment is fitness for surgery and aligning interventions with patient goals of care.

Geriatric patients present unique challenges in surgical care and cancer treatment. Special consideration must be taken for the individual physiologic reserve and frailty prior to presenting different treatment options. Currently, geriatric patients make up about 50% of the total operations in the United States [24]. This percentage will be expected to increase as the baby boomer population ages. The US Census Bureau anticipates that the baby boomer population (born between 1946 and 1964) is expected to increase from 13% of the total population to at least 20% of the total population by the year 2030 [25]. At that point, nearly one in five US citizens will be age 65 or older [26]. Given the aging of the population, assessment for surgical resection of gastric cancer can be expected to increase, and special approaches must be taken to ensure that patients are appropriately selected for specific treatments and procedures. This includes special assessment tools for those patients carrying a higher risk for increased postoperative morbidity and mortality.

The concept of frailty is multidimensional and incorporates health outcomes including any potential serious adverse effects, like loss of the ability to care for oneself [27]. Frailty has been recognized as a more sensitive and specific predictor of postoperative outcomes in the aging population, particularly in gastric cancer, resulting in the development of several direct and surrogate estimates [28–30]. These estimates have been recommended from various professional organizations and have been shown to assist in decreasing morbidity and mortality when utilized [31–33]. Geriatric frailty is most likely due to a lowered physiologic reserve combined with multiple comorbidities [34]. The concern over physiologic reserve becomes critical when considering an elderly patient for gastrectomy.

These variables, such as the activity level, use of assistive devices, nutritional status, polypharmacy, and cognition, have been individually examined for the association with mortality, length of stay, and/or readmission after surgery [28–30, 35, 36]. In circumstances where surgery reduces nutrient absorption, such as in total gastrectomy, nutrition parameters like albumin and weight loss are of especial importance to postoperative recovery [30, 37].

These are just a few of the many factors that may contribute to or be markers for frailty; the challenge lies in determining the best modalities for frailty measurement and how to use them to maximize improvement preoperatively [38]. In the authors' institution, the combined efforts of surgical and geriatric specialists have created a standardized assessment of patients at high risk for postsurgical complications. Patients over the age of 80, or over 65 with multiple comorbidities, dementia, polypharmacy, weight loss, or visual impairment, are eligible for evaluation in this Perioperative Optimization of Senior Health (POSH) clinic. The majority of the patients seen in this clinic undergo partial or total colectomy, hernia repair, cholecystectomy, or pancreatectomy. Team-based care between surgery, geriatrics, nursing, and anesthesia is focused on risk stratification, then developing a patient-centered optimization plan including planning for post-hospital care. Evaluations and recommendations are evidence based, and they target the gamut of barriers to postoperative recovery: physical function, social planning, mobility and activity, nutrition, cognition, and medication (Fig. 4).

A comprehensive preoperative geriatric assessment allows the team to provide recommendations for perioperative plan in and out of the hospital. These recommendations range from management of comorbidities, reduction of unnecessary medication, nutrition and exercise counseling, sensory augmentation, sleep enhancement strategies, multimodal pain management, planning reorientation strategies and cognitive stimulation, delirium education for prevention, patient activation for preparing for surgery, enlisting social support and family engagement, advance care planning, and anticipating postsurgical discharge needs (Table 1).

Preoperative interventions that can be carried out by the patient, such as improving mobility and nutrition and discontinuing high-risk medications, are also explained to the patient and family. Patients with other diseases or findings of high potential for poor outcomes are referred to the

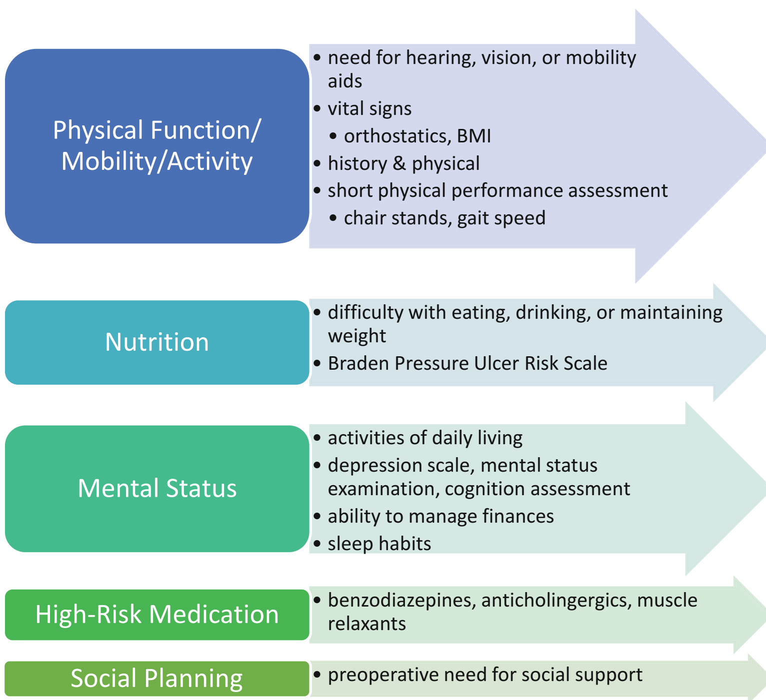

Fig. 4 Frailty-directed preoperative assessment through POSH Clinic. Phone and clinic screening assesses the patient's previous experience with surgery and delirium and reviews family and social history, current living situation, activity level, social support pre- and post-discharge, and advance directives. This screening also aims to identify any difficulties with exhaustion, hearing, vision, nutrition, mobility, sleep, memory, mood, or activities of daily living. Braden Pressure Ulcer Risk Scale [79]

Table 1 American Joint Committee on Cancer (AJCC). TNM Staging Classification for Carcinoma of the Stomach. (7th ed., 2010) (Used with permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original and primary source for this information is the AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer Science + Business Media)

Primary Tumor (T)	
TX	Primary tumor cannot be assessed
TO	No evidence of primary tumor
Tis	Carcinoma in situ: intraepithelial tumor without invasion of the lamina propria
T1	Tumor invades lamina propria, muscuiaris mucosae or submucosa
T1a	Tumor invades lamina propria or muscuiaris mucosae
T1b	Tumor invades submucosa
T2	Tumor invades muscuiaris propria[a]
T3	Tumor penetrates subserosal connective tissue without invasion of visceral peritoneum or adjacent structures[b],[c]
T4	Tumor invades serosa (visceral peritoneum) or adjacent structures[b],[c]
T4a	Tumor invades serosa (visceral peritoneum)
T4b	Tumor invades adjacent structures
Regional Lymph Nodes (N)	
NX	Regional lymph node(s) cannot be assessed
NO	No regional lymph node metastasis[d]
N1	Metastasis in 1–2 regional lymph nodes
N2	Metastasis in 3–6 regional lymph nodes
N3	Metastasis in seven or more regional lymph nodes
N3a	Metastasis in 7–15 regional lymph nodes
N3b	Metastasis in 16 or more regional lymph nodes
Distant Metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis
Histologic Grade (G)	
GX	Grade cannot be assessed
G1	Weil differentiated
G2	Moderately differentiated
G3	Poorly differentiated
G4	Un differentiated

Anatomic	Stage/prognostic		Groups
Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T2	N0	M0
	T1	N1	M0
Stage IIA	T3	N0	M0
	T2	N1	M0
	T1	N2	M0
Stage IIB	T4a	N0	M0
	T3	N1	M0
	T2	N2	M0
	T1	N3	M0
Stage IIIA	T4a	N1	M0
	T3	N2	M0
	T2	N3	M0
Stage IIIB	T4b	N0	M0
	T4b	N1	M0
	T4a	N2	M0
	T3	N3	M0
Stage IIIC	T4b	N2	M0
	T4b	N3	M0
	T4a	N3	M0
Stage IV	Any T	Any N	M1

[a]A tumor may penetrate the muscuiaris propria with extension into the gastnocolic or gastrohepatic ligaments, or into the greater or lesser omentum, without perforation of the visceral peritoneum covering these structures. In this case, the tumor is classified T3. If there is perforation of the visceral peritoneum covering the gastric ligaments or the omentum, the tumor should be classified T4

[b]The adjacent structures of the stomach include the spleen, transverse colon, liver, diaphragm, pancreas, abdominal wall, adrenal gland, Kidney, small intestine, and netroperitoneum

[c]Intramural extension to the duodenum or esophagus is classified by the depth of the greatest invasion in any of these sites, including the stomach

[d]A designation of pN0 should be used if all examined lymph nodes are negative, regardless of the total number removed and examined

correct specialist for preoperative evaluation and surgical clearance, as necessary. These evaluations and interventions carry out the POSH clinic's intention to integrate care plans and communications between various providers; reconcile best practices; standardize care; diminish delirium, length of stay, ICU admission, and readmission; and improve rate of and rescue from complications of the patient and caregiver satisfaction and discharge destination.

Gastrectomy for a surgical cure is the optimal goal for gastric cancer treatment but may carry significant morbidity and mortality [39]. In an analysis utilizing the American College of Surgeons (ACS) National Surgical Quality Improvement (NSQIP) database, 23.6% of patients undergoing gastrectomy for gastric cancer suffered serious morbidity and 30-day mortality was 4.1%. Mean age in this patient population was 66 years old, and age was an independent predictor of serious morbidity and 30-day mortality on univariate and multivariate analyses.

As the surgical procedure for treating gastric cancer carries a high risk for morbidity and mortality in a patient population that is often frail and deconditioned, geriatric assessments can be utilized to help refine treatment decisions for these patients. A recent publication demonstrated the utility of a multidimensional frailty score to more accurately predict a 1-year all-cause mortality in elderly patients ($\geq$ 65 years of age) undergoing intermediate-risk or high-risk elective operations than the American Society of Anesthesiologists (ASA) classification [33]. This frailty score was generated on multiple domains: Charlson Comorbidity Index (CCI), dependence in activities of daily living, dependence in instrumental activities of daily living, dementia, risk of delirium, short mid-arm circumference, and malnutrition [33]. Tools such as these hold great promise in better assessing surgical risk and better informing patients considering major surgical procedures.

Comprehensive geriatric assessments (CGAs) have been demonstrated to better assess surgical risk in gastrectomy patients. A recent publication from MD Anderson Cancer Center reported their experience utilizing preoperative geriatric assessments [29]. Patients were assessed on the following variables preoperatively within 30 days: falls within the last month, pain scores (0 vs. $\geq$1), use of assistive devices, activity level of Eastern Cooperative Oncology Group (ECOG) performance status, ASA presurgical fitness score, CCI, polypharmacy ($\geq$5 daily medications), weight loss $\geq$10% in the past 6 months, and albumin level $\leq$ 3.3 g/dL. In this study, they demonstrated that CGA variables such as pain score, ECOG performance status >0, and polypharmacy were independently associated with major morbidity on multivariate analysis in patients undergoing gastrectomy.

CGAs may also help predict long-term complications in patients undergoing gastrectomy. One recent publication investigated whether the Study of Osteoporotic Fractures (SOF) frailty index could predict readmission within 1 year [40]. In their study patients classified preoperatively as “pre-frail and frail” had a readmission rate of 19.1% versus those patients categorized preoperatively as “robust” with a readmission rate of 6.7%.

With the use of the comprehensive geriatric assessments (CGAs), practitioners have the opportunity to identify areas of need and can utilize a multidisciplinary approach to optimize patient outcomes. CGAs hold promise in decreasing in hospital complications as well as anticipating and decreasing complications post-discharge. Specific recommendations have been established by the American College of Surgeons National Surgical Quality Improvement Program and the American Geriatrics Society and were recently published [32].

Surgery

Long-term survival in patients with gastric cancer is only achievable with surgical resection. Resection goals include margin-negative resection and appropriate lymphadenectomy. Endoscopic resection may be a suitable alternative for T1a lesions, and this recommendation is supported by ESMO and NCCN guidelines [5, 16]. Lymph node positivity in this group is nearly zero. Endoscopic resection techniques include endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD). Guidelines limit Local Excision to lesions $\leq$2 cm in diameter, well or moderately well differentiated on biopsy, does not exhibit lymphovascular invasion and has clear lateral and deep margins. EMR/ESD should only be performed by experienced endoscopists. The presence of any of these high-risk features after resection should also mandate interval formal gastrectomy and lymphadenectomy.

For stage Ib–III tumors, gastrectomy should be performed. In general, location of tumor dictates resection strategy. Recommended gross luminal margins are 4–5 cm proximally [2, 5, 16]. For diffuse cancers, a margin of 8 cm is advocated

[5]. For this reason, proximal tumors (about 50% of all gastric carcinomas) and midbody tumors (15–30%) require total gastrectomy. More distal tumors (approximately 35% of all gastric carcinomas) may be managed with partial/subtotal gastrectomy. T4 lesions may require en bloc resection of involved structures.

Surgeons should routinely freeze the proximal margin. The surgeon should discretely document completeness of resection:

R0: no residual gross disease and negative microscopic margin
R1: microscopic residual disease only
R2: gross residual disease

Lymphadenectomy

The role of lymphadenectomy in the management of surgically resectable gastric cancer remains controversial. In the current parlance, investigators typically utilize the following classification to describe the extent of lymphadenectomy:

D1: removal of perigastric lymph nodes (within 3 cm of primary tumor)
D2: D1 plus clearance of celiac, common hepatic, splenic, and left gastric lymph nodes
D2+: D2 plus omentectomy, splenectomy, and distal pancreatectomy and clearance of porta hepatis and periaortic lymph nodes.

The Japanese have long advocated at least D2 resection. This recommendation stems from the original report by Kodama et al. in 1981 [41]. In patients undergoing curative attempt resection, a 5-year survival in patients with extensive regional node dissection was 45% compared to 18% in patients undergoing simple resection alone. In node-positive patients, a 5-year survival advantage was maintained at 39% versus 18%. Extensive node dissection included all perigastric lymph nodes (D1) in addition to left gastric artery, common hepatic artery, celiac artery, and splenic artery (D2), including splenic hilum, hepatic pedicle, retropancreatic, mesenteric root, middle colic artery, and para-aortic stations (D2+ or D3).

Though clearly D2 dissection leads to more accurate staging, this technique's contribution to improved survival remains controversial, and these results have not been reproduced reliably in the Western world and widespread adoption has been resisted in Western countries.

The Dutch Gastric Cancer Trial randomized 711 patients with resectable gastric cancer to a D1 dissection versus D2 dissection [42–44]. D2 dissections were performed by nine surgeons trained in D2 dissections by Japanese experts. Morbidity (25% vs. 43%) and mortality (4% vs. 10%) were significantly higher in patients undergoing D2 dissection. Notably, in this study, D2 dissection included distal pancreatectomy and splenectomy. After 11 years, there was no statistical difference in survival (30% vs. 35%, $p = 0.53$). However, a 15-year follow-up ultimately demonstrated a survival difference. A 15-year survival was 21% (82 patients) in D1 versus 29% (92 patients) in D2 patients.

Similarly, the Medical Research Council (MRC) Gastric Cancer Surgical Trial randomized D1 versus D2 resections for patients with resectable gastric cancer [45]. Again, routine pancreaticosplenectomy was routinely included in the D2 resection. There was no difference in a 5-year survival between the two groups (35% vs. 33%).

Finally, the Italian Gastric Cancer Study Group performed a randomized trial of D1 versus D2 resection [46]. Due to the evolution in many centers of abandoning routine pancreaticosplenectomy as part of D2 dissection, this trial did not include routine resection of distal pancreas and spleen, but rather incorporated only when suspected to be directly invaded by gastric cancer. In this study, operative morbidity was similar. Again, there was no difference in a 5-year survival between the two groups (66.5% vs. 64.2%, D1 vs. D2, $p = 0.695$). A subgroup analysis did suggest a possible benefit to D2 dissection in patients with more advanced disease.

These studies have all been somewhat criticized for quality control in the D2 dissection groups. For these reasons, ESMO guidelines do recommend D2 dissection for medically fit patients, and the recommendation is that patients should undergo these procedures in specialized, high-volume centers [5]. Routine pancreatico-splenectomy is no longer advocated.

In the United States, given the technical expertise required to perform routine D2 dissection and the controversy regarding its impact on patient survival (stage migration rather than true impact on survival), NCCN recommends a minimum of 15 nodes evaluated at the time of gastrectomy and the current AJCC staging system supports these guidelines (Tables 1 and 2) [16]. This recommendation is supported by a large analysis by Schwarz et al. [47]. Utilizing the SEER 1973–2000 database to evaluate outcomes from 1377 patients who underwent gastrectomy, these investigators identified a significant cut point in survival for patients with a minimum of more than 15 lymph nodes examined.

As the guidelines state, surgeons should perform "gastrectomy with D1 or a modified D2 lymph node dissection, with a goal of examining at least 15 if not more lymph nodes" [16]. In practice, reliably obtaining >15 lymph nodes requires technical skill beyond a D1 dissection alone, and practitioners performing gastrectomy for gastric cancer should pursue D2 dissection. The NCCN also emphasizes that these dissections should be performed by experienced surgeons in high-volume centers.

Table 2 Perioperative Optimization of Senior Health

Recommended evaluations specific to frailty assessment	Improving postoperative outcomes
Orthostatic vital signs	Communication between all providers and patient/family
Nutritional assessment	Preoperative optimization of physical performance and nutrition, other comorbid conditions
Mental status exam	Use of hearing, vision, and ambulatory aids
Physical performance exam	Limit pre- and postoperative high-risk medications
Medications/substances at high risk for delirium	Pain control with multimodality, nonnarcotic medications
Aids for hearing, vision, ambulation	Sleep cycle optimization

Minimally Invasive Surgery

Over the last decade, minimally invasive approaches to gastrectomy have emerged as a promising technique to decrease morbidity while maintaining important oncologic principles. Several randomized trials in the East have been conducted, but high-quality Western studies are rare and small. For example, an Italian group randomized only 59 patients with resectable, distal gastric cancers [48] to open subtotal gastrectomy ($n = 29$) versus laparoscopic subtotal gastrectomy ($n = 30$). Lymph node retrieval was similar between groups. Operative mortality rates were low overall (two patients vs. one patient). Operative morbidity was similar (27.6% vs. 26.7%). A 5-year overall survival was 55.7% in the open group versus 58.9% in the laparoscopic ($p = \text{NS}$).

Scattered high-volume centers in the United States have begun to demonstrate the feasibility of minimally invasive gastrectomy for gastric cancer. A recent single-institution analysis from Kelly et al. compared outcomes from 87 consecutive patients undergoing laparoscopic gastrectomy to 87 patients undergoing open resection during that same time period [49]. Patients were matched by age, stage, body mass index (BMI), and procedure (subtotal vs. total). Operative time was longer in the laparoscopic group but was associated with less blood loss. Microscopic margin positivity was higher in the laparoscopic group (9% vs. 1%). Lymph node retrieval was similar (median of 20). Postoperatively, laparoscopy was associated with decreased use of narcotics and epidural, decreased minor complications, decreased length of stay, and increased likelihood of receiving adjuvant therapy. Major morbidity and 30-day mortality were similar.

In all likelihood, large robust clinical trials in the United States will be difficult to perform, and reliance upon the experience of these high-volume centers will lead surgeons to an appropriate understanding of the role. Almost certainly, as has been demonstrated in other gastrointestinal oncologic surgeries, minimally invasive techniques, when appropriately applied, provide equivalent oncologic outcomes while providing advantages in postoperative recovery.

However, it is critical to understand that, unlike other high-volume malignancies such as colorectal cancer where oncologic equivalence has been demonstrated with laparoscopic techniques, the challenge of low patient volume is unique to surgeons performing gastrectomy for gastric cancer in the United States. In a recent editorial, Strong points out that in a recent high-quality Eastern report, 42 cases were required before surgeons achieved equivalence with lymph node retrieval, complication rate, and outcomes [50]. In general, she notes that it is likely that 50–60 laparoscopic gastrectomies are necessary to achieve proficiency [51]. For gastric cancer in the United States, few centers can achieve this learning curve and the appropriate strategy for adoption is unclear.

Staging

Following gastrectomy, patients can be assigned a formal pathologic stage.

Overall, outcomes are dictated by pathologic stage. According to contemporary SEER data, 5-year survival outcomes by stage are as follows [9]:

IA – 71%
IB – 57%
IIA – 46%
IIB – 33%
IIIA – 20%
IIIB – 14%
IIIC – 9%
IV – 4%

Outcomes in the Elderly

Stage-by-stage survival rates do not necessarily capture the difficulty of predicting outcomes in elderly patients. Efforts to better understand surgical outcomes in the elderly include nomogram strategies. For instance, the Memorial Sloan Kettering Cancer Center group published a nomogram in 2003 predicting disease-specific survival in patients undergoing surgical resection [52]. Of note, these predicted outcomes did not incorporate the impact of perioperative chemotherapy or radiation therapy, but instead predicted outcomes for patients undergoing complete surgical resection. Predictive factors included age, tumor size, sex, tumor location, Lauren classification, T stage, and the number of positive and negative lymph nodes. In this model, increasing patient age is a potentially more powerful predictor of patient outcome than sex, Lauren classification, tumor size, or tumor location.

Historically, surgical outcomes in the elderly were considered quite poor, and many patients did not undergo attempted resection. In an analysis of an English registry from 1957 to 1981, less than 20% of patients over age 80 years underwent surgical resection and resection rates in 70–79 year olds were still only 25% [53]. Similarly, a Dutch registry analysis from 1982 to 1992 demonstrated resection rates of 54% for 70–79-year-olds versus only 35% for 80+ –year-olds [54]. Over time, as perioperative care has improved and the understanding of geriatric physiology has improved, resection rates have increased and have begun to approach rates in other age cohorts.

In addition, elderly patients may not undergo resections which adhere to recommended oncologic principles, thus potentially compromising their oncologic outcomes. A recent SEER analysis addressed this question for patients ≥65 years old undergoing gastrectomy for gastric cancer [55]. In this analysis, though 61% of the patients undergoing resection were elderly patients, less than 30% of patients in this cohort underwent appropriate lymphadenectomy (≥ 15 lymph nodes examined). Older age was also associated with worse cancer-specific mortality, especially in proximal gastric cancers.

Investigators have also looked at outcomes in octogenarians, sometimes called the super-elderly. In a recent Japanese report, though 80+ –year-olds had significantly more comorbidities (74.7% vs. 49.5%) than a matched 60–69-year-old cohort, postoperative complication rate was equivalent (23.2% for each group) [56]. However, initiation of adjuvant chemotherapy was markedly less

(9.5% versus 29.0%) in the super-elderly group. And finally, disease-specific survival (DSS) was worse for super-elderly patients with stage II and stage III disease.

A recent National Surgical Quality Improvement Program (NSQIP) publication again highlights some of the differences seen between Eastern and Western experiences. Teng et al. evaluated all patients undergoing gastrectomy for malignancy in the 2005–2011 dataset [57]. Octogenarians had higher 30-day mortality (7.2% vs. 2.5%, $p < 0.01$) and higher complication rates despite fewer undergoing total gastrectomy (24.0% vs. 43.2%, $p < 0.01$) and extended lymphadenectomy (10.1% vs. 17.4%, $p < 0.01$). Again, these poorer outcomes in Western series may be related to increased frailty in Western patients or may represent high-volume experience in Eastern countries.

Advances in minimally invasive techniques hold promise for reducing perioperative morbidity for elderly patients undergoing gastrectomy. As mentioned earlier in this chapter, much of this work has been published in the Eastern literature, where gastric cancer is more common. A recent meta-analysis of Eastern studies comparing laparoscopic and open outcomes in elderly patients undergoing gastrectomy showed less intraoperative blood loss, earlier time to first ambulation, earlier oral intake, shorter postoperative hospital stay, and few postoperative complications with no significant difference in lymph node retrieval [58]. Other analyses have demonstrated similar findings [59]. Clearly, these endpoints may be disproportionately influential in a patient population that is more frail and less resilient.

Perioperative Locoregional and Systemic Therapy

Despite advances in preoperative staging, surgical technique, and perioperative care over the past few decades, the majority of patients with a diagnosis of gastric cancer will die from this disease. As stated previously, the overall relative survival rate in the United States is 29%, regardless of stage. In patients with resectable disease, overall survival remains well less than 50%. For this reason, continued progress with locoregional and systemic therapies is critical.

Preoperative Chemoradiation Therapy

Several institutions in the United States have favored preoperative chemoradiation strategies. In a critical pilot study, Lowy et al. reported on the feasibility of a preoperative chemoradiation pilot study [60]. In this study, 24 patients were administered 45 Gy of external beam radiotherapy with concurrent 5-FU with plans for interval surgical resection. Twenty-three patients completed the planned chemoradiotherapy protocol. Nineteen of 23 (83%) patients underwent interval surgical resection. Reported morbidity and operative mortality rates were 32% and 5%, respectively. Fourteen of 19 patients had some pathologic evidence of treatment effect, including two patients with complete pathologic response.

To date, there is no level 1 evidence for the benefit of preoperative chemoradiation therapy in patients with true gastric cancer, only extrapolation from studies in resectable adenocarcinoma of the esophagus, inclusive of gastric cardia tumors. Currently, there is an ongoing randomized trial by the Australasian Gastrointestinal Trials Group evaluating this question (Trial of Preoperative Therapy for Gastric and Esophagogastric Junction Adenocarcinoma [TOPGEAR] trial) (ClinicalTrials.gov Identifier NCT01924819). In this trial, patients are randomized to preoperative chemotherapy, preoperative chemoradiotherapy, surgery and postoperative chemotherapy versus preoperative chemotherapy, and surgery and postoperative chemotherapy. The perioperative chemotherapy regimens include epirubicin + cisplatin +5-fluorouracil (ECF chemotherapy), and the radiotherapy arm includes 45 Gy of radiation in 25 fractions. This trial is currently recruiting and will be an important advance in understanding optimal treatment of patients preoperatively. Currently, preoperative chemoradiation therapy carries a category 2B recommendation by the NCCN for resectable patients with T2 or higher, any N disease [16]. ESMO guidelines do not include preoperative chemoradiation in its recommended treatment algorithms [5].

Adjuvant Chemoradiation Therapy

The landmark Southwest Oncology Group (SWOG) 9008/INT-0116 trial provided level 1 evidence for the benefit of postoperative chemoradiation in patients with resectable gastric or GEJ tumors [61]. In this trial, 556 patients with resected adenocarcinoma of the stomach or GE junction were randomly assigned to surgery plus chemoradiotherapy ($n = 281$) versus surgery alone ($n = 275$). Adjuvant therapy included 5-fluorouracil (FU) and leucovorin (LV) plus 45 Gy of radiation therapy followed by 5-FU/LV. Median overall survival in the surgery-only group was 27 months versus 36 months in the chemoradiotherapy group ($p = 0.005$). Three-year OS (50% vs. 41%) and RFS (48% vs. 31%) were also improved in the chemoradiotherapy group.

This trial has several limitations. It has been criticized for poor standardization of surgical therapy. Though a D2 dissection was recommended, only about 10% received a D2 dissection. Only 36% underwent formal D1 dissection. Thus, the majority of patients (54%) underwent less than a D1 dissection. In addition, only 64% of patients ($n = 181$) completed their planned treatment in the chemoradiotherapy group. Reasons for incomplete treatment included toxicity (17%), patient declined further treatment (8%), disease progression (5%), death (1%), and others (4%). Despite these shortcomings, this trial has established postoperative chemoradiation therapy as an important regimen in patients who have not received preoperative therapy.

It should also be noted that though the Intergroup trial established a role for adjuvant chemoradiation therapy in patients with resected gastric cancer, the toxicity was significant. Currently, regimens typically include infusional fluorouracil or oral capecitabine. In addition, the benefit of adjuvant radiation for patients with T2 disease remains controversial. Finally, the role of adjuvant radiation therapy remains controversial for patients who have undergone D2 dissection. The ongoing phase III Adjuvant Chemoradiotherapy in Stomach Tumors-II (ARTIST-II) trial (ClinicalTrials.gov Identifier NCT01761461) may help answer this question. In this trial, patients with true gastric cancer or GEJ cancers who have undergone at least D2 dissection are randomized to one of the three arms: adjuvant S-1, adjuvant S-1 + oxaliplatin, or adjuvant S-1 + oxaliplatin, then chemoradiation (45 Gy), and then S-1 + oxaliplatin. This trial is currently recruiting.

Currently, the NCCN recommends an adjuvant regimen which includes chemoradiation for all patients who have not undergone preoperative therapy and who have undergone an R1 or R2 resection. In addition, in those patients with no preoperative therapy and an R0 resection, a chemoradiation-based regimen is recommended in T3 or T4, any N patients who have not undergone primary D2 dissection (chemotherapy alone is considered sufficient for these patients) [16]. ESMO guidelines also support adjuvant chemoradiation but similarly note that benefit likely accrues to primarily patients who have undergone incomplete lymph node dissection [5].

Perioperative Therapy

Another critical landmark trial establishing the role of systemic chemotherapy in the management of resected gastric cancer was the MAGIC trial conducted by the British Medical Research Council [62]. In this trial, patients with resectable adenocarcinoma of the stomach, GEJ, and lower esophagus were randomized to either perioperative chemotherapy with surgery ($n = 250$) or surgery alone ($n = 253$). Of note, only 74% of the patients in this trial were true gastric cancers. Chemotherapy consisted of three cycles of preoperative and three cycles of postoperative ECF. Again, in this trial, systemic therapy carried significant toxicity. Only 104 of 250 patients (41.6%) completed all six cycles of perioperative chemotherapy. Primary endpoint was overall survival. A 5-year OS was 36% in the perioperative chemotherapy group and 23% in the surgery-alone group.

This trial has similarly been criticized similarly for surgical technique. As reported, less than one-third of the patients underwent D2 dissection.

Currently, ESMO guidelines consider perioperative chemotherapy the "preferred pathway" for patients with >T1 disease [5]. The NCCN considers perioperative chemotherapy a category 1 recommendation for patients with T2 or higher, any N disease though up-front surgery is still considered an option, along with preoperative chemoradiation (category 2B, previously discussed) [16].

Adjuvant Systemic Therapy

Typically, for patients with resected T1 disease, adjuvant chemotherapy is not offered. There was no benefit demonstrated in a large randomized trial from Japan evaluating adjuvant mitomycin and fluorouracil [63].

In patients with T2 or greater disease, the benefit of postoperative systemic chemotherapy alone is best supported in patients who have undergone D2 dissection. In another important Japanese study, 1059 patients with resected stage II (excluding T1) or stage III disease (all patients underwent extended D2 lymph node dissection) were randomized to postoperative S-1 (an oral fluoropyrimidine) ($n = 529$) versus surgery alone ($n = 530$) [64]. The trial was terminated early due to significant difference in outcomes. A 3-year overall survival was 80% in the S-1 group and 70% in the surgery-only group ($p = 0.002$). Of note, S-1 remains an investigational agent in North America.

Another important trial that has helped frame the role of adjuvant systemic therapy was the CLASSIC trial [65]. This trial was conducted in South Korea, China, and Taiwan. In this trial, which again included only patients undergoing gastrectomy with D2 lymph node dissection, 1035 patients with stage II–IIIb disease were randomized following surgical resection to oral capecitabine and oxaliplatin ($n = 520$) versus surgery alone ($n = 515$). The primary endpoint was a 3-year disease-free survival (DFS). A 3-year DFS was 74% in the surgery plus chemotherapy group versus 59% in the surgery-alone group ($p < 0.0001$).

These two large, high-quality randomized Eastern cooperative group trials have clearly established the benefit of adjuvant systemic chemotherapy in patients with at least T2 disease undergoing resection for gastric cancer. Of note, in patients who do not undergo D2 dissection, current guidelines recommend adjuvant regimens that include radiation therapy [16]. ESMO guidelines also recommend caution in applying these results in Western countries, noting that perioperative chemotherapy regimens remain the preferred strategy, given the increased difficulty for patients to tolerate adjuvant therapy versus neoadjuvant therapy [5]. This issue may be especially notable for elderly patients undergoing gastrectomy.

Clinical Trials in the Elderly

Despite high-level evidence regarding the survival benefits of perioperative therapy for resected gastric cancer, it is well known that elderly patients are underrepresented in clinical trials and the applicability of the results from these trials to the elderly may not be fully known. In an analysis of the participation of elderly patients in clinical trials sponsored by the National Cancer Institute (NCI) from 1997 to 2000, investigators found that the elderly comprised only 32% of participants in phase II and phase III cancer clinical trials, despite comprising 61% of patients with newly diagnosed cancers in the United States [66]. Similarly, in an analysis of patients enrolled in SWOG treatment trials between 1993 and 1996, patients aged 65 years or older represented only 25% of trial participants [67].

In a recent SEER analysis of elderly patients undergoing gastrectomy for gastric cancer, older patients were less likely to undergo recommended radiation therapy [55]. In this analysis, patients older than 65 years of age received indicated adjuvant radiation therapy only 23% of the time. Much of the data regarding strategies for systemic therapies in the elderly come from trials in advanced gastric cancer originating in the Eastern literature.

Xiang et al. assessed the efficacy and safety of oxaliplatin plus oral capecitabine (XELOX) as a first-line regimen in 46 patients aged $\geq$70 years in a recent publication from China [68]. A median of six cycles was administered, and the overall response rate was nearly 50%. The investigators concluded that toxicities were well tolerated: grade 3 toxicities included neutropenia (6.5%), thrombocytopenia (2.2%), nausea (2.2%), vomiting (4.3%), diarrhea (4.3%), and peripheral neuropathy (2.2%). No grade 4 toxicities were reported.

Lee et al. performed a randomized phase II study from Korea on 91 patients comparing oral capecitabine versus S-1 as first-line treatment in elderly patients [69]. In this study, response rates were 27–28%. Toxicities included granulocytopenia, asthenia, anorexia, diarrhea, and hand-foot syndrome. Toxicity rates were similar between groups and less than 10% overall.

In a recent Italian study, Catalano et al. evaluated the efficacy and safety of 43 elderly patients ($\geq$ 70 years) undergoing a modified FOLFOX regimen for advanced gastric cancer [70]. In this phase II study, overall response rate was 35%. Toxicities included grade 3 neutropenia, fatigue, vomiting, and peripheral neuropathy – again, primarily less than 10%. No treatment-related deaths were seen.

A recent meta-analysis from the United Kingdom pooled data from three clinical trials evaluating chemotherapy for patients with locally advanced or metastatic cancer of the esophagus, GEJ, and stomach [71]. Outcomes were compared between patients $\geq$70 years and those younger. In this analysis of 1080 patients, there were no significant differences between the groups in grade 3 or 4 toxicities. Response rates and survival were also not significantly different between groups, and age was not an independent predictor of outcome. However, low performance status did predict worse outcome. This analysis is a compelling challenge to the traditional nihilism associated with treating elderly patients with gastric cancer, based on age alone.

Advanced Disease

Outcomes in patients with metastatic disease are poor, in any age cohort, ranging from 4 to 12 months. However, in patients with advanced disease, systemic chemotherapy has been demonstrated to prolong survival and improve quality of life. This understanding of the potential palliative benefit of systemic chemotherapy is critical when considering therapeutic options for the elderly patient.

The cytotoxic agents which have demonstrated the most activity against advanced gastric cancer include fluoropyrimidines, platinums, taxanes, epirubicin, and irinotecan [2]. Most of the response rates are around 20% with single-agent use. A recent large Cochrane review concluded that combination chemotherapy demonstrates survival benefit over best supportive care (8.3 months vs. 6.7 months) and also compared to single-agent 5-FU [72]. In general, the most commonly used first-line chemotherapy regimen in metastatic gastric cancer is a combination of a fluoropyrimidine with a platinum. The role of triplet regimens is controversial.

As stated previously, systemic chemotherapy for advanced gastric cancer has also been shown to improve quality of life [73]. In an important study conducted in Sweden, investigators randomized 61 patients with advanced gastric cancer to best supportive care versus best supportive care plus systemic chemotherapy (ELF regimen: 5-fluorouracil, leucovorin, and etoposide). Quality of life was evaluated utilizing the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ)-C30 instrument. In this trial, more patients in the chemotherapy group reported improved or prolonged high quality of life for a minimum of 4 months. A similar difference was noted subjectively by the treating physician evaluation.

Currently, ESMO guidelines recommend doublet or triplet platinum/fluoropyrimidine combinations as first-line therapy for advanced gastric cancer.

Targeted Therapies

To date, trastuzumab and ramucirumab are the only two targeted agents approved for the treatment of advanced gastric cancer.

Overexpression of HER2-neu is observed in 10–15% of gastric cancers [5]. Currently, the NCCN recommends assessment of HER2-neu overexpression in patients with inoperable locally advanced, recurrent, or metastatic disease. ESMO guidelines currently recommend assessment of HER2-neu overexpression in patients with metastatic disease (level 1 recommendation).

These recommendations emerged from the Trastuzumab for Gastric Cancer (ToGA) trial [74]. In this trial, 594 patients with HER2-positive (3+ on immunohistochemistry or FISH-positive) advanced gastric or GEJ cancers were randomized to trastuzumab plus chemotherapy (fluorouracil or capecitabine and cisplatin) versus chemotherapy alone. The majority of patients (>80% in each group) had true gastric cancer. This phase III trial demonstrated statistically significant improvements in response rate, progression-free survival (PFS), and overall survival (OS) (13.8 vs. 11.1 months, $p = 0.046$) with the addition of trastuzumab to systemic chemotherapy [74]. This trial represents one of the first meaningful advances in targeted therapy for advanced gastric cancer.

Ramucirumab, a VEGFR-2 antibody, has demonstrated a survival benefit in two randomized trials as a second-line agent over best supportive care alone [75, 76]. In the REGARD trial, a randomized phase III trial conducted in 29 primarily Western countries, 355 patients with advanced gastric cancer and disease progression on first-line therapy were randomized to ramucirumab versus best supportive care [75]. In this trial, median survival was 5.2 months in the treatment group versus 3.8 months in the placebo group.

In the RAINBOW trial, a randomized phase III trial conducted in 27 countries, 665 patients with advanced gastric cancer who had progressed on first-line therapy were randomized to paclitaxel plus ramucirumab versus paclitaxel alone [76]. Overall survival was significantly longer in the ramucirumab plus paclitaxel group than the paclitaxel group alone (9.6 months vs. 7.4 months).

These trials highlight significant advances being made in personalized treatment strategies and novel agents for patients with advanced gastric cancer. The favorable toxicity profiles of many of these agents are well suited to the geriatric population.

Palliative Surgery

Palliation in advanced gastric cancer may involve resection, bypass, or both. Though partial gastrectomy may be performed with reasonable morbidity, caution should be exercised when considering palliative total gastrectomy. In an analysis of palliative gastrectomy in patients with gastric cancer from Memorial Sloan Kettering Cancer Center, reasons for palliative resection included bleeding (20%), obstruction (43%), pain (29%), unexplained weight loss (4%), and others (4%) [77]. About 20% of these palliative patients underwent total gastrectomy. Of note, patient age > 65 years was an independent predictor of worse outcomes.

Since this important publication, continued advances have been made in nonsurgical strategies for palliation. Patients with bleeding may be palliated by endoscopic or embolization strategies. These strategies include injection therapy, endoscopic clip placement, ablative therapy, or angiographic embolization. External beam radiation therapy may also be effective. Obstruction may be relieved with endoscopic stenting. Pain may be controlled through radiation therapy or pharmacologic means. These other modalities should be explored thoroughly before subjecting the patient to the greater morbidity of surgical resection.

Future Directions

Given the relatively low incidence of gastric cancer in Western countries, it is unlikely that widespread endoscopic screening programs will be adopted. Therefore, earlier detection of gastric cancer remains a challenge. Certainly, the promise of serum biomarkers is an intriguing and less invasive strategy. Noninvasive methods of detection such as protein and nucleic acid tumor markers, circulating tumor cells, and tumor-associated autoantibodies in peripheral blood have shown promise but remain far from widespread clinical application [78].

Though traditional classification systems such as the Lauren and WHO have provided useful prognostic information, they have essentially had little impact in guiding therapeutic decision-making. The promise of a more robust molecular classification, such as the recent efforts by The Cancer Genome Atlas (TCGA) Research Network, will provide molecular insights for better tumor targeting [19].

With these advances, targeted therapies will also be increasingly utilized. As discussed previously, trastuzumab has been shown to improve median overall survival in patients with HER2-positive advanced gastric cancer [74] and is approved as a first-line therapy for patients with HER2-positive advanced gastric cancer. Targeted therapies also hold promise as less toxic alternatives to traditional cytotoxic chemotherapeutics, an especially crucial issue in the elderly population, a population that is more often frail with decreased performance status.

Advances in minimally invasive techniques, including the emergence of robotic technologies, and the more widespread adoption of these techniques will also decrease morbidity associated with surgical resection. In Western countries, increased emphasis on appropriate lymphadenectomy will also be critical for accurate staging and optimal oncologic outcomes.

Finally, in addition to better characterization of tumors and more precise targeting of tumors with systemic therapy, better "targeting" of patients will also be necessary. Gastric cancer is a disease that predominantly impacts the elderly. Strategies for "prehabilitation" and better risk characterization will provide providers and patients with the tools to make better decisions about which patients will benefit from the spectrum of available treatment options.

Conclusion

As the worldwide population continues to age, the global burden of cancer will continue to increase. Though the age-adjusted incidence of gastric cancer has demonstrated an overall decline, the absolute incidence is increasing due to global aging. Appropriate management of elderly patients with gastric cancer will be critical to enhance longevity, optimize quality of life, and decrease the burden that these patients will have on healthcare systems.

Clinical Vignette 1

An 84-year-old physician with a history of an appendectomy and glaucoma, status post corneal transplant, was under endoscopic surveillance for gastritis and mucosal abnormalities over the previous 2 years. His only notable family history was paternal colon cancer at 75 years of age, and he had no personal tobacco or alcohol use history. Biopsies were negative for malignancy as late as 1 month prior to presentation, but on computed tomography (CT) scan, he was found to have antral thickening with corresponding hypermetabolic activity on positron emission tomography (PET). He did endorse early satiety around this time. Further workup with endoscopic ultrasound and biopsy revealed Her2-negative linitis plastica. A D2 total gastrectomy with Roux-en-Y reconstruction was then performed, yielding a diagnosis of signet ring cell carcinoma that was microsatellite stable. It involved the entire stomach and 41 of 42 lymph nodes.

He completed 6 months of adjuvant chemotherapy but 2 months later presented with large bowel obstruction from extrinsic compression of the hepatic flexure (Fig. 5). On laparotomy, a mass in the right upper quadrant adherent to the flexure,

Fig. 5 CT Imaging demonstrates large bowel obstruction at hepatic flexure secondary to recurrent gastric cancer

as well as adhesions and a perforation distal to the initial jejunojejunal anastomosis, was discovered. Peritoneal nodules and ascites were also encountered, the former of which was consistent with metastasis of the original carcinoma. The perforated bowel, also consistent with metastasis on pathologic examination, was resected and the jejunojejunal anastomosis recreated. The mass encroaching on the colon was unable to be resected and was instead bypassed via diverting loop ileostomy.

During this hospital admission, the patient was first referred to palliative care for pain control alone, but on subsequent hospitalizations (for bacteremia from line infection and biliary obstruction requiring percutaneous biliary drain), discussion of hospice care was introduced to him and his family. He went on to complete a further two doses of chemotherapy, and he survived a month and a half after referral to hospice, 5 months after palliative bypass, and 16 months after the initial resection.

This case highlights one of the significant complications of advanced disease in gastric cancer. Peritoneal carcinomatosis is a common site for metastatic disease. Diagnosis and management of malignant bowel obstruction can be a difficult challenge for clinicians, patients, and their families.

Clinical Vignette 2

A frail 73-year-old man with a complex medical history was diagnosed with gastric adenocarcinoma on esophagogastroduodenoscopy (EGD) for hematemesis. He had a history of tissue valve replacements for endocarditis, non-insulin-dependent diabetes, COPD, and iliac aneurysms. He reported previous tobacco and heavy ethanol use.

He required multiple hospitalizations over the next few weeks for repeated hematemesis, severe anemia, poor oral intake, and cachexia. He finally developed aspiration pneumonia bilaterally, and a non-contrasted CT demonstrated a dilated, fluid-filled stomach and esophagus; an 11 cm distal gastric mass extending to the duodenal bulb; lymphadenopathy in the perigastric, porta hepatis, and aortocaval nodes; liver lesions of uncertain character; and pulmonary emboli of unknown chronicity. A contrasted CT further demonstrated thickening of the antrum (Fig. 6).

After a week of conservative management, an upper endoscopy demonstrated benign-appearing lymph nodes that were not biopsied. He was then taken to operating room for palliative laparoscopic loop gastrojejunostomy, placed a few centimeters proximal to the tumor.

Despite a patent anastomosis on swallow study, he failed to demonstrate oral tolerance, and 2 weeks later, he returned to OR for open subtotal gastrectomy with Roux-en-Y gastrojejunostomy. He was staged T3N3bM1 with poorly differentiated signet ring adenocarcinoma, *H. pylori* negative. There were foci of tumor at the distal and omental margins, 24 of 39 lymph nodes were involved, and an excised umbilical hernia sac was also positive for metastatic tumor.

The rest of his prolonged hospital course was notable for pancreatic leak, acute kidney injury, respiratory failure requiring re-intubation, anemia/bleeding on anticoagulation requiring transfusions, catheter and surgical site infections, and pleural effusion requiring thoracenteses. Once

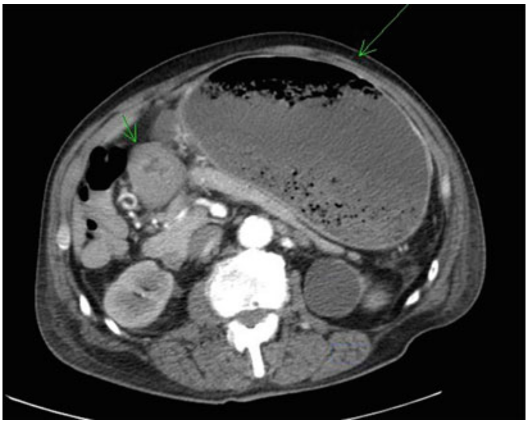

Fig. 6 CT Imaging demonstrates gastric outlet secondary to large gastric antrum malignancy

stabilized 3 weeks after the partial gastrectomy, he was discharged to his local medical oncologist for care.

This case highlights a common problem with gastric cancer in Western countries. Patients frequently present with advanced and symptomatic disease. In this case, the patient presented with gastric outlet obstruction. Despite efforts to palliate this frail, malnourished patient with a lesser operation (from a morbidity standpoint), he ultimately required palliative resection of the tumor.

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Esophageal Cancer in the Elderly

48

Manisha Shende and Neha Reddy

Contents

Abstract

Esophageal cancer is the sixth leading cause of cancer-related mortality and the eighth most common cancer worldwide. In 2016, 16,000 new cases of esophageal cancer were diagnosed in the United States. An increasing number of elderly patients are diagnosed with esophageal cancer and subsequently referred for surgical treatment. Operative management of esophageal cancer in the very elderly still remains a subject of controversy. Even with substantial advances in preoperative risk evaluation, surgical technology, intensive care medicine, and nutritional supplementation, the in-hospital mortality and morbidity associated with esophagectomy remains high when compared to other GI malignancies Begg et al. (JAMA 280:1747–1753, 1998). However, recent studies published from high volume centers are showing that carefully selected elderly patients can undergo esophagectomy with postoperative morbidity and mortality rates similar to those of younger patients.

Keywords

Esophageal cancer · Elderly · Esophagectomy · MIE · Palliation · Stents

Case Studies

Patient 1

Background: 76-year-old female diagnosed with Stage T3 N2 esophageal adenocarcinoma with long-segment Barretts disease extending from 23 cm from incisors. Her comorbid conditions included diabetes, hypertension, hyperlipidemia,

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and history of ongoing nicotine abuse. Preoperative PFTs included FEV1 of 90% predicted and DLCO of 60% predicted. She received neoadjuvant chemotherapy and radiation (45 Gy). Restaging was done with PET scan, diagnostic laparoscopy, and deemed resectable. However, she was very weak and deconditioned and underwent rehabilitation prior to surgery. ECOG score was 2 prior to rehab and 1 afterwards.

Management: She underwent minimally invasive McKeown esophagectomy. She had no surgical complications such as anastomotic leak, bleeding, or recurrent laryngeal nerve injury. She did develop drug resistant pneumonia that required tracheostomy, prolonged ICU stay, and innumerable toilet bronchoscopies. No aspiration could be demonstrated on modified barium esophagram or endoscopy. The conduit was narrow and emptied well. However, she continued to have recurrent pneumonias. She had a hospital stay of 2 months and was still in inpatient rehab 4 months later. CT scan now shows chronic bibasilar fibrotic changes.

This case demonstrates how aspiration and recurrent pneumonia contributes to increased morbidity and potential mortality after an esophagectomy despite careful preoperative evaluation.

Patient 2

Background: 86 year old male was diagnosed with T3 N1 esophageal cancer at an outside institution and treated with definitive chemoradiation. Surgery was not offered due to his advanced age. Unfortunately, 1 year after treatment, at the age of 87, cancer recurred. He was referred for management. He was a healthy man and quite active. Cardiac and pulmonary function testing was within normal limits. Repeat staging showed a T3 tumor.

Management: Patient underwent a minimally invasive Ivor Lewis esophagectomy. Surgery was technically difficult due to extreme fibrotic reaction due to prior radiation. Patient did well but developed a small anastomotic leak which was well contained by the JP drain. He was managed with serial dilations and drain manipulations and leak healed over next 3–4 weeks. Patient had a hospital stay of 3 weeks and was able to be discharged home to a supportive family. His feeding tube was removed at 2 months and patient lived past 90 years of age when he developed malignant pleural effusion and lung metastases.

This case demonstrates that esophagectomy can be accomplished safely in the elderly patient even after radiation treatment, if carefully selected.

Introduction

Esophageal cancer is the sixth leading cause of cancer-related mortality and the eighth most common cancer worldwide. In 2016, 16,000 new cases of esophageal cancer were diagnosed in the United States. It affects 450,000 people worldwide and the incidence is rapidly increasing. Despite trimodality therapy and multidisciplinary approach, the overall 5 year survival ranges from 15% to 25% [1]. Treatment remains challenging and the majority of esophageal cancer cases are diagnosed at advanced stages. Simultaneously, worldwide increase in life expectancy leads to an increased number of elderly patients diagnosed with esophageal cancer and the subsequent referrals for surgical treatment [2]. Based on SEERS database, the median age at diagnosis of esophageal cancer was 67 and most commonly diagnosed among the age group of 65–74 years (Fig. 1) [3].

Squamous-cell carcinoma (SCC) remains the predominant form of esophageal carcinoma worldwide. Countries such as Turkey, northeastern Iran, Kazakhstan, and northern and central China have a very high incidence of esophageal SCC, with more than 100 cases per 100,000 people annually. The incidence of esophageal SCC also remains high in southern and eastern African countries. Tobacco use and alcohol consumption along with low socioeconomic status, poor oral hygiene, and nutritional deficiencies are associated with increased risk of SCC of the esophagus [1].

Over the last few years however, there has been a shift in epidemiology that has been seen in Australia, the UK, the USA, and some western European countries (e.g., Finland, France,

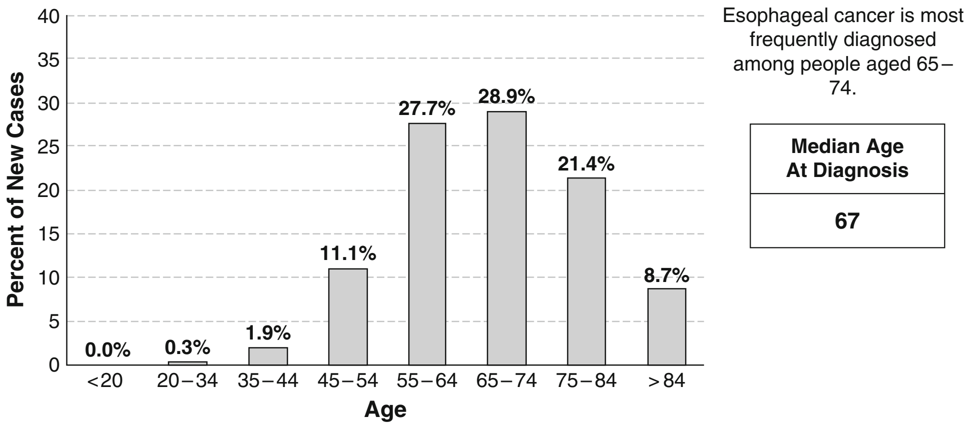


Fig. 1 Percent of new esophageal cancer cases by age group (SEER 18 2009–2013, All Races, Both Sexes)

and the Netherlands), where the incidence of adenocarcinoma now exceeds that of SCC. This major epidemiologic shift is thought to be related to gastroesophageal reflux disease, obesity, and Barrett's esophagus, the dominant risk factors for esophageal adenocarcinoma. The risk of esophageal adenocarcinoma in patients with Barrett's esophagus has been estimated to be in the range of 0.12–0.5% per year. The risk is highest in patients with high-grade dysplasia (HGD) of the esophagus which progresses to adenocarcinoma in 16–59% of patients [1].

According to SEER database, the stages of esophageal cancer at the time of diagnosis are as follows: 20% are localized (confined to the primary site), 31% are regional (spread to regional lymph nodes), 38% have distant spread (metastasis), and 11% are unstaged (Fig. 2). Cancer stage at the time of diagnosis determines treatment options and has a strong correlation to length of survival [4]. Outcomes after treatment of esophageal cancer are suboptimal, with an overall 5-year survival rate of 25.2%; for those in Stage I 94.4%, stage IIa 36%, stage IIb 14.3%, stage III 10%, and stage IV 0% [5].

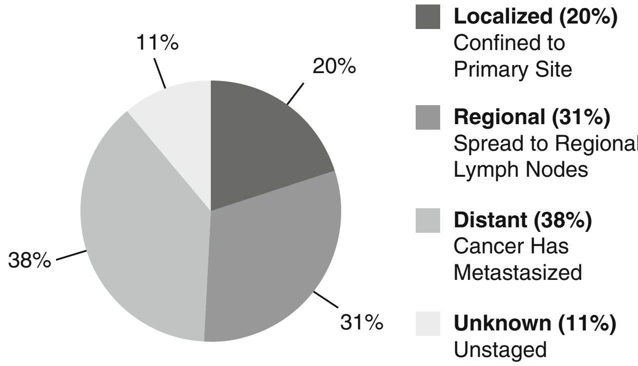
Treatment Options for Esophageal Cancer

Patients with early stage esophageal cancer, staged as T1a lesions, are candidates for endoscopic mucosal resection (EMR) for treatment and potential cure of their disease. T1a lesions have a less than 2% risk of lymph node metastases, making them appropriate candidates for this approach. The incidence of regional lymph node involvement however, increases with the depth of invasion of the cancer; T1b lesions have a reported incidence of 25–30% lymph node involvement. Thus, this group benefits most from surgery with curative intent. Local treatment with EMR in T1b lesions should be considered on a case-by-case basis [6]. Moreover, since the majority of patients present with Stage III cancer, local treatment is a feasible option in only a small number of patients [1, 7].

Operative management of esophageal cancer in the very elderly still remains a subject of controversy. Even with substantial advances in preoperative risk evaluation, surgical technology, intensive care medicine and nutritional supplementation, the in-hospital mortality and morbidity associated with esophagectomy remain high when compared to other GI malignancies [8]. However, recent studies published from high volume centers are showing that carefully selected elderly patients can undergo esophagectomy with postoperative morbidity and mortality rates similar to those of younger patients.

Although there is no well-established cutoff to define a patient as "elderly" for esophageal surgery, 65–75 years has been used for assessing treatment outcome of esophageal cancer in most studies. There are also several studies that examined outcomes in the octogenarians.

Fig. 2 Percent of cases by stage (SEER 18 2006–2012, All Races, Both Sexes by SEER Summary Stage 2000)



Studies examining the relationship of volume and outcome for specific surgical procedures including esophagectomy have demonstrated a consistent improvement in clinical outcomes with increased hospital volumes. High volume center is defined as a hospital doing greater than 20 esophagectomies per year. Analysis of the literature of the last 10 years shows a clear reduction in postoperative mortality with increasing case volumes per year. For a given hospital, an experience of more than 20 esophagectomies per year can lead to a significant reduction of the mortality to 4.9% [9].

It has been demonstrated that when complex surgical oncological procedures are performed in high-volume hospitals (HVHs) with specialty expertise, operative mortality and morbidity is lower [8, 10]. Dimick and colleagues were able to show that pulmonary complications were particularly prevalent at low-volume hospitals (LVHs) [11]. In addition, there is new growing body of evidence to suggest improved patient outcome in high-volume hospitals with specialty expertise irrespective of individual surgeon case volume. Surgeons with appropriate training in esophageal resection may get good results despite lower individual case volumes when a standardized approach is taken in an institution with a high-case volume. In conclusion, to reduce mortality and morbidity of esophagectomy, the procedure should be performed at a high-volume center, by a surgeon who is trained, and where patient care is approached in a multidisciplinary manner. The studies also showed that when complications did occur in HVHs, they were recognized earlier and treated more effectively [12].

There are several different approaches in performing an esophagectomy whether open or minimally invasive: the two main approaches are transhiatal and transthoracic approach. The transthoracic esophagectomy (TTE) approach includes Ivor Lewis esophagectomy, “3-incision” McKeown-type esophagectomy, and lastly, a left thoracotomy or left thoracoabdominal incision. The surgical approach depends on various factors, including the location of the tumor, surgeon preference, and the conduit and route chosen for reconstruction. Large single-institution series have adopted various approaches, but there is no single ideal approach [13].

Visbal and colleagues retrospectively examined 220 consecutive patients from 1992 to 1995 who all underwent an open Ivor Lewis esophagectomy for esophageal cancer. In this study, the operative mortality was 1.4%, and all of the mortalities were secondary to postoperative MI. The overall morbidity was 37.7% and the most common complication being atrial fibrillation at 17.3%, which was followed by pneumonia in 12.3% [5]. Swanson et al. looked at 250 consecutive patients that had undergone a 3-hole esophagectomy. The 30-day mortality was 3.6% (9 patients) with 4 out of 9 patients dying from pneumonia, aspiration, and respiratory failure. The morbidity rate of 33% is similar to the previous study. However, they do report a recurrent laryngeal nerve injury of 14%, which can cause a marked increase in pulmonary problems [14].

Orringer et al. published in 2007 a retrospective analysis of over 2000 transhiatal esophagectomies (THE) performed at a single institution from 1976 to 2006. Orringer observed that the in-hospital mortality, mean blood loss, rate of anastomotic leak, and recurrent nerve injury have significantly decreased overtime. The hospital mortality rate steadily fell as the volume of THE operations increased, averaging 10% from 1978 to 1982 with an average of 23 THE operations annually to 1% since 1998, with more than 100 THE operations annually. Clearly, there has been an evolving refinement in surgical technique and perioperative management of patients undergoing esophageal resection over the years [15].

Lastly, Luketich et al. reported on over 1000 patients who underwent an esophagectomy from 1996 to 2011. MIE-McKeown (neck) was performed in 481 (48%) and MIE-Ivor Lewis (chest) in 530 (52%). The primary approach originally used was a 3-incision McKeown MIE and by 2006 the Ivor Lewis MIE became the preferred approach [16]. In 2002, an additional paper was published from the University of Pittsburgh which specifically looked at mortality and morbidity in 41 patients that were 75 years of age or older [17]. All patients underwent an MIE (neck) from 1997 to 2001 for esophageal cancer. The study showed no increase in incidence of mortality or morbidity in this age group when compared to the younger counterpart.

The overall 30-day mortality, morbidity, and mean age from these studies are listed in Table 1. Mortality rates at high-volume centers ranges from 1% to 3.6%, and mortality rates have improved with time. The reported mortalities are secondary to postoperative MI, progression of respiratory failure, massive aspiration, sepsis, and multiorgan failure from anastomotic leak, ischemic bowel, ischemic conduit, and massive PE. The major morbidity rate, however, is high even at high-volume centers ranging from 17.7% to 37.7%. Major morbidity included in these studies are RLN injury, prolonged respiratory failure, postoperative MI, anastomotic leak, gastric tube necrosis, and chylothorax [5, 14–16].

Each approach to esophagectomy has its own advantages and disadvantages. Patients who underwent THE had shorter duration of surgery and overall less morbidity then compared TTE approach. However, patients that underwent TTE had significantly more lymph nodes resected (improved 5-year disease-free survival, but did not reach statistical significance), better exposure, and safer dissection of the mediastinum [42]. Pulmonary morbidity is increased with TTE approach due to entrance into the chest cavity in addition to the abdominal cavity.

Some recent trials have demonstrated improved survival with neoadjuvant chemoradiotherapy over surgery alone in patients with locally advanced disease. The MAGIC trial randomized 503 patients with gastric or GE junction adenocarcinomas to three cycles each of pre- and postoperative epirubicin/cisplatin/5-FU and surgery alone. There was a significant improvement in overall 5-year survival rate (36% vs. 23%). There were no pathologic complete responders (pCR) in this trial [18]. The low rates of pCRs led to interest in examining the role of radiation combined with chemotherapy in a neoadjuvant fashion. Patients that achieve pathologic complete response consistently achieve increased survival [19]. CALGB trial 9781 randomized patients to two cycles of preoperative cisplatic/5-FU and radiation or to surgery alone. Patients that received neoadjuvant treatment had significantly improved median survival (4.5 vs. 1.8 years) compared with surgery alone [20].

There are several studies looking at differences in outcomes after open versus minimally invasive esophagectomy for the transthoracic approach. Patients who were treated at an academic center or comprehensive cancer facilities were more likely to undergo MIE. Patients who underwent MIE had significantly more lymph nodes examined (15 versus 13; $p = 0.016$) and shorter hospital lengths of stay (10 versus 11 days; $p = 0.046$) but similar resection margin positivity, readmission, and 30-day mortality [21]. MIE was also shown to offer short-term risk reduction in postoperative respiratory complications [22, 23] The TIME trial is the only randomized, prospective, multicenter study comparing traditional transthoracic esophageal resection with minimally invasive resection for esophageal cancer. It was also shown to decrease overall in-hospital incidence of pulmonary infections from 34% to 12%. Thus, MIE can offer a decrease in short-term

Table 1 Outcomes after esophagectomy at four different high-volume centers. Most recent morbidity rates range from 1% to 3.6%; however, the morbidity rates remain high ranging from 17.7% to 37.7%

	Study Date	Surgical Approach	Number of Patients in study	Mean age	Overall 30 day mortality	Morbidity	Anastomotic leak rate	RLN injury	Chylothorax	Gastric Tube Necrosis
Luketich et al	1996-2011	1996-2006 MIE neck (preferred) 2006-2011 MIE chest (preferred)	MIE neck = 481 MIE chest=530 Total 1033	64	0.9% MIE chest 2.5% MIE neck	MIE neck = 32% MIE chest = 17.7%	MIE neck 5% (requiring additional surgery) MIE chest 4% (requiring additional surgery)	MIE neck = 8% MIE chest = 1%	3.90%	MIE neck = 3% MIE chest = 2%
Visbal et al	1992- 1995	Open Ivor Lewis	220	65	1.40%	37.70%	0.9 % (requiring additional surgery) 3.6% (overall leak rate)	0.90%	1.80%	NA
Swanson et al	1989-2000	3-hole	250	62.7	3.60%	33%	5.6% (all treated by simple cervical drainage)	14%	9%	0.80%
Orringer et al	1976-2006	Trans hiatal	1976-1998 group I 1063 1998-2006 group II 944	62	10% (group I) 1% (group II)	24.70%	14% (group I) 9% (group II) 6.46% of all leaks required surgical exploration	7% (group I) 2% (group II)	1%	2%

and 30-day morbidity from a pulmonary standpoint without significant differences in 30-day mortality when compared to an open esophagectomy [22].

Studies have also looked at outcomes after esophagectomy specifically in the octagenerian group. Elderly patients undergo a more detailed risk assessment prior to surgery given that they may have concomitant cardiovascular and respiratory disease [24]. For example, the inclusion criteria for operating on patients greater than age of 80-years-old were performance status score of 0 or 1, normal cardiac function (abnormal EKG findings or LVEF <55% were considered to have cardiac risk), and acceptable pulmonary function (hx of COPD or FEV < 70% were considered high risk for the surgery) in one study. The study reported a morbidity rate of 25% and a mortality rate of 0%, comparable to that of the younger group [25]. However, other studies without such stringent inclusion criteria reported increase in mortality (8.4 versus 3.8%) and morbidity secondary to nonsurgical complications from cardiovascular and pulmonary disease [13, 26]. Octogenarians were found to have significantly more Stage III disease but received less neoadjuvant therapy than younger counterparts and more likely to undergo transhiatal resection as opposed to transthoracic [27]. Other institutions have showed that patients older than 80 years have age-related increased mortality risk after esophagectomy, independent of comorbidity [28].

Atkins et al. retrospectively looked at records of 379 patients who underwent an esophagectomy at tertiary medical centers between 1996 and 2002. This study was performed to identify prognostic variables that might be used to develop a strategy for optimizing outcomes after esophagectomy. Study concluded that increasing age, anastomotic leak, Charlson comorbidity index of 3, worse swallowing scores, and pneumonia were associated with increased risk of mortality by univariate analysis. However, only age and pneumonia were independently associated with mortality by multivariable analysis. Pneumonia was associated with a 20% incidence of death. Patients with pneumonia had significantly worse deglutition and anastomotic integrity on barium swallow compared to patients without pneumonia. This study has identified pneumonia to be the major factor associated with early death after esophagectomy [29].

The decision whether or not to perform an esophagectomy on an elderly patient with esophageal cancer is often difficult to make and encompasses many immeasurable factors. Although cardiovascular complications are more likely to occur in elderly patients, some authors suggested that advanced age alone should no longer be considered a contraindication to esophageal resection or neoadjuvant therapy in carefully selected patients [24, 43]. Esophagectomy in elderly patients can be performed after an accurate preoperative selection based on evaluation of comorbidities.

The risk of pulmonary complications after esophagectomy is higher than after any other common operation including major lung resection. The reasons for this includes entry into two separate body cavities, disruption of bronchial innervation and lymphatic circulation, placement of reconstructive organ in substernal space, cachexia, RLN injury, and discoordinated deglutition [7].

Pulmonary risk after esophagectomy is predicted on the bases of a number of preoperative factors, including patient age, spirometric values, diffusing capacity, performance status, and diagnosis of COPD [40]. Age and spirometry are objective measurements, and performance status is based on clinical observation which can be easily obtained with brief patient interview. A review of the STS database showed that only 40% of the patients that underwent esophagectomy for cancer had preoperative PFTS. Surgeons need to be encouraged to increase the frequency of ordering PFTS to better risk stratify patients [30]. FEV1 < 65% predicted were associated with prolonged mechanical ventilation and length of stay (LOS) in the ICU and hospital [31].

Geriatric surgery patients have physiologic vulnerability requiring assessment beyond the traditional preoperative evaluation of older adults. In addition to cardiopulmonary testing and comorbidity assessment, frailty and disability are two clinical entities that must be investigated prior to any major surgical resection.

Frailty markers include: advanced age, impaired cognitive function, recent weight loss with BMI $<$ 25, unexplained falls, depression, and anemia. Disability defined as loss of independence in activities of daily living should also be assessed in the office setting. The presence of four or more markers of frailty, dependence in one or more activities, and a high burden of comorbid conditions, was related to 6-month mortality with high sensitivity and specificity [32].

Any preexisting swallowing disorders in the elderly should be teased out in the clinical settings, especially since swallowing disorders are a major cause of pulmonary complications. Bartels et al. developed a composite scoring system to predict the risk of esophagectomy, based on quantitative assessment of preoperatively available physiological parameters. The scoring system was reviewed retrospectively on operated patients and was evaluated prospectively. The study concluded that compromised general status, poor cardiac, hepatic, and respiratory functions are independent predictors of a fatal postoperative course [33].

Intraoperative factors such as increased volume of blood loss, length of operation, use of substernal rather than the posterior mediastinal route for esophageal reconstruction, and the routine use of ventilator support rather than early extubation also have an increase in postop pulmonary complications [41]. Postoperatively, good pain management control (use of epidural analgesia), aggressive pulmonary toileting, and use of bronchoscopy to clear secretions are all important to successfully avoid pulmonary complications [7].

They are high risk for aspiration particularly in the early postoperative period when transient diminished airway protection occurs in 47–67% esophagectomy patients. There should be low threshold for postoperative patients to undergo a formal MBS or fiber-optic endoscopic evaluation of swallowing. Aggressive ongoing therapy with speech is recommended for those patients that do have swallowing abnormalities [29].

More than 50% patients will have incurable disease at diagnosis, either due to advanced disease or poor medical condition [34]. Many modalities of palliation are available for those who cannot undergo an esophagectomy. The goals of palliation are to relieve dysphagia, avoid malnutrition, control pain, and improve quality of life. The palliative treatment that is best suited for the patient is based on the location of the tumor, performance status, and expected survival. Definitive chemoradiotherapy alone may be an acceptable option for patients who have a decent performance status and a contraindication to surgery. A Scandinavian phase III trial of 91 patients randomized between chemoradiation alone or surgery showed no survival difference at median follow-up of almost 52 months [35].

Endoscopic palliative options include placing esophageal stents, laser therapy, and placing feeding tubes. Stents are used extensively to palliate dysphagia because of relatively low cost with wide availability in most institutions. Stents can effectively palliate dysphagia very quickly but are associated with complications such as stent migration, esophageal perforation, aspiration pneumonia, bleeding, and pain. Approximately 30–35% of patients will develop recurrent dysphagia due to tumor over growth or stent migration. In one study of 100 patients who were stented for malignant dysphagia, 85% had immediate relief from dysphagia, 49% had palliation until their death, and 51% required re-intervention [36]. Stents are also useful in the unfortunate patient with fistulous formation to the trachea or surrounding structures. Effective closure of the fistulous opening can be achieved in most patients with an appropriately placed stent [37].

Brachytherapy is another option for palliation of dysphagia. This modality delivers high-dose radiation to the tumor in short periods. The advantages of brachytherapy are that it is cost effective when compared with other modalities and is suitable for frail elderly patients. The disadvantages are the lack of homogenicity in dose distribution of the radiation and approximately 6-week lag time before symptomatic relief of dysphagia is seen [3]. Nonetheless, it offers better long-term control of dysphagia as compared to stenting [38].

Photodynamic therapy, a tissue ablative technique, uses endoscopically delivered light of a specific wavelength to activate a previously administered photosensitizer. Photofrin is quite costly, and it is the most commonly administered photosensitizer. A study of 215 patients showed relief of dysphagia in 85% of patients. Sunburn was the most frequent complication and occurred in 6% of patients [39]. Other complications were perforation, fistula formation, and stricture formation.

Conclusion

Refinement in surgical technique and ICU care has allowed high-volume centers to reduce mortality from esophagectomies to 1–3.6% in the overall population. However, morbidity from the procedure remains high even at centers of excellence. Several studies have shown that complications are diagnosed earlier and treated effectively at high-volume centers compared to low-volume centers. Nonsurgical complications from cardiopulmonary comorbidity contributed to increased mortality and morbidity in the elderly population. Age-associated changes in the cardiovascular, pulmonary, hepatorenal, and endocrine systems lead to a decrease in functional reserve in the older population. Preoperative evaluation in a multidisciplinary team can provide accurate selection of the patients for whom esophagectomy may be feasible at reasonable risk. When the decision of proceeding to an esophagectomy is unclear, the judgment of the multidisciplinary team may be an invaluable opinion to the surgeon. For those patients who are a marginal performance status, we recommend that they undergo for a short-period cardiopulmonary rehabilitation prior to categorizing them as nonsurgical. Many effective palliative options are available for the patient with advanced disease or the inoperable patient.

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49 Breast Cancer in Elderly Women

Monica Morrow and Oriana Petruolo

Contents

Abstract

In the setting where breast cancer is the second leading cause of cancer death in American women, and in which the incidence of breast cancer increases with age, herein we review the important issues related to the management of breast cancer in the elderly (defined as those older than 70 years of age), including the impact of age on the value of mammographic screening, the selection of local surgical therapy, the need for adjuvant radiotherapy, the efficacy and toxicity of systemic therapy, and the effect of mortality due to breast cancer in this population.

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We conclude that screening mammography in healthy women up to 75–80 years of age appears beneficial, that healthy elderly breast cancer patients should undergo surgery of the primary tumor (excision to negative margins or mastectomy) using standard selection criteria, that sentinel node biopsy is the axillary staging procedure of choice for clinically node-negative women if the finding of nodal metastases would alter treatment, and that axillary dissection remains standard management for patients presenting with clinically evident metastases. We also conclude that good local control is obtained with excision alone and endocrine therapy for T1, estrogen receptor-positive tumors, while radiotherapy should be given for others undergoing breast-conserving therapy.

Keywords
Breast cancer · Elderly · Screening · Mastectomy · Radiation · Adjuvant therapy

Introduction

Breast cancer is the most common malignancy in American women aside from skin cancer and the second leading cause of cancer death, exceeded only by lung cancer. It is estimated that there were 231,840 new breast cancer cases diagnosed in the United States in 2015 and 40,290 deaths. In addition to invasive breast cancer, carcinoma in situ (CIS), the earliest form of breast cancer, accounted for about 60,290 new cases in 2015 [1].

The incidence of breast cancer increases with age, and despite competing causes of mortality, breast cancer remains a significant cause of death in elderly women. Cancer is the leading cause of death in those 55–74 years of age and is second only to heart disease in the 75+ age group [2]. As life expectancy increases and the elderly population continues to grow, there will be an increasing number of elderly women diagnosed with breast cancer. Despite the high prevalence of this disease in the elderly, they largely have been excluded or discouraged from participating in clinical trials and often are not given the same therapeutic options as their younger counterparts [2, 3].

The goal of this chapter is to review the important issues related to the management of breast cancer in the elderly. These include age-specific issues regarding the value of mammographic screening, the selection of local surgical therapy, the need for adjuvant radiotherapy, the efficacy and toxicity of systemic therapy, and the effect of mortality due to breast cancer in this population. Because there is no standard definition of "elderly," for the purposes of this chapter, an elderly patient is defined as one older than 70 years of age.

Epidemiology

Breast cancer incidence and mortality increase with age, with the greatest increase observed during the childbearing years. In Western countries, a continued increase in incidence is seen after menopause, whereas in Asian countries, the incidence decreases in elderly women [4, 5]. Approximately one-half of the breast cancers in the United States are diagnosed in women 65 years of age and over. For women in this age group, an age-adjusted incidence rate of 426 cases per 100,000 population was noted in the SEER database [6], compared with 82 cases per 100,000 for women younger than age 65. The age-specific incidence rate for women 85 years of age or older rose to 350 cases per 100,000 population. Although the overall incidence of breast cancer is similar among black women (121.5 cases/100,000 population) and white women (123.6 cases/100,000), differences by age are seen with breast cancer incidence higher among black women <60 years of age but lower among those age 60 years and older compared to white women [7].

Breast cancer incidence rates in the United States increased by 32% from 1980 to 1987 [8]. Since that time, data from the National Program of Cancer Registries (NPCR) and the SEER registries [9] indicate that age-adjusted incidence rates for invasive breast cancer decreased significantly in women 50 years of age and older each year between 1999 and

2003, with the greatest decrease (6.1%) occurring from 2002 to 2003. The largest decreases were seen in women 55–59 years of age (11.3%), 60–64 years (10.6%), and 65–69 years (14.3%). After the sharp decrease from 2002 to 2003, there was no significant change in overall incidence rates in any age group from 2003 to 2007 [10]; however, SEER data showed incidence rates were increasing in women in their 60s and 70s through 2012 [11] (Fig. 1). Rates of in situ breast cancer also stabilized from 1999 to 2003 after increasing by more than 6.6% per year since 1981, with women 50–79 of age years experiencing a significant decrease in incidence during this period [12].

Over the past 25 years, the incidence of in situ carcinoma has increased in association with a decrease in regional disease and a stable metastatic disease rate [8]. Between 1987 and 1997, a decrease in breast cancer mortality was observed in the United States, with a 9% reduction in mortality for those 70–79 years of age. Approximately 50% of this mortality reduction is attributed to screening and 50% to improvements in therapy [13]. Despite the reported decreases in breast cancer mortality, it is important to keep in mind that breast cancer represents the underlying cause of death in 54.5, 37.1, and 30.7% of women aged 60–69, 70–79, and 80+ years, respectively, who are diagnosed with the disease [14].

As in young women, infiltrating ductal carcinoma is the most common histologic tumor type in the elderly, accounting for 77–85% of cases [15, 16]. The relatively favorable subtypes of colloid and papillary carcinoma are observed more frequently in elderly women but still account for less than 10% of mammary carcinomas even in women 85 years of age or older [15–17], whereas inflammatory and medullary carcinoma are seen less commonly in elderly women than in their younger counterparts [16, 17]. Breast cancers in elderly women are more likely to be estrogen receptor positive, and less likely to overexpress HER2, than those in younger women. The proportion of estrogen receptor-positive cancers was 55.9% among women ages 30–34 compared to 85.1% among those ages 80–84 [18].

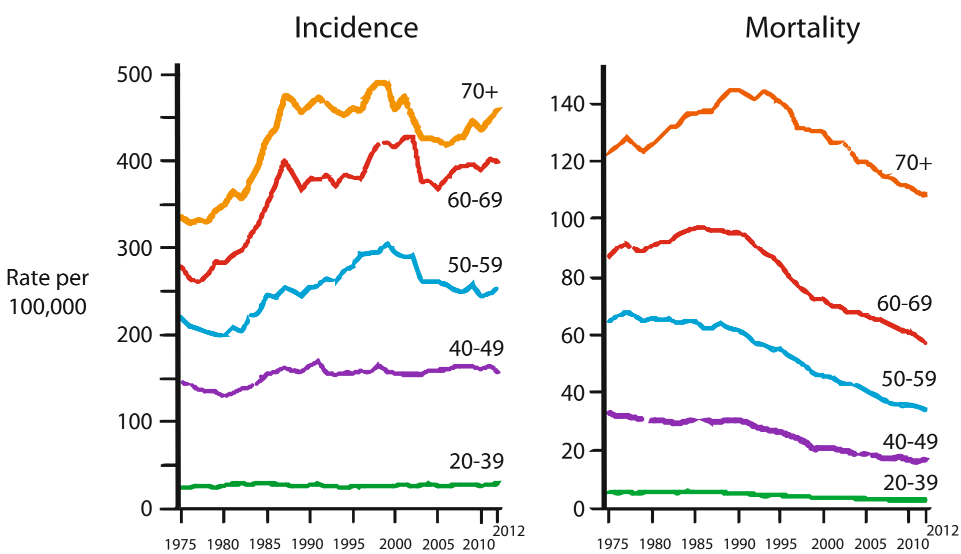

Fig. 1 Incidence and mortality rates of female breast cancer by age from 1975 to 2012. Rates are per 100,000 females and age adjusted to the 2000 US standard population. Incidence rates were adjusted for reporting delay (Republished with permission of John Wiley and Sons Inc, from CA: A Cancer Journal for Clinicians, DeSantis CE et al. Volume No. 66, Issue No. 1, 2016; permission conveyed through Copyright Clearance Center, Inc. [11])

Screening

Randomized studies have shown that screening for breast cancer with mammography reduces breast cancer mortality by approximately one-third, especially for women 50–69 years of age at invitation to screening [19–21]. As life expectancy increases, attention has turned to determining an appropriate upper age limit for population-based mammography screening. Current guidelines are vague, indicating that chronological age alone should not be the reason for the cessation of regular screening. Theoretically, screening should be beneficial for women 70 years of age or older, but evidence to support this statement is limited. To date, the only randomized screening trial that included women 70 years of age and older was the Swedish Two-County trial [21]. In this study, 162,981 women 40–74 years of age were randomized to a screening or a control group. A 31% reduction in mortality from breast cancer and a 25% reduction in the rate of stage II or higher cancers were seen in the group invited to screening, and the benefit extended to patients 70–74 years of age.

Van Dijck et al. [22] reported the results of a nonrandomized trial of screening in 6,773 women 68–83 years of age, enrolled during 1977–1978 and followed through 1990. Women from the same birth cohort in a neighboring city without a screening program served as controls. Over the entire study period, the cumulative mortality rate ratio was 0.80 (95% confidence interval [CI], 0.53–1.22) for the screened women; at 9–13 years after the start of screening, it had decreased to 0.53 (95% CI, 0.27–1.04). A subsequent study by Jonsson et al. [23] attempted to evaluate the contribution of screening to decreasing breast cancer mortality in women 70–74 years of age. Breast cancer mortality for both the screened and not-screened groups decreased during the study period, but with a mean screening interval of 22.8 months and a mean follow-up time of 10.1 years, a 24% reduction in breast cancer mortality was estimated in the screened group after adjusting for lead time bias.

In 2000 Smith-Bindman et al. in a study of 690,993 women 66–79 years of age reported that screening mammography was associated with a decreased risk of detecting metastatic breast cancer among elderly women [24]. Taplin et al. [25] retrospectively reviewed data from seven health-care plans dating from 1995 to 1999, comparing women 50 years of age or older who were diagnosed with late-stage (metastatic and/or tumor size $\geq$3 cm; $n = 1{,}347$) or early-stage (control subjects, $n = 1{,}347$) breast cancers. The odds of having late-stage breast cancer were higher among women not undergoing screening (odds ratio [OR] = 2.17, 95% CI, 1.84–2.56; $p < 0.001$); failure to screen was significantly associated with age >75 years (OR = 2.77, 95% CI, 2.10–3.65), as well as lower socioeconomic status.

Mandelblatt et al. [26] used a decision analysis model to determine whether mammographic screening extends life for women 65 years of age and older in the presence and absence of comorbid conditions. Patients were stratified into age groups of 65–69, 70–74, 75–79, 80–84, and 85 years or older. In each age category, women were further stratified into those with average health, those with mild diastolic hypertension, and those with symptomatic congestive heart failure, to determine the effect of comorbid conditions on screening benefit. Screening was found to save lives for elderly women of all ages, although the magnitude of benefit decreased as the severity of the comorbidity increased. For a woman with breast cancer, screening prolonged life 617 days for the woman of average health 65–69 years of age, and 311 days for women in the same age group with congestive heart failure. The prolongations of survival for women older than 85 years in the same health groups were 178 and 126 days, respectively. The cost-effectiveness of annual screening ranged from $13,200 to $34,600 per year of life saved. In comparison, the cost per year of life saved by treating mild to moderate hypertension in the nonelderly is $16,000–$72,000 [26]. These estimates of cost are based on the use of annual screening mammograms. Moskowitz [27] calculated that owing to the longer lead times seen with breast cancer in older women, most of the benefits of screening could be obtained with a 2- to 3-year interval between studies. In a study of women 66–89 years of age, Braithwaite et al. found that biennial versus annual screening was not associated with more adverse tumor characteristics at diagnosis and that the cumulative probability of a false-positive recall was higher among annual than biennial screeners [28].

Boer et al. [29] used a model incorporating the natural history of breast cancer and the known effect of screening to identify the optimum upper age limit for screening. Using a model in which preclinical duration of breast cancer was assumed not to increase after age 65, no upper limit for screening benefit was identified. If the duration of the preclinical phase was "pessimistically" assumed to increase in the elderly, screening up to age 80 was found to be of benefit. In a study of 2,067 million screening exams performed between 1998 and 2000, the overall breast cancer detection rates in the 50–69 and 70–75 age groups were, respectively, 4.2 and 14.2 per 1,000 initially screened women. The referral, biopsy, and detection rates were substantially higher in women 70–75 years of age than in their younger counterparts, and a significant trend toward a smaller tumor size distribution was observed [30]. These findings suggest that mammographic screening is a beneficial technique in the elderly (Table 1) [30].

The U.S. Preventive Services Task Force (USPSTF) changed their guidelines in 2009, recommending that screening mammography in women younger than 50 should be on an individual basis, and biennial screening mammography for women 50–74 years of age [31]. They also noted insufficient evidence regarding the benefits or harms in screening women 75 years or older. The following year, there was a 4% decrease in screening mammography utilization in the Medicare population [32]. Since the publication of these recommendations, results of studies examining changes in screening mammography rates have been mixed [33–35], with some studies showing decreased rates of screening mammography in older women 50–64 [36] and 50–74 [37] years of age, and a continuing decline in rates of screening mammography in women >75 years of age [38, 39]. In the 2016 update of the USPSTF guidelines, it was again noted that the greatest benefit of screening was seen in women 50–74 years of age and that randomized trials including women older than 74 years of age were lacking [40]. A number of studies indicate that breast cancer screening in the elderly, whether by mammography or clinical breast examination, is underutilized. The National Cancer Institute Breast Cancer Screening Consortium [41] reported the results of seven population-based surveys of women 50–74 years of age. In five of the seven studies, the rates of breast screening by mammography and breast examination in the 70–74 years age group were lower than those reported for other ages. This occurred despite the fact that more than 90% of women surveyed had a regular source of medical care.

Table 1 Outcomes of screening in older women

	Age group (years)	
	50–69	70–75
No. of screening exams	1,880,082	187,207
No. of women	18,902	3,429
% Additional imaging	33.9	24.9
% Biopsy	5.1	4.2
Screen detected cancers/1000	4.2	10.3
% In situ	14.8	11.6
% Node neg. (invasive only)	66.3	69.7
Positive predictive value of biopsy	70.0	79.0

Source: Data from Fracheboud et al. [30]

In a prospective cohort study, Malmgren et al. assessed mammography-detected breast cancer in women 75 years of age and older [42]. They found a significant difference in tumor stage between patient- or physician-detected versus mammography-detected cancers; 62% of mammography-detected cancers were stage I, whereas 59% of patient- and physician-detected cancers were stage II and III ($p < 0.001$). Patients with mammography-detected cancer were more likely to have lumpectomies (87%) versus non-mammographically detected cancers (56%) and fewer mastectomies ($p < 0.001$). They also found a significant difference in type of treatment administered ($p < 0.001$), with patients with mammography-detected cancers less frequently having chemotherapy as part of their treatment. With a median follow-up of 6.4 years, when adjusted for age and treatment, mammography detection was significantly associated with decreased breast cancer mortality (hazard ratio [HR] 0.50; 95% CI 0.31–0.82; $p < 0.001$). This supports the potential benefits of continued screening in the elderly age group.

Lack of awareness of breast cancer risk and screening procedures in elderly women contributes to the underutilization of these techniques. Leathar and Roberts [43] identified a lack of knowledge among elderly women about breast cancer, a pessimistic attitude toward disease outcome, and embarrassment about being examined as major barriers to screening. Fox et al. [44] conducted a telephone survey of 724 women 65 years of age and older to assess factors influencing the use of mammography. Only physician recommendation predicted a recent mammogram, with age, race, and health status found to be insignificant factors.

In 2001 data from the state-based Behavioral Risk Factor Surveillance System (BRFSS) and the National Health Interview Survey (NHIS) confirmed that the percentage of women who reported receiving mammography and clinical breast exam within 2 years was lower among older women (56.7% of women 70 years of age and older) compared with younger women (71.1% of women 50–69 years of age). Among both groups, those unable to perform a major activity of daily living were less likely to report receiving mammography within 2 years. Interestingly, most (62.7%) women 70 years of age and older reported having no activity limitation, and only 5.5% reported being unable to perform a major daily activity [45].

In 2007 Field et al. studied women 65 years of age or older when diagnosed with early-stage invasive breast cancer ($n = 1{,}762$). They assessed mammography use during 4 years of follow-up and found that the percentage of women having mammograms after treatment declined significantly during the studied time frame, from 82% in the first year post-treatment to 68.5% in the fourth year of follow-up. Women at higher risk of recurrence (breast conservation without radiation therapy or higher stage) were less likely to have yearly mammograms, as were women without visits to breast cancer surgeons or oncologists, suggesting that underutilization of mammography is a problem for women at all levels of breast cancer risk [46]. Massimino et al. evaluated rates of mammographically detected cancer and benign biopsy rates for follow-up mammograms in elderly breast cancer survivors 80 years of age or older [47]. Four hundred twenty-nine women were included and had a median of four mammograms over a mean 50-month follow-up period. Eighteen women (5.9%) had a local recurrence; 50% detected by mammography alone and 50% by palpation. Of the four contralateral cancers, all were detected mammographically. While the rates of local recurrences and contralateral cancers were low in this subset of patients (0.9%), the risks of mammographic surveillance were minimal, with only a 1.2% benign biopsy rate. These results suggest that annual mammography is not necessary for elderly breast cancer survivors and confirm the need for further studies to determine the most effective follow-up in this population.

Local Therapy of Breast Cancer

What constitutes appropriate local treatment for the elderly woman with breast cancer remains controversial. In the past, when mastectomy was the standard surgical therapy, the major debate in older women centered on dissection of the axillary nodes. The emergence of breast-conserving surgery and sentinel lymph node biopsy as accepted modalities for the local therapy of breast cancer and the development of endocrine therapies such as tamoxifen and the aromatase inhibitors have increased the available options for local treatment in this population. When evaluating therapeutic options, it is important to consider not only the immediate morbidity and mortality of treatment but also the efficacy of the therapy in maintaining local control for the duration of the woman's life. Current options for the local management of breast carcinoma in the elderly include mastectomy, breast-conserving therapy consisting of excision and irradiation, or excision alone, and endocrine therapy.

Mastectomy

Mastectomy remains a common treatment in the elderly patient. A modified radical mastectomy includes removal of breast tissue, the underlying pectoralis fascia, and the axillary lymph nodes. In patients with clinically negative axillary lymph nodes, the modified radical mastectomy has been replaced by total (simple) mastectomy plus sentinel lymph node biopsy, an operative technique that is discussed later in this chapter. The 30-day operative mortality rate of any type of mastectomy is uniformly low, and the procedure is physically well tolerated. Petkke et al. used the National Surgical Quality Improvement Program database from 2005 to 2013 to compare postoperative outcomes in patients older and younger than 80 years of age [48]. They found low rates of morbidity and mortality regardless of age, with a 30-day mortality postmastectomy of 0.3% for those >80 years of age (0.1% for the <80-year-old age group, $p < 0.01$). They observed significantly higher rates of systemic complications such as urinary tract infection and pneumonia in the elderly age group postmastectomy, but these were seen in fewer than 1.5% of patients. In contrast, return to the operating room occurred for 2.3% of patients <80 years of age compared to 2.1% of those ≥80 years of age ($p = 0.57$). Similar results have been noted in other studies, with mortality rates less than 4% commonly observed [49–52]. Davis et al. reported a 3% mortality rate for women 80 years of age or older treated by mastectomy and a 7% incidence of major complications [49]. Hunt et al. in a study of 94 patients reported a complication rate of 20% in elderly patients, but the operative mortality was still only 1% [50]. Wound problems accounted for most of the complications in this series, while Kessler and Seton found cardiovascular and neurologic problems to be the most common cause of postoperative morbidity in their series [51]. Data on the morbidity and mortality of mastectomy in the elderly are summarized in Table 2 [49–56]. In patients with severe comorbidities, mastectomy has been performed using local anesthesia and regional nerve blocks [57]. Mastectomy under local anesthesia alone using the tumescent technique of infiltrating dilute lidocaine with epinephrine (25 ml of 1% lidocaine [250 mg] and 1 ml of 1:1,000 epinephrine [1 mg] in 1 L of Ringer's lactate) via an infusion pump has also been reported [58]. Although mastectomy is an excellent method for obtaining local control of breast cancer with a minimum number of outpatient visits, and although elderly women can undergo the procedure safely, these results are obtained at the expense of cosmesis. Older women are less likely to have a reconstructive procedure postmastectomy compared to younger women [59–61] in spite of studies showing that older age groups do not have significantly higher rates of complications after reconstruction [62, 63]. In et al. examined data from the SEER-Medicare database from 2000 to 2005 on postmastectomy reconstruction rates in women >65 years of age with ductal carcinoma in situ or stage I–II breast cancer. They found that of 19,234 women, only 6% underwent reconstruction and only 2.4% of patients >75 years of age had reconstruction [60]. Oh et al. performed a meta-analysis including 42 studies from eight countries published from 1993 to 2015 evaluating rates of breast reconstruction in women >60 years of age and found a pooled breast reconstruction rate of 6.1% [61]. While it is unclear from these studies whether low reconstruction rates reflect patient preference or the failure of surgeons to discuss the availability of reconstruction with healthy

Table 2 Morbidity and mortality of mastectomy in the elderly

Study	Age (years)	No	Operative mortality (%)	Complications **(%)**
Hunt et al. [50]	>65	94	1.0	20
Schottenfield and Robbins [56]	>65	437	0.2	NS
Singletary et al. [52]	>69	157	1.9	24
Kesseler and Seton [51]	>70	82	1.2	11
Berg and Robbins [53]	>70	242	2.0	NS
Kraft and Block [54]	>75	75	4.5	NS
SEER 1967–1973 [55]	>75	NS	0.9	NS
Davis et al. [49]	>80	96	3.0	7

NS not stated

older women, a study from 11 institutions using patient-reported outcomes found that older women reported higher levels of sexual well-being than their younger counterparts after breast reconstruction [62], suggesting quality of life benefits for reconstruction across the spectrum of age.

Breast-Conserving Surgery in the Elderly

Since 1970, multiple prospective randomized trials have compared survival after breast-conserving treatment to survival after mastectomy for stage I and II breast cancer. No survival advantage has been noted for mastectomy. Although most of these trials did not include women older than 70 years of age, the biologic rationale for breast preservation can be extrapolated to the elderly population. Several studies have suggested that elderly women may have a lower rate of breast recurrence after partial mastectomy and radiotherapy than their younger counterparts [64–66]. Fourquet et al. reported a 97% rate of control at 10 years for women older than 55 years of age compared to 85% for women 33–45 years of age and 71% for women 32 years of age or younger in a series of 518 patients [65]. Veronesi et al. [66] and Clark et al. [64] have also reported a decreasing frequency of breast recurrence with increasing age. Some of these differences in local failure rates may be due to a higher incidence of adverse pathologic features, such as an extensive intraductal component or lymphatic invasion in young women, but older women appear to have lower local failure rates even after correction for pathologic features.

In addition, local recurrence rates can be affected by a number of treatment factors, such as the extent of surgical resection, the status of the surgical margin, and the use and duration of adjuvant endocrine therapy. Five years of tamoxifen reduces the relative risk of locoregional recurrence to 0.47 compared to placebo, and the use of aromatase inhibitors alone or in sequence with tamoxifen reduces the relative risk to 0.50–0.83 compared to tamoxifen [67]. Thus, in women treated with breast-conserving therapy, including breast irradiation and endocrine therapy, the incidence of local failure is low, and the small risk of a second surgery is not an appropriate reason to recommend that elderly women routinely undergo mastectomy. The standard contraindications to breast-conserving therapy (Table 3) [68] used to determine the suitability of young women for breast-conserving therapy are applicable in older women as well [68].

High rates of mastectomy in the elderly have been attributed to patient choice. Some studies have indeed shown that breast-conserving therapy is chosen less frequently as age increases [69–71]. In contrast, Bleicher et al. [72] examined the role of age in the surgery decision-making process by surveying 1,279 patients 79 years of age or younger from two SEER program registries. A majority of patients (80.3%) underwent breast-conserving therapy. There were no differences in patient preference for mastectomy on the basis of age, and in a logistic regression analysis, age and comorbidities were not significant predictors of mastectomy use.

The necessity for adjuvant radiotherapy in patients treated with breast conservation is a matter of particular interest in the elderly population. The Early Breast Cancer Trialists' Collaborative Group (EBCTCG) overview of randomized trials included ten trials of post-breast-conserving therapy radiotherapy with a total of 23,500 patients. The main analyses of local recurrence, breast cancer mortality, and overall mortality were stratified by age into five groups (<40, 40–49, 50–59, 60–69, and >70 years of age) [73]. The relative risk of recurrence, comparing those allocated to radiation therapy with those not, was about 0.3 in every trial, corresponding to a 5-year risk of local

Table 3 Contraindications to breast-conserving therapy with irradiation

Two or more primary tumors in separate quadrants of the breast
Diffuse malignant-appearing microcalcifications
Prior therapeutic irradiation to the breast region that requires retreatment to an excessively high total radiation dose
Persistent positive margins after reasonable surgical attempts

Source: American College of Radiology [68] recurrence of 7% in the radiation therapy group versus 26% in the control. The absolute effects of post-breast-conserving surgery radiation therapy on local recurrence were greater in younger than in older women (5-year risk reductions of 22, 16, 12, and 11% for those <50, 50–59, 60–69, and >70 years of age, respectively). The proportional risk reduction for breast cancer mortality was less pronounced than that for local recurrence, with one breast cancer death averted at 15 years for every four local recurrences prevented in year 5. The lower absolute benefit of RT in older women coupled with the long follow-up period needed for mortality reductions to be observed makes it unlikely that RT will have a major impact upon survival in this population [73].

A similar age-related difference in the magnitude of benefit achieved with a boost dose of radiation was demonstrated in a randomized trial by Bartelink et al. [74]. Although the use of a boost resulted in a statistically significant reduction in local recurrence in all age groups, the absolute benefit ranged from 10.4% at 10 years in women <40 years of age to approximately 3% in those older than 60 years of age [74].

Although the value of radiation therapy in the setting of breast-conserving surgery in the general population, and to some extent in elderly patients, has been demonstrated, the argument that older age may be associated with lower rates of recurrence, less aggressive tumor biology, and increased comorbidity has prompted investigation into the need for radiation therapy after breast-conserving surgery in this subgroup of patients. Hughes et al. [75] designed a prospective randomized trial that included 636 women 70 years of age or older who were randomly assigned to receive tamoxifen plus radiation therapy or tamoxifen alone to examine the benefit of radiation therapy in older women with small breast cancers. Eligibility criteria included estrogen receptor-positive clinical stage I (tumor <2 cm, clinically node negative) breast carcinoma treated by lumpectomy. At a median follow-up of 12.6 years, the 10-year rate of locoregional recurrence was 2% in the tamoxifen plus+ radiation therapy group versus 10% in the tamoxifen alone group ($p < 0.001$) [76]. There were no significant differences in the rates of mastectomy, distant metastases, or overall survival between groups [76]. These findings suggest that lumpectomy plus adjuvant tamoxifen is a reasonable treatment choice for women 70 years of age or older with small, estrogen receptor-positive breast cancers. In the PRIME II trial, 1,326 women 65 years of age or older with hormone receptor-positive, node-negative breast cancers <3 cm undergoing breast-conserving surgery and receiving adjuvant endocrine therapy were randomized to either whole breast radiation therapy or no radiation therapy [77]. At a median 5-year follow-up, ipsilateral breast recurrence was 1.3% in the whole breast radiation therapy group and 4.1% in the no radiation therapy group (95% CI 0.2–2.3 and 95% CI 2.4–5.7, respectively). No significant differences in regional recurrences, distant metastases, contralateral breast cancers, new cancers, or 5-year overall survival were seen between groups. These findings mirror those of Hughes et al. [76] discussed above, leading the authors to conclude that in older patients with lower-risk hormone receptor-positive breast cancer, endocrine therapy alone is a safe option.

Practical issues, such as the difficulty in traveling to radiation therapy appointments daily for 6 weeks, play a significant role in the omission of radiation therapy in elderly women, and studies have examined the feasibility of alternative methods of radiation delivery. Hypofractionated whole breast irradiation which allows treatment to be completed in 3–4 weeks rather than the conventional 5–6-week period has been demonstrated in prospective randomized trials to result in local recurrence-free survival and overall survival rates which do not differ significantly from those seen with conventional fractionation (Table 4) [78, 79]. These results support the conclusion that hypofractionation is a safe, more convenient approach for elderly patients requiring radiation therapy. In recent years, hypofractionation has also been used to deliver partial breast irradiation (PBI). PBI is defined as the delivery of radiation to the surgical cavity plus a 1–2 cm margin after breast-conserving surgery. The rationale for PBI is that most local recurrences occur at the primary tumor site or immediately adjacent to it, rather

Table 4 Randomized trials comparing standard and hypofractionated radiotherapy (RT). Long-term follow-up shows no difference in locoregional recurrence rates and no worsening of overall survival rates [78, 79]

Study	Total patients	Median follow-up (years)	RT type[a]	Locoregional recurrence rate[b]	p-value	Overall survival rate[b]	p-value
Ontario Clinical Oncology Group	1,234	12	Standard	6.7%	<0.001 for non-inferiority	84.4%	0.79
			hypofractionated (42.5 Gy, 16 fractions, over 22 days)	6.2%		84.6%	
START A	2,236	9.3	Standard	7.4%	0.65 (41.6 Gy)	80.2%	0.74 (41.6 Gy)
			hypofractionated (41.6 Gy or 39 Gy, 13 fractions, over 5 weeks)	6.3% (41.6 Gy)	0.41 (39 Gy)	81.6% (41.6 Gy)	0.69 (39 Gy)
				8.8% (39 Gy)		79.7% (39 Gy)	
START B	2,215	9.9	Standard	5.5%	0.21	80.8%	0.042
			hypofractionated (40 Gy, 15 fractions, over 3 weeks)	4.3%		84.1%	

[a]Standard RT = 50 Gy, 25 fractions, over 5 weeks
[b]10-year rate for Ontario Clinical Oncology Group trial and estimated 10-year rate for START A and START B trials

than elsewhere in the breast. Numerous techniques have been developed to deliver PBI, including interstitial brachytherapy, a single-source balloon catheter brachytherapy, three-dimensional conformal treatment with external beam, and intraoperative treatment (IORT). There are a limited number of studies assessing long-term outcomes after accelerated PBI (APBI). Polgar et al. reported the 10-year results of their single institution trial [80] in which 258 patients with T1N0-1mi breast cancer treated with breast-conserving surgery and axillary dissection were randomized to receive either 50 Gy of whole breast irradiation or PBI with brachytherapy catheters, or electron beam irradiation. At a median follow-up of 10.2 years, the 10-year actuarial local recurrence rate was 5.9% for the APBI group and 5.1% for the WBI group ($p = 0.77$), with no significant difference in overall or disease-free survival. Significantly higher rates of good or excellent cosmetic outcomes were seen in the PBI group, with superior results for those treated with brachytherapy compared to external beam PBI. At William Beaumont Hospital, Wobb et al. conducted a matched-pair analysis comparing 274 patients prospectively followed after treatment with brachytherapy post-breast-conserving surgery to controls treated with WBI matched in a one-to-one ratio [81]. At 10 years, there was no significant difference in the rate of local recurrence–4.2% for APBI and 3.7% for WBI ($p = 0.11$)–or in disease-free survival or overall survival. Long-term outcomes, however, are still limited for most techniques of PBI, and many of the patients selected for PBI were at very low risk for local recurrence in the absence of radiation therapy, raising questions as to whether the favorable outcomes are applicable to a wider spectrum of women with breast cancer. In spite of these concerns, the very brief period of time needed for treatment with PBI (5 days, or on the day of surgery in the case of IORT) makes this an attractive approach for elderly women. Meattini et al. [82] performed a subgroup analysis of the group's previously published phase 3 trial to assess the role of APBI in elderly breast cancer patients. In the initial study, 520 BCS patients with invasive cancer and ductal carcinoma in situ, and a maximum tumor size of 2.5 cm, were randomized to receive either APBI using intensity-modulated radiotherapy technique or conventional whole breast radiation therapy [83].

The subgroup analysis included 117 women 70 years of age or older. Similar to the overall study results, the subgroup analysis showed no significant difference in locoregional recurrence between treatment groups, 3.9% in the WBI group and 1.9% in the APBI group ($p = 0.60$), with no significant difference in disease-free survival. The largest ongoing trial comparing WBI and APBI is the NSABP B39/RTOG 0413 phase III multi-institutional study enrolling patients with ductal carcinoma in situ or stage I–II invasive breast cancer with tumors no larger than 3.0 cm and randomizing to one of several APBI techniques (multi-catheter brachytherapy, balloon catheter, or external beam radiation) or WBI [84]. The results of this study and the long-term results of other randomized studies will provide definitive data on the safety and efficacy of PBI, but existing data indicate that hypofractionated whole breast irradiation and PBI are reasonable options for older women undergoing breast-conserving surgery who do not meet criteria for elimination of radiotherapy or who desire the local control benefit of radiotherapy.

Overall, breast irradiation has been shown to be well tolerated in the elderly population. A tolerance study by Wyckoff et al. demonstrated that radiation dose, duration of therapy, number of treatment interruptions, and toxicities were no different in women older than 65 years of age compared to women less than 65 years of age [85]. When considering whether to omit breast irradiation after limited surgery, it is important to remember that most local failures occur within 6 years of surgery, leaving many elderly women at risk of this occurrence. Irradiation is well tolerated in the elderly population, and chronologic age alone is not an indication for its omission from breast-conserving therapy. However, Schonberg et al. evaluated SEER data from 1992 to 2005 to determine how life expectancy affected treatment for women 80 years of age or older and found that 37% of women with a Charlson Comorbidity Index (CCI) of 3 or greater (72% 5-year mortality) received radiation therapy after breast-conserving surgery although they were unlikely to benefit, indicating a greater need for individualization of therapy [86].

Sentinel Lymph Node Biopsy

The sentinel node is defined as the first lymph node/nodes to receive drainage from a particular cancer and can be identified by lymphatic mapping with a blue dye, a radioactive tracer, or both. Injection of the breast tissue around the tumor, the subareolar space, and the skin overlying the tumor has all successfully been utilized to identify a sentinel node. The success rate for identification of the sentinel node in prospective, multi-institutional studies is greater than 95% and improves with experience [87, 88]. When identified, the sentinel node is an accurate predictor of the status of the remaining nodes in the axilla in more than 90% of cases [87, 89, 90]. In the American College of Surgeons Oncology Group (ACOSOG) Z10 trial, increasing patient age was significantly associated with failure to identify a sentinel node [88], with the failure rate increasing from less than 1% in women less than 50 years of age to 2.7% for those 70 years of age and older ($p = 0.0004$). Others have reported excellent outcomes for sentinel node biopsy in older patients. Gennari et al. reported a sentinel node identification rate of 100% in 241 consecutive patients 70 years of age or older who underwent sentinel node biopsy [91].

In the past, many elderly patients were not offered axillary staging because the complications associated with axillary lymph node dissection were felt to outweigh the potential benefits of the procedure. The sentinel lymph node biopsy technique allows patients with clinically node-negative breast cancer to undergo axillary staging with a significant decrease in morbidity. There are complications associated with the procedure, however. After 6 months of follow-up in the ACOSOG Z10 trial, decreased range of motion was observed in 4% of patients, axillary paresthesias in 9%, and lymphedema in 7%. Although paresthesias were more common in younger women, the incidence of lymphedema increased with age [92]. Thus, it is important to ensure that knowledge of nodal status is important for overall patient management prior to performing a sentinel node biopsy, since excellent outcomes have been reported after observation of the clinically negative axilla in older women.

The International Breast Cancer Study Group conducted a prospective, randomized trial of axillary dissection versus observation in women 60 years of age and older [93]. The median patient age was 74 years, and all patients received tamoxifen. At a median follow-up of 6.6 years, axillary recurrence as a first event was observed in 2% of patients and did not differ between groups. This low rate of axillary failure is particularly noteworthy since most of the study participants did not receive radiotherapy. Differences in quality of life favoring no axillary surgery were present in the first 6–12 months postoperatively, but were minimal with longer follow-up. This study indicates that axillary observation is associated with a low risk of axillary recurrence but that when axillary dissection is necessary, it can be performed with a limited effect on quality of life. The impact of knowledge of axillary nodal status on treatment has been examined, with changes in planned therapy occurring in 14–38% of patients based on knowledge of nodal status [94, 95]. In aggregate, these studies suggest that when knowledge of axillary nodal status will not change therapy, axillary observation is a safe approach. When axillary staging is indicated, sentinel node biopsy is the procedure of choice, and axillary dissection can be safely carried out with acceptable morbidity in patients presenting with clinical nodal involvement and those found to have metastases to the sentinel nodes who are having mastectomy. In clinically node-negative patients undergoing breast-conserving surgery with whole breast irradiation and found to have metastases to 1 or 2 sentinel nodes, 10-year follow-up of the ACOSOG Z0011 trial demonstrated axillary recurrence rates of less than 2% after treatment with sentinel node biopsy alone and no difference in disease-free or overall survival compared to patients randomized to axillary dissection [96], allowing a greater proportion of women to avoid the sequelae of axillary dissection if these results are applied in practice. The morbidity of sentinel node biopsy and axillary dissection is compared in Table 5 [97–99].

Axillary dissection is an effective method for maintaining local control in the axilla with isolated axillary failures seen in only 1–2% of patients after the procedure [100, 101]. Major complications of axillary dissection, including injury or thrombosis of the axillary vein and injury to the motor nerves of the axilla, are uncommon, although significant short- and long-term morbidity are associated with the procedure (Table 5). Of the potential sequelae of the procedure, lymphedema of the arm is potentially associated with the greatest disability. The incidence of lymphedema following axillary dissection ranges from 1.5% to 62.5% [102–105] depending on the definition used, the length of follow-up, the method of detection employed, and the population studied. Several studies have suggested that older age is a risk factor for the development of lymphedema. Pezner et al. [105] noted lymphedema following breast-conserving treatment (including radiation therapy) in 25% of women 60 years of age or older compared to 3 of 46 younger women (7%) ($p = 0.02$). Other studies have failed to identify an association between age and lymphedema [102–104]. Axillary dissection has also been shown to cause pain and decreased upper arm mobility [106], factors that can cause significant functional impairment in women with preexisting limitations due to neurologic disease or arthritis. In patients with microscopic nodal involvement, axillary irradiation is an alternative to dissection to maintain local control [107], but in the presence of clinically evident, histologically confirmed nodal disease, axillary dissection remains the procedure of choice because failure rates after irradiation alone are higher than those seen with surgery in this clinical setting.

Table 5 Comparison of the morbidity of sentinel node biopsy and axillary dissection

Symptom	SN biopsy (%)	Axillary dissection (%)
Pain	8–14	23–72
Paresthesia	2–9	24–85
Decreased range of motion	0–6	18–27
Lymphedema	1–11	7–69

Source: Data from Lucci et al. [97], Veronesi et al. [99], and Schijven et al. [98]
SN Sentinel node

Primary Endocrine Therapy as an Alternative Local Therapy

Because of concerns regarding the morbidity and mortality of conventional surgical therapy for breast cancer in elderly women with comorbid conditions, considerable attention has been given to the use of tamoxifen as a primary treatment. In 2007, Hind et al. reviewed the evidence from randomized trials comparing primary endocrine therapy to surgery, with or without adjuvant endocrine therapy and/or radiation, in women 70 years of age or older [108]. Seven studies were included in the review, three reporting outcome data on surgery versus primary tamoxifen, and four analyzing surgery plus endocrine therapy versus primary tamoxifen. Only one study selected patients on the basis of estrogen receptor status. When comparing surgery alone to primary endocrine therapy, no significant difference in overall survival between interventions (HR 0.98, 95% CI, 0.74–1.30, $p = 0.9$) was noted. One trial [109] reported adequate summary data to show a significant difference in progression-free survival (PFS) favoring surgery (HR 0.55, 95% CI, 0.39–0.77, $p = 0.0006$). In the three trials comparing surgery plus adjuvant endocrine therapy to primary endocrine therapy [110–112], there was a nonsignificant trend in favor of surgery plus endocrine therapy (HR 0.86, 95% CI, 0.73–1.00, $p = 0.06$). Only one trial [111] reported adequate data on PFS to calculate a significant difference favoring surgery plus endocrine therapy (HR 0.65, 95% CI, 0.53–0.81, $p = 0.0001$), and two trials [110, 111] showed a significant decrease in local recurrence favoring surgery plus endocrine therapy (HR 0.28, 95% CI, 0.23–0.35, $p < 0.00001$). These results are summarized in Table 6 [108]. The results of this review are based on a limited number of small studies of variable methodological quality, with significant heterogeneity among studies. Nonetheless, this review demonstrates that primary endocrine therapy is inferior to surgery plus endocrine therapy for the local control of breast cancer in estrogen receptor unselected, medically fit older women, independent of the type of surgery (mastectomy or wide excision alone). The meta-analysis showed no significant difference in overall survival between the two treatments, although one trial showed a small but significant survival advantage for surgery with adjuvant endocrine therapy where follow-up was extended to 13 years [110]. These results suggest that primary endocrine therapy should only be offered to women with estrogen receptor-positive tumors who are not surgical candidates or who refuse surgery. In a cohort of women with reduced life expectancy due to significant comorbid disease, primary endocrine therapy may be an appropriate treatment choice. The ESTEEM trial (Endocrine +/− Surgical Therapy for Elderly Women with Mammary Cancer), a national trial in the United Kingdom, was designed to evaluate selection criteria for the use

Table 6 Primary endocrine therapy for breast cancer

Surgery vs. primary endocrine therapy			
Trial	Median follow-up (years)	HR death (95% CI)	
EORTC 10851	10	1.11 (0.75–1.65)	
Nottingham 1	5	1.06 (0.59–1.92)	
St. Georges	6	0.75 (0.44–1.26)	
Surgery plus endocrine therapy vs. endocrine therapy			
Trial	Median follow-up (years)	HR death (95% CI)	HR local failure (95% CI)
CRC	13	0.78 (0.63–0.96)	0.25(0.19–0.32)
GRETA	7	0.98 (0.77–1.25)	0.38 (0.25–0.57)
Nottingham 2	5	0.80 (0.73–2.32)	Not available

Source: Data from Hind et al. [108]

HR hazard ratio; *EORTC* European Organization for Research and Treatment of Cancer; *CRC* Cancer Research Campaign; *GRETA* Italian Cooperative Group of primary endocrine therapy and hopefully clarify the indications for its use [108]. The trial included patients 75 years of age and older with operable estrogen receptor-positive breast cancer randomized to primary endocrine therapy with anastrozole or surgery and adjuvant anastrozole. Unfortunately, these questions were not answered, as the trial closed early due to failure to recruit, an issue that has been seen with several other studies attempting to address management controversies in this age group [113].

Systemic Therapy

The majority of older women have hormone receptor-positive breast cancers and will receive adjuvant endocrine therapy.

Tamoxifen is well established as an effective endocrine therapy for postmenopausal, estrogen receptor-positive women with node-positive or node-negative breast cancer. The 2005 update of the meta-analysis by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) [114] demonstrated that only for estrogen receptor-positive disease, adjuvant tamoxifen reduced the annual breast cancer death rate by 31% in all age groups (50, 50–69, and >70 years) and that the absolute risk reduction after 5 years of tamoxifen was found to be similar for younger and older women [114]. The EBCTCG found similar results in a meta-analysis assessing the relevance of breast cancer hormone receptors on the efficacy of tamoxifen [115], which showed that even in marginally estrogen receptor-positive disease (10–19 fmol/mg cytosol protein), there was a substantial recurrence reduction (rate ratio 0.67 [SE 0.08]) in estrogen receptor-positive disease which was independent of progesterone receptor status, age, nodal status, or use of chemotherapy.

Adjuvant therapy with tamoxifen for 5 years was the standard of care for women with early-stage, endocrine-responsive breast cancer for many years [114]. However, the partial estrogen agonistic activity of tamoxifen and other selective estrogen receptor modulators (SERMs) increases the risk of endometrial cancer and thromboembolic events [116]. Aromatase inhibitors (AIs) are an alternate form of endocrine therapy that profoundly reduce the already low-circulating endogenous levels of estrogens in postmenopausal women by blocking the synthesis of estrogens in non-ovarian tissues, including breast tissue [117]. AIs have been shown to prolong disease-free survival compared to tamoxifen. The EBCTCG conducted a meta-analysis of randomized trials comparing AIs to tamoxifen in early breast cancer [118] and demonstrated that in a comparison of 5 years of AI versus 5 years of tamoxifen, recurrence rate ratios were better for AIs during years 0–1 after surgery (recurrence rate ratio 0.64, 95% CI 0.52–0.78) and years 2–4 (recurrence rate ratio 0.80, 95% CI 0.68–0.93) with no significant differences after 5 years. The 10-year breast cancer mortality with AIs was 12.1% compared to 14.2% with tamoxifen ($2p = 0.009$). In an aggregate evaluation of all comparisons of AIs versus tamoxifen, including switching strategies between tamoxifen and AI in sequence, recurrence rate ratios significantly favored AIs during periods when treatments differed (recurrence rate ratio 0.70, 95% CI 0.64–0.77) and breast cancer mortality was reduced for all time periods combined compared to treatment with tamoxifen alone (recurrence rate ratio 0.86; 95% CI 0.80–0.94; $2p = 0.0005$) [118]. However, the side effect profiles of the AIs and tamoxifen differ, with AIs being associated with an increased risk of osteoporosis, bone fractures, and musculoskeletal complaints; and tamoxifen with an increased incidence of venous thrombosis, endometrial cancer, and cataracts. Crivellari et al. [119] investigated whether the observed effects of letrozole compared to tamoxifen identified in the Breast International Group (BIG) 1–98 trial differed by age to determine whether treatment recommendations should be modified for elderly patients. In the elderly, letrozole significantly improved disease-free survival and was effective in reducing relapses, including distant metastases, when compared to tamoxifen; even though no convincing differences were observed in thromboembolic or cardiac events in the elderly group, data in the older (64–75 years of age) cohort indicated that thromboembolic events appeared more common with tamoxifen, and cardiac events appeared more common with letrozole. Letrozole was also associated with a higher incidence of bone fractures, independent of age [119]. In an update of the BIG 1-98 trial at 8 years median follow-up, letrozole monotherapy continued to show significantly better disease-free survival, overall survival, distant recurrence-free interval, and breast cancer-free interval than tamoxifen, whether by inverse probability of censoring weighting or by intention-to-treat analysis [120]. They found that sequential treatments involving tamoxifen and letrozole did not improve outcome compared with letrozole monotherapy and concluded that use of a sequence might be a reasonable option for patients with risk factors or treatment intolerability that make letrozole contraindicated. The choice between an AI and tamoxifen in the individual patient is often made on the basis of preexisting conditions, such as the presence of significant osteoporosis or a history of deep venous thrombosis, which would influence the risk/benefit ratio of one of the drugs. A follow-up study by Chirgwin et al. assessing adherence to tamoxifen and letrozole in the BIG 1-98 cohort found that older age and sequential treatments were both associated with decreased adherence to treatment, leading to reduced disease-free survival [121]. This should be taken into account during patient education and in developing an optimal treatment regimen.

There is considerable controversy regarding the use of adjuvant chemotherapy in elderly women. The EBCTCG overview [114] only included about 1,200 older women in trials of chemotherapy versus no chemotherapy, making it difficult to draw firm conclusions about efficacy, although the proportional reductions in recurrence and death were smaller in older women than in their younger counterparts. A retrospective review of randomized trial data indicated similar reductions in breast cancer mortality from regimens containing more versus less chemotherapy in older and younger women, but toxicity, including treatment-related mortality, was higher among older women [122]. Chemotherapy is an appropriate treatment for many elderly patients with early breast cancer, but its use requires careful consideration of life expectancy, comorbidity, functional status, and other factors. Unlike endocrine therapy, toxicity can be substantial with a major effect on functional status. Hospitalization rates of 13–24% in women older than 65 years of age receiving various common adjuvant chemotherapy combinations were reported in one retrospective study [123]. For healthy elderly women with hormone receptor-negative tumors and life expectancies of at least 5 years, chemotherapy should be considered for node-positive patients and high-risk node-negative patients. In an effort to reduce the toxicity of treatment, Muss et al. compared the efficacy of oral capecitabine in patients older than 65 years of age to standard chemotherapy (cyclophosphamide, methotrexate, fluorouracil [CMF] or doxorubicin, and cyclophosphamide) and demonstrated that capecitabine was inferior to standard therapy [124]. Similarly, von Minckwitz et al. conducted a randomized study comparing epirubicin, cyclophosphamide (EC), or CMF versus nab-paclitaxel plus capecitabine for non-frail elderly patients [125]. At a median follow-up of 22.8 months, they found no survival differences; however, they noted a significantly more frequent discontinuation of treatment with nab-paclitaxel.

Systemic therapy includes endocrine therapy, chemotherapy, and, more recently, HER2 directed therapy. Trastuzumab combined with chemotherapy significantly improves survival in HER2 positive patients compared to treatment with chemotherapy alone [126, 127]. Cardiac toxicity, reversible in most cases, is a major side effect of trastuzumab, and its incidence increases with age and anthracycline use [128]. Elderly patients with HER2 positive tumors at high risk for recurrence should be considered for non-anthracycline trastuzumab-containing regimens such as docetaxel, carboplatin, and trastuzumab (TCH) if cardiac toxicity is a concern [129]. In a further attempt at reducing toxicity in lower-risk patients, a single-arm trial with one-third of enrolled patients 60 years of age and older examined the use of trastuzumab and weekly paclitaxel in predominantly stage I HER2 positive breast cancer and reported a 2% risk of recurrence at 4 years median follow-up, and a low rate of adverse events [130].

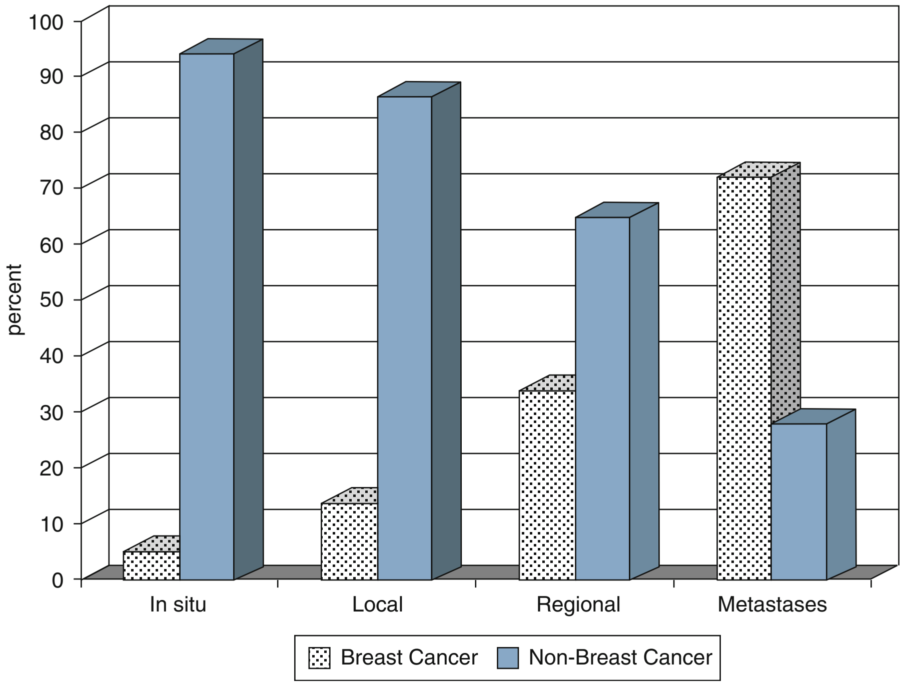

Fig. 2 Causes of death (breast cancer vs non-breast cancer) by stage at diagnosis in women aged 70 years and older at diagnosis (From Schairer et al. [132])

The decision to use adjuvant systemic therapy in elderly women must take into consideration coexisting morbidities and functional status; these may affect a woman's ability to tolerate breast cancer treatment and may decrease survival, regardless of age. The effects of comorbidity on survival can be reliably estimated from mathematical models that are publicly available [131]. This is important in view of the fact that non-breast cancer causes of death are substantial in women 70 years of age and older, even in those with axillary nodal metastases [132] (Fig. 2).

Additional clinical trials are needed to answer questions concerning the risks and benefits of adjuvant therapy in elders.

Breast Cancer Survival and Patterns of Care in the Elderly

In spite of having more biologically favorable tumors, older age at breast cancer diagnosis has been associated with significantly worse breast cancer-specific survival. Chen et al. studied 133,057 women diagnosed with breast cancer between 2004 and 2008 and reported to the Surveillance, Epidemiology, and End Results (SEER) registry [133], including 32,147 70 years of age and older. In multivariate analysis, age over 60 years was an independent predictor of poor prognosis with an HR of 1.46 (95% CI 1.37–1.56, $p < 0.0001$) for death due to breast cancer compared to patients less than 40 years of age. This finding has been confirmed in other studies [18, 134]. Even among women with stage I breast cancer, the adjusted HR for death from breast cancer among those 90 years of age and older was 2.6 compared to those 67–69 years of age [135]. A number of studies suggest that age-related undertreatment may account for the seeming paradox of more favorable biology and poorer survival.

Owusu et al. [136] investigated whether the observed age-related disparities in breast cancer survival were related to differences in treatment received by evaluating 659 women 65 years of age or older with early breast cancer. Women older than 75 years of age were less likely to receive axillary lymph node dissection, radiotherapy, definitive primary therapy, chemotherapy, and guideline-specified therapy. In patients receiving guideline-specified therapy, no age-related differences in breast cancer-specific survival were noted, but 5-year breast cancer-specific survival for those >75 years of age who did not receive guideline-specified therapy was 83% compared to 95% and 94% for those 75 years of age or younger who did and did not receive guideline-specified therapy, respectively. Findings from this study indicated that as many as 66% of women >75 years of age and 45% of women 65–75 years of age received less than guideline-specified therapy. Van de Water et al. retrospectively analyzed patients with early-stage breast cancer from the Netherlands Cancer Registry either less than 65 years of age, or 75 years of age or more, to assess adherence to treatment guidelines for breast and axillary surgery, radiotherapy, chemotherapy, and endocrine therapy in the two age groups [137]. They also found that patients 75 years of age and older were less frequently treated in concordance with guidelines compared to those <65 years of age (55.6% versus 62%, respectively, $p < 0.001$) but did not demonstrate an association with adherence to the guidelines and overall survival in either age group.

Healthy Versus Frail Elderly Patients

Almost 30% of all invasive breast carcinomas occur in women older than 70 years of age [138]. By the year 2030, an even larger portion of breast cancer patients will be 65 years of age or older, and many will be affected by comorbid conditions. In a study of 184 women 65 years of age or older with newly diagnosed, nonmetastatic breast cancer, approximately 1 in 5 declined and/or died within 12 months of breast cancer diagnosis. In multivariable analysis, an increasing score on the vulnerable Elders Survey and having a high school education or less were independent predictors of functional decline or death [139]. These results emphasize the importance of distinguishing healthy from frail elderly patients and the need for clinical tools that guide clinicians when planning care. The following principles have been proposed for the management of frail elderly women. The benefit of screening mammography in these patients is questionable, and a clinical breast exam is likely to identify breast cancers that warrant intervention. Endocrine therapy may be a reasonable primary therapy in older, frail women with hormone receptor-positive lesions. For estrogen receptor-negative and progesterone receptor-negative lesions, excision of the primary tumor may be adequate. Adjuvant endocrine therapy may be appropriate in frail elders with high-risk hormone receptor-positive breast cancer; chemotherapy is rarely indicated regardless of tumor status. The majority of frail elders with metastases will have hormone receptor-positive breast cancers, and endocrine therapy should be considered; those with receptor-negative tumors may be treated with single-agent chemotherapy or supportive care measures. Oncologists need to acquire the skills to appropriately identify frail elders so that they select appropriate therapies that will minimize toxicity and maintain quality of life.

Finally, when considering healthy elderly breast cancer patients, the data included above suggest that compliance with evidence-based recommendations for definitive locoregional treatment, usually defined as breast surgery with evaluation of the axillary lymph nodes and radiation therapy in patients undergoing breast-conserving procedures, is warranted. Tailoring of these recommendations based upon studies specific to elderly patients may include elimination of sentinel node biopsy when results will not change adjuvant therapy recommendations, and omission of radiotherapy in patients with stage I, estrogen receptor-positive cancers receiving endocrine therapy. Standard guidelines for adjuvant systemic therapy, including chemotherapy, should also be utilized in this group [140].

Conclusion

The important issues regarding breast cancer management in the elderly (defined as those older than 70 years of age) are the impact of age on the value of mammographic screening, the selection of local surgical therapy, the need for adjuvant radiotherapy, the efficacy and toxicity of systemic therapy, and the effect of mortality due to breast cancer in this population.

Here we conclude that screening mammography, while not indicated in frail elders, appears beneficial in healthy women up to 75–80 years of age and that healthy elderly breast cancer patients should undergo surgery of the primary tumor (excision to negative margins or mastectomy) using standard selection criteria. We also conclude that sentinel node biopsy is the axillary staging procedure of choice for clinically node-negative women if the finding of nodal metastases would alter treatment, that axillary dissection remains standard management for patients presenting with clinically evident metastases, and that good local control is obtained with excision alone and endocrine therapy for T1, estrogen receptor-positive tumors (while radiotherapy should be given for others undergoing breast-conserving therapy).

Regarding breast cancer management for frail elders, primary endocrine therapy (tamoxifen or an aromatase inhibitor) is the appropriate management of hormone receptor-positive breast cancer. In the rare frail elderly patient with a hormone receptor-negative tumor, excision alone may be the appropriate therapy.

Case Study

Background

An 80-year-old wheelchair-confined diabetic female is s/p right above the knee amputation after failed bypass grafting, and s/p 2 myocardial infarctions, most recently 3 years ago. She is not felt to be a candidate for revascularization. Her ejection fraction is 20%. She has occasional chest pain at rest. She also has an 80 packs per year smoking history, moderately severe arthritis, and mild dementia. She is managed by an endocrinologist, a cardiologist, her family doctor, and a rheumatologist. Her family doctor obtains a screening mammogram which demonstrates a 1.0 cm spiculated mass in the upper outer quadrant of the right breast. Breast exam is normal and there is no adenopathy.

Management

This patient is highly unlikely to have her life prolonged by the detection of this cancer prior to the development of a palpable mass. Ideally, she would never have had a screening mammogram. Since she did, optimal management would include obtaining an ultrasound (US) to see if the mass is visible by US. If yes, an US-guided core biopsy would be far more comfortable for the patient than lying prone, with her breast in compression, for a stereotactic biopsy. The core biopsy demonstrates a grade II, strongly estrogen receptor- and progesterone receptor-positive, HER2 negative infiltrating ductal cancer. This patient is an appropriate candidate for primary endocrine therapy with tamoxifen or an aromatase inhibitor. Although removal of the primary tumor optimizes local control, in her case this would entail localization prior to surgery, which would require her cooperation, as would a procedure done under local anesthesia. Her cardiopulmonary status places her at significant risk for general anesthesia. There is no indication for sentinel node biopsy since the identification of nodal metastases would not change her management. She should be followed with clinical breast exam. If a palpable mass develops in the breast, then surgical excision is warranted.

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Small Bowel Obstruction in the Elderly

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Contents

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Abstract
Small bowel obstructions may occur in patients of any age; however, the underlying cause and management may differ in the elderly population.

Keywords
Small bowel obstruction · Elderly · Hernias · Adhesions · Strangulation · Large bowel obstruction · Frailty · Biologic barriers · Nasogastric decompression · Malignant obstruction · Lysis of adhesions

Case Study 1

An 82-year-old female presents to the emergency department with acute onset of right lower quadrant abdominal pain, nausea, and vomiting beginning 8 h prior to presentation. She notes the pain began as nagging, but has steadily worsened. She states she has no significant surgical history. Medical history is significant for hypertension and hyperlipidemia. Her white blood cell count is 16,000, while her creatinine is elevated to 1.6 from her baseline of 0.7. Physical examination demonstrates a distended abdomen with rebound and guarding, as well as an incarcerated hernia in the right femoral canal.

Background

In the elderly patient presenting with obstructive symptoms, and no previous surgical history, the cause of obstruction is likely either from malignancy or hernia. Physical examination may reveal the inciting herniation, though many patients will undergo CT of the abdomen and pelvis in the emergency department. Physicians should take particular attention to look for incarcerated femoral/obturator hernias in the elderly, female patient. The patient's worsening pain, peritoneal signs, and elevated white blood cell count are likely signs of possible strangulation and require emergent surgical intervention.

Management

Nasogastric decompression should be initiated due to the patient's significant symptoms. Fluid resuscitation and correction of electrolyte abnormalities should be initiated after initial assessment of the patient. If physical examination did not reveal the source of obstruction, then CT imaging is warranted. In this patient, the biggest concern is strangulated bowel, considering the examination and laboratory findings. The patient will require emergent surgery after appropriate resuscitation.

Case Study 2

A 76-year-old male presents with a 2-day history of worsening nausea, vomiting, and abdominal distention. He states the symptoms began suddenly, but have slowly worsened. He began vomiting prior to coming to the emergency department. His last bowel movement was 2 days ago and most recently passed flatus in the early morning. He notes a past medical history of type 2 diabetes, hypertension, and a surgical history significant for an open right hemicolectomy 10 years prior for a colonic neoplasm, which required no further treatment. He is distended, tympanic to percussion, and tender on palpation diffusely, but has no rebound or guarding on abdominal exam. A CBC sent by the emergency department physician demonstrates a WBC count of 10.

Background

Adhesions remain the most common cause of small bowel obstruction in the elderly patient, despite increased risk of obstruction from other etiologies. In this patient with prior open surgery, obstruction secondary to adhesions should be considered. A full history, physical, and diagnostic testing will likely reveal the cause.

Management

This patient should undergo imaging to aid in diagnosing the cause of his obstruction. Fluid resuscitation and nasogastric decompression will be the first steps toward managing this patient's obstruction, as he currently does not show signs that would point toward urgent need for operative intervention. CT will likely reveal a discrete transition point, and in many cases NG tube decompression may be potentially curative.

Introduction

Small bowel obstruction (SBO) is a common surgical entity that can occur at any patient age. Although the general principles of diagnosis and treatment of SBO has remained consistent across all age groups, recent shifts in both incidence and etiology among patients of more advanced years now requires focused treatment considerations [1]. Historically, the classical dilemmas associated with management of SBO has remained steadfast for the elderly and include (1) differentiating strangulated from nonstrangulated SBO, (2) delineating ileus from SBO, and (3) determining optimal duration of nonoperative management for partial SBO. Indeed, a better understanding and approach to these clinical scenarios is especially pertinent for the elderly due to their increased risk for perioperative morbidity and mortality [2].

No current data suggests much change in the primary etiologies of SBO, which remain adhesions, neoplasms, and hernias [2, 3]. Likewise, standard operative management still includes an "open" exploratory approach along with adhesiolysis, herniorraphy, enteric bypass, and/or bowel resection. Importantly, advances in clinical imaging (e.g., multidetector computed tomography or MDCT) and biotechnology now provide more effective modalities for accurate detection as well as preventative measures for reducing recurrence of SBO following major abdominal surgery, ultimately leading to better patient management and outcome.

This chapter will focus on fundamentals for approaching the assessment and management of SBO in the geriatric population. Operative versus nonoperative management in the elderly will be addressed. This review will also highlight the important pathophysiology of adhesion formation and resultant SBO as well as current data supporting patient selection and minimally invasive approaches for the treatment of this disease. Moreover, operative intervention and developments in preventative measures, e.g., biological barriers, will be discussed. Throughout, an algorithmic, evidence-based approach for the evaluation and appropriate therapeutic management will be emphasized.

Epidemiology

Geriatric persons are now the largest growing segment of our population, with the number of persons 65 years of age and older more than doubling by the middle of this century, to approximately 80 million [4]. What remains problematic is accurately determining the incidence of SBO among this cohort. Previously, patient statistics were derived from population-based samples, primarily through national hospital-based discharge registries predicated upon imprecise coding schema for SBO, now seemingly more standardized in the International Classification of Diseases (ICD-10 CM) [5]. Therefore, current data likely reflect an underestimation of this escalating clinical problem.

Nevertheless, recent trends in aging have shown that patients 65 years of age and older make up 38% of all hospital discharges accounting for nearly 43% of in-patient care days. These rising figures remain in accord with overall age-adjusted national rates of hospitalization for intestinal obstruction occurring in 44.8 per 10,000 [4]. Similarly, census data based upon National Health Statistics, published in 2011, reported an increasing rise in intestinal obstruction with advancing age (Fig. 1) [6].

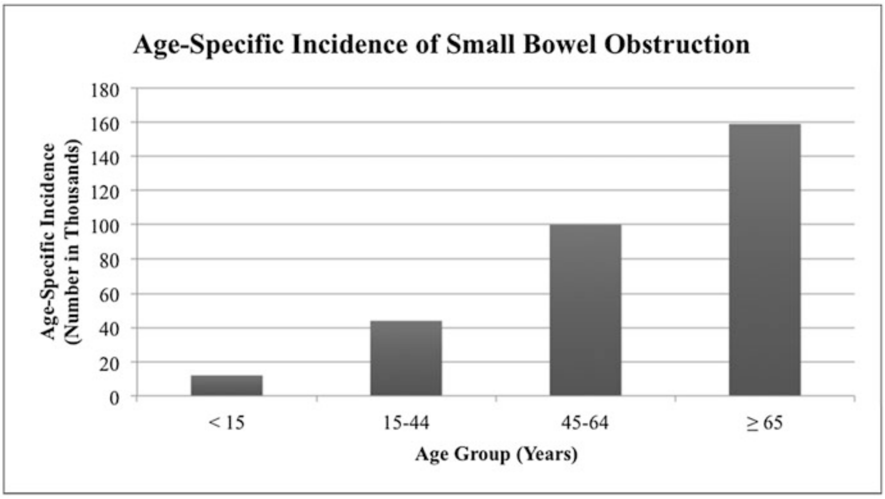

Fig. 1 Age-specific incidence of small bowel obstruction (From the National Center for Health Statistics, 2010)

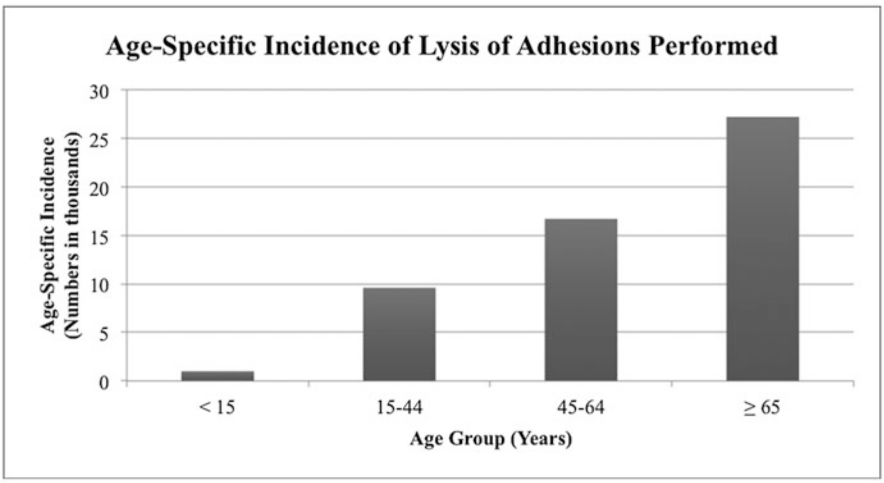

Fig. 2 Age-specific incidence of patients that underwent lysis of adhesions (From the National Center for Health Statistics, 2010)

Moreover, as small bowel obstruction increases with age, so also does the rate of reported operative procedures (lysis of adhesions, only) performed on elderly patients (Fig. 2), as well as a small increase in length of stay (Fig. 3) [6]. However, more concerning is the age-specific mortality rate due to vascular disorders and obstruction of the intestines (without hernia) derived from the National Center for Health Statistics, demonstrating age-specific increase in death rates, especially among individuals over age 75 (Fig. 4) [7].

Etiology-Specific Considerations in the Elderly

To predict the etiology of SBO and direct its treatment, it is first useful to classify SBO using several defining characteristics. Upon initial presentation, the degree of luminal obstruction should be described as either partial or complete. Equally important is *where* along the axis of the small bowel does the obstruction occur (e.g., proximal, mid, or distal). Underscoring the

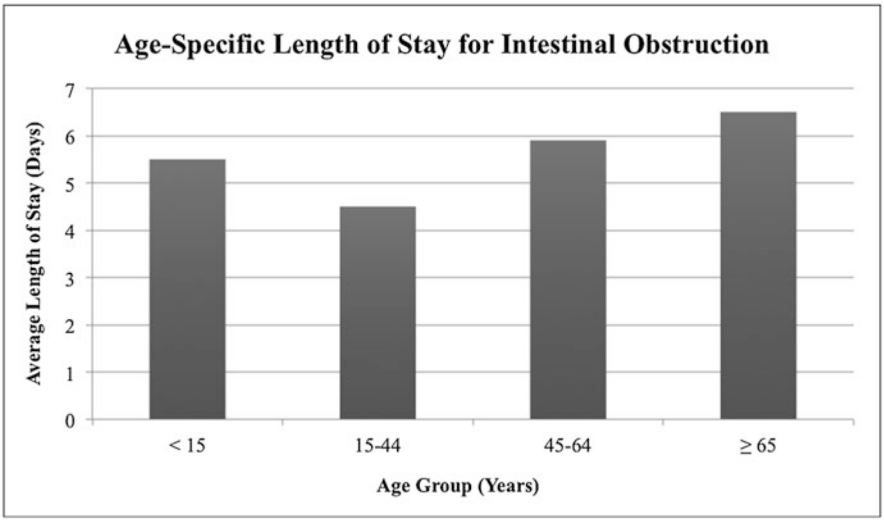

Fig. 3 Age-specific length of hospital stay for patients with admitting diagnosis of intestinal obstruction (From the National Center for Health Statistics, 2010)

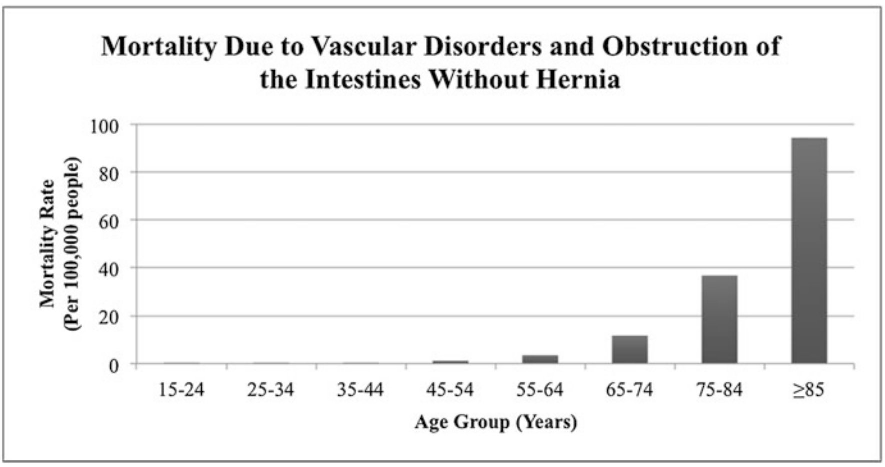

Fig. 4 Age-specific mortality rates of patients with diagnosis of "vascular disorder and obstruction of the intestines without hernia" (From the National Center for Health Statistics, 2007)

importance of these descriptors is the clinical scenario of the worrisome "closed"-loop obstruction where two areas of complete obstruction prevent axial flow of intestinal contents from the involved bowel loop in either direction. Similarly, structures causing obstruction can also be classified by their anatomic location as they relate to the perpendicular axis of the bowel. These structures may be either extrinsic and/or intrinsic to the bowel wall [8–10], both capable of comprising the entire lumen. Table 1 depicts some of the more common etiologies for SBO, keeping in mind that increasing age is a risk factor for most [11].

By definition, mechanical bowel obstruction is an abnormal decrease in the caliber of the involved bowel such that the passage of liquid or solid intestinal contents is impeded. In the majority of cases, SBO starts out as a simple mechanical obstruction with adequate blood supply to the intestinal wall such that the bowel remains viable. However, SBO can progress to strangulation where local bowel ischemia occurs either by direct compression of the affected segment by the obstructing lesion or by extreme dilation and increased pressure in the bowel just proximal to the obstruction, leading to mesenteric occlusion and diminished vascular perfusion.

Table 1 Common etiologies of small bowel obstruction in the elderly

Extrinsic causes
Postoperative adhesions
Hernias Inguinal, femoral, obturator, umbilical, ventral, internal
Malignancy Mass effect, peritoneal metastases
Volvulus
Intrinsic causes
IBD Crohn's disease, ulcerative colitis
Small bowel malignancy Primary, metastatic
Radiation enteritis/stricture
Bowel wall abscess/hematoma
Intraluminal obstruction
Gallstones
Fecal impaction
Bezoars
Foreign bodies

By comparison, the etiology and pathophysiology of large bowel obstruction (LBO) is considerably different from those of SBO, due to the mostly retroperitoneal nature of the large bowel, its relatively short mesentery, along with the competency of the ileocecal valve. Indeed, both types of obstruction occur frequently in the elderly, but nearly 80% of intestinal obstruction involves the small bowel, the predominant cause of obstruction in the elderly being due to adhesions from prior abdominal surgery [12]. Thus, emphasis of this chapter will focus on the pathophysiology, management, and measures to prevent intra-abdominal adhesions. Figure 5 illustrates the incidence of the three most common causes of SBO in the elderly – postoperative adhesions, neoplasms, and hernias – again all have increasing prevalence in the elderly population [10].

Adhesions

More than 90% of abdominal adhesions develop after surgery [13, 14]. The formation of adhesive bands following surgical manipulation is a dynamic process that can occur within several days after surgically traumatized tissues appose one another. Under normal circumstances, following nonsurgical traumatic injury, an inflammatory

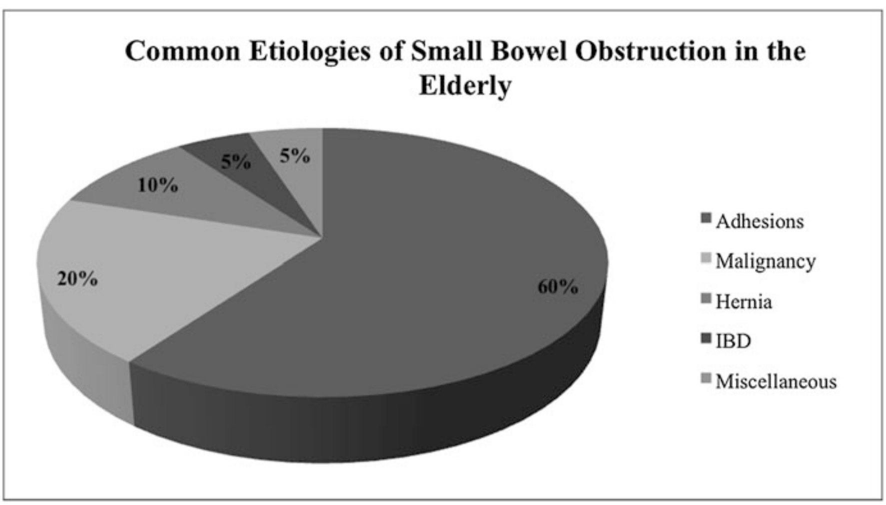

Fig. 5 Percentages of the most common causes of small bowel obstruction in the elderly

response ensues with recruitment and release of proinflammatory cells and cytokines (e.g., interleukin-1) along with activation of the coagulation cascade resulting in the deposition of a fibrinous matrix between apposing tissue surfaces. This fibrin matrix consists primarily of polymorphonuclear cells (PMNs), macrophages, eosinophils, red blood cells, platelets, and tissue debris encased within fibrinous strands. In most cases, such an early fibrin matrix is temporary and undergoes fibrinolysis following activation of tissue plasminogen. Degradation occurs within 72 h leading to tissue remodeling and repairs as mesothelial and mesenchymal cells proliferate to restore peritoneal defects. This process occurs 4–5 days after tissue injury preventing permanent attachment of adjacent tissue surfaces. In contrast, following surgically induced trauma, these involved tissues become ischemic from reduced blood flow resulting in suppression of fibrinolytic activity. With an absence of fibrin degradation (days 5 through 7), the fibrinous matrix now matures into an adhesive band from continued deposition of collagen and organization by fibroblasts. Over time, these adhesive bands represent a well-organized composition of connective tissues containing arterioles, venules, capillaries, and nerve fibers.

Remarkably, postoperative adhesions account for approximately 60% of all cases of intestinal obstruction in the elderly since many patients by the age of 65 have already undergone some form of abdominal surgery [15]. Whereby, the remaining causes of adhesions are typically secondary to inflammatory processes: such as pelvic inflammatory disease, diverticulitis, tuberculosis, and peritonitis.

The onset of adhesion-associated SBO may occur from several days up to 65 years from the initial operation. However, most SBOs develop earlier on during this interval period with reported median times to occurrence between 1.5 and 5.0 years [16–18]. Interestingly, the incidence of SBO after abdominal surgery appears to decrease over time; however, the cumulative risk remains substantial over the increasing lifetime of the patient. Nieuwenhuijzen et al. reported on a series of 234 patients who underwent colectomy and found that 11% of patients developed SBO within the first postoperative year and 30% within the first 10 years [19]. Similarly, a series from Norway demonstrated a 9% cumulative incidence of SBO after colorectal resection over 5 years [20]. Associated procedure-related formation of adhesions typically results after colorectal procedures, appendectomies, as well as multiple prior abdominal surgeries (including adhesiolysis for SBO) each accounting for 20–25% occurrence of adhesive SBO. Gynecologic procedures comprise the remaining 10–15% [18, 21, 22]. These procedures have been found to lead to the formation of single and multiple matted adhesive bands. Interestingly, vascular procedures have also been found to contribute substantially to the occurrence of adhesive SBO [23–25]. Therefore, not surprisingly, more than half of all adhesions causing SBO typically involves the ileum and occur within the pelvis. Moreover, in a recent Mayo Clinic series report, 48% of adhesion-associated SBO resulted from only single bands, whereas nearly 40% were multiple, among these 10% were categorized as dense [16]. In part, these findings clearly support adopting a less traumatic surgical approach (e.g., laparoscopy) in the treatment of certain diseases.

Malignancy

Neoplasms represent the second most common cause of SBO and are responsible for nearly 20% of intestinal obstruction in the elderly. Malignant obstruction occurs by the following mechanism (s): (1) via direct tumor extension causing extrinsic compression of bowel, (2) bulky lymphatic metastases which impinge on adjacent bowel, (3) and, more commonly, peritoneal implants (e.g., carcinomatosis), typically ovarian in origin, leading to a large burden of peritoneal disease and SBO [10]. While typically caused by benign lesions, acute SBO due to intussusception may result from malignancy, most commonly carcinomatosis, and in rare instances carcinoids, lymphoma, or metastatic melanoma [26]. Of greatest concern in these patients are the risk of a potentially palliative procedure and the needs for further treatment of malignancy. Decision to operate on these patients should be considered carefully, identifying potential risk factors that could lead to higher morbidity and short-term mortality [27].

Hernia

The third most common etiology found in the geriatric population is derived from hernias, which accounts for the remaining 10% of cases of SBO. Clinically, hernias are more often associated with bowel strangulation than adhesive bands: these include ventral, umbilical, incisional, inguinal, and internal hernias [8]. In addition, there are certain hernias that occur more frequently in the elderly, also requiring special consideration if a diagnosis of hernia-associated small bowel obstruction is suspected; these include femoral and obturator hernias. There is a well-known preponderance of femoral hernias among female patients; therefore, a high incidence of suspicion is warranted and femoral hernias should never be overlooked. By comparison, obturator hernias, however less common, should also be considered in the aging population with chronic disease, also more prevalent in the elderly and often associated with bowel strangulation [10].

Other miscellaneous causes of small bowel obstruction (10%) in older patients include inflammatory disease processes, such as Crohn disease, diverticulitis, and radiation-induced colitis. Moreover, gallstone ileus, which is rare in the general population, is more common in the elderly and can lead to SBO. Volvulus, bezoars (particularly in edentulous patients with prior gastrectomy), foreign bodies, fecal impaction, intestinal wall hematomas from blunt traumas (i.e., traumatic falls), and intestinal wall abscesses are also potential causes of small bowel obstruction in the elderly. Clinicians must be aware of these possibilities when differentiating an underlying cause for small bowel obstruction.

Moreover, as minimally invasive techniques become a larger part of our diagnostic and treatment armamentarium, application of these techniques is likewise expanding in the elderly due to the potential advantages for reduced morbidity. However, with these changes, new etiologic subclasses of iatrogenic causes of SBO are now being reported with increasing frequency. For example, endoscopically placed foreign objects, such as percutaneous endoscopic gastrostomy tubes and endoscopic retrograde cholangiopancreatography (ERCP) stents, can become dislodged and lead to luminal obstruction [28–33]. Similarly, SBO after laparoscopic procedures is well established [34]. Hernias can occur in trocar sites as well as through peritoneal defects created during laparoscopic procedures [35, 36]. Although postoperative adhesions are less likely, they also can occur. Because of the different etiologies of obstruction after laparoscopy, the general approach to SBO after laparoscopy may differ from that after laparotomy. One recent report examining a series of patients with early postoperative SBO after laparoscopy found that all patients eventually required surgical intervention [37].

Pathophysiology of SBO and Evaluation

Mechanical small bowel obstruction (e.g., adhesion, neoplasia, and hernia) is accompanied by proximal intestinal distension, which is a result of the accumulation of normal gastrointestinal secretions and gas above the obstructed segment. Initially, hyperperistalsis of the bowel is stimulated from intestinal distension leading to frequent loose bowel movements distal to the point of obstruction. Typically, this occurs in the early onset both in partial and complete obstruction. Paradoxically, presentation of frequent bowel movements in the elderly has been found to contribute to high rates of misdiagnosis, delayed treatment, and resultant increased morbidity and mortality [38–40].

As the distension becomes more severe, intraluminal hydrostatic pressures increase leading to the compression of the intestinal mucosal villus lymphatics. This results in the hindrance of lymphatic flow and development of bowel wall lymphedema. Consequently, the venules of the capillaries become congested from the increased hydrostatic pressure at the level of the capillary bed. Resultant fluids accumulate in the lumen as luminal pressures exceed 20 cm H_2O, thereby inhibiting absorption and stimulating secretions of salt and water into the lumen, proximal to the obstruction. Moreover, other causes of accumulation of intraluminal fluid may include (1) release of endocrine and paracrine substances, (2) changes in mesenteric circulation, (3) luminal release of bacterial toxins, and (4) excess release of prostaglandins. These may all contribute to promoting small bowel epithelial secretion, therefore, inhibiting absorption [38–40]. As a result, loss of intravascular fluid into the bowel manifests clinically as dehydration and hypovolemia. Consequently, prolonged dehydration can result in oliguria, azotemia, hemoconcentration, and eventually hypotension and hypovolemic shock. Furthermore, congested loops of bowel may twist upon themselves and accompanying mesentery resulting in vascular occlusion. In turn, bowel ischemia and necrosis develop, and if untreated, perforation, peritonitis, and sepsis may occur.

In general, the pathophysiologic changes that occur in small bowel obstruction are similar between the nongeriatric and geriatric patient population. However, and very importantly, as a result of inherent comorbidities found in the elderly, any delay in diagnosis may negatively impact on patient outcome with mortality exceeding 20% [11].

Clinical Features of SBO in the Elderly

Symptoms of SBO are primarily determined by the anatomic level and degree of obstruction. These include nausea and emesis, abdominal distension, abdominal pain, and obstipation (lack of passage of stool or flatus). Proximal SBO is characterized by frequent vomiting of bilious material and dehydration early in the course of disease with relatively little abdominal distension. With distal SBO, swallowed air and gastrointestinal secretions leads first to small bowel and abdominal distension. Only later do patients develop vomiting, usually after bacterial overgrowth has resulted in a feculent character to the enteric content. Partial obstruction is accompanied by continued, though potentially diminished, passage of flatus or stool. Early complete obstruction may also be accompanied by seemingly normal bowel movements, but eventually obstipation occurs.

Strangulation is notoriously difficult to detect reliably. Classic signs include fever, tachycardia, hypotension, and severe pain or focal tenderness, which are especially unreliable in the elderly, whereby the inflammatory response may be muted. Similarly, an elevated white blood cell (WBC) count may be absent in the elderly patient. From a previous Mayo Clinic series, strangulation was present in 13% of patients operated for SBO and was most commonly seen with the etiologies of hernia and small bowel volvulus [16]. Only 52% of patients with strangulation had an elevated WBC count, and the mean WBC count for patients with strangulation was just 2,000 cells/mm higher than that observed for patients with simple obstruction [3].

Diagnostic Considerations for the Elderly

Symptoms of SBO are common presenting complaints of elderly patients. The differential diagnosis for abdominal pain, nausea, and vomiting includes gastroenteritis, food poisoning, pancreatitis, biliary colic, porphyria, diabetic ketoacidosis, intestinal ischemia, constipation, paralytic ileus, and intestinal pseudo-obstruction. Compounding this problem in the elderly are age-related concurrent comorbidities that have been shown in a recent large retrospective study to be attributed to misdiagnosis, delay in surgical evaluation, and increased mortality [41]. Among these diagnoses, SBO is fairly common. In a review of ER visits to a regional trauma center by patients over 65 years of age, 12% of patients presenting with nontraumatic abdominal pain were ultimately found to have SBO [42]. Patients should be asked about any history of abdominal surgery or SBO, and during the physical examination, evidence of abdominal wall hernias should be vigilantly elicited. Laboratory values that can aid in the diagnosis and management of these patients include a complete blood count (CBC), basic metabolic profile, and serum amylase. As the classic signs of strangulation are often absent in the elderly, a leukocytosis, elevated hematocrit, and blood urea nitrogen (BUN) levels are often seen as a consequence of dehydration. Serum bicarbonate may be elevated because of loss of chloride-rich emesis and as part of a contraction alkalosis. These findings indicate a significant fluid deficit, which should be aggressively corrected upon initial presentation.

Diagnostic imaging is an important part of the evaluation of every patient with suspected SBO. Supine and upright abdomen and upright PA chest films are typically all that is required to confirm the diagnosis of complete SBO and to plan its treatment. Dilation of small bowel, paucity of colon and rectal gas, and air-fluid levels suggest complete SBO. Forty-eight percent of patients with proven SBO will have abdominal plain films that are consistent with SBO [16]. This, of course, means that almost half of patients with SBO have equivocal or even normal plain films, with residual colonic or rectal gas.

When these films are not diagnostic of complete SBO, the decision has traditionally been to rely on the clinical examination and serial plain films. In our experience, other CT scans has been useful in equivocal cases as an early diagnostic test and alters management in up to 20% of patients [43, 44]. Some centers have reported high accuracy of CT in identifying strangulation obstruction. A prospective evaluation of CT in 60 patients with high-grade SBO (with a 48% strangulation rate) showed that CT had 100% sensitivity and 61% specificity for detecting bowel ischemia [45]. The CT findings consistent with strangulation included bowel thickening and a high attenuation bowel wall on nonenhanced CT and abnormal bowel wall enhancement and mesenteric fluid on enhanced CT. A similar series of 100 patients from different institutions found a sensitivity of 83% and a specificity of 93% [46]. In contradistinction to these studies, several studies have compared CT with plain radiography and have found only modest differences in the overall accuracy of these tests when evaluating the grade of obstruction [47, 48]. CT also is helpful in patients with closed-loop obstructions and patients who swallow little air and thus have a gasless proximal bowel, as these problems are difficult to detect on plain films.

CT scans are more likely to demonstrate the cause of SBO, particularly when the obstruction is not secondary to adhesions. Current generation multidetector computed tomography or MDCT now permit high-quality reformatted images to be obtained in multiple planes which facilitate identification of the transition point and other findings in SBO: presence of a high degree of SBO and abnormal vascular course around the transition zone. Ultimately, MDCT may result in a paradigm shift toward earlier cross-sectional imaging in the elderly by its inherent ability to better predict the necessity for emergent surgery (i.e., ischemia) in the elderly when SBO is caused by adhesions [49, 50].

Less commonly used diagnostic imaging modalities in the acute setting include ultrasonography and MRI [51–55]. In the more subacute and chronic setting in patients with an intermittent or partial SBO, enteroclysis (small bowel enema) and small bowel follow-through may be useful [56, 57]. The passage of water-soluble oral contrast into the cecum within 4 h after CT or small bowel follow-through remains highly predictive of nonsurgical resolution of SBO [58, 59]. Interestingly, there have also been two randomized controlled trials examining whether water-soluble contrast speeds the resolution of partial SBO. Assalia et al. found a therapeutic benefit in terms of a shorter hospital stay in those patients receiving oral contrast with SBO from a variety of etiologies, whereas Feigin et al. reported no therapeutic benefit in patients with postoperative SBO [60, 61].

A special case of the diagnostic dilemma between SBO and paralytic ileus may occur during the early postoperative period. At 1–6 weeks after abdominal surgery, inflammatory adhesion can be thick and highly vascular. For these reasons, the morbidity of reoperation can be considerable. Because these early adhesions are also in a fluid state of constant remodeling, there is also a good chance of resolution of even high-grade partial obstructions without surgical intervention. It therefore becomes even more critical to define the degree of obstruction in these patients to avoid the higher morbidity of reoperation. In such circumstances, MDCT scanning may prove more beneficial for accurately distinguishing these equivocal cases [49, 50]. In very selected cases, when persistent partial SBO is a problem, endoscopic placement of a long intestinal tube may prove to be therapeutic and allow for a high-quality small bowel contrast study that more clearly characterizes the site of partial obstruction.

Initial Treatment

The traditional adage of "never let the sun set or rise on a small bowel obstruction," in part, underscores the severity of this diagnosis, particularly in the elderly [16]. Recently, however, this has been largely modified by a multifactorial assessment and approach that first considers the physiologic abnormality that has occurred since the onset of the SBO (i.e., hemodynamic status), type of SBO (partial, complete, strangulated), and patient comorbidities/performance status.

Even the patient who clearly has a complete bowel obstruction benefits from initial nonsurgical measures including proximal decompression, aggressive fluid resuscitation, and correction of electrolyte abnormalities. A Foley catheter is critical in the elderly to assess organ perfusion and fluid status. Generally, a nasogastric tube is adequate to decompress the gastrointestinal (GI) tract, but in some patients in whom a prolonged course of nonoperative management is contemplated, as for early postoperative SBO or the patient with multiple previous laparotomies or known severe adhesions, a long nasogastric (Miller–Abbott without mercury) tube may be considered.

Patients with complete SBO or with obvious signs of strangulation should be expeditiously resuscitated and then brought to the operating room. This strategy particularly applies to patients in whom the etiology is thought unlikely due to adhesions or neoplasm. However, most patients admitted for an SBO do not fall into this category. Two-thirds to three-fourths of patients with partial (primarily adhesive) SBO can be treated conservatively, with resolution of their acute episode [62–65]. In patients with a partial SBO, the duration of medical therapy continues to be a debated issue. Recent series examining this question have consistently shown that partial SBOs that ultimately resolve generally do so within 24–72 h. Delays beyond 48 h have been associated with increased morbidity in some series, whereas others have shown no increased morbidity with even longer delays [65, 66].

The potential arguments against maintaining a nonoperative approach are that the diagnosis of strangulation is inaccurate and the duration of medical treatment may be proportional to the incidence of strangulation or need for bowel resection and the subsequent higher incidence of complications [67]. These concerns are particularly relevant in elderly patients. Adhesive SBO requiring surgery in elderly patients ultimately requires bowel resection in up to 50% of cases, whereas only 8% of patients of all ages required bowel resection in the Mayo Clinic series [16, 68]. In that series, among patients in whom strangulation was found, delays of more than 4 h from presentation to surgery were associated with higher morbidity rates. Much emphasized is the importance of the underlying etiology when determining the mortality risk of delayed surgical intervention [16]. Data from the Mayo Clinic series showed that in the case of obstruction due to hernia, the time from presentation to operation was directly related to the mortality rate, but this relation with mortality did not exist for SBO caused by adhesions or malignancy.

A selective approach may be more appropriate in the elderly patient with SBO. The immediate strategy should be determined by consideration of (1) the evidence for current bowel ischemia, (2) the presumed etiology of the SBO, and (3) degree of obstruction. Patients with two or more signs of strangulation, radiographic signs of complete SBO, or both are operated on as soon as possible after adequate resuscitation. Nasogastric decompression and serial examinations are then planned for those in whom an adhesive, partial SBO is likely. For those in whom the diagnosis of SBO is unclear or the etiology is in question, CT is performed. The longer-term strategy in patients initially treated nonoperatively

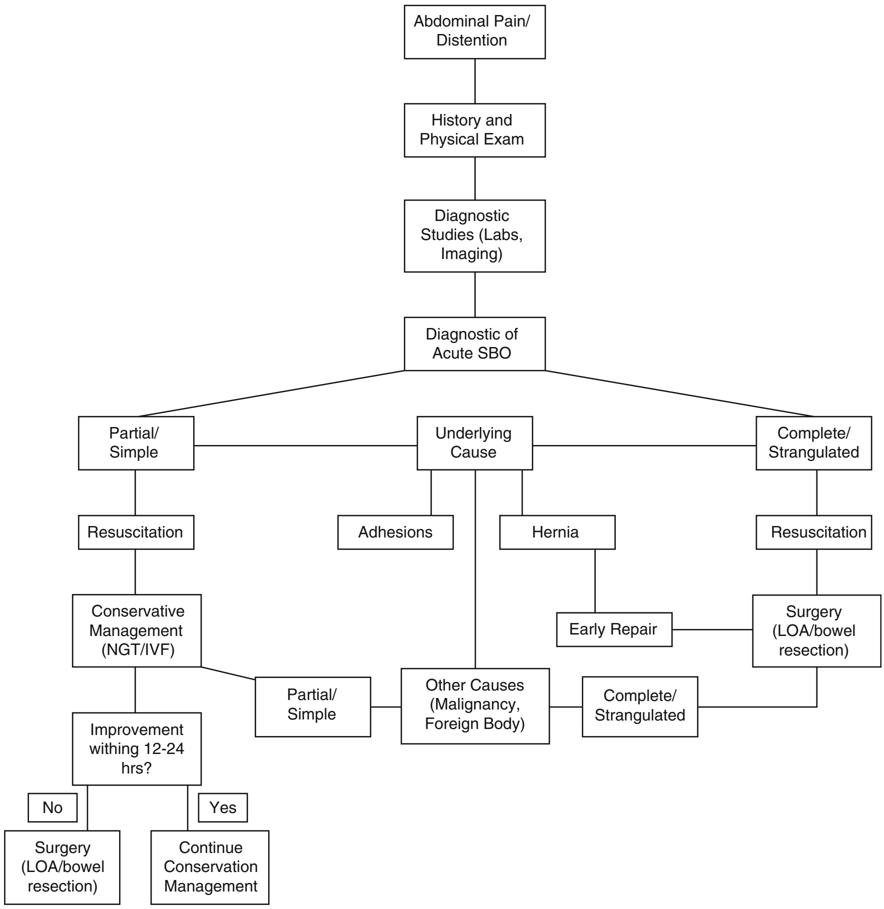

Fig. 6 Recommended algorithm for the management of small bowel obstruction in the elderly. *SBO* small bowel obstruction, *LOA* lysis of adhesions, *SBR* small bowel resection, *LBR* large bowel resection, *IVF* intravenous fluids, *NGT* nasogastric tube, *IBD* inflammatory bowel disease

should include both the above factors as well as [3] the likelihood of intraoperative and postoperative complications. These factors should be weighed against the likelihood of success using continued nonsurgical management. Figure 6 shows our diagnostic and treatment algorithm for patients with SBO.

Surgical Treatment: General Principles

Preoperative antibiotic coverage to cover enteric organisms, as per SCIP guidelines, should be administered, as a number of cases involve bowel resection or inadvertent enterotomy [69]. Although elderly patients are more likely to have underlying cardiovascular disease, increasing the risk of a perioperative cardiac event, invasive monitoring devices are rarely required. Hypotension upon induction of anesthesia should be avoided by attention to adequate preoperative fluid resuscitation often requiring 3–4 L of intravenous isotonic crystalloid. The surgical adage, “rush to resuscitate, then operate,” must always be remembered in the elderly patient with SBO.

Open approach remains the standard of care for treatment of SBO in the elderly; however, use of laparoscopy has increased in frequency over the last decade [70]. Laparotomy should be performed through a midline approach with at least part of the initial incision over virgin/scarless skin, if possible. Entry through the fascia is done with extreme care, avoiding the use of cautery, as transmitted heat can injure underlying bowel. Adhesions are usually stronger than the junctions between the small bowel muscle layer and the muscularis propria and submucosa, and this seems particularly true in the elderly patient. Sharp dissection with scissors or knife should therefore be performed to avoid seromuscular injuries. We generally lyse adhesions from the anterior abdominal wall first and then proceed to run the small bowel lysing adhesions as we progress from the ligament of Treitz to the terminal ileum.

While running the bowel, the etiology of the SBO and local bowel viability are assessed. The commonly available parameters include bowel color, peristalsis, and mesenteric pulsations. Although clearly viable and clearly nonviable extremes are easy to identify, many gradations of color are difficult to judge, and assessment of ultimate viability is prone to error. Adjuncts to these methods continue to include Doppler flow probe assessment of mesenteric and antimesenteric blood flow, intravenous fluorescein perfusion, and electromyography (EMG) [71–73]. Although these methods have their advocates, none has consistently been shown to have higher accuracy than "clinical judgment" using visual and manual inspection. Our general strategy is to resect questionable bowel, if possible. If resection would result in less than 4–5 ft of clearly viable intestine, questionable segments with the highest likelihood of viability should be left in situ with a planned "second-look" reoperation within 24–48 h.

To allow abdominal wall closure, frequently the bowel must be decompressed. This can be achieved with a long nasogastric tube, but we favor gentle retrograde milking of the intestine toward the duodenum with fluid evacuation via a nasogastric tube. To minimize excessive distension and the risk of serosal tears, this process is first started in the mid-jejunum. The proximal jejunal segment is then evacuated of luminal content. The process is then repeated starting progressively more distally on the bowel. Prior to closing the abdomen, the bowel loops should be laid back in the abdomen in gentle folds. Some have advocated the use of long intestinal tubes to act as stents, particularly in the patient with recurrent SBO or pervasive adhesions [74]. Another option gaining popularity is the application of hyaluronidase-containing films to inhibit adhesion formation [75]. Clinical trial data (see section "Biological Barriers") demonstrate safety and potential efficacy for reducing adhesions and adhesion-associated SBO.

Laparoscopic Treatment of SBO

Laparoscopic surgery has theoretical advantages over open surgery including decreased postoperative pain, reduced wound complications, decreased respiratory complications, and shorter hospital stay. These advantages are particularly attractive in elderly patients and have led to a decreased threshold for elderly patients seeking surgical management by a minimally invasive approach. Recent reports of SBO management with favorable outcomes using a laparoscopic approach have been documented [76]. The challenge of laparoscopic treatment for SBO rests not in the diagnostic efficiency, which is between 60% and 100%, but the therapeutic efficacy, which is generally low (40–88%). Not surprisingly, the conversion rate to laparotomy has been reported to be as high as 52% [77–81].

Several factors make laparoscopic treatment of SBO difficult and have prevented many surgeons from adopting this approach to SBO. Most significant is the concern for the physiologic effects of laparoscopy on the elderly patient's cardiovascular system [82]. Insufflation may decrease excursion of the diaphragm, leading to elevated peak airway pressures, and decreased pulmonary compliance and vital capacity. Increased abdominal pressure may also decrease venous return to the heart, elevating systemic vascular resistance and mean arterial pressures. This increased abdominal pressure may also decrease renal and hepatic perfusion. Lastly, insufflation can worsen gastroesophageal reflux in an elderly patient with weakened lower esophageal sphincter, increasing risk of aspiration, especially in Trendelenburg position [82].

Additionally, exposure with laparoscopy can be problematic because of diffuse adhesions to the anterior abdominal wall and because distended bowel may have already increased the intra-abdominal pressure and decreased the volume of pneumoperitoneum that can be achieved. Therefore, it is generally best to use an open insertion technique and to select an initial insertion site remote from previous scars. In a case with concern for extensive adhesions, we recommend open, trocar insertion technique at Palmer's Point (left upper quadrant, 3 cm below the coastal margin in the mid-clavicular line). We typically do not recommend insufflation and creation of pneumoperitoneum by Veress needle approach in the setting of SBO. Bowel distension should be minimized by preoperative nasogastric decompression, and in selected cases using a long intestinal tube prior to attempting laparoscopic treatment. Perhaps the most common reason for reluctance to use laparoscopy for SBO is a concern that treatment may require an extensive adhesiolysis or resection that is problematic to achieve laparoscopically. Therefore, proper patient selection is paramount before choosing a minimally invasive approach. A recent Medline, Embase, Cochrane review from 1980 to 2007 identified predictive factors for a successful laparoscopic adhesiolysis, which includes two previous laparotomies, adhesions associated with appendectomy, single adhesive band, early <24 h laparoscopic management from onset of symptoms, no peritonitis, and surgical expertise [78]. Despite the aforementioned concerns, the number of laparoscopically managed SBOs has increased over time. An analysis of the National Surgical Quality Improvement Program (NSQIP) database demonstrated an increase in laparoscopic management from 17.2% in 2006 to 28.7% in 2013 [70].

The laparoscopic approach is particularly attractive for adhesive SBOs where there is a single adhesive band. Conventional laparotomy is recommended for malignant SBOs and hernia-related SBOs, where there is a high rate of strangulation. The general principles of the laparoscopic approach are similar to those of the open approach. Adhesions are dissected sharply, and after adhesiolysis, the bowel is inspected from the ileocecal valve to the ligament of Treitz.

Although one-half to two-thirds of patients may be managed laparoscopically, one must anticipate a high conversion rate to open laparotomy. A study by Bailey et al. compared SBOs treated in two surgical units, one with a special interest in laparoscopy [83]. The laparoscopy unit attempted laparoscopic treatment in 80% of SBOs, and among those cases, they completed treatment laparoscopically in 56%. The laparoscopically treated patients left the hospital 5 days earlier than the open procedure patients, but they also had a higher rate of unplanned reoperation (14% vs. 5%). The safety and efficacy of diagnostic laparoscopy for SBO appears well established from retrospective studies, whereas laparoscopic adhesiolysis requires careful patient selection and laparoscopic surgical expertise, using an operative plan that includes converting to an open approach if extensive adhesions or nonadhesive causes are encountered. Ultimately, prospective randomized trials assessing all clinically relevant outcomes are needed.

Nonoperative Management

In many cases of SBO due to malignancy, surgery may be high risk, and often for palliative relief. Risk of performing a surgical procedure in these patients may outweigh the benefits. Placement of self-expandable metal stent (SEMS) has become a viable alternative cases of malignant gastric outlet obstruction or large bowel obstruction, and its use is being investigated for management of malignant SBO [84, 85]. Small prospective studies have been performed describing three different techniques: (1) through-the-scope insertion with colonoscope, (2) through-the-overtube using double balloon/single balloon/spiral enteroscopy, and (3) withdrawal-reinsertion using double balloon enteroscopy [86–90]. Most publications regarding this topic are case series or reports, though with favorable outcomes with regard to morbidity and relief of symptoms. Decision to employ this strategy requires attention to patient selection, as some patients will have more than one site of obstruction, in particular those with peritoneal metastases. However, there may be significant benefits toward this tactic in select patients including shorter hospital stay, decreased cost, lower short-term mortality, and early continuation of chemotherapy [91].

Outcomes of Treatment of SBO

Most studies of the outcomes of treatment of SBO have centered on traditional surgical outcomes, such as perioperative mortality, survival, and post-operative complications. Increased age is a risk factor for mortality from SBO (Fig. 4). Perioperative mortality is also related to the etiology of the SBO. For example, SBO from malignancy has an in-hospital mortality of 21% and a median survival of 6 months, compared to a 4–5% mortality risk for hernia and adhesive etiologies. Similarly, a large prospective experience by Miner et al. showed that the potential benefits of palliative surgery are minimized by the inherent morbidity (29%) and mortality (11%) of these procedures [92]. Of note, delay from symptom onset to presentation is not generally related to mortality risk except in the case of hernias, where there is also a higher risk of strangulation; overall, in-hospital morbidity is 30% but is increased in patients with strangulation to 60%.

As adhesions represent the most common cause of SBO in the elderly, identifying pertinent risk factors for adverse outcome following surgery for adhesion-associated SBO may provide the clinician with important information for stratifying the risk-to-benefit ratio for clinical decision making especially in the more concerning elderly population. A recent VA National Surgical Quality Improvement Program developed a morbidity and mortality risk index assessment based on a cumulative score that predicts the probability of an adverse outcome [93]. Not surprisingly, the odds of mortality in a patient 70–79 years of age are increased by a factor of 1.855 compared to a patient younger than 50 years. Similarly, better outcomes are associated with adhesiolysis only, compared to bowel resection.

Attempts were also made to ascertain the longevity of treatment of SBO, specifically, for patients treated nonsurgically, the likelihood and timing of recurrence, and how this compares to patients treated surgically. These questions were largely addressed from a statewide longitudinal population-based outcome analysis derived from 32,583 hospitalized patients (mean age 63 years) admitted with a diagnosis of SBO (index admission). From this study, Foster et al. showed that in California, from data derived from patients hospitalized in 1997, SBO was primarily managed non-operatively in 76% of these patients. Of the patients that underwent operative management (24%), there was a longer length of stay, lower mortality rate, fewer SBO readmissions, and longer time to readmission. In general, patients who did not have operations were usually older and with more comorbidities. However, regardless of the treatment, 81% of patients had no subsequent SBO requiring readmission over the 5-year study follow-up period [63]. Similarly, Landercasper et al. retrospectively reviewed 309 consecutive patients with SBO and followed them for recurrence [57, 94]. The SBOs recurred in 34% by 4 years and in 42% by 10 years. Those who were operated on had a lower recurrence rate (29%) than those who were treated non-operatively (53%). Among those who had surgery, recurrences differed by etiology: malignant (56%), adhesive (28%), and hernia (0%). In this study, the number of prior obstructive episodes was not a risk factor for recurrence. However, Fevang et al. retrospectively studied 500 patients with adhesive-associated SBO (ASBO) for up to 40 years for recurrence [58, 95]. They found that the cumulative recurrence rate for patients operated once for ASBO was 18% after 10 years and 29% at 30 years. The likelihood of a recurrent ASBO was highest within 5 years after the previous one, but a considerable risk was still present 10–20 years after an ASBO episode.

In addition to recurrence risk, treatment choice affects the cost of care and utilization of health-care resources. The costs of caring for patients with SBO are considerable. From a Swedish study, 60% of all bowel obstructions were due to adhesions, 65% of them required more than a

1-day hospital stay, and 45% of these required surgery. Calculating direct costs and extrapolating these data, $13 million are spent on adhesive SBO in Sweden (a country of 8.5 million population) annually [96]. In many cases, treatment choice is determined solely by the initial clinical presentation. Either the decision to undergo surgery occurs early or an initial short duration of medical management results in rapid clinical improvement and resolution of the SBO. However, in patients with high-grade partial obstruction likely due to adhesions, an early decision to treat surgically is likely to have a favorable clinical outcome but may result in a longer hospital stay and higher cost of care compared to a nonsurgical approach. As one might expect, retrospective analysis of patients treated medically and surgically show that surgically treated patients have clinical outcomes similar to those treated medically but with longer lengths of stay [17]. The additional costs of care in patients ultimately treated surgically may be as much as eight times higher than nonsurgically treated patients. This differential makes tests with improved diagnostic accuracy, such as CT or MDCT, more cost-effective for questionable partial SBO [97].

Preoperative frailty scores have been more recently used as a predictor of postoperative morbidity and mortality in various surgical specialties [98–100]. Commonly used markers, such as the American Society of Anesthesiology (ASA) score and the Lee and Eagle Criteria, are either subjective estimates or evaluate only one organ system, leaving outcomes in the elderly difficult to predict [101]. For this reason, frailty scores may act as a surrogate marker of an elderly patient's physiologic reserve and vulnerability. One such example, Makary et al. prospectively measured frailty in 594 patients presenting for elective surgery. Their score was composed of five validated criteria including shrinking (weight loss), decreased strength (weakness), exhaustion, low physical activity, and slowed walking speed. Frailty score improved the power of the previously mentioned indices to predict surgical complications and discharge to nursing facility [101]. A systematic review of 23 studies assessing various instruments for measuring frailty (mean age range 75–87 years), demonstrated associations between these markers and 30-day, 90-day, and 1-year mortality, as well as postoperative complications and length of stay [98]. When planning operative intervention for SBO, frailty is an important predictor of the potential for postoperative morbidity and mortality that should be considered in the decision-making process.

Biological Barriers

Barriers are biosynthetic membranes or gels that have been shown to be effective in decreasing surgically induced adhesions. One of the first prototypes successful in reducing postoperative adhesions in humans was Interceed®, which was composed of modified oxidized regenerated cellulose. This particular barrier was found to be applicable following gynecologic procedures; however, its efficacy in general surgical procedures is unknown [102]. Another type of biological barrier is expanded polytetrafluoroethylene (PTFE). This was shown to prevent pelvic adhesions. However, PTFE was not cost-effective or bioabsorbable and required a large piece of material and suturing to keep it in place for adhesion prevention.

To date, the most efficacious barrier is a hyaluronan and carboxymethylcellulose bioresorbable membrane called Seprafilm®. The mechanism of action of adhesion prevention is believed to occur by one of the components known as sodium hyaluronate. It is believed to improve peritoneal healing by increasing the proliferation of mesothelial cells and facilitating their detachment and migration, leading to the restoration of the mesothelial lining within the abdomen. It is also thought to increase the fibrinolytic response of mesothelial cells, aiding in adhesion prevention.

Seprafilm® is typically prepared as a membranous sheet that is applied over potential sites of adhesion formation (e.g., traumatized tissue), prior to closure following an abdominal surgical procedure. Placement of the membrane requires that the peritoneal cavity, as well as the instruments and gloves used to handle the barrier, be as

Table 2 Clinical trials regarding safety and efficacy for use of Seprafilm® for prevention of small bowel obstruction recurrence

Study	No. of Patients	Pathology	Occurrence of SBO		Reoperation for SBO		Complication	
			Y	N	Y	N	Y	N
Becker et al. [103]	183	Ulcerative colitis/FAP	42	85	NR	NR	82	86
Diamond [104]	127	Uterine fibroids	27	54	NR	NR	NR	NR
Beck et al. [105]	1791	IBD	NR	NR	NR	NR	249	223
Fazio et al. [106]	1791	IBD	15	29	8	4	249	223
Kusunoki et al. [107]	62	Rectal cancer	2	5	1	3	NR	NR
Hayashi et al. [108]	150	Gastric cancer	4	7	0	1	23	22
Vrijland et al. [109]	42	Diverticulitis/obstructed sigmoid	21	21	NR	NR	8	3

FAP familial adenomatous polyposis syndrome, *IBD* inflammatory bowel disease, *NR* not recorded

Table 3 Statistical significance of clinical trials regarding the use of Seprafilm® for prevention of adhesion formation and recurrence of small bowel obstruction

Study	Occurrence of SBO (p-value)	Complications (p-value)
Becker et al. [103]	<0.00000000001	>0.05
Diamond [104]	<0.0001	NR
Beck et al. [105]	NR	<0.05
Fazio et al. [106]	<0.05	NR
Kusunoki et al. [107]	0.22	NR
Hayashi et al. [108]	0.534	0.722
Vrijland et al. [109]	NR	NR

NR not recorded

dry as possible. Approximately, 1–2 cm of the membrane should be exposed from its holder prior to application. When entering the abdominal cavity, the membrane can be curved or slightly folded to facilitate placement over the desired area. To ensure adequate adherence to the tissue, a dry instrument or gloved hand can be used to gently press down on the membrane. Seprafilm® should be sufficiently placed over the margins of the incision or surgically traumatized tissue and overlapped to achieve sufficient coverage. Importantly, a bowel anastomosis should not be wrapped with Seprafilm®, as this practice has been associated with adverse events. Seprafilm® slowly resorbs within 7 days of placement and is fully excreted by 28 days.

Seprafilm® was evaluated in a number of prospectively, randomized, controlled, multicenter studies and consistently demonstrated overall safety (Table 2) [103–108]. The larger clinical trials did show a significant reduction in the formation of adhesions and adhesion-associated SBO (Table 3) [103–109]. Still other trials have demonstrated limited efficacy while confirming its safety [110]. These barriers potentially provide an excellent form of adjunctive therapy for preventing postoperative adhesions, the number one cause of SBO, not only in the elderly but also in the general population.

Conclusion

Small bowel obstruction is a common pathological process that can occur in any patient population. Its effects, however, are devastating in the elderly and warrants prompt appropriate management. Utilization of a thorough clinical history, physical examination, and investigative studies provide the necessary information to determine a diagnosis and direct the next step in treatment. Immediate aggressive resuscitation is required with monitoring of hemodynamic parameters especially in older patients because of their limited physiologic reserve and comorbidities.

Based on the type of SBO, a trial of conservative management may be initiated or definitive surgery may be performed. Either the standard laparotomy or laparoscopic surgical technique may be used dependent on surgeon experience, patient stability, or underlying cause, with further consideration for patient comorbidities. Recent developments of biosynthetic products have made a positive impact in the management of SBO that help in the prevention of surgically induced adhesions in the elderly.

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Ischemic Disorders of Small and Large Intestine

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Gregorio A. Sicard and Joshua Balderman

Contents

Abstract

Mesenteric ischemia is a condition that can be fatal if not diagnosed early and treated efficiently. The acute form of mesenteric ischemia can present with pain out of proportion of abdominal findings by exam and is usually due to an acute embolus to the superior mesenteric artery. The chronic form of mesenteric ischemia tends to be indolent and presents with postprandial pain and significant weight loss over a long period of time. Accurate diagnosis of chronic

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mesenteric ischemia is important to avoid the continuum to acute mesenteric ischemia which has an extremely high mortality. Common risk factors are cardiac arrhythmias, age, and systemic atherosclerosis. In any patient suspected of having chronic mesenteric ischemia, CT angiogram can be diagnostic. A third form of mesenteric ischemia is nonocclusive venous mesenteric ischemia which is usually associated with elderly patients in congestive heart failure or with other intra-abdominal pathologies. That condition if diagnosed appropriately can be managed with anticoagulation and close monitoring.

Standard treatment for chronic and acute mesenteric ischemia is open surgical procedure with embolectomy for an embolus and a bypass either antegrade or retrograde for the chronic form of atherosclerotic mesenteric ischemia. Percutaneous stenting of the SMA has yielded excellent short-term results and in very acute or high-risk patients. The long-term results of superior mesenteric artery stenting are not as good as surgical bypass, and some investigators feel that close monitoring of the stent is required and in many cases only used as a bridge until the patient medically stabilizes. Early diagnostic suspicion and appropriate treatment has a significant impact in good outcomes.

Keywords

Mesenteric ischemia acute and chronic · Early diagnosis · Angiographic imaging · Open surgical or endovascular treatment · Pain out of proportion to physical findings · Post prandial pain and weight loss · Mesenteric bypass versus stenting · Second look procedure

Mesenteric Ischemia Vignettes

Case Study: SMV Thrombosis

A 51-year-old male with no PMH presents with 6 days of increasing abdominal pain. He states on Sunday evening he was at a wake and started noticing epigastric abdominal pain that was aching but not severe at the time. Over the next day, the pain increased and began radiating to his back. The pain was sometimes worsened with eating but not always. It is, however, always worsened by movement/activity. Tylenol did not relieve his symptoms. He had no nausea, vomiting, or hematochezia and no recent weight loss, fever, chills, or night sweats. He additionally denies recent chest pain or shortness of breath. He went to see his primary care physician on Tuesday and was given omeprazole, which he took Tuesday night and Wednesday morning. On Wednesday, he was switched to pantoprazole, which he took on Wednesday evening and Thursday morning. Due to no relief on pain by either omeprazole or pantoprazole, he stopped taking them Thursday night. He was scheduled to see a cardiologist on Friday; however, the pain had increased to 9/10 and was so great that patient was in tears when trying to move, so he came to the emergency department instead.

In the emergency department, vitals were stable, and labs were significant only for hgb of 17.7 (hct 51.3%). Chest X-ray showed mild bilateral atelectasis without acute pulmonary process. EKG was unremarkable. CT body/pelvis with contrast showed complete occlusion of the SMV with fat stranding at the root of the mesentery. He was given fluids and started on Heparin gtt.

Management

The patient was admitted to the hospital and started on a heparin drip. A coagulopathy workup was sent to the lab. Serial abdominal exams were performed. He improved over the course of his hospital stay, and no surgical intervention was offered. By discharge, his pain had resolved and he was tolerating an oral diet. He was discharged on oral anticoagulation therapy.

Case Study: Mesenteric Ischemia

A 42-year-old female presented to clinic with a 3-month history of pain associated with eating and 30 pound weight loss. Three months prior to presentation in our clinic, she had suffered from significant vomiting and abdominal pain. She had a CT at an outside hospital which revealed an isolated aneurysm of the superior mesenteric artery. She underwent resection and interposition grafting at the other institution. On repeat imaging at our institution, she was found to have an occluded interposition graft.

Management

The patient was admitted to the hospital and taken for a diagnostic angiogram. This confirmed the previous diagnosis of occluded SMA interposition graft. She was also found to have a severely disease celiac artery at its origin with a patent common hepatic artery but non-visualized splenic artery. She was brought to the operating room a few weeks later for bypass grafting. She underwent re-operative exploratory laparotomy with bypass grafting from the aorta to the common hepatic artery with greater saphenous vein. The SMA was unable to be safely dissected due to scar tissue. She did well postoperatively and is now tolerating an oral diet and has regained a normal BMI.

Case Study: Mesenteric Ischemia

A 60-year-old male with a history of CAD status post CABG, PAD s/p left BKA, and hypertension presented to the emergency department with acute onset of severe abdominal pain. Patient described this as severe, crampy, and worse with activity. Initially, he thought it was due to constipation and took laxative but without resolution of symptoms. In the emergency room, he had a CT scan which showed portal venous gas and severe stenoses of the celiac and SMA without complete occlusion.

Management

The patient was taken to the operating room for diagnostic laparoscopy and diagnostic angiogram with possible interventions. Laparoscopy revealed a dead right colon. Angiogram showed severe stenosis of the celiac and SMA. It was then decided to stent the SMA with a covered, balloon expandable stent. Exploratory laparotomy was performed, and the right colon was resected and bowel left in discontinuity. The patient was brought back to the operating room 2 days later for a second look. At that point, the remaining bowel looked healthy, and a good Doppler signal was obtained at the base of the mesentery. The bowel was re-anastomosed, and the abdomen was closed in the standard fashion.

Epidemiology

The frequency of atherosclerosis of the mesenteric vessels increases with age and is found in 20% of patients over 65 years old in North America. In a population study of all patients undergoing autopsy or operation in Malmo, Sweden, 12.9% of patients were found to have fatal acute mesenteric ischemia. Chronic mesenteric ischemia accounts for approximately 5% of mesenteric ischemic conditions. On the other hand, acute mesenteric ischemia (AMI) is more common and has a devastating outcome.

The risk factors for acute mesenteric ischemia are all related to advanced age. They include low cardiac output due to congestive heart failure, cardiac arrhythmias, valvular disease, atherosclerosis, and intra-abdominal malignancy.

Anatomy

Understanding the gut blood supply and extensive collaterals is critical to understanding the cause(s) of acute and chronic mesenteric ischemia.

The gastrointestinal tract derives its blood supply from the celiac, superior mesenteric, and inferior mesenteric arteries (Fig. 1). The celiac axis branches into the common hepatic, left gastric, and splenic arteries. The common hepatic artery gives off the gastroduodenal artery which terminate in functional anastomoses to the anterior and inferior pancreaticoduodenal arteries from the superior mesenteric artery. The SMA arises from the aorta just distal to the celiac access. The SMA gives rise to the aforementioned inferior pancreaticoduodenal branches, the middle colic artery, right colic artery, ileal branches, and ileocolic artery. The middle colic artery comes off the proximal SMA and supplies the transverse colon. It also communicates directly with branches of the IMA. The ileocolic artery is the terminal branch of the SMA and supplies the terminal ileum, cecum, and ascending colon. The IMA is the most distal and

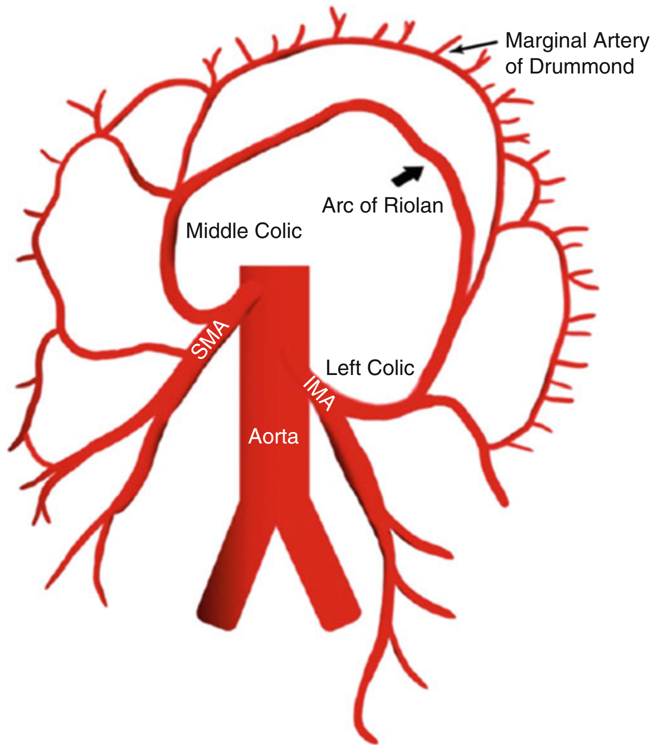

Fig. 1 Drawing demonstrating collateral pathways between superior mesenteric artery (SMA) and inferior mesenteric artery (IMA)

smallest of the mesenteric arteries and is also a ventral branch of the aorta. It arises approximately 6–7 cm below the SMA, which corresponds to the L3 level of the vertebra. It supplies the hindgut, which includes the distal transverse colon, descending colon, sigmoid colon and rectum. The left colic artery communicates with the SMA via the marginal artery.

To understand the pathophysiology of mesenteric ischemia, it is important to understand the anatomic collateral pathways. For collateral circulation between the celiac axis and the SMA, the principle pathways are the gastroduodenal and pancreaticoduodenal arteries. Unusual anatomic variations can also provide collateral flow, such as a replaced right hepatic artery or a pancreatic or middle colic artery originating from the CA. In addition, there is an infrequent but well-recognized collateral pathway known as the arc of Buhler, which represents a direct collateral pathway between the CA and the SMA. This is thought to be due to a persistence of an embryonic ventral segmental artery.

There are three major and consequential anastomotic pathways between the SMA and the IMA, the most significant of which is the marginal artery of Drummond. This artery runs within the mesentery of the colon and gives rise to the vasa recta. It receives branches from the ileocolic, right colic, middle colic, and the left colic arteries. It usually runs close to the mesenteric border of the colon. Normally, this artery is not particularly large; but with occlusion of the SMA, it can enlarge significantly. The arc of Riolan also lies within the mesentery but is much closer to its base. This collateral connects the middle and left colic arteries. The final potential collateral pathway between the SMA and IMA is the meandering or wandering mesenteric artery. Occasionally, this is markedly hypertrophied arc of Riolan, and other times, there is a distinct anastomotic pathway between the SMA and IMA (Fig. 1). The IMA can be collateralized not only by the MSA but also by the lumbar branches of the aorta as well as the hypogastric arteries.

The venous drainage of the gut is principally via the splenic vein for the foregut, the superior mesenteric vein for the hindgut, and the inferior mesenteric vein for the hindgut. These vessels all drain into the portal vein and hence through the liver.

Mesenteric blood vessels are highly reactive, and accordingly, mesenteric blood flow can fluctuate between 10% and 35% of cardiac output. They react to a large variety of endogenous cytokines and exogenous medications. The GI tract requires varying amounts of blood flow based on the metabolic needs of the gut during fasting and fed states. At rest, the mesenteric flow is low due to high resistance with low diastolic flow with flow reversal, which is typical of high-resistance beds. In the fed state, there is both systolic and continuous diastolic flow.

Imaging/Diagnosis

Radiographic imaging plays an increasingly significant role in the diagnosis of mesenteric ischemia. Plain radiographs are commonly used to exclude other causes of the acute abdomen such as bowel obstruction or a perforated viscus. As an early diagnostic aid in acute mesenteric ischemia, plain radiographs lack sensitivity, being reported as normal in up to 25% of cases involving acute mesenteric ischemia. Unfortunately, definitive plain radiographic findings of acute mesenteric ischemia are those associated with progressive loss of tissue integrity, such as pneumatosis and portal venous air and with a much poorer prognosis at this stage.

Duplex ultrasound of the mesenteric vessels is noninvasive and does not require administration of nephrotoxic contrast agents. Its utilization has primarily been in the diagnosis of CMI. As with all duplex examination, this modality is operator-dependent. An optimal patient setting, such as a thin patient with minimal bowel gas, is required to achieve quality results. Duplex ultrasonography accurately identifies high-grade stenoses of the celiac artery and SMA. In patient thought to have CMI, the reported technical adequacy approaches 100%. Studies from Dartmouth and the Oregon Health Sciences University attempted to established duplex criteria for the diagnosis of splanchnic artery stenosis and occlusion. Based on repeat studies, they have determined the peak systolic velocity (PSV) and end diastolic velocity (EDV) that correlates with a significant degree of stenosis. For the SMA, a PSV of >275 cm/s correlated with a > 70% angiographic stenosis with sensitivity of 92% and specificity of 96%. An EDV of >45 cm/s correlated with a > 50% angiographic stenosis with sensitivity of 90% and specificity 91%. For the celiac artery, a PSV of >200 cm/s suggests a stenosis of >70% with sensitivity of 90% and specificity of 91%. Retrograde hepatic artery flow is 100% predictive of a severe celiac artery stenosis or occlusion. Celiac EDV >55 cm/s indicates a stenosis of >50% with sensitivity of 93% and specificity of 100%.

Catheter angiography has long been the gold standard in delineating mesenteric arterial anatomy. However, as the availably of multidetector helical CT scan as spread, the ability to rapidly acquire high-quality CT angiographic images has made this modality the study of choice when evaluating a patient with possible mesenteric ischemia. A significant amount of information can be obtained about the central arterial and venous circulation with CT angiography. Accurate timing of contrast injection and fine slices (0.5–1.5 mm) through the upper abdomen usually provides excellent visualization of the celiac artery and SMA distributions. Other causes of abdominal pathology can also be assessed with CT. Nonspecific findings for bowel ischemia or infarction may include mesenteric stranding, bowel wall edema, or even air within the bowel wall or mesenteric vessels. The exact timing of intravenous contrast administration is tailored to the specified clinical question; usually, a non-contrasted study is performed first to establish a baseline of the appearance of the bowel wall. The tradition as of “positive” oral contrast agents detracts from image quality, and most visceral computed tomography angiography (CTA) protocols recommend the use of a “negative” oral contrast agent, such as water, given before the scan. The negative contrast agent prevents image artifact from pooled areas of high opacification within the intestinal tract and actually enhances the ability to see bowel wall enhancement (or lack thereof) in the late arterial phase of the contrast bolus. Three-dimensional reconstructions may be generated from the raw CT data set, yielding a spatially oriented image that allows for the clinician to evaluate the diseased segments from different perspectives. Some protocols may offer the use of biphasic scanning, a technique borrowed from standard pancreatic and liver studies. A delayed set of images are acquired approximately 1 min after the administration of IV contrast to obtain portal venous phase imaging.

Magnetic resonance angiography (MRA) provides excellent evaluation of the splanchnic vessels. MRI/MRA is noninvasive and avoids the risk of allergic reaction with iodinated contrast agents. There are several caveats to the use of MRI/MRA, such as avoidance of patients with ferrous-containing implants and concern for gadolinium-induced nephrogenic systemic fibrosis (NSF) in patients with impaired renal function. Anatomic imaging of the visceral vessels relies on contrast-enhanced MRI techniques; noncontrast three-dimensional phase contrast MRA identifies on 66% of angiographic stenoses and crates some false-positive results. The most common error of visceral MRA is overestimation of the stenosis. This weakness may result from the relatively poor spatial resolution of MRA. Even on the best systems, resolution is limited to 1 mm^3. Gadolinium-enhanced MRA currently does not provide sufficient resolution to show distal emboli non-occlusive, low-flow states, small vessel occlusion, or vasculitis. One study evaluated 14 patients with CMI; three-dimensional contrast-enhanced MRA had a sensitivity of 100% and a specificity of 87% in the overall detection of 50% or greater stenosis. In a similar, more recent study by Carlos et al., two blinded observers reviewed gadolinium-enhanced MRA studies and compared them with conventional angiography in 26 patients suspected to have CMI. The overall accuracies for the detection of 50% or greater stenosis or occlusion in the celiac artery, SMA, or IMA were 95% and 97%. Secondary signs of mesenteric ischemia, such as fat or bowel wall thickening, which are routinely delineated by CT, are more difficult to assess with MRI. In general, the anatomic evaluation of the mesenteric arteries is limited to the proximal celiac artery and SMA only, and the evaluation of SMA branches or IMA is limited by the spatial resolution of MRI techniques. MRA is not routinely the first imaging study to obtain in the setting of AMI because of time delay. The utility of MRA in CMI depends on the quality of the instrumentation, the sophistication of the software, and the skill of the interpreting radiologist, especially when other modalities are available.

Finally, catheter-based arteriography is a time-tested modality offers superbly detailed images of the visceral arterial tree, and venous patency may also be assessed on delayed images. Due to the time urgency in the treatment of AMI, as well as the burgeoning availability of CTA, the use of catheter angiography prior to laparotomy is now distinctly uncommon. In the setting of CMI, diagnostic angiography may be combined with therapeutic intervention in selected candidates. To document stenosis of the origins of the SMA and celiac axes, lateral views are best. Usually, involvement of at least two mesenteric vessels is required to diagnose symptomatic CMI. It is unusual for a patient to be symptomatic from occlusion of only one vessel. Additional evidence of chronic ischemia is evidenced by hypertrophy of collateral pathways, including the marginal artery of Drummond and the arc of Riolan (Fig. 2). Relative drawbacks of this technique include the need for arterial instrumentation and administration of nephrotoxic contrast agents.

Arterial Mesenteric Ischemia

Acute Pathology

Acute arterial insufficiency to the small bowel results from occlusion of the superior mesenteric artery. This represents the most dramatic and lethal form of mesenteric ischemia. Stoney found that about half of acute SMA occlusions are due to embolic phenomenon, most of which have cardiac origin (Fig. 2). These emboli generally occur in the setting of cardiac arrhythmias, particularly atrial

Fig. 2 Sagittal CTA reconstruction of cardiac embolus in mid-SMA (red arrow) in patient with AMI

fibrillation or following acute myocardial infarction. The can also stem from valve-associated thrombi especially in the inadequately anticoagulated patient with mechanical valve replacement. The vast majority of emboli lodge distal to the SMA origin just beyond the middle colic artery as the SMA begins to taper. In approximately 20% of cases, patients with SMA emboli will also have emboli to other vascular beds.

Patients with acute mesenteric ischemia will have the pathognomonic, "pain out of portion to physical exam." They also usually have elevated white blood cell counts and lactate levels.

Approximately 25% of acute mesenteric ischemic events are due to thrombosis of a preexisting atherosclerotic lesion (Figs. 3, and 4). Although these patients may present acutely, on questioning they generally give a history of chronic mesenteric ischemia symptoms. These lesions occur at the SMA origin, not distally as with embolic disease.

Fig. 3 Sagittal 3D reconstruction of patient with atherosclerotic obstruction proximal SMA (arrow) in patient with CMI

Fig. 4 Drawing of surgical exposure of proximal SMA at root of mesentery. Notice distal embolectomy (first insert) and closure transverse arteriotomy (second insert)

Nonocclusive mesenteric ischemia (NOMI) is a low-flow state in the setting of preexisting atherosclerotic lesions. This ischemia is often unveiled by the administration of vasoconstrictive agents in the setting of septic or cardiogenic shock. NOMI should be thought of as a rule-out diagnosis in that it is relatively uncommon. It is a relatively lethal diagnosis with a mortality rate of about 70%; this is mostly due to the underlying clinical condition that precipitates it. Treatment of NOMI requires diagnosis and treatment of the underlying pathology. Low-flow states result in peripheral hypoxemia and paradoxical splanchnic vasospasm, thereby precipitating intestinal ischemia. Angiotensin and vasopressin have been found to play an important role in the instigation of this ischemic state.

Chronic Pathology

Chronic mesenteric ischemia (CMI) is a "rule-out" diagnosis for chronic abdominal pain. However, the incidence is increasing due to the overall aging population and so to have the number of surgical interventions for this malady. CMI is more common in late middle-aged smokers; 60% of the afflicted are female which is a contradistinction from other vascular diseases where the majority of patients are male. Atherosclerosis in the SMA is a relatively common phenomenon; despite this, clinically significant mesenteric stenosis is relatively rare. In fact, autopsy series have found that up to two third of patients have a significant SMA lesion.

A history of a patient with CMI must include the pathognomonic of postprandial pain. Patients will usually describe dull pain that begins 1–2 h after a meal. This postprandial pain is what is often called "food fear." CMI patients frequently present with significant weight loss.

Ischemic Colitis

Ischemic colitis is the result of decreased perfusion to the colon. Because of the collateral pathways that exist between the SMA, the IMA, and the hypogastric arteries, this problem is uncommon in patients with well-developed collaterals. Patients are susceptible to this problem when they have had surgically ligated collaterals from prior colon surgery or congenitally absent arteries. The marginal artery of Drummond is absent in approximately 5% of the population.

Venous Mesenteric Ischemia

Mesenteric venous thrombosis is the least common form of mesenteric ischemia, accounting for 5–15% of cases. It is divided into acute and chronic presentations in which the cutoff is 4 weeks of symptoms. The etiology of mesenteric venous thrombosis is divided into either primary or secondary. Primary thrombosis is spontaneous and idiopathic and is not associated with any other disease process or hypercoagulable state. Secondary venous thrombosis is associated with hypercoagulability, malignancy, cirrhosis, splenomegaly, intra-abdominal infection, trauma, and pancreatitis. Hypercoagulable states associated with thrombosis included protein C and S deficiency, antithrombin III deficiency, polycythemia vera, thrombocytosis, sickle cell disease, factor V Leiden mutation, and others.

Mesenteric venous thrombosis is generally not as severe as arterial thrombosis in symptomatology. These patients generally present with several days to weeks of diffuse, nonspecific, and often intermittent abdominal pain. Physical exam findings are vague, but most commonly they have abdominal distension. These patients rarely have peritonitis, since it is only present with advanced cases with bowel infarction.

CT is the most sensitive test for mesenteric venous thrombosis. MRI and ultrasound have also been used. Once the diagnosis is made, therapeutic anticoagulation should be started. Unlike arterial ischemia, thrombectomy has not been shown to have proven benefit except in select cases. Generally, chronic, lifelong anticoagulation is recommended in patients that survive the initial episodes. Obviously, any patient with peritonitis should be explored emergently and dead bowel should be resected.

Nonocclusive Mesenteric Ischemia

The cause of nonocclusive mesenteric ischemia is usually a low-flow state in the setting of preexisting atherosclerotic lesions and then coupled with the administration of vasoconstricting medications or digitalis. Low-flow states are generally cardiogenic shock or sepsis.

Treatment

Preoperative Planning

Preoperative planning for mesenteric revascularization is similar to that of other major revascularization procedures. Patients should be evaluated to coronary and cerebrovascular disease. They require the same basic workup as other surgical candidates. A major difference for these patients is that they are generally nutritionally debilitated. They are generally hypovolemic, dehydrated, and anemic. It is generally recommended that these patients have invasive arterial blood pressure monitoring during the procedure as they may be particularly sensitive to episodes of hypotension.

Open Surgery

Once the diagnosis of acute mesenteric ischemia has been made, prompt exploration and revascularization are essential. Open exploration remains the gold standard. The first critical step is to examine the bowel for viability and to surgically resolve the cause of the ischemia. Preoperative imaging should determine if it is CMI or others. Bowel ischemia is determined by visual inspection. Direct signs of bowel ischemia are a dull, ashen gray color, absence of the normal glistening sheen, and lack of peristalsis. Adjunctive maneuvers that can help determine viability include Doppler signals along the antimesenteric border, intravenous fluorescein, and use of a Wood's lamp. In catastrophic cases when the extent of ischemia is too great and any remaining bowel would not be enough to sustain life, it is reasonable to close the laparotomy without restoration of blood flow. In all other cases, it is essential to proceed with revascularization prior to bowel resection because bowel that appears dusky may, in fact, be resuscitated with adequate blood supply. Once blood flow is restored, any dead bowel should be resected, and the patient should be left open to return for a second look exploration.

Embolectomy

SMA exposure for embolectomy begins with retraction of the transverse colon cephalad, while the small bowel and its mesentery are retracted inferiorly. The SMA can be found by tracing the middle colic artery to its junction with the SMA (Fig. 5). A vessel loop is passed around the proximal SMA and the middle colic and jejunal branches for distal control. If direct repair is planned after embolectomy, a transverse incision is made to avoid narrowing the SMA on closure. If the vessel itself seems diseased, then a longitudinal incision is made with a plan to patch the vessel prior to blood flow restored. Proximal embolectomy is performed with a 3 or 4 French (F) Fogarty catheter. The catheter should be passed until pulsatile inflow is achieved. Gentle distal embolectomy is then performed, usually with a 2 or 3 (F) catheter. Preoperative clinical assessment along with imaging should indicate if the patient has acute ischemia on top of CMI or embolic acute mesenteric ischemia. The mortality for acute mesenteric ischemia is around 70%. Factors such as age, delay to surgery from presentation, level of adhesions, and amount of small and large bowel involvement, significantly affect the perioperative mortality. This catastrophic presentation of acute mesenteric ischemia differs significantly from the perioperative mortality of CMI which is 10–20%.

Bypass

Mesenteric bypasses can be categorized as either antegrade or retrograde. Antegrade bypasses are

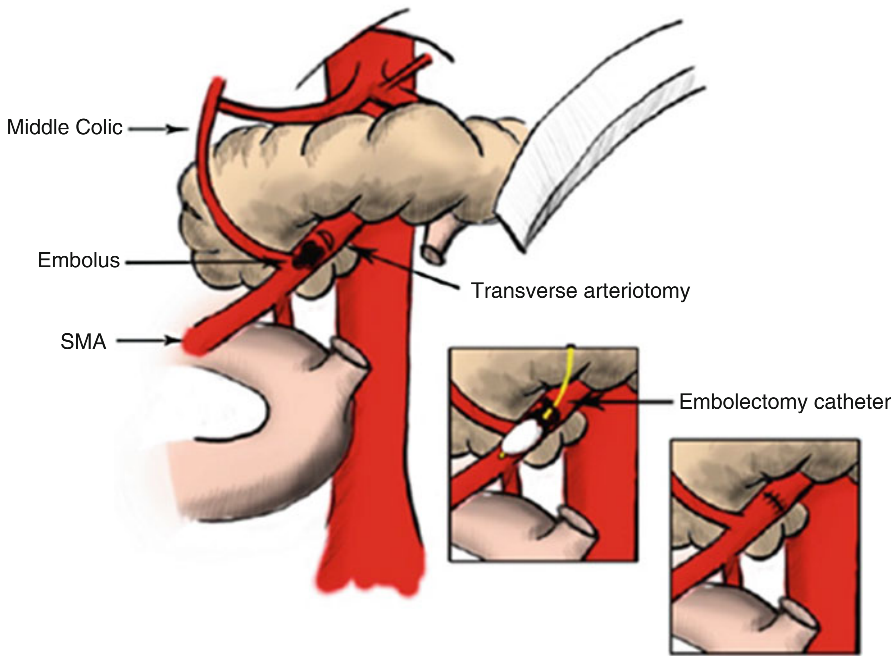

Fig. 5 Sagittal CTA 3D reconstruction in patient with embolus to SMA (arrow) of cardiac source

usually from the supraceliac/thoracic aorta which is an excellent site for inflow because it is generally spared from atherosclerotic disease. Either autologous or synthetic conduit can be used with equal efficacy and no data showing superior of one material over the other. Of course, if any concern for contamination is present, then using autologous vein graft is mandatory.

Exposure of the supraceliac aorta is typically performed through a midline incision or alternatively through bilateral subcostal incisions. The left lobe of the liver is mobilized by dividing the left triangular ligament and retracting the left lobe of the liver inferior and to the right. At this juncture, it is vital that a nasogastric tube is placed in order to identify and protect the esophagus during mobilization and clamping. The gastrohepatic omentum is divided, and the lesser sac is entered. The right crus of the diaphragm is divided with electrocautery. The celiac axis and SMA are then skeletonized. If possible, multilevel (hepatic and SMA) reconstruction should be performed for optimal outcomes and patency. With multilevel reconstruction, there is a better chance of long-term benefit; in case one of the bypasses thrombosis, collateral flow may prevent symptomatic recurrence. If possible, it is preferable to place a side-biting clamp on the aorta. Occasionally, it may be technically necessary to completely cross-clamp the supraceliac aorta; in these cases, the proximal anastomosis can usually be completed in less than 20 min, and the ischemic time is usually well tolerated. Most surgeons will perform the SMA anastomosis to the proximal SMA anterior to the pancreas, but it can also be tunneled retropancreatic and sewn to the SMA at the point distal to where it passes through the uncinate process of the pancreas.

A retrograde bypass is indicated when the supraceliac aorta is not suitable for the proximal anastomosis, i.e., it is aneurysmal or is atherosclerotic. It may also be scarred in from prior surgery, or the patient may not tolerate a supraceliac clamp. In these situations, retrograde bypass from the infrarenal aorta or the iliac vessels can be performed. By mobilizing the ligament of Treitz, the proximal SMA can be isolated below the inferior border of the pancreas at the base of the small bowel mesentery. The proximal anastomosis to the aorta or the right common iliac artery

Fig. 6 Lateral arteriography demonstrating long proximal SMA stenosis. Notice wire in SMA

is performed in an end-to-side fashion. The graft is brought in a gentle curve to the SMA which can then be sewn in end-to-side fashion. It is imperative to review the gentle curve with restoration of the small bowel to the abdominal cavity to avoid kinking of the conduit (Fig. 6).

Overall, the perioperative mortality for mesenteric revascularization for chronic disease is around 6%. Primary patency at 5 years is almost 90% whether performing retrograde or antegrade bypass, and there is no known patency difference for synthetic or autologous conduit. Overall patient survival is 75–80% at 3 years which is acceptable for this disease-burdened population.

Endarterectomy

Transaortic mesenteric endarterectomy is a useful technique for occlusive disease that is limited to the origins of the visceral vessels. Endarterectomy can be advantageous in that it resects the occlusive lesion; it is anatomic revascularization and avoids the turbulent flow that plagues grafts, and it is autogenous. The visceral aorta can be exposed through a midline or a thoracoabdominal incision. This procedure is generally reserved for patients with a "coral reef" aorta as it necessitates aortic cross clamping at the supraceliac aorta.

Exposure of the visceral aorta by midline incision is accomplished with left-sided medial visceral rotation. The splenic flexure is mobilized as well as the descending colon by dividing the peritoneal attachments. The spleen and pancreas are mobilized medially, and the left renal vein is identified and dissected free from the hilum to the cava. In order to retract the vein inferiorly, the adrenal and lumbar branches can be ligated. The left crus of the diaphragm is divided, and the distal thoracic aorta is thus exposed. Distal control is obtained in the infrarenal aorta. Finally, the mesenteric vessels are dissected out until disease free segments are found. After systemic heparinization, clamps are placed, and an aortotomy is created. Generally, gentle eversion endarterectomy is sufficient to treat ostial disease. If the SMA is diseased beyond the origin, it is beneficial to make a separate arteriotomy and vein patch angioplasty.

Endovascular

Percutaneous revascularization is a useful alternative to open reconstruction in patients with intestinal angina. In a retrospective comparison between open and endovascular revascularization, symptom relief and long-term patency were better achieved with open surgery, but the complication rate was also significantly higher in this group. Therefore, a full evaluation of the patient's health status and life expectancy should be considered when deciding the best approach.

Angioplasty and stenting of the mesenteric vessels follow similar rules as that of any other vessel. Ideal lesions are short, non-calcified and not caused by lesions that are not care by extrinsic compression (Figs. 5, 6, and 7). One major difference in SMA angioplasty is that approach is generally easier from left brachial access due to the acute angle of the artery. Purely endovascular techniques cannot be used in the acute setting when a thorough evaluation of bowel viability is mandated. In malnourished patients, this approach should be initially considered even if there is a complete occlusion. Modern endovascular techniques can many times cross totally occluded SMA.

Fig. 7 Repeat lateral intra procedure arteriography demonstrating full deployment of SMA stent and restoration of blood flow

This approach becomes an effective bridge to eventual formal revascularization.

Retrograde open mesenteric stenting (ROMS) is another viable option for a hybrid approach to this disease process. This technique still requires laparotomy for exposure and assessment of bowel integrity. In this modality, the SMA distal to the occlusion or one of the branches are punctures and recanalization is undertaken. One retrospective review found this to be an especially helpful alternative when percutaneous antegrade mesenteric stenting is unsuccessful. The mortality of ROMS is still 20% at 1 year, and primary patency was reported to be 83%.

Conclusion

Patient history is vital to distinguish between acute or acute on chronic pathology and can dictate surgical management. “Pain out of proportion to exam” is a key clinical finding for patient suffering acute mesenteric ischemia and should raise high suspicion. While atherosclerosis of the mesenteric vessels is quite common, mesenteric ischemia remains rare. Exploration via laparotomy is mandatory in any patient with peritonitic signs and suspicion for mesenteric ischemia.

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52 Benign Disease of Stomach and Duodenum

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Abstract
The normal physiology of the stomach and duodenum undergoes several changes as patients increase in age. Patients become more susceptible to *H. pylori* infection and the complications related to it, such as peptic ulcer disease, gastric volvulus, and gastric polyps. In addition, patients develop more comorbidities as they age, causing the impact of their disease and complications to be greater. Due to the changes of aging, patients require special perioperative considerations that involve the entire care team. Medical and surgical therapies must be tailored for the elderly patient.

Keywords
Peptic ulcer disease · Peptic bleeding · Duodenal diverticula · Gastric volvulus · Gastroparesis

Case #1

Background

An 81-year-old Caucasian female with kyphosis arrives to the emergency department complaining of acute abdominal pain and chest pain for the last 3 h. She has associated retching and recently vomited a small amount of rust-colored blood. She denies any other symptoms, but her family affirms that she has some difficulty swallowing tough meats and breads for the past year, as well as heartburn. She has a history of scoliosis that has not required any interventions, as well as hypertension. She underwent a laparoscopic cholecystectomy approximately 10 years ago. Her current medications are hydrochlorothiazide and over-the-counter Tums. She has mild tachycardia with a heart rate of 103 but otherwise is not in distress. While examining her, she begins to have small amounts of emesis, which are bloody.

Management

An acute abdominal series is ordered which shows a large gastric bubble within the lower chest, consistent with a paraesophageal hernia. A CT scan is ordered and is concerning for an incarcerated paraesophageal hernia with gastric volvulus and impending ischemia. The patient remains stable. Nasogastric tube placement is attempted, but it will not pass beyond 35 cm.

An EGD is performed which shows a large hiatal hernia with retained food and liquid content.

A small area of mucosal ischemia is seen. The patient is prepped and draped for a laparoscopic reduction of paraesophageal hernia with reduction of gastric volvulus, gastropexy and gastrostomy tube placement, and repair of hiatal hernia by cruroplasty.

Case #2

Background

A 65-year-old female presents to her endocrinologist complaining of an increasing frequency of vomiting after meals. She states that she has had a long history of occasional vomiting after eating, but over the last 6 months the frequency has increased. She currently vomits after every meal and has associated bloating. She has tried home remedies and an elimination diet, as well as promethazine. She was unable to tolerate promethazine as it caused her confusion. Her past medical history includes diabetes since age 43, hypertension, peripheral vascular disease, and COPD. She is a current smoker. Her prior surgeries include a hysterectomy and tonsillectomy. She is currently using oral medications only to control her diabetes. On examination, her abdomen is bloated, and her mucous membranes are dry. Her physician orders a hemoglobin A1C and gastric emptying study which reveals that greater than 60% of the ingested meal remained within her stomach after 2 h. Her hemoglobin A1C reveals poor glucose control.

Management

It is recommended that the patient gain better control of her glucose level prior to considering a surgical intervention. She is started on short-acting insulin and commits to keeping a glucose log. Dietary modification is also recommended, with the patient encouraged to avoid high-fiber and high-fat foods, as well as carbonated beverages, and to eat six small meals a day. In addition, she was prescribed ondansetron for symptom control. Prior to leaving the clinic, she was given a bolus to correct her dehydration.

Anatomy and Physiology of the Stomach and Duodenum

The stomach comprises five anatomical regions: the cardia, fundus, body or corpus, antrum, and pylorus. The cardia is contiguous to the lower esophageal sphincter and is the transition between the esophagus and the stomach. The cardia is used to create a reference horizontal plane that delineates the second and third regions of the stomach, the fundus, and the body, respectively. The fundus is located above this horizontal plane. The body is delineated proximally by the horizontal plane at the level of the cardia and distally by the incisura angularis. The incisura angularis is located at the abrupt right angle created by the lesser curvature in the distal portion of the stomach; it marks the transition between the body and the antrum [1]. The pylorus lies at the junction of the stomach and aids with digestion and gastric emptying [2].

The duodenum is divided into four anatomical regions. The first part is the duodenal bulb, which is approximately 5 cm. It attaches to the pylorus and crosses over the common bile duct, portal vein, pancreatic head, and gastroduodenal artery [3]. Beyond this is the second portion of the duodenum, the descending duodenum. The second portion contains concentric folds of mucosa called the Kerckring folds, which are seen on endoscopy. This portion of the duodenum is approximately 10 cm and travels over the right renal vasculature, the inferior vena cava, and to the right of the lumbar vertebrae (L1 and L2). The ampulla of Vater, where the common bile duct and main pancreatic duct join the duodenum, is located here. The third portion of the duodenum is referred to as the transverse duodenum and is also 10 cm in length. It crosses from right to left anterior to the spine, aorta, and inferior vena cava. The superior mesenteric artery and vein travel above this portion of the duodenum and delineate the third portion from the fourth portion, called the ascending portion of the duodenum. This portion is approximately 5 cm long and travels upward and obliquely to the ligament of Treitz, where the bowel becomes intraperitoneal and joins the jejunum [3].

Microscopically, the stomach has four different layers. The external layer or serosa is an extension of the visceral peritoneum that covers the entire stomach. Beneath this is the muscularis propria which is formed by three different layers of muscle: an inner oblique layer, a middle circular layer, and an outer longitudinal layer. The middle muscular layer forms the pylorus at the end of the stomach. The muscularis propria contains many ganglion cells that create a neuronal plexus known as myenteric or Auerbach's plexus. The third layer or submucosa is a firm matrix of collagen and elastin that contains plasma cells, lymphocytes, lymphatics, and blood vessels. Numerous ganglion cells are also located in this layer; they form the submucosal or Meissner's plexus. The gastric lumen is lined by the innermost layer, the gastric mucosa, which is formed by a columnar epithelium that covers a layer of connective tissue (lamina propria) and a thin muscular layer known as the muscularis mucosa. The columnar epithelium invaginates and contains different gastric pits. Each gastric pit opens to four or five different gastric glands [4]. While the entire surface of the stomach is lined with glands, each region has a different function and histology except for mucous cells. Mucous cells are the most common type of gastric cell and are present in the surface throughout the stomach. The mucus and bicarbonate secreted by them create a neutral mucous film that prevents back diffusion of hydrogen ions (H +) from the gastric lumen to the cells. This film is very viscous due to the high concentration of long-chain oligosaccharides. Mucous cells also produce a hydrophobic film of phospholipids that blocks back diffusion of hydrogen ions [5].

The duodenum contains the same four distinct layers; however the retroperitoneal segments are only covered by serosa on the anterior portion. The mucosa has a crypt and villus structure. The villi project into the lumen and contain epithelial cells and lamina propria, with the principal roles of absorption and secretion. Within the submucosa of the duodenum are Brunner glands that secrete mucus and bicarbonate into the lumen to neutralize the gastric acid as it enters from the stomach [3].

Gastric glands can be classified as oxyntic or antral based on the main type of cell present. Oxyntic glands are present in the proximal stomach (fundus and body), while antral glands are found in the distal stomach (antrum). Oxyntic glands produce pepsin and gastric acid. The main component of oxyntic glands are parietal cells. These cells contain multiple mitochondria that generate the energy required for acid secretion. The apical membrane of parietal cells contains the H+/K+-ATPase pump, responsible for gastric acid secretion. Parietal cells are mainly present in the proximal stomach (fundus and the body) [1]. Chief cells are located at the base of the oxyntic glands. They store pepsinogen inside intracytoplasmic granules that are secreted shortly after eating. This effect is mediated by acetylcholine. Pepsinogen is converted to pepsin in the gastric lumen; it breaks down ingested proteins into smaller peptides. Pepsin has optimal activity at pH 2.5, but if the intraluminal pH rises above 5, pepsin becomes deactivated [6]. The body of the stomach also contains enterochromaffin-like cells (ECL) that express histidine decarboxylase. ECL cells secrete histamine in response to acetylcholine release during the cephalic or vagal phase of gastric secretion. Histamine is also secreted in response to gastric distention, a response mediated by gastrin. Histamine induces the release of gastric acid by parietal cells [4].

The major function of antral glands is to produce gastrin [7]. G cells are the major component of antral glands and are also located in the duodenum [3]. They secrete gastrin in response to gastric distention, vagal stimulation, or with increase of the intraluminal concentration of peptides and amino acids. Gastrin increases the secretion of gastric acid and pepsinogen. It also induces cell growth and differentiation of parietal cells. D cells release somatostatin into the bloodstream when the concentration of gastric acid increases. The primary location of these cells is the antrum, but the body of the stomach and the duodenum also has D cells. Somatostatin inhibits the secretion of gastric acid, histamine, and gastrin [6].

The duodenum produces and secretes cholecystokinin (CCK) within the I cells, which causes contraction and emptying of the gallbladder, increased bile flow, and relaxation of the sphincter of Oddi, as well as stimulating pancreatic enzyme secretion. This is directly stimulated by amino or fatty acids. Secretin is produced in the S cells of the duodenum and causes the release of water and bicarbonate from the pancreas. It is released when there is low intraluminal pH, fatty acids, and bile salts [3]. The K cells of the duodenum release gastric inhibitory peptide in response to glucose, fat, protein, and adrenergic stimulation. It inhibits the gastric acid and pepsin production and stimulates the secretion of insulin [3]. The enteroendocrine cells of the duodenum secrete motilin in response to alkalinization of the duodenum; motilin causes stimulation of the migrating myoelectric complex and promotes GI motility. Finally, neurotensin and glucagon are secreted in small part by the duodenum. Neurotensin is produced in response to fat and stimulates bicarbonate secretion from the pancreas and GI motility. Glucagon is released in states of hypoglycemia and promotes glycogenolysis, lipolysis, gluconeogenesis, and ketogenesis [3].

Effect of Age on Physiology

Gastric and duodenal diseases are influenced by age. The surgeon caring for elderly patients has to understand that not only comorbidities influence the clinical scenario; aging affects the normal physiology, histology, and pathology of the stomach and duodenum. The major changes in physiology and histology associated with normal aging are:

1. Gastric motility. Aging is associated with normal gastric emptying of liquids but slower gastric emptying with solid foods. In healthy subjects the presence of nutrients in the small intestine decreases antral contractions, increases the pyloric tone, and induces relaxation of the gastric fundus. These responses are mediated by different hormones, but cholecystokinin (CCK) is most responsible for this response. The plasma concentrations of CCK are persistently elevated in older patients before and after meals. As a consequence, they experience decreased appetite and slower gastric emptying [8]. The decrease in gastric motility can influence drug absorption. This is one of the reasons older patients have more side effects as compared to younger patients [9].
2. Bicarbonate secretion. Aging decreases both the basal and induced secretion of bicarbonate in the stomach which decreases acid neutralization in elderly patients [8].
3. Mucous. The quality of the mucus in the stomach decreases with age; this effect is independent of *Helicobacter pylori* infection and any medication. The total number of mucous secreting cells decreases after *H. pylori* infection [9].
4. Prostaglandin (PG) synthesis. The main types of PGs identified in the gastric mucosa are PGE2 and PGI2 and lesser amounts of PGF2 and PGD2 [5]. Mucous cells release PGE2 and PGI2 on epithelial injury. Both molecules increase the mucosal blood flow and induce the release of mucous and bicarbonate secretion. The mucus and bicarbonate create a pre-epithelial barrier that keeps the pH neutral [6]. Gastric biopsies from elderly patients show a decrease in PGE2 and PGF2 levels [10].
5. Pepsin. Studies evaluating the secretory function of the stomach have indicated that pepsin secretion decreases in elderly subjects [11].
6. *H. pylori* infection prevalence. The prevalence of *H. pylori* infection increases with age, with rates up to 80% in patients older than 80 years. Chronic infection with *H. pylori* induces atrophic gastritis, causing hypochlorhydria. Aside from *H. pylori* status, current evidence suggests that gastric acid secretion is not influenced by aging [12].
7. Changes in gastric mucosa. A recent histopathology database study showed an age-dependent change in gastric mucosa over a lifetime. While the majority of these are

caused by *H. pylori* infection, reactive gastropathy is the second most common change in gastric mucosa. This is likely caused by the cumulative effect of exposure to damaging factors over an individual's lifetime, such as NSAIDS [13]. There is no evidence that mucosal blood flow changes in older healthy patients.

8. Decreased number of Brunner's glands. The number of Brunner's glands in the duodenum is decreased, which may cause impaired ability of the duodenum to neutralize the acid secretions from the stomach. It may also affect the activation of pancreatic enzymes that are dependent on a certain pH. Of note, this may also affect drug solubility [14].

Perioperative Considerations in the Elderly Patient

The aging population means that an increasing number of operations will be performed in the elderly patient population. Special perioperative considerations should be taken to improve outcomes in this growing patient population. Efforts to improve geriatric surgical outcomes must involve the entire surgical team, pre- and postoperatively. Strong consideration should be made to consulting geriatric medicine if available as a resource.

1. Risk assessment. Thoughtful care of the geriatric patient starts with an understanding of the specific risks associated with surgical intervention, in particular emergency surgery. This allows the surgeon to have informed conversations with the patient and family pre- and postoperatively and to align the care of the patient with their wishes. Acute kidney injury, ASA class IV or higher, and a Charlson score of 4 or higher are significantly predictive of 30-day mortality [15]. Although initially developed in internal medicine patients and used among oncology patients, the Charlson score takes into consideration comorbid conditions of elderly patients and has been shown to be useful in the surgical setting [15, 16]. The impact of a surgical intervention on an elderly patient extends beyond 30 days, with ASA class IV or higher, Charlson score of 4 or higher, BMI <18.5 kg/m^2, and a low serum albumin being predictive of 1 year mortality. BMI >30 kg/m^2 was protective against death [15].
2. Analgesia. Due to the higher sensitivity to narcotics in elderly patients, a multimodal and balanced use of pain control agents is recommended, including local or topical anesthetics, acetaminophen, NSAIDs (with PPI prophylaxis for stomach protection), and other nontraditional pain management agents such as gabapentin or ketamine. Peripheral nerve blocks and spinal or epidural anesthesia may be considered [17]. These modalities can be particularly useful in managing the pain associated with abdominal incisions.
3. Postoperative delirium. Rapid treatment of the underlying disease state, dehydration, and infection helps prevent or improve delirium, as well as normalization of the patient by providing eye glasses, hearing aids, daytime activities to encourage wakefulness, and a normal sleep-wake cycle [17]. If feasible, minimize nighttime interruptions such as lab draws and vital signs. In addition, encouraging family members or familiar caretakers to stay with the patient will normalize the environment and help orient the patient.
4. Fluid resuscitation. Elderly patients are more susceptible to dehydration but also have reduced total body water volume, as well as reduced glomerular filtration rate and reduced ability to concentrate urine, making them more susceptible to fluid retention and volume overload. Cautious and thoughtful fluid resuscitation using chloride-restricted IV fluids and small colloid boluses results in better outcomes in the elderly [17].
5. Aggressive pulmonary toilet. Incentive spirometry, early mobilization, and upright position are helpful in the elderly population [17].
6. Posthospital care. Every effort should be made to return patients to independent care, as research suggests that many elderly patients are discharged to post-acute care facilities

when they are functionally independent and without postoperative complications [18]. Being placed in a post-acute care setting may be associated with worse outcomes [19].

Peptic Ulcer Disease

Epidemiology

The number of admissions, operations, and mortalities related to peptic ulcer disease (PUD) has generally decreased; however, the proportion of patients older than 65 years admitted for duodenal or gastric ulcer complications is increasing [20]. The first clinical manifestation of PUD is an acute abdomen in up to 50% of elderly patients [21]. Acute upper gastrointestinal (GI) bleeding related to PUD is more frequent in elderly patients [22, 23].

Pathophysiology

PUD results from multiple factors that either injure the mucosal barrier in the stomach and duodenum or increase the production of gastric acid. In the healthy gastric mucosa, the mucus and bicarbonate form a hydrophobic pre-epithelial barrier that prevents backflow of H+ and maintains a neutral pH even with an increased intraluminal concentration of gastric acid [6]. Mucosal injury occurs regularly but is repaired by the mucosal defense system. Cells in the gastric mucosa are replaced continuously, so that the epithelium is renewed every 2–4 days. The normal response after epithelium damage is migration of healthy cells from the gastric pits to denuded areas of the basement membrane, as well as an increase in the release of mucus by damaged cells and the release of plasma by the mucosal vessels. When mucus and plasma mix, they create a mucoid cap that protects the denuded area. Although the basement membrane is highly sensitive to gastric acid, the mucoid cap prevents further damage because it has a neutral pH. This response is dependent on mucosal blood flow. Sensory afferent nerve endings in the mucosa release calcitonin gene-related peptide (CGRP) if the gastric mucosa gets exposed to gastric acid. CGRP vasodilates mucosal vessels. The increase in blood flow is mediated by nitric oxide. The enhanced blood flow buffers, dilutes, and removes gastric acid. PGs are crucial for this defense because they induce the release of mucus, bicarbonate, and phospholipids from the mucous cells. PGE2 and PGI2 also increase blood flow to the gastric mucosa [5]. True ulcers occur if the insult continues and extends into the muscularis propria.

Classification of Gastric Ulcers

Gastric ulcers are classified according to location and possible physiopathology into four types: Type I are gastric ulcers located in the antrum, typically along the lesser curvature; Type II are gastric ulcers associated with a history of previous or active duodenal ulcer; Type III are prepyloric ulcers; Type IV are ulcers located near the GE junction. While Types II and III are associated with increased acid production, Types I and IV are associated either with malignancy or decreased mucosal defense [24]. Type V are secondary gastric ulcers, such as from NSAID use, and can occur anywhere in the stomach.

Etiology

The main factors that predispose to PUD are as follows:

Helicobacter pylori

This microaerophilic gram-negative spiral bacterium colonizes the pre-epithelial mucous layer of the stomach and is one of the most common human chronic infections worldwide. The transmission is either fecal–oral or oral–oral. Prevalence is influenced by socioeconomic status, ethnicity, and age. Approximately 50% of the world's population is infected; the frequency is higher in developing countries with poor sanitation and household hygiene and with low family income and educational level. In the USA, the prevalence increases with age: less than 10%

before 30 years, 50% around 50 years, and up to 80% in patients older than 80 years [9, 20, 25]. *H. pylori* secretes urease, which produces ammonium, which favors gastric colonization with *H. pylori* and damages epithelial cells. *H. pylori* also produces proteases and phospholipases that affect the efficacy of the mucous-bicarbonate layer. *H. pylori* has a rich catalase activity that blocks the neutrophil response [26]. These bacteria also release toxins that generate a chronic inflammatory response which results in type B atrophic gastritis. Why *H. pylori* induces duodenal inflammation is not fully understood. Some studies suggest that gastric metaplasia in the first portion of the duodenum facilitates *H. pylori* colonization and further inflammation. Other studies posit that antral *H. pylori* infection increases gastric acid secretion because the ammonia produced by *H. pylori* increases the pH to which G cells are exposed and because the population of the D cells decreases with *H. pylori* infection. Duodenal *H. pylori* infection decreases bicarbonate secretion in the duodenal cells [26].

Nonsteroidal Anti-inflammatory Drugs

At least 40% of the patients older than 65 years use NSAIDs. Between 1% and 8% of these patients will require a hospitalization to treat a NSAID-related complication. Duodenal and gastric ulcers develop in 5–8% and 15–20% of patients taking NSAIDs, respectively. Proton pump inhibitors (PPI) or misoprostol decreases the risk of PUD, but only 10–20% of the patients receive prophylaxis [22]. The risk of NSAIDs' toxicity increases with age; the risk of serious GI complications after 1 year of NSAID ingestion is 0.32% in patients older than 65 as compared to 0.039% in younger patients [27]. NSAIDs significantly decrease the production of mucus, bicarbonate, and phospholipids in the stomach and duodenum because these drugs inhibit the activity of COX-1 and COX-2. The final result is a pre-epithelial barrier that cannot prevent H+ backflow. NSAIDs also disrupt mucosal healing because they decrease PG synthesis; therefore the mucoid cap cannot be formed, and the increase in mucosal flow and mucosal regeneration cannot occur. COX-1 inhibition also releases endothelin-1, a potent vasoconstrictor, and for that reason blood flow to the mucosa decreases in patients with mucosal injury induced by NSAIDs [27]. NSAIDs also increase the expression of leukocyte adhesion molecules and neutrophil adherence. Neutrophils cause further damage because they release proteases and reactive oxygen metabolites [5]. The toxic effects of NSAIDs are mainly systemic, but these drugs also induce topical cytotoxic injury in the gastric mucosa because they increase cellular permeability with diffusion of the drugs to mucosal cells [5]. NSAID ingestion and *H. pylori* infection are independent risk factors for PUD, but if both factors coexist, the risk of PUD is synergistically increased [28]. This is particularly likely in elderly patients because both risk factors are more prevalent in older populations [20].

Zollinger–Ellison Syndrome

This syndrome is associated with neuroendocrine tumors that secrete excessive amounts of gastrin into the bloodstream. Gastric acid greatly increases in these patients. Zollinger–Ellison syndrome (ZE syndrome) accounts for 0.1–1% of all peptic ulcers. The diagnosis requires an elevated gastrin (>500 pg/ml) in the presence of an acidic gastric pH (pH <5). In patients with non-diagnostic gastric elevations (>150 but less than 500 pg/ml), a rise of more than 120 pg/ml after the intravenous administration of secretin (0.2 mg/kg) is diagnostic. The tumor can be localized with CT, MRI, endoscopic ultrasound, selective arterial secretin stimulation test, and somatostatin receptor scintigraphy, but surgical exploration of the gastrinoma triangle with intraoperative ultrasound is the best method to localize the tumor. This entity is more common in young patients (mean age 41), but it should be considered in patients with atypical PUD localization (ulcers in the second, third, or fourth portion of the duodenum or jejunum), severe gastroesophageal reflux, diarrhea, PUD refractory to treatment, and recurrent disease in patients without *H. pylori* infection or NSAID ingestion [29].

Smoking

Smoking decreases wound healing, increases the risk of *H. pylori* infection, and is an independent risk factor that predicts failure to antibiotic treatment [30].

Clinical Manifestations of Uncomplicated Peptic Ulcer Disease

The cardinal symptom is epigastric pain without radiation. This pain is frequently described as "burning," "gnawing," or "hunger pain." It is usually exacerbated with fasting and relieved with the ingestion of food or antacids. The presence of symptoms other than pain such as weight loss, anorexia, melena, hematemesis, constant pain, or pain radiating to the back suggests complicated PUD. Differential diagnosis includes dyspepsia, upper GI malignancies, symptomatic cholelithiasis, pancreatitis, and GERD. Elderly patients always require an extensive workup because the risk of malignancy increases with age. The gold standard test to diagnose PUD is an upper endoscopy. Duodenal ulcers typically occur in the first portion of the duodenum; they are usually not associated with malignancy (risk less than 1%). The presence of multiple ulcers or ulcers located beyond the second portion of the duodenum suggests ZE syndrome. Gastric adenocarcinoma exists in up to 5% of the patients with gastric ulcers with gross benign appearance; therefore all gastric ulcers should be biopsied [24].

Medical Treatment for Uncomplicated Peptic Ulcer Disease

The mainstay of treatment is to inhibit gastric acid secretion. This can be achieved with proton pump inhibitors (PPIs) or with histamine H2-receptor antagonists (H2RA or H2 blockers). PPIs are irreversible inhibitors of the H+/K+-ATPase. The recommended therapy for duodenal ulcers is 4–6 weeks with the rate of healing between 80% and 100%. For gastric ulcers the recommended therapy is 8 weeks, and the healing rate is 70 and 85%. In cases of associated hypergastrinemia or NSAID ingestion, the treatment should be continued. H2RAs are reversible inhibitors of the histamine H2-receptor in the membrane of parietal cells. The healing rate is 70–80% in duodenal ulcers and 55–65% in gastric ulcers. The duration of therapy is the same as with PPIs [6]. An alternative in the treatment of PUD is sucralfate. This agent improves mucosal healing by creating a protective barrier in the ulcer, as well as stimulating bicarbonate, mucous, and growth factor release. Misoprostol is a PG analogue that improves ulcer healing; however, it is frequently associated with GI side effects such as diarrhea.

The presence of *H. pylori* infection is associated with a high recurrence rate; in duodenal ulcers the recurrence rate is 95% without *H. pylori* eradication compared to 12% for those patients who receive eradication treatment. The recurrence rate for gastric ulcers without *H. pylori* eradication is 74% vs. 13% after eradication [26]. The two most common techniques to diagnose *H. pylori* infection are urea breath test and gastric biopsy; other tools are rapid urease testing, culture, polymerase chain reaction, antibody testing, and the fecal antigen test. Eradication treatment is always indicated in patients with PUD, complicated or uncomplicated. The current regimens approved by the FDA for the eradication of *H. pylori* are listed in Table 1. The success rate is approximately 80% [31].

Patients with gastric or duodenal ulcers associated with NSAIDs require replacement of the NSAIDs with an alternative pain regimen plus the administration of a PPI. Prophylaxis with misoprostol or PPIs is indicated in elderly patients who cannot stop NSAIDs. With prophylaxis, the incidence of ulceration decreases from 20% to 4.5% [5].

Clinical Manifestations of Complicated Peptic Ulcer Disease

The first clinical manifestation is a complication in 50–60% of elderly patients [27]. Elderly

Table 1 FDA approved regimens for Helicobacter pylori eradication[a]

Regimen	Duration (days)
1. Omeprazole 20 mg b.i.d. + Clarithromycin 500 mg b.i.d. + Amoxicillin 1 g b.i.d.	10
2. Lansoprazole 30 mg b.i.d. + Clarithromycin 500 mg b.i.d. + Amoxicillin 1 g b.i.d.	10
3. Esomeprazole 40 mg q.d. + Clarithromycin 500 mg b.i.d. + Amoxicillin 1 g b.i.d.	10
4. Rabeprazole 20 mg b.i.d. + Clarithromycin 500 mg b.i.d. + Amoxicillin 1 g b.i.d.	7
5. Bismuth 525 mg q.i.d. + Metronidazole 250 mg q.i.d. + Tetracycline 500 mg q.i.d. + Histamine-2 Receptor Antagonists[b]	14

[a]The success rate is around 80%
[b]In this regimen the total duration of Histamine-2 receptor antagonists therapy is 4 weeks

patients frequently have comorbidities that affect their mental status or pain perception (uncompensated diabetes, stroke, dementia) or they are receiving drugs that create or mask PUD (i.e., NSAIDs, narcotics, steroids). The diagnosis is frequently challenging because the normal systemic inflammatory response (fever, leukocytosis) may be absent in elderly patients or may be affected by drugs (steroids, beta-blockers) [21, 23]. PPI, H2RA, and antibiotic therapy for *H. pylori* have decreased the number of elective surgical procedures required for PUD, but the incidence of complications such as perforation or bleeding has not changed significantly over time.

Perforation

Between 2% and 10% of the patients with duodenal ulcers present with a perforated ulcer. Elderly patients frequently present to the emergency room without any history of PUD. The diagnosis is suggested by acute epigastric pain that rapidly becomes generalized. The patient is often diaphoretic and tachycardic; low-grade fever can also occur. The presence of generalized tenderness, positive rebound, and abolished peristalsis is usually evident, but the physical examination in very old or immunocompromised patients can be nonspecific. The diagnosis may be confirmed with chest radiography because 70–80% of the patients have free subdiaphragmatic air. If the physical examination is inconclusive or in the absence of free air, the most useful test is a CT scan of the abdomen and pelvis; this study excludes other diagnoses and is highly sensitive to detect free intra-abdominal air. Although conservative treatment with antibiotics and IV fluids has been described in hemodynamically stable patients with contained perforations, elderly patients usually require surgical treatment. After the initial evaluation, fluid resuscitation is crucial. Elderly patients frequently have cardiovascular comorbidities that require careful management, and external and/or internal monitoring of their hemodynamic status may be useful. Broad spectrum antibiotics should be started on diagnosis. The initial assessment and medical therapy should not delay operation. The most frequent surgical procedure for perforated ulcers is primary closure plus reinforcement with an omental patch. The treatment for perforated ulcers is summarized in Fig. 1.

Primary Closure Reinforced with Omental Patch

The patient is placed in the supine position under general endotracheal anesthesia; a nasogastric tube and Foley catheter are placed. The repair may be approached laparoscopically or via a midline supraumbilical incision. After ruling out other diagnoses, attention is turned to the perforation. If the ulcer is on the posterior wall of the stomach, the gastrocolic ligament is divided to enter the lesser sac. Ulcer biopsies should be sent as gastric cancer can simulate perforated PUD. The defect is closed with a full-thickness single layer of interrupted 3-0 silk or vicryl stitches (Fig. 2). The primary closure is reinforced with omentum

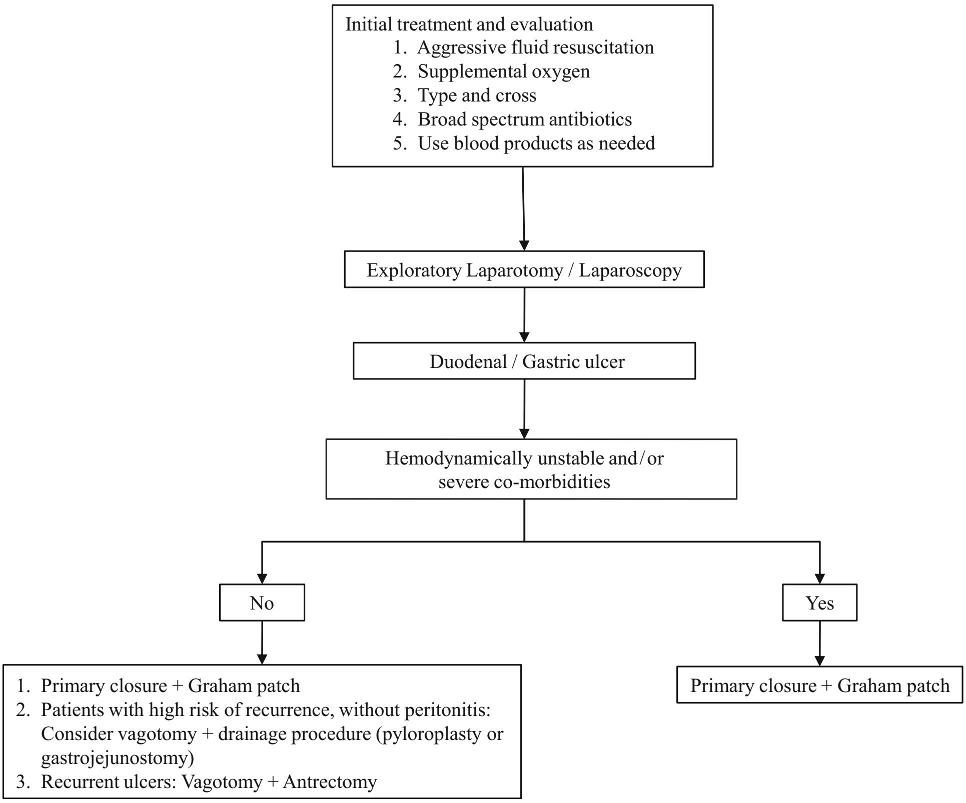
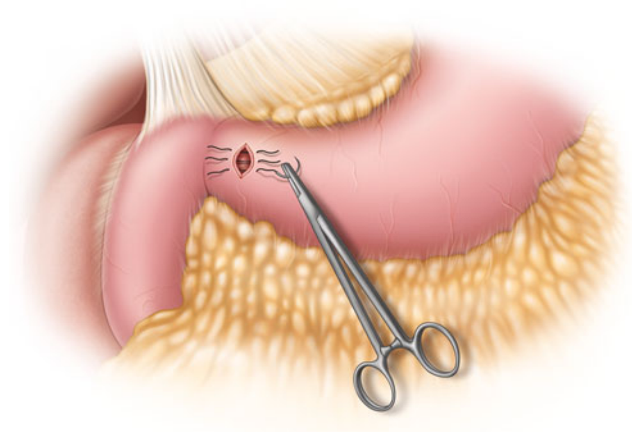


Fig. 1 Algorithm for the management of perforated peptic ulcers in elderly patients

Fig. 2 Primary closure of a perforated ulcer



(omental patch) (Fig. 3). The tails of the sutures are used to hold the omental pedicle, avoiding ischemia, while the sutures are tied (Fig. 4). It is important to avoid vascular injury to the omentum during dissection of the gastrocolic ligament. The abdominal cavity is copiously irrigated.

For duodenal ulcers, after a complete exploration is done, the duodenum is mobilized anteriorly and medially (Kocher maneuver). This maneuver avoids excessive tension on the primary closure. Both the anterior and posterior surfaces are carefully inspected. Routine biopsies are not required

Fig. 3 Reinforcement of the primary closure using an omental patch

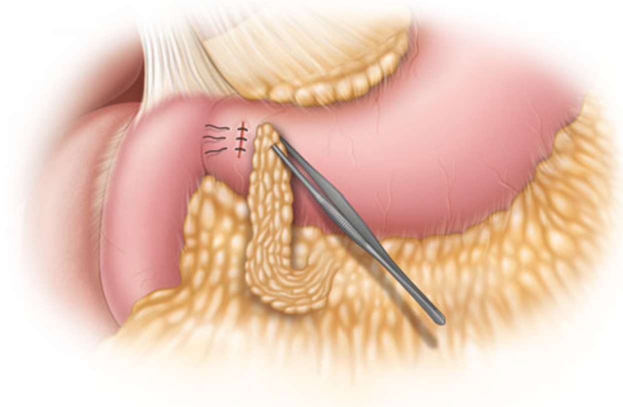
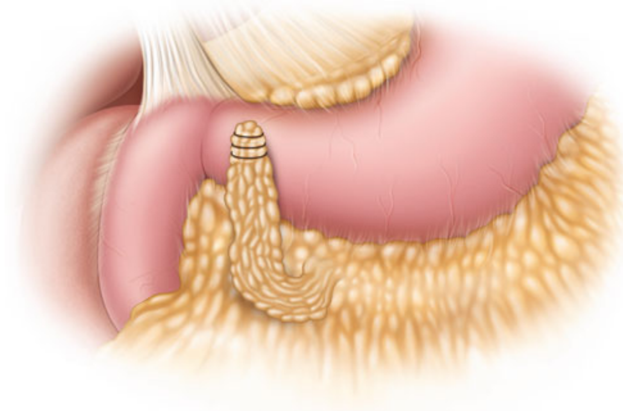


Fig. 4 Final view of the primary repair of a perforated ulcer with an omental patch



because the risk of malignancy in duodenal ulcers is very low. The duodenal defect is closed following the same principles for a gastric ulcer: interrupted full-thickness sutures reinforced with an omental patch. Duodenal ulcers are associated with more inflammation and defects larger than gastric ulcers, so if a primary closure is not possible, a true omental patch (Graham patch) is used. In this repair the ulcer margins are not approximated, the orifice is only plugged with omentum sutured to the duodenal defect. For very large perforations, a jejunal serosal patch can be used, which involves suturing a loop of jejunum to the perforated ulcer. Drain placement and distal feeding access should be considered based upon the size of the ulcer, difficulty of repair, and patient factors.

Patients are usually extubated unless they have persistent hemodynamic instability and/or if the patient has any respiratory issues. The integrity of the repair is evaluated with an upper GI study using water-soluble contrast, typically 3–7 days after operation. The nasogastric tube is kept to prevent gastric or duodenal distention, and it is removed after there has been an imaging study negative for leak, the output is low, and bowel function has returned. An esophagogastroduodenoscopy is recommended in the postoperative period, typically 6–8 weeks following surgery, to verify healing of the ulcer.

Performing additional procedures that decrease gastric acid secretion is not recommended because elderly patients frequently present with shock and severe comorbidities that require a rapid intervention. Often, these patients have a delay in diagnosis, and generalized peritonitis is found during the laparotomy; therefore, further dissection of the hiatus increases the risk of other complications such as mediastinitis. It is also important to consider that PPIs and *H. pylori* eradication treatment decrease the risk of recurrence.

The morbidity and mortality associated with perforated PUD are between 25–89% and 4–30%, respectively. Risk factors associated with increased morbidity and mortality are age, delay in diagnosis, high ASA score (III and IV), and shock during the operation. Age is crucial because patients older than 65 years have a mortality rate of 37.7% as compared with 1.4% in younger patients. A delay in diagnosis (>24 h) increases the mortality rate in elderly patients. The most common causes of mortality are myocardial infarct, arrhythmias, septic shock, and pneumonia. Resection procedures (i.e., antrectomy) are also associated with more mortality than primary closure in these patients [32].

Bleeding

Bleeding is the most common complication of PUD, which in turn is the most common source of upper GI bleeding. It is seen in 15–20% of the patients [33, 34]. The frequency of acute upper GI bleeding has decreased in general, but the proportion of patients older than 60 years who have bleeding is increasing; recent studies have published that 65% and 25% of the patients are older than 65 and 80 years old, respectively [22, 23]. This trend is a result of increased life expectancy; older patients have more comorbidities that predispose them to PUD (i.e., chronic renal failure, myeloproliferative disorders, portal hypertension) or that require anticoagulation. Elderly patients ingest more NSAIDs either as analgesics or as a preventive measure for other disorders. The most important risk factor to develop GI bleeding is NSAID ingestion. These drugs decrease the mucosal defense to gastric acid and inhibit platelet aggregation by decreasing thromboxane A2 production. The risk is dose dependent, but bleeding also occurs with low aspirin doses (75–325 mg/day) [35]. The risk of bleeding is considerably lower with COX-2 inhibitors as compared with nonselective NSAIDs, but COX-2 inhibitors can induce bleeding when they are combined with anticoagulants, aspirin, or any other NSAIDs [33]. The risk of bleeding significantly increases in patients taking anticoagulants, serotonin reuptake inhibitors, or drugs that prevent platelet aggregation [27]. *H. pylori* infection marginally increases the risk of bleeding; however, concomitant NSAIDs use and *H. pylori* infection significantly increase the risk of bleeding [28].

Symptoms include melena, hematemesis, fatigue, and/or hematochezia. The primary focus during the initial evaluation is assessment of the hemodynamic status. The presence of tachycardia, systolic blood pressure <100 mmHg, postural hypotension, or altered mental status suggests a significant blood loss. The initial goals of resuscitation are to establish a secure airway if needed, to ensure proper oxygenation and ventilation, and to administer IV fluids. It is mandatory to obtain a complete blood count, glucose, blood urea nitrogen, creatinine, electrolytes, INR, type, and crossmatch in all patients. The use of blood products needs to be individualized for each patient; any history of coronary artery disease lowers the threshold for packed red blood cells. Plasma or anticoagulation reversal agents should be considered in any patient with a coagulopathy associated with drugs or comorbidities; however, the risks and benefits should be considered in light of the patient's clinical condition. Once the patient is hemodynamically stable, he or she should be thoroughly examined. In the absence of any other disease, the physical examination of the abdomen is usually unremarkable.

Upper endoscopy is the gold standard in the initial evaluation because it can be diagnostic and therapeutic. Upper endoscopy may identify the source of the bleeding, and bleeding can be stopped using hemoclips, sclerosing agents, epinephrine, thrombin or fibrin glue, or thermal contact with bipolar electrocoagulation, heater probe, or argon plasma. Except for epinephrine, all these techniques can be used either to stop active bleeding or to prevent it in visible vessels. Epinephrine injection can partially control the bleeding before implementation of other techniques. Endoscopic therapy has a low complication rate (0.5%) [36]. The two most common complications are perforation and induced bleeding.

Most bleeding duodenal ulcers are in the posterior wall of the first portion of the duodenum; the bleeding almost always arises from the gastroduodenal artery (GDA) [20]. The most common vessels that bleed in the stomach branch off the inferior branch of the left gastric artery in the lesser curvature [24]. Approximately 20% of the patients will rebleed after endoscopy. For these patients, a second endoscopy is indicated because the success rate is high without significant morbidity; however, if bleeding persists, surgery or interventional radiology intervention is necessary [37]. Interventional radiology can often selectively cannulate and embolize the bleeding vessel.

Another indication for surgery or another intervention is a persistent transfusion requirement, typically considered to be more than 4 units given during a 24-h time span. However, since elderly patients develop coagulopathy more quickly than younger patients and they are at risk of rebleeding when coagulopathic, intervention needs to be considered in elderly patients before four units of blood are required. In addition, ongoing bleeding may aggravate preexisting comorbidities and cause myocardial infarction, renal failure, and stroke. Ulcer size is not considered a surgical indication, but ulcers bigger than 2 cm are associated with an increased risk of rebleeding. If a patient has an ulcer >2 cm and presents with persistent hypotension, surgical treatment should be considered [23].

Adequate platelet aggregation and hemostasis require an intragastric pH >6. Different studies have shown that high doses of PPI decrease the rebleeding rate by 54% and the need for surgery by 41%. The recommended regimens are pantoprazole 80 mg IV bolus followed by 8 mg/h for 3 days or pantoprazole 80 mg IV bolus followed by pantoprazole 40 mg IV every 12 h [38]. Figure 5 summarizes the diagnosis and treatment of bleeding ulcers.

Surgical Treatment of Bleeding Gastric Ulcers

Most gastric ulcers that bleed are type I. The anesthesia, patient's position, and incision are similar to duodenal bleeding ulcers. Treatment depends on the hemodynamic status of the patient. For those with shock, a conservative approach that only aims to control bleeding is recommended. Through an anterior gastrotomy, the ulcer is biopsied and oversewn with figure of eight stitches. The gastrotomy is closed in two layers using the same technique described below for closing bleeding duodenal ulcers. Stable patients with recurrent or large ulcers may require an antrectomy. The gastrocolic ligament is divided to enter the lesser sac; this dissection begins in the middle point between the pylorus and the cardia and is continued distally to the pylorus where the right gastroepiploic vessels are transected. Adhesions between the posterior gastric wall and the pancreas are divided. The gastrohepatic ligament is divided in order to control the inferior branch of the left gastric artery. The proximal and distal margins of this dissection are the incisura angularis and the beginning of the first portion of the duodenum, respectively. The stomach is divided proximally with a gastrointestinal anastomosis (GIA) stapler. The first portion of the duodenum is divided immediately after the pylorus with a stapler. The integrity can be restored with a Billroth I, Billroth II, or a Roux-en-Y gastrojejunostomy. The first option for reconstruction is a gastroduodenostomy, or Billroth I, which requires a complete Kocher maneuver to avoid tension on the anastomosis. The duodenum is mobilized close to the gastric remnant. The anastomosis is done in two layers. The internal layer is a continuous full-thickness layer using a 3-0 absorbable suture reinforced by a second layer of interrupted seromuscular sutures with 3-0 silk (Lembert type). This anastomosis is considered the most physiological reconstruction as the normal transit of the stomach goes to the duodenum; however, alkaline gastritis can occur. Previous scarring can limit the Kocher maneuver and prevent a tension-free anastomosis. The second reconstruction is a Billroth II procedure or gastrojejunostomy, which is preferred in cases with excessive scarring that prevent duodenal mobilization. This side-to-side anastomosis is created between the posterior gastric wall and the anti-mesenteric border of a jejunal limb (10–20 cm distal to the ligament of Treitz). The jejunum is brought up to the stomach, anterior or posterior to the transverse colon

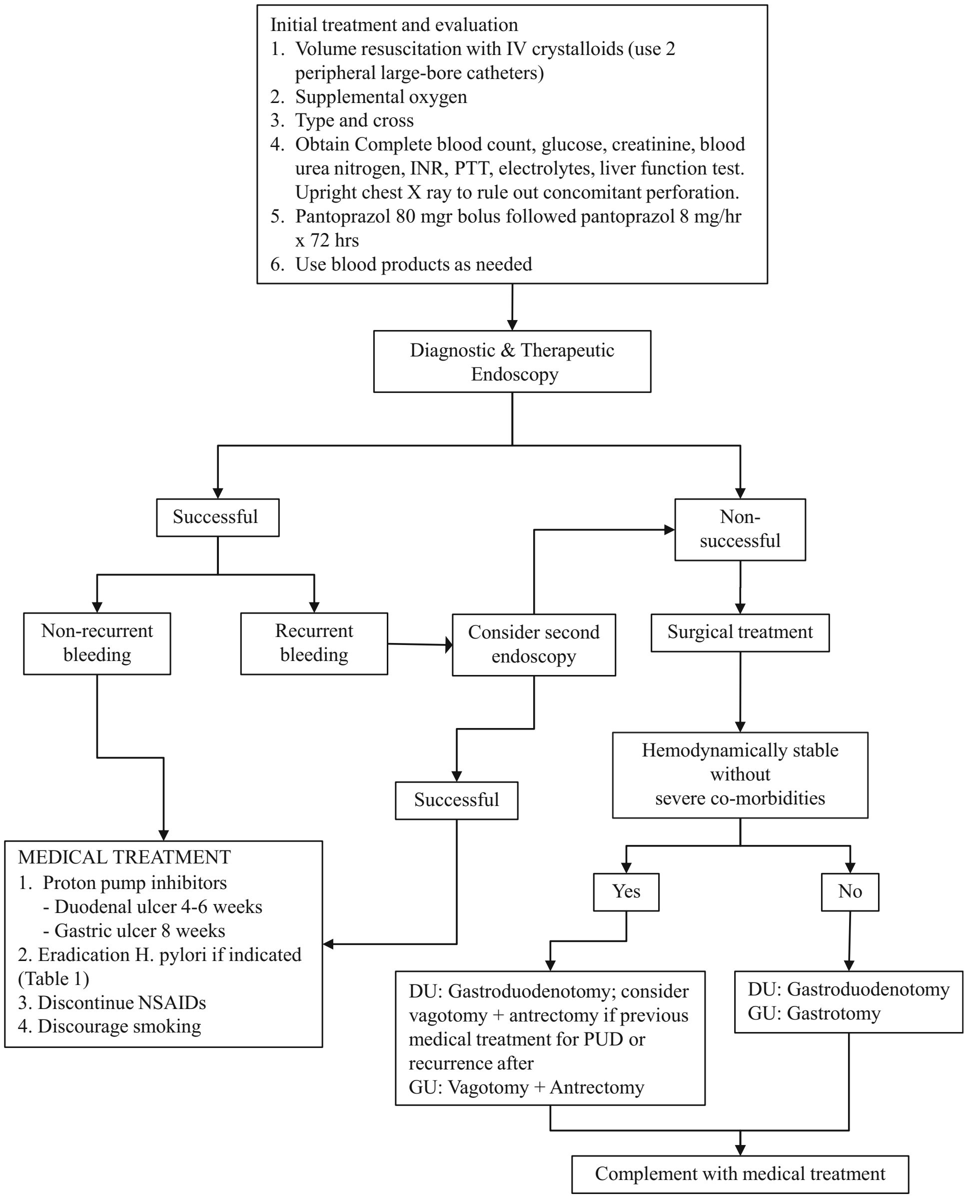


Fig. 5 Algorithm for the management of acute peptic ulcer bleeding in elderly patients

(antecolic or retrocolic, respectively). There is no functional difference in benign diseases. The anastomosis is created with a stapler or manually using the Hofmeister technique. The anastomosis is stapled through a small gastrotomy and enterostomy. The stapler is introduced through these defects, and the anastomosis is created. Both orifices are closed manually with a continuous full-thickness layer reinforced by an interrupted seromuscular layer. The mesenteric defect in the mesocolon is closed with interrupted 3-0 silk stitches in order to avoid internal hernias. The two most common options to restore are Billroth I and II, but both anastomoses predispose patients to alkaline gastritis or reflux; therefore, some surgeons recommend a reconstruction using a Roux-en-Y gastrojejunostomy for benign conditions.

Truncal vagotomy was previously performed in conjunction with a resection but with advances in the medical treatment of ulcer disease and the understanding of *H. pylori* disease is now rarely indicated. It is typically not used in the setting of perforation and is only indicated for patients who bleed on active PPI therapy, have a high risk of recurrent gastric outlet obstruction due to ulcer disease, or for intractable ulcer pain after all medical therapies are exhausted. It should always be combined with a gastric emptying procedure [39].

Surgical Treatment of Bleeding Duodenal Ulcers

The anesthesia, positioning, and incision are the same as for perforated ulcers. A full Kocher maneuver follows an exploratory laparotomy. Profuse bleeding in the first portion of the duodenum can be partially stopped by compressing the duodenal bulb. The pylorus is identified by the palpation of the concentric ring between the stomach and the duodenum or by visual identification of the pyloric vein that crosses anterior to the pylorus (Mayo's vein). Two 3-0 silk sutures are placed in the superior and inferior borders of the anterior surface of the pylorus. A 3-cm longitudinal gastrotomy perpendicular to the pylorus is followed by 3-cm extension toward the duodenum. The most common bleeding vessel is the GDA, which is located in the posterior duodenal wall (Fig. 6). Three stitches are placed to stop bleeding: two initial figure of eight stitches in the superior and inferior margin of the ulcer followed by a third figure of 8 or U-stitch that controls the pancreatic branch of the GDA (Fig. 7). Each suture must be placed carefully to avoid injury to the common bile duct. Once vascular control is achieved, the duodenum and stomach are carefully inspected to rule out any other source of bleeding. The aperture is closed transversely. The internal layer is a full-thickness continuous closure with an absorbable 3-0 suture reinforced by a second layer of interrupted seromuscular stitches using 3-0 silk (Lembert type) (Fig. 8). The closure can be reinforced with omentum, similar to a Graham patch.

This complication has a mortality rate that ranges between 10% and 35% in patients older than 60 years as compared with 10% in younger patients. Bleeding is the most common complication that causes death in PUD. Risk factors that predict high mortality are increased age, severe associated comorbidities, rebleeding, or patients that present with hypotension, shock, or in-hospital bleeding [20, 22, 24].

Gastric Volvulus

Gastric volvulus occurs when the stomach rotates more than 180° and may lead to vascular compromise, ischemia, and perforation, which is life-threatening. This condition has a peak incidence in the fifth decade of life. The volvulus may happen with an intra-abdominal stomach or an intrathoracic stomach within a paraesophageal hernia or due to a congenital or traumatic disruption of the diaphragm [40].

The presentation may be acute or chronic. Acute volvulus often presents with pain and vomiting. Associated hematemesis is a concerning sign, as it suggests mucosal damage due to ischemia. Patients with chronic volvulus often present with difficulty swallowing, mild abdominal pain, and bloating [40]. Diagnosis is typically confirmed acutely with a CT scan or chest X-ray. Chronic volvulus may be diagnosed on an upper GI series.

Treatment of the gastric volvulus depends on the clinical condition of the patient. In a stable patient, gastric decompression with an NGT can be attempted. An EGD may be performed as well to assess the mucosa for ischemia. This may also facilitate placement of the NGT for decompression. If there are no signs of ischemia and the patient is stable, this allows time for operative planning and often facilitates a laparoscopic repair. In the case of an unstable patient or concerns for ischemia, then immediate operative repair should be undertaken. A laparoscopic approach is still recommended if

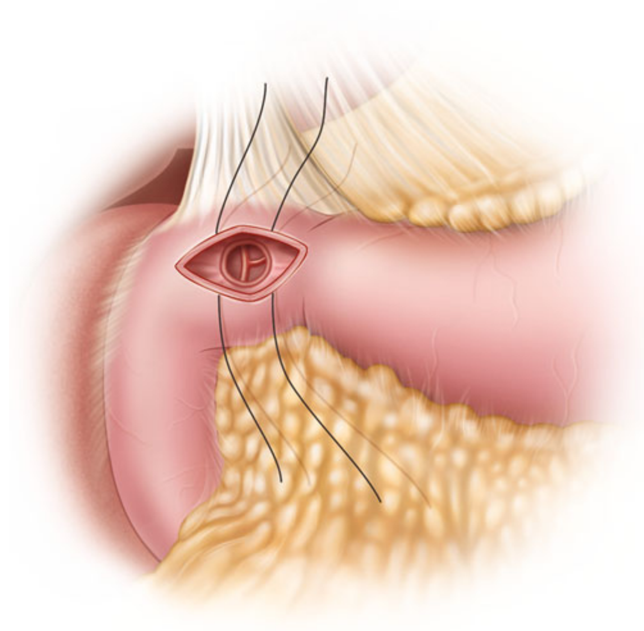


Fig. 6 Bleeding ulcer in the posterior wall of the rst portion of the duodenum

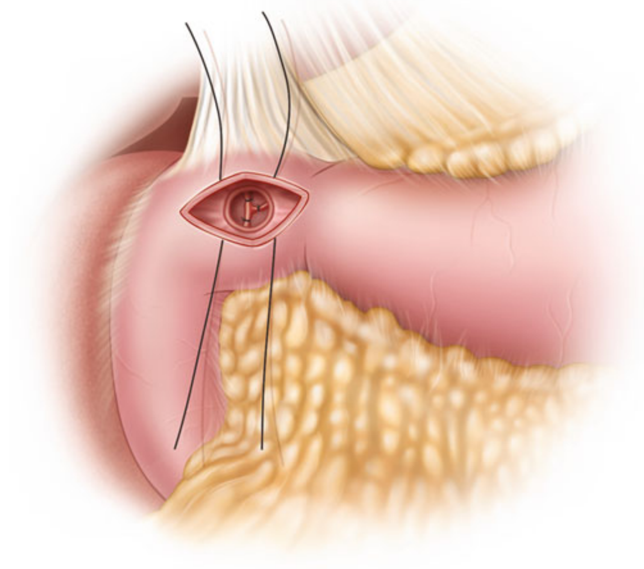


Fig. 7 Hemostasis of the GDA using 3-0 silk stitches

feasible. The aim of the operation is to reduce the volvulus, prevent recurrence, and repair any predisposing factors [40]. In addition, any ischemic tissue will need to be resected and reconstructed. Gastric reduction is accomplished by dividing any adhesions and/or reducing any herniation of the stomach and returning it to its normal anatomical position. Prevention of recurrence often involves pexy of the stomach to the abdominal wall and/or placing a gastrostomy tube to encourage the stomach to adhere to the abdominal wall. These maneuvers do not

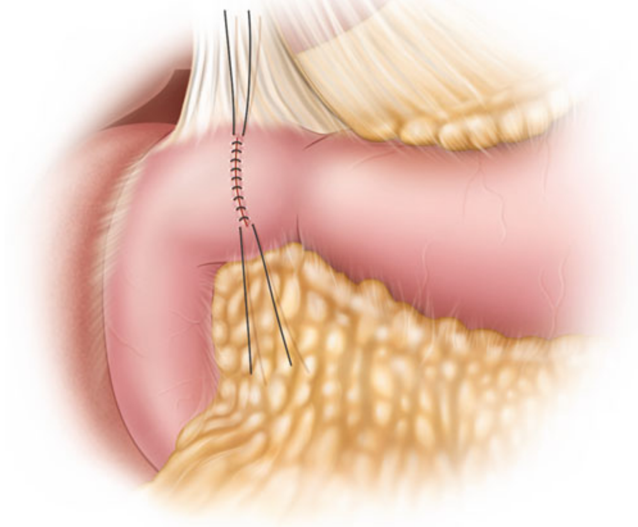


Fig. 8 Primary closure of the duodenotomy

necessarily prevent reherniation of the stomach into the chest but rather may reduce the risk of volvulus. Repairing any predisposing factors includes addressing diaphragmatic or hiatal hernias.

Gastric Outlet Obstruction

Gastric outlet obstruction (GOO) is the result of chronic edema, scarring, and fibrosis of the distal stomach or duodenum. The area proximal to the stenosis becomes chronically dilated; gastric dilation induces gastrin release, which is further aggravating because it increases gastric acid production. The incidence of GOO has declined with the advances in the medical therapy for PUD. GOO accounts for less than 5–8% of all PUD complications. The typical symptoms are early satiety, nausea, vomiting undigested food, heartburn, and weight loss. The most common GOO etiology is malignancy (60–80%); therefore multiple biopsies from the stenosis need to be taken [41]. Only 5–8% of patients with GOO have PUD [34]. Other diagnoses to consider are external duodenal or gastric compression (i.e., pancreatic pseudocysts, tumors) or GOO caused by a large gallstone (Bouveret syndrome), bezoars, or gastroparesis.

The initial evaluation relies on an upper endoscopy with multiple biopsies plus a water-soluble contrast upper GI series. If external compression is suspected, a CT scan is required. The initial treatment is conservative decompression using an NGT, IV infusion of PPIs, and correction of any electrolyte or acid–base disorder. Prokinetics are contraindicated. If *H. pylori* infection is proven, therapy is indicated because some studies report that symptoms improve after *H. pylori* eradication [41]. Nutritional status is also crucial; a liquid diet should be attempted unless the patient cannot tolerate ingestion. Severe GOO requires total parenteral nutrition.

Medical treatment improves GOO obstruction in 50% of the patients [42]. Endoscopic therapy with endoscopic balloon dilation increases the success rate up to 70% [43]. Serial dilations can be attempted in patients with recurrent stenosis, but the failure rate is proportional to the number of dilations attempted. The most common complication is perforation. Although experience with endoscopic stenting for malignancies is increasing, current data on benign disease is limited [44].

Surgical treatment may be indicated if medical therapies fail. The operation depends on the underlying etiology. In cases of GOO caused by recurrent PUD, a truncal vagotomy with antrectomy is indicated. A diverting laparoscopic or open gastrojejunostomy may also be sufficient in other disease states. Chronic gastric obstruction dilates the stomach with subsequent accumulation of food and secretions; this condition predisposes patients to aspiration pneumonia and wound infection due to bacterial overgrowth, so decompressing the stomach with an NGT is indicated before surgery. Duodenal dissection can be difficult in patients with chronic scarring; oversewing the duodenal stump is recommended due to the risk of duodenal stump leak.

Gastric Polyps

Gastric polyps are nodules of tissue, either sessile or pedunculated, which protrude into the gastric lumen [45]. Gastric polyps are seen in 0.5–2% of all endoscopies; most of them are asymptomatic but occasionally gastric polyps can grow, erode, and bleed. Large polyps can produce GOO [46–48]. Several types of gastric polyps can be found, but the three most common in elderly patients are hyperplastic polyps, fundic gland polyps, and adenomatous polyps. Uncommon type of polyps include inflammatory fibroid polyps, xanthomas, Peutz–Jeghers-type hamartomatous polyps, juvenile polyps, gastric polyps associated with Cowden disease, and finally gastric polyps associated with Cronkhite–Canada syndrome [49].

Hyperplastic Polyps

Hyperplastic polyps are the most common variety found during endoscopies in areas where *H. pylori* infection is common [47–49]. The incidence increases with age (mean age of diagnosis is 64–75 years), and they are more prevalent in women. Hyperplastic polyps are usually asymptomatic but are associated with other gastric diseases such as autoimmune gastritis, ZES, antral vascular ectasia, gastric amyloidosis, or cytomegalovirus gastritis [49]. Gastrin plasma levels are higher than controls [45]. The most common location is the antrum followed by the fundus and body. The mean size is 1 cm, although larger hyperplastic polyps have been reported. They are typically an incidental finding during an upper endoscopy. These polyps are usually sessile. The typical histological findings show elongated, dilated, tortuous foveolae lined by mucin-containing epithelium and edema of the lamina propria [48]. The natural history is variable. *H. pylori* eradication is associated with regression [46]. Most hyperplastic polyps are benign and asymptomatic, though a routine biopsy is recommended because final histology reports dysplasia or carcinoma in 1.5–4% of the patients. This risk of malignancy is higher in polyps larger than 2 cm [48, 49].

Fundic Gland Polyps

These polyps are the most common type of benign gastric polyps found in areas with low prevalence of *H. pylori* infection but common use of PPIs. They can be found sporadically or associated with familial adenomatous polyposis at any age, and they are also now recognized as sequelae of long-term PPI use. The most common location is in the fundus. Gastrin values are usually normal [45, 47]. Histology reveals cystic dilated glands lined by parietal and chief cells [48]. When sporadic or associated with PPI use, these polyps can regress spontaneously; routine follow-up is not required because they are ot premalignant [45]. However, when associated with a familial syndrome, surveillance is recommended [50].

Adenomatous Polyps

The incidence of these polyps also increases with age. They are associated with atrophic gastritis and are more prevalent in countries with a high incidence of gastric cancer [48]. The median age of diagnosis is 67 years [46]. The most common location is the antrum, and gastrin levels do not differ from controls. The risk of malignancy is higher in adenomatous polyps than any other gastric polyp, especially if the size is greater than 2 cm (40–50% risk of malignancy) [48]. *H. pylori* eradication does not cause regression. Routine excision is recommended because they may be malignant [46].

Dieulafoy Lesion/Malformation

Dieulafoy lesion is an abnormal submucosal artery associated with a minute mucosal defect frequently associated with bleeding. It causes between 1% and 5.8% of acute nonvariceal upper GI bleeding. The most common location is the stomach followed by the first portion of the duodenum, but they can occur throughout GI tract or in the bronchial tree. The most common location in the stomach is the fundus and body [51]. Histology reveals a submucosal artery that does not undergo the usual ramification within the wall of the stomach or failure to diminish to the minute size of the mucosal capillary vasculature without any inflammation or defect in the mucosa [52]. It is more common in men. The mean age of diagnosis is 63 years, so they are frequently associated with comorbidities. Most patients develop melena and hematemesis along with hemodynamic instability. The treatment follows the same principles described previously for bleeding peptic ulcers; the initial goal is hemodynamic stabilization followed by an upper endoscopy. The same endoscopic techniques described for PUD are used to stop bleeding. The success rate is >90% [53]. In patients who do not respond to endoscopic therapy, local wedge resection of the lesion is indicated.

Gastroparesis

Gastroparesis indicates impaired transit of intraluminal content from the stomach to the duodenum without a mechanical obstruction [54]. It affects 4% of the population.

Etiology

The most common causes of gastroparesis are diabetes, idiopathic, and surgery; however, the most common etiologies in the elderly patient are as follows:

1. Diabetes. Gastroparesis is present in 30% of the patients with type 2 diabetes [55]. Different theories explain this effect. Since gastroparesis is seen in patients with other manifestations of autonomic neuropathy, it is believed that autonomic neuropathy contributes to the development of gastroparesis. Diabetes decreases the number of interstitial Cajal cells, induces smooth muscle fibrosis, and decreases the neurons present in Auerbach's plexus. Hyperglycemia decreases gastric emptying [55]. Diabetes is the most common cause of gastroparesis in elderly patients because diabetes is one of the most common comorbidities seen in this population.

2. Upper GI surgery. Any operation that involves the distal esophagus, stomach, or duodenum can be complicated by delayed gastric emptying. Unfortunately, upper GI malignancies that require surgery are more common in older patients. This complication is also seen in benign diseases; gastroparesis may occur after any operation for PUD or anti-reflux procedures.
3. Neurologic diseases. Parkinson disease and strokes are associated with gastroparesis. Parkinson disease is present in 7% of patients with gastroparesis [55].

4. Drugs. Elderly patients often require drugs that delay gastric emptying such as calcium channel antagonists, L-dopa, opiates, tricyclic antidepressants, and aluminum antacids [54].
5. Other comorbidities. Renal insufficiency, hypothyroidism, previous abdominal radiation, cirrhosis, chronic pancreatitis, and paraneoplastic syndromes can produce gastroparesis.

Clinical Manifestation

The most common symptoms are nausea, vomiting, bloating, early satiety, epigastric pain, and belching. Although in severe gastroparesis the previous symptoms are present with liquid meals, they are more frequent with solid meals. Physical examination usually shows abdominal distention, mild pain, and tympanic percussion in the epigastrium, but in severe cases dehydration is evidenced by tachycardia, orthostatic hypotension, poor skin turgor, and dry mucous membranes. Succussion splash is also present in severe cases. Gastroparesis should be suspected in any patient with predisposing conditions associated with the symptoms previously described. An extensive workup can rule out cancer, dyspepsia, GOO secondary to PUD, pancreatitis, GERD, cyclic vomiting syndrome, chronic pancreatitis, and superior mesenteric or rumination syndromes. An upper GI radiographic study with contrast plus an upper endoscopy is frequently required to rule out any anatomical obstruction. Retained food in the stomach (with proper fasting) without anatomical obstruction increases the probability of gastroparesis. The gold standard for diagnosis is gastric emptying scintigraphy. In this test the patient receives a solid meal (typically scrambled eggs) mixed with technetium-99 sulfur colloid. Gastric emptying is measured after 2, 3, and 4 h. The diagnosis is confirmed if more than 60% of the meal is retained after 2 h or 10% after 4 h [56].

Treatment

The initial goal of therapy is to correct any preexisting dehydration or electrolyte disorders. The medical treatment has different components: dietary recommendations, control of predisposing conditions, and drug therapy. In elderly patients, predisposing conditions are irreversible or difficult to treat. However, good metabolic control and replacement of any drug that delays gastric emptying are required. Meals rich in fiber or fat should be avoided because they delay gastric emptying; carbonated beverages should also be avoided. Frequent small meals are better tolerated than larger meals [55]. Prokinetic drugs such as erythromycin and metoclopramide improve gastric emptying. Different studies have shown that erythromycin is the most potent agent because it activates motilin receptors and increases both antral peristalsis and gastric emptying. Metoclopramide is a benzamide that increases the contraction in the esophagus, fundus, and antrum; it also elevates the lower esophageal sphincter pressure and improves antral–pylorus–duodenal coordination. It is also helpful to control vomiting [57]. However, metoclopramide should be used with caution in the elderly, who may be more likely to experience side effects such as tardive dyskinesia or confusion.

Nausea and vomiting are present in 92% and 84% of the patients, respectively; therefore antiemetics are also indicated. The most useful agents are phenothiazines (prochlorperazine and tiethyperazine). Serotonin 5-HT3 receptor antagonists such as ondansetron may be helpful because they do not affect gastric emptying. Muscarinic M1 receptors antagonists such as scopolamine and H1RA such as promethazine are not recommended because they inhibit gastric emptying [55]. They should also be avoided in the elderly due to their anticholinergic effects.

The role of surgery in gastroparesis is limited to patients with severe gastroparesis that require multiple hospitalizations plus enteral or parenteral nutrition and those patients who fail medical treatment. Surgery relies on the placement of gastric stimulation devices that alter the gastric myenteric neural network and interrupt gastric arrhythmias [58]. Through laparoscopy or open approach, two electrodes are placed 1 cm apart in the muscularis propria along the greater curvature 10 cm proximal to the pylorus. The electrodes are connected to a neurostimulator located in a subcutaneous pocket outside the abdomen [58]. A recent study showed that gastric electrical stimulation produces a good outcome in 70% of the patients, most of whom are able to tolerate oral diets after placement and have a significant increase in the body mass index [58]. In addition, there is a growing role for other therapies, including pyloroplasty, transpyloric stenting, endoscopic pyloromyotomy, and Botox treatment of the pylorus [59]. For patients with refractory symptoms, placement of a palliative gastrostomy or feeding jejunostomy should be considered.

Duodenal Diverticula

Diverticula of the duodenum occur in approximately 5–22% of individuals, typically located along the pancreatic or mesenteric border of the second portion of the duodenum [60]. Often they are asymptomatic but may be diagnosed at the time of a complication, such as inflammation, bleeding, obstruction, or perforation. CT scan is the most useful imaging in the diagnosis of duodenal diverticula. If perforated, management ranges from conservative treatment with antibiotics and percutaneous drainage to a surgical diverticulectomy, with or without duodenal diversion based upon the amount of inflammation and the clinical status of the patient. In the case of a diverticulectomy, a single- or double-layer duodenal closure with placement of drainage tubes is recommended. A patch of omentum over the repair may be considered. Care should be taken to avoid the ampulla of Vater, as diverticula occur commonly around this area [60]. Distal feeding access should be considered at the time of the operation.

Complications After Gastric Surgery

It is not uncommon for elderly patients to develop complications after gastric surgery. Each region has a particular response to food ingestion, which is mediated by the vagus nerve. The proximal stomach is the main reservoir for liquids; and shortly after liquid ingestion there is a decrease in the tone in the fundus, which allows liquid storage. Antral motility is increased by the ingestion of solid meals, and it triturates large particles; only 1–2 mm particles pass through the duodenum. The pylorus controls the transit of food particles to the duodenum and limits alkaline reflux. Any operation that involves the intra-abdominal esophagus, stomach, and duodenum can affect the motor functions of the stomach. The most common postgastrectomy syndromes are as follows:

Dumping Syndrome

This syndrome can present after any vagotomy, drainage procedure, or gastric resection. Between 25% and 50% of the patients have some manifestations related to dumping syndrome. In approximately 10% of the patients, these symptoms are significant. After vagal denervation, the stomach loses the relaxation and accommodation reflexes; therefore, it cannot function as a reservoir. When a drainage procedure is added, gastric emptying cannot be controlled because the size of the particles is no longer regulated [61].

Dumping syndrome can be divided into early and late dumping syndrome. Early dumping syndrome presents within 30 min after food ingestion. This causes diaphoresis, weakness, dizziness, flushing, palpitations, fullness, crampy abdominal pain, nausea, vomiting, and diarrhea. Late dumping is seen 1–3 h after the ingestion of food. The rapid increase of carbohydrate concentration in the intestinal lumen induces a rapid absorption of carbohydrates with subsequent hyperinsulinemia, which then creates reactive hypoglycemia. Clinically, patients present only with vasomotor symptoms and no GI symptoms [61].

The pathophysiology of dumping syndrome is explained by the rapid transit of chyme, fluid shifts from the general circulation to the intestinal lumen, and pooling of the blood supply within the splanchnic circulation. This causes the increased heart rate, vasoconstriction, and elevated plasma norepinephrine levels seen in dumping syndrome. The symptoms are also caused by excessive secretion of gastrointestinal hormones, such as VIP, serotonin, and bradykinin, GLP-1, and norepinephrine levels.

The diagnosis is suspected in patients with a previous gastric surgery. It can be confirmed with a glucose oral challenge test or with gastric emptying scintigraphy. The mainstay of treatment is diet modification: liquids should be ingested 1 h after the ingestion of solids, simple carbohydrates should be avoided, and supplemental fiber is recommended, because it slows gastric emptying. Octreotide or acarbose, as well as antidiarrheal medications such as loperamide and tincture of opium, can help to control symptoms. Surgical therapy is a last resort if all other therapies have failed. If feasible, takedown of the gastrojejunostomy should be performed if the pyloric channel has reopened. If a pyloroplasty was previously performed, performing a longitudinal closure to re-create the original alignment can modify it and slow gastric emptying. Conversion to a

Roux-en-Y gastrojejunostomy may also be helpful [61].

Postvagotomy Diarrhea

The pathophysiology of this condition is unclear; some theories that may explain this complication are denervation of the small intestine, gallbladder, and common bile duct or rapid gastric emptying associated with rapid intestinal transit that leads to malabsorption. The diagnosis should be suspected in every patient with prior gastric surgery and a negative workup that excludes other causes of diarrhea. The initial treatment is dietary modification (avoid lactose and decrease liquid ingestion before meals) and the use of antidiarrheal agents (e.g., loperamide). For refractory untreatable diarrhea, the antiperistaltic interposition of a jejunal limb 100 cm downstream of the gastrojejunostomy may be considered [62].

Gastroparesis or Delayed Gastric Emptying

Gastric surgery is responsible for approximately 10% of all gastroparesis cases [54]. This complication was described previously.

Afferent Loop Syndrome

This is the result of an obstructed afferent limb secondary to stomal edema, kinking, scarring, stricture, adhesions, internal hernias, or cancer. It can occur acutely or chronically. It occurs in 0.3% of the patients that have a Billroth II. The typical manifestations are abdominal pain, nausea, and non-bilious vomiting. If the limb is partially obstructed, the abdominal pain may be relieved by vomiting. In severe cases the chronic obstruction can result in jaundice or pancreatitis. The diagnosis is confirmed with an endoscopy that demonstrates the obstruction. The initial treatment can be endoscopic using balloon dilation, but if it persists the gastrojejunostomy should be converted to a Roux-en-Y gastrojejunostomy. A second option is a Braun enteroenterostomy between the afferent and the efferent limb [63].

Efferent Syndrome

This syndrome results when the efferent limb of the gastrojejunostomy is obstructed. It can be acute or chronic and is manifested as abdominal pain, epigastric distention, and bilious vomiting. Upper endoscopy or an upper GI transit study is typically diagnostic. Possible etiologies are limb kinking, retroanastomotic herniation of the efferent limb, or adhesions. The treatment is surgical, either converting a Billroth II procedure into a Roux-en-Y gastrojejunostomy or revising the initial anastomosis [62].

Duodenal Stump Leak

Dehiscence of the initial duodenal closure after antrectomy is the typical cause of duodenal stump leak. This is more common in the setting of inflammation and scarring in this area but can also be a consequence of an incomplete duodenal mobilization or distal obstruction. It can be avoided with a Kocher maneuver to ensure that the closure is tension-free; however, if the area has fibrosis or acute inflammation, a lateral duodenostomy in the second portion of the duodenum to create a controlled duodenal fistula may be helpful. In a postoperative patient, percutaneous transhepatic duodenal diversion has also been described [64].

Alkaline Gastritis

After a Billroth I, Billroth II, or pyloroplasty, 5–15% of the patients develop gastritis associated with bilious reflux. Patients complain of epigastric pain, nausea, and bilious emesis. The diagnosis is obtained at time of endoscopy that shows gastric inflammation and the presence of bile. The diagnosis can also be made with bile acid scintigraphy. For patients with severe symptoms, the previous anastomosis can be converted to a Roux-en-Y gastrojejunostomy or a Braun enteroenterostomy.

Conclusion

H. pylori infection and NSAID ingestion are the major risk factors for the development of peptic ulcer disease in elderly patients. Unfortunately, an acute complication such as bleeding or perforation will be the first clinical manifestation in 50–60% of patients. Eradication of *H. pylori* decreases the risk of recurrent PUD, especially in light of the fact that elderly patients have worse outcomes than younger patients. Elderly patients are also at unique risk of other complications, such as gastric volvulus, which typically occurs in the setting of a paraesophageal hernia. These can be either chronic or acute, and initial conservative management is recommended once gastric ischemia is ruled out. The geriatric population is also at increased risk of a malignancy arising within adenomatous gastric polyps, and they also suffer with gastroparesis. The most common etiology of gastroparesis is diabetes, and its treatment is very difficult due to the undesirable side effects associated with most antiemetics and prokinetics. It is important to consider the unique risks and treatments required for elderly patients in a multidisciplinary setting.

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Benign Disease of the Gallbladder and Pancreas in the Elderly

53

Morgan L. Cox and Alexander Perez

Contents

Abstract

Benign disorders of both the gallbladder and pancreas are important diseases to account for within the elderly population. The incidence of cholelithiasis increases with age, and acute cholecystitis is a common presentation in the elderly. Pancreatic disease including pancreatitis, most likely due to gallstones, is less common in the elderly, compared to the general population. Elderly patients are more likely to present with nonspecific, constitutional symptoms often leading to a delay in diagnosis. However, many of the diagnostic modalities and treatment algorithms essentially remain the same as endoscopic, percutaneous, and surgical interventions are safe and feasible in the elderly population. The higher risk of morbidity and mortality with biliary or pancreatic disease is due to decreased reserve and exacerbation of comorbidities making it critical to identify and optimize the comorbidities of these patients. A multidisciplinary team approach to a focused comprehensive geriatric assessment in the perioperative period helps identify risk factors and informs postoperative management, with improved outcomes.

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Introduction

This chapter explores benign biliary and pancreatic disease in patients with advanced age. We will address the varying incidence of these diseases in the elderly compared to their younger counterparts and how they might present differently for medical care. Diagnosis and treatment algorithms are provided for each of the diseases discussed in addition to pitfalls in the treatment of benign biliary or pancreatic disease in the elderly population. Finally, the importance of adequate treatment of comorbidities and the role of specialized multidisciplinary, geriatric teams in perioperative care will be emphasized.

Gallbladder

Cholelithiasis

Cholelithiasis is the presence of gallstones within the gallbladder. The incidence of cholelithiasis increases greatly with age, and therefore, the most common cause of abdominal pain in elderly adults is due to biliary tract stones [1]. In a large autopsy series of elderly patients, about 30% had gallstones present while another 5% had a prior cholecystectomy [2]. In addition to increasing age, risk factors for the development of cholesterol gallstones include obesity, female gender, metabolic syndrome, rapid weight loss, diabetes, gallbladder dysmotility, and a sedentary lifestyle [3, 4].

Cholesterol stones are the most common type of gallstone in the general population including the elderly. These stones are typically yellow in color and consist of 70–80% cholesterol. Calcium bilirubinate stones are the second most common type of gallstone. These are black pigmented stones containing mostly insoluble bilirubin and calcium phosphate with less than 20% cholesterol. Black stones tend to be multiple and are commonly seen in patients with hemolytic anemia. The third type of gallstone is mixed or brown pigmented stones, and these stones typically form due to infection in the biliary tract when bacterial enzymes hydrolyze conjugated bilirubin. Mixed stones are more likely to be radiographically apparent due to the high calcium content. They commonly form de novo in the bile ducts which makes them primary gallstones [5].

Although there is an increased incidence in this population, elderly patients are less likely to present with typical symptoms of biliary disease. Cholelithiasis is most likely to have a silent presentation as most patients remain asymptomatic for decades. Only about 10% of individuals with known cholelithiasis will develop symptoms within 5 years and about 25% within 10 years [4].

Given the indolent course of asymptomatic cholelithiasis that is diagnosed incidentally when investigating a separate disease process, it is recommended that surgery be avoided. The risk of perioperative morbidity and mortality in the elderly outweighs the low incidence of developing symptoms or complications from gallstones.

The most common presenting symptom due to biliary colic or symptomatic cholelithiasis is recurrent abdominal pain. One third of elderly patients who present with symptomatic biliary disease for the first time will have recurrence with nonoperative management [6]. Compared to younger patients, the elderly are more likely to represent with complications of gallstones such as acute cholecystitis (40% versus 18%), gallstone pancreatitis (19% versus 6%), and choledocholithiasis (21% versus 5%) [7].

A prognostic nomogram has been developed by Parmer and colleagues to provide a 2-year risk of developing gallstone-related complications in elderly patients after their first presentation. Factors associated with acute hospitalization included male gender, increased age, fewer comorbid conditions, presentation to emergency department (ED) compared to primary care office, and complicated biliary disease. The 2-year emergent hospitalization rate due to biliary disease was 11.1% [8].

Therefore, due to the increased risk of complications and hospitalization, medical therapy or observation of the elderly patient with symptomatic gallstones is not optimal. Less than 10% of patients are suitable for a nonoperative plan as all of the following criteria must be met: stone <20 mm in diameter, less than four stones, and a functioning gallbladder [4]. Medical treatment consisting of oral dissolution therapy with ursodeoxycholic acid (UDCA) has an unpredictable success rate even within these very select patients.

Given elective or emergent laparoscopic cholecystectomy is safe and effective for cholelithiasis in the elderly population, surgical management of symptomatic cholelithiasis is the preferred option [9, 10]. Elderly patients have a slightly higher risk of postoperative complications and a longer hospital stay compared to younger patients, so the benefits of surgery need to outweigh the risks based on the individual patient's comorbidity profile [4, 11]. The goal of early surgical intervention is to reduce the risk of complications and the development of cholecystitis or cholangitis which can be fatal in the elderly population [12].

Choledocholithiasis

About 10–20% of individuals with gallstones will progress to have common bile duct (CBD) stones which are defined as choledocholithiasis [1]. About 25% of those patients will go on to develop serious complications due to the retained stones. Elderly patients are more susceptible to choledocholithiasis due to an increased diameter of the extrahepatic bile duct; this is thought to be from the fragmentation of longitudinal smooth muscle myocyte bands and connective tissues of the CBD [1]. This dilation of the CBD is age-dependent with an increase of about 0.04 mm per year. Therefore, the upper limit of normal for the diameter of the CBD in an elderly patient should be considered 8.5 mm [13].

Elderly patients with choledocholithiasis are more likely to present with generalized symptoms such as malaise or debility compared to the more characteristic symptoms of biliary disease seen in their younger counterparts. Nausea, emesis, and right upper quadrant or epigastric pain are more typical of patients with CBD stones. Other presentations include biliary colic, jaundice, cholangitis, and pancreatitis. Given the wide range of possible presentations within the elderly population, it is important to perform a timely and thorough workup in order to prevent a delay in diagnosis and the development of acute cholangitis which can be devastating in an elderly patient [1].

Laboratory testing in the elderly patient with abdominal pain should be broad including serum alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase (ALP), fractionated bilirubin, white blood cell count (WBC), hemoglobin, hematocrit, blood urea nitrogen (BUN), and creatinine (Cr). Patients suffering from choledocholithiasis most commonly have elevated ALP in addition to elevated gamma-glutamyltransferase which differentiates an elevated ALP due to bone disease. Liver enzymes can also be elevated in the setting of CBD stones especially with a longer duration of symptoms. An increased WBC is concerning for concomitant acute cholecystitis or cholangitis.

Imaging studies are typically obtained as adjuncts to physical exam and laboratory values in the diagnosis of biliary disease. Transabdominal ultrasound is the most recommended method given it is noninvasive with acceptable sensitivity and specificity. Transabdominal ultrasound actually has an increased sensitivity and accuracy for CBD stones with increasing age [1]. However, magnetic resonance cholangiopancreatography (MRCP) and endoscopic retrograde cholangiopancreatography (ERCP) are the most sensitive in detection of CBD stones. Without direct visualization of a stone, dilation of CBD on imaging is an independent predictor of the presence of a CBD stone [1].

Intravenous fluids and analgesia are the appropriate initial treatment for suspicion of choledocholithiasis. The elderly are believed to have an increased risk of infection and inflammation due to decreased immune competence [14]. Antibiotics should be administered in a timely fashion for those patients with stones complicated by cholangitis, to prevent systemic bacteremia. Allergies as well as declining renal and hepatic function should be considered when selecting antibiotics, analgesia, and dosages.

Pharmacologic choices are complicated further by sarcopenia in elderly patients, making serum creatinine a less sensitive determinant of renal function. Therefore, BUN and glomerular filtration rate should be evaluated as well.

After initial resuscitation and stabilization, the clearance of CBD stones for adequate drainage of the biliary tract is the highest priority. Pharmacological treatment of CBD stones with UDCA is not recommended in the elderly population as it has not been shown to make a difference in stone size or rate of successful duct clearance [1]. The time required for medical treatment, successful or not, puts the patient at risk for infection from persistent obstruction.

ERCP is first-line therapy for choledocholithiasis in all patients including the elderly. Complete extraction of stones from the bile ducts in choledocholithiasis is associated with a longer survival [15]. ERCP has been shown to have an overall complete clearance of CBD stones in over 95% of elderly patients [16]. During ERCP, there are a variety of interventions capable of clearing the CBD and preventing further obstruction including sphincterotomy and papillary balloon dilation [17]. Furthermore, endoscopic biliary stenting with a double-pigtail stent is a safe and feasible therapy following endoscopic sphincterotomy in elderly patients with choledocholithiasis [18]. This is an indicated procedure for patients with three or more common bile duct stones and/or stones greater than 20 mm in size [19].

Rates of post-procedural ERCP complications range 3–10% in elderly patients with no higher incidence due to advanced age [1, 20]. These complications include pancreatitis, hemorrhage, duodenal perforation, and events due to exacerbation of comorbid conditions such as myocardial infarction or stroke. Elderly patients with a concomitant malignancy have been noted to have a higher risk of adverse events following ERCP. Additionally, within the elderly population, those patients greater than 80 years old are more likely to suffer from bleeding, cardiopulmonary events, and death [1].

ERCP with sphincterotomy has a higher risk of peri-procedural bleeding but a lower risk of post-procedural pancreatitis compared to balloon dilation [1]. Therefore, it is recommended that elderly patients on antithrombotic therapy for cardiovascular, cerebrovascular, or peripheral vascular disease undergo papillary balloon dilation preferentially to reduce the risk of procedural bleeding. These patients should also be evaluated for extent of anemia and anticoagulation prior to undergoing a procedure of any kind [1].

As with many other diseases requiring procedural or surgical intervention in the elderly population, there is a higher risk of decompensation from an adverse event due to concomitant comorbidities and decreased functional reserve. Optimization of concurrent medical conditions is imperative in the peri-procedural period including an anesthetic assessment to tailor the sedation approach. A multidisciplinary team approach to a focused comprehensive geriatric assessment can help improve outcomes by providing a geriatric consultation to high-risk patients prior to surgery to identify risk factors preoperatively and manage them postoperatively [21]. With attention to detail, therapeutic ERCP in the elderly patient is safe, effective, and imperative to prevent progression of the disease and overall deterioration [1, 16, 20, 22].

Once endoscopic intervention or advanced imaging has ensured the CBD is clear of stones, definitive treatment with laparoscopic cholecystectomy is indicated to prevent recurrence and subsequent complications. Laparoscopic cholecystectomy has very good results in the elderly population allowing for a shorter length of stay (LOS) and decreased number of postoperative complications compared to an open approach. Alternatively, an open procedure is most commonly planned due to associated pathophysiology from pneumoperitoneum, acid-base disturbances, renal hypoperfusion, or pulmonary physiology leading to an increased anesthetic risk [23].

The importance of extracting CBD stones at the time of surgery for patients who did not have preoperative endoscopic intervention has been well described by Moller and colleagues [24]. Patients who did not undergo measures to remove ductal stones had a 25% chance of suffering postoperative complications including pancreatitis, cholangitis, and jaundice. This risk was decreased to 12.7% in patients who underwent intervention to clear the ducts [24].

Although not as commonly performed as ERCP, a surgical approach to clearance of CBD stones with a common bile duct exploration is considered safe and feasible in the elderly population [25–27]. A laparoscopic approach to CBD exploration carries a morbidity of 30% and a mortality of 3.4% [28]. These are similar results to those described in the general population [29]. Age should not preclude a common bile duct exploration at the time of surgery if the biliary tract was not previously cleared; however, the success rate of stone clearance from the CBD with surgery has been reported as significantly lower within the elderly population, 50% for >65 years old and 90% for <65 years old) [11]. This suggests preoperative clearance of the biliary tract with ERCP followed by definitive treatment with laparoscopic cholecystectomy is the optimal treatment of choledocholithiasis in the elderly population.

Gallstone Ileus

Gallstone ileus is a mechanical small bowel obstruction due to the impaction of a gallstone within the lumen of the intestine via a cholecystoenteric fistula. The most common fistula, accounting for almost 60%, occurs between the gallbladder and duodenum (cholecystoduodenal fistula) [30]. The obstruction most commonly occurs at the ileocecal valve where the stone is unable to pass.

The diagnosis of gallstone ileus is quite rare within the general population but it has a higher propensity to affect females and the elderly. While it causes only 1–4% of all small bowel obstructions, gallstone ileus accounts for 25% of nonstrangulated small bowel obstructions within the elderly population [31]. Overall, mortality is high at 8–18% making early diagnosis critical [32, 33].

Nonspecific history and clinical findings make the diagnosis of gallstone ileus more difficult. Many patients are treated for small bowel obstruction alone leading to a delay in the operative treatment of gallstone ileus. Plain abdominal radiograph is also nonspecific and only suggests intestinal obstruction. Cross-sectional imaging with computed topography (CT) scan is diagnostic with the triad of pneumobilia, small intestine dilation, and a radio-opaque gallstone located within the bowel lumen.

Surgical intervention is required for the treatment of gallstone ileus. However, there is persistent debate over the extent of surgery required. At minimum, an enterotomy with removal of the obstructing stone is necessary, and this is typically performed in an urgent or emergent fashion. Differing opinion suggests completion of the enterolithotomy in addition to cholecystectomy and closure of the fistula tract, known as the one-stage procedure, is required.

Postoperative mortality is lower with only a simple enterolithotomy, 12% versus 17% [32]. However, this leaves the risk of further obstruction if more stones are present within the gallbladder, persistent symptoms due to an inflamed gallbladder, and possibly increased risk of gallbladder cancer [33]. Older literature suggests recurrence of gallstone ileus is only 5% after enterolithotomy alone with 10% of patients having persistent biliary symptoms without recurrence of the ileus [32].

The one-stage procedure results in a longer operative time due to the complexity of the procedure. Although it does offer definitive treatment, it leads to a higher rate of morbidity and mortality. Therefore, this should only be considered in healthier patients with fewer comorbidities and a longer life expectancy leading to less operative risk [31, 33].

Acute Cholecystitis

Symptomatic gallstones progress to acute cholecystitis in 10% of patients [4]. Acute cholecystitis is an acute inflammatory process that occurs in response to an obstruction of the cystic duct by a gallstone. Acute cholecystitis is a very common cause of ED visits in the elderly population [34]. Presenting symptoms most commonly include right upper quadrant abdominal pain, fever, emesis, palpable mass, and jaundice. Up to 12% of elderly patients with acute cholecystitis meet criteria for septic shock upon admission [34].

The workup of the elderly patient with abdominal pain due to suspected biliary disease is similar to that described above for cholelithiasis and choledocholithiasis. Laboratory tests should evaluate for leukocytosis, liver function, renal function, and coagulation status. Imaging typically starts with transabdominal ultrasound given its high sensitivity and specificity for biliary disease and its ability to accurately determine the severity of acute cholecystitis in the elderly population. Severity of disease on imaging can be used to help guide therapy and as a reference for the timing of surgical intervention [35]. Findings such as pericholecystic fluid, wall enhancement, wall thickening (>3 mm), positive sonographic Murphy sign, and a nonmobile stone at the neck of the gallbladder are all consistent with acute cholecystitis. A dilated CBD or elevated ALP and liver enzymes are suggestive of a retained CBD stone and should prompt further evaluation of the biliary tract with either MRCP or ERCP prior to definitive treatment of acute cholecystitis.

Based on the 2007 Tokyo Guidelines, acute cholecystitis is classified into three grades. Elderly age is not a criterion for gauging the severity of acute cholecystitis, but rather it indicates the propensity to progress to a severe form of the disease. Grade I is considered mild with the inflammation limited to the gallbladder and no associated organ dysfunction. Grade II is moderate cholecystitis defined by elevated WBC, significant inflammatory changes on imaging studies, and a duration of symptoms for more than 72 h. Severe acute cholecystitis is considered grade III and involves organ dysfunction. Identifying the grade of acute cholecystitis helps guide treatment options including timing and type of intervention [36].

Treatment of acute biliary disease including cholecystitis requires supportive care including early resuscitation with intravenous fluids, antibiotics, and supportive care in addition to invasive procedures in order to accomplish adequate drainage. Prior to invasive treatment, evaluation should include the severity of disease, the American Society of Anesthesiologists (ASA) score, and the patient's general condition prior to the acute episode especially within the elderly population with multiple comorbidities [37]. Compared to younger patients, the elderly who ultimately undergo cholecystectomy for mild or moderate acute cholecystitis tend to have higher ASA scores and higher serum Cr, and they are more likely to have gangrenous cholecystitis [38].

Given declined functional status and reserve, the majority of elderly patients have a higher propensity to decompensate quickly due to infection or inflammation. Acute cholecystitis is the most common indication for surgery in elderly patients admitted to the intensive care unit (ICU) with severe sepsis. These patients have a high in-hospital mortality of 48% and an additional 1-year mortality of 64%. ICU scoring systems including acute physiology, age, chronic health evaluation (APACHE), simplified acute physiology score (SAPS), and sequential organ failure assessment (SOFA) as well as elevated lactate levels are predictive of increased mortality [39].

Definitively treating these sick, elderly patients with an emergency operation becomes a more difficult decision compared to their younger counterparts. In general, emergency abdominal surgery in the elderly population is more likely to include an open operation with about 26% of laparoscopic procedures being converted to open. These operations still have a relatively high morbidity of 32% and mortality of 14% [40]. Acute cholangitis holds the highest risk of mortality compared to acute cholecystitis and acute pancreatitis [41]. Poor prognostic indicators in elderly patients undergoing an emergent operation include panperitonitis, positive blood cultures, and hypoalbuminemia [42]. On the other hand, relative contraindications to surgery include increased age, myocardial infarction, dementia, diabetes, malignancy, and severe liver disease [41].

Specifically in acute cholecystitis, early surgical intervention with laparoscopic cholecystectomy compared to late surgical intervention results in a decreased length of hospital LOS, but it has no effect on overall complication rate. This has led to early cholecystectomy becoming the gold standard treatment for grades I and II cholecystitis. In addition to systemic illness with hemodynamic instability, serious local inflammation can preclude early cholecystectomy in grade II cholecystitis making early percutaneous or operative drainage recommended with elective cholecystectomy after improvement of the acute inflammatory response [43].

Laparoscopic cholecystectomy is a safe, efficient, and feasible treatment of acute cholecystitis in the elderly population [10, 12, 44–46]. This includes elective, urgent, and emergent cases [9]. Consequently, cholecystectomy should be recommended after the first acute biliary presentation in order to reduce the risk of recurrence in the elderly patient [41].

The literature is conflicting when it comes to the rate of postoperative complications after laparoscopic cholecystectomy in the elderly population. Haltmeier and colleagues evaluated perioperative variables utilizing the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) for over 4,000 elderly patients who underwent laparoscopic cholecystectomy. They found early intervention was associated with a shorter postoperative stay with no increase in postoperative complications or conversion to an open procedure including those with significant comorbidities (ASA < =2 versus ASA>2) [47].

However, other studies have revealed that patients over 80 years old are more likely to have longer LOS and operative times [46]. Additionally, higher ASA scores have been identified as a major risk factor for postoperative complications in extremely elderly patients [10]. Postoperative complications are correlated to the severity of concomitant diseases at the time of diagnosis. Interestingly, patients with fever and leukocytosis have been shown to have better outcomes possibly reflecting the ability to mount a better immunologic response [34].

Although the laparoscopic approach has been deemed safe and feasible in elderly patients, the rate of primary open cholecystectomy remains doubled in the elderly (9%) compared to a younger population (4%) [12]. Evaluation of the surgical approach within an elderly population alone, 47% underwent an open cholecystectomy while 53% had a laparoscopic approach [45]. The conversion rate from laparoscopic to open cholecystectomy is also higher in the elderly ranging from 7% to 36% [12]. The most common reasons for conversion include concern with anatomy, the presence of CBD stones, and a difficult dissection due to severe inflammation [45].

Given the apprehension for surgery due to severe comorbidities and poor functional status in many elderly patients, an alternate treatment option for acute cholecystitis includes percutaneous cholecystostomy tube with antibiotics, analgesia, and interval or delayed cholecystectomy after the resolution of the acute inflammation making the risk of surgery and complications much less [4]. This is recommended for patients with grade III cholecystitis and those patients with less severe acute cholecystitis but a clinical status that precludes an urgent or emergent operation [36, 48].

In fact, those patients who undergo drainage with percutaneous cholecystectomy tube instead of surgery typically have a higher ASA score indicating poor overall health [49]. The mortality rate in patients undergoing percutaneous drainage can be greatly reduced by combining cholecystostomy tube placement with ERCP for common bile duct stones and a subsequent, interval cholecystectomy [50, 51].

Cystic duct stent insertion can be considered as an alternative to percutaneous cholecystostomy tube in elderly patients deemed unfit for surgical intervention. Stenting has been shown to have a 91% success rate with 13% complication rate and 3% mortality rate at 30 days [52]. This procedure can be performed concomitantly during ERCP for clearance of CBD stones.

Unfortunately, patients treated with percutaneous cholecystostomy tube or a delayed cholecystectomy are more likely to have recurrent episodes of cholecystitis, cholangitis, or pancreatitis. Furthermore, cholecystostomy tube is associated with lower rates of definitive treatment, higher mortality, and higher readmission rates in the elderly population [48]. However, those who do subsequently undergo definitive treatment with laparoscopic cholecystectomy have similar rates for conversion to an open procedure at the time of surgery compared to those who had an early cholecystectomy [49]. Therefore, elderly patients treated with percutaneous cholecystostomy tube due to poor clinical status in the acute setting should be recommended for delayed definitive treatment with laparoscopic cholecystectomy at the earliest feasible time.

Pancreas

As a patient ages, overall body composition changes along with functional and morphological changes of the pancreas. Peripheral body composition evolves with an increase in visceral adipose tissue and a decrease in skeletal muscle mass. In addition, insulin-secreting beta cells of the pancreas are reduced in number and function over time [53, 54]. This leads to elevated insulin resistance and an increased incidence of diabetes that is multifactorial in etiology within the elderly population [53, 54].

The morphological changes that occur overtime in the pancreas can be readily seen on imaging studies. It is important that these physiological changes of the pancreas are not confused for pathology. Many of these findings have been well described including a lower position of the pancreas causing the ampulla of Vater to be located below the vertebral level of L3. Calcification of the superior mesenteric artery (SMA) and splenic arteries creates hyperdensities around the pancreas evident on cross-sectional imaging. The width of the pancreatic duct (PD) has been noted to increase significantly with age. For instance, a normal caliber of the PD is 1–3 mm, but this can increase to 1–2 cm in the elderly without any evidence of obstruction. In addition to the increased caliber of the PD, the elderly also have increased linear defects or strictures of the PD due to compression from the SMA, splenic artery, vertebral osteophytes, and local lymph nodes. Ductal ectasia also affects intra- and interlobular ductules to the point some ducts can reach the size of a cyst [55].

Even with these functional and morphological changes of the pancreas over time, the incidence of benign pancreatic disease in the elderly is comparable to the general population.

Pancreatitis

Acute

Pancreatitis is an inflammatory reaction in the pancreatic parenchyma due to an obstruction of secretory function which leads to the activation of pancreatic enzymes and subsequent autodigestion of the tissue. The course of pancreatitis spans in severity from completely benign and self-limiting to multiple system organ failure leading to death [56]. Fortunately, acute pancreatitis is not a common condition diagnosed in the elderly.

As in the general population, there are several different etiologies of acute pancreatitis in the elderly population [57]. However, the incidence of the various etiologies differs with advanced age. Biliary causes remain the most common etiology in both the elderly and general population. With age, there is an increased incidence of cholelithiasis in addition to an increased diameter of the CBD which makes the elderly more susceptible to gallstone pancreatitis [58, 59].

The second most common etiology in the elderly includes unknown or idiopathic causes which differs from alcohol in the general population [56]. Together, biliary stones and unknown etiologies account for about 90% of acute pancreatitis cases in the elderly [57, 60]. Additionally, drug-induced pancreatitis is seen more commonly in the elderly compared to younger patients [57, 60]. This etiology is much more difficult to diagnose requiring the medication to be active at the time of diagnosis, resolution with cessation, and recurrence upon restarting the drug. Medications most commonly incited as inducing pancreatitis include several antibiotics, corticosteroids, diuretics, azathioprine, valproate, and estrogen [60]. A recent case-control study noted a dose-dependent association of polypharmacy and the risk of acute pancreatitis [61]. This is of critical importance within the elderly population given the high incidence of polypharmacy where taking six or more medications is common and puts the patient at highest risk.

Alcohol-induced pancreatitis is less common within the elderly population compared to the general population. It is also a more common cause of chronic pancreatitis. A thorough history still needs to be obtained to rule out this etiology even in the elderly population. Much less common causes of acute pancreatitis in both young and elderly patients include hypertriglyceridemia, hypercalcemia, ischemia, and malignancy.

There is often a delay in diagnosis of acute pancreatitis in the elderly population given its low incidence and nonspecific symptoms upon presentation. Older patients who present with abdominal pain or vague symptoms often undergo a cardiac workup followed by treatment of duodenal or gastric ulcers prior to the diagnosis of pancreatitis [59, 62].

Laboratory values in acute pancreatitis typically reveal an elevated serum amylase and lipase with the lipase level being more specific than amylase. Necrotizing or infectious pancreatitis can have elevated WBC. Elevated total bilirubin and liver enzymes are usually indicative of a biliary cause of acute pancreatitis. Lab evaluation should also include triglyceride and calcium levels as these can cause pancreatitis when severely elevated which affects the proper treatment. Hypoglycemia and a low hemoglobin A1c is a prognostic indicator of patients with frailty and an increased risk of mortality [53]. It is crucial to obtain complete laboratory studies on these patients given their extensive comorbidities and decreased reserve. Early signs of organ dysfunction should be thoroughly investigated.

While age alone is helpful for stratification of severity of acute pancreatitis, several clinical scoring systems have been developed to help determine mortality risk in the setting of acute pancreatitis and critically ill patients [57]. Ranson's criteria are a system specific to pancreatitis which assesses the severity of pancreatitis on admission and within 48 h. This system accounts for age and multiple laboratory values including WBC, blood glucose, lactate dehydrogenase, aspartate aminotransferase, BUN, calcium, oxygen partial pressure, and base deficit. The APACHE III score predicts hospital mortality for all critically ill adults after admission to the ICU which can apply to those with pancreatitis. This system utilizes over 20 variables including age, vital signs, laboratory values, blood gas, primary comorbidity, and the Glasgow Coma Scale in order to risk stratify in-hospital death. Both of these scoring systems can help the clinician assess the severity of acute pancreatitis and the risk of complication and mortality [63].

Imaging for unknown or vague abdominal pain in the elderly typically consists of a contrast-enhanced CT scan of the abdomen and pelvis. A dual phase protocol which includes arterial and portal venous contrast phases is preferred for evaluation of the pancreas. CT imaging findings suggestive of pancreatitis include a change in the density of the pancreatic parenchymal tissue due to local edema and fat stranding in the surrounding retroperitoneal fat. Signs of pancreatic necrosis and the development of pseudocysts also need to be evaluated. Necrotic tissue will not enhance on CT images, and the presence of gas is indicative of infected necrosis. Any associated hemorrhage would be identified as high-attenuation fluid.

Scoring systems based on CT imaging including the Balthazar score within the CT severity index (CTSI) have been developed to help grade acute pancreatitis based on imaging findings. The Balthazar score stratifies pancreatitis as mild (interstitial), intermediate (exudative), or severe (necrotizing) based on the size of the pancreas, inflammatory changes in the pancreas and surrounding fat, fluid collections, and the amount of necrosis present. The CTSI has a similar predictive accuracy to the clinical scoring systems described above. Therefore, CT imaging should not be performed solely for the assessment of severity of acute pancreatitis [64].

At the time of diagnosis, the severity of pancreatitis is much higher in elderly patients leading to an increase in mortality which can be as high as 25% in patients >80 years old [57]. This is most likely due to the comorbidities and fragility of the elderly population [59]. Severe acute pancreatitis defined as pancreatitis with associated organ failure, pancreatic necrosis, pseudocyst, or abscess can increase the mortality to >50% in the elderly population [60].

Interestingly, local complications of acute pancreatitis including abscess, necrosis, and pseudocyst have the same incidence and mortality in the elderly as the general population [65]. However, multisystem organ dysfunction and failure is more common in the elderly. This suggests the higher risk of organ failure as a sequela of acute pancreatitis in the elderly is due to the greater number of comorbidities and frailty [60, 65].

Overall, we can conclude that age and comorbidities contribute to organ failure and mortality while local complications are independent of these factors. This is important in that special attention should be given to the elderly in order to best treat and control comorbid conditions in addition to supportive therapy for acute pancreatitis [66].

Ideal treatment of acute pancreatitis in the general population as well as the elderly requires accurate diagnosis, early supportive care, adequate management of complications and comorbidities, and ultimately the prevention of further episodes [56]. Therefore, the initial treatment of acute pancreatitis in the elderly is consistent with the supportive care we provide to younger patients. This requires intravenous fluid resuscitation, analgesia, and enteral feeding. Antibiotics are reserved for signs of necrosis with infection unless an infectious cause is thought to be the etiology of the acute pancreatitis.

Fluid resuscitation with a balanced crystalloid solution is vitally important and often requires large volumes, on average 2.5–4 L over the first 24 h, in the setting of acute pancreatitis [56]. The patient's respiratory, renal, and cardiac function need to be considered in order to prevent exacerbation of comorbidities which leads to suboptimal outcomes. Pain control is also important and complicated in the elderly population due to high risk of delirium. This can be caused by either uncontrolled pain or overuse of narcotics. Nonnarcotic analgesic agents should be utilized whenever possible.

Enteral feeding should be emphasized in the treatment plan of any patient with acute pancreatitis including the elderly patient. Patients with mild pancreatitis can typically tolerate an oral diet shortly after admission. There is no need to wait for the complete resolution of elevated laboratory values or pain in order to start oral feeds. If the patient is unable to tolerate oral feeds within the first 3–5 days of admission, enteral feeding via a post-pyloric tube should be attempted. Enteral feeding has been shown to be superior to parenteral feeding in the setting of acute pancreatitis [67]. Therefore, total parenteral feeding should be reserved for the rare case where oral and artificial enteral feeds cannot be tolerated for a prolonged period of time [56].

Many studies suggest a diagnosis of acute pancreatitis in the elderly requires an early admission to the ICU given the concern of comorbidities and risk of rapid decompensation [62]. These patients have limited cardiac and respiratory reserve, so treatment of the acute pancreatitis alone can very easily exacerbate coinciding medical conditions, leading to morbidity and mortality. An ICU setting is better equipped to closely and continuously monitor for multiple organ dysfunction in the ill, elderly patient.

Beyond diagnosis and initial supportive care, next steps in treatment should be based on the etiology of pancreatitis. Acute pancreatitis due to biliary causes automatically implies a stone outside of the gallbladder that traveled down the CBD causing obstruction of the pancreatic duct. Clinical course and laboratory values can help determine if a stone is still present causing ongoing obstruction.

For persistent obstruction, the main concern is worsening pancreatitis as well as the risk of cholangitis. In this case, urgent endoscopic intervention to clear the ductal system is indicated even in the elderly population. Advanced endoscopic procedures including ERCP and endoscopic ultrasound (EUS) are not contraindicated in the elderly population as there is no increase in procedure-related complications compared to a younger cohort [68, 69]. Even endoscopic sphincterotomy can be safely performed in the elderly population with comparable success and complication rates similar to the general population [70].

Elderly patients have a lower incidence of post-ERCP pancreatitis compared to the younger population [71, 72]. However, they do have a similar to increased risk of peri-procedural bleeding suggesting hemoglobin, hematocrit, and coagulation studies are important laboratory values to obtain pre-procedure [68]. The risk of perforation during ERCP has been shown to be similar to that in the general population [71].

While endoscopic intervention is safe with a favorable risk profile, the comorbidities, functional status, and metabolism of elderly patients need to be considered when undergoing a procedure, just as they were important in the initial treatment of acute pancreatitis. For instance, lower doses of sedative medications should be administered because elderly patients undergoing ERCP are more likely to experience adverse effects due to prolonged conscious sedation or post-procedural hypotension [72–74].

Once the ductal system is cleared and the current episode of acute pancreatitis steadily improves, definitive therapy for gallstone pancreatitis needs to be considered. Cholecystectomy during the initial hospitalization is the recommended therapy for gallstone pancreatitis in the majority of patients regardless of age [75]. Unfortunately, studies have shown that elderly patients are less likely to undergo cholecystectomy during their initial hospitalization (about 50%) suggesting a hesitation to operate on these older patients with acute gallstone pancreatitis. However, based on readmissions and a subsequent operation within this population, about 40% of these patients would have benefited from early definitive, surgical therapy [75]. Given the acceptable mortality and morbidity associated with laparoscopic surgery, which is less than that of a repeat episode of acute pancreatitis in this age group, laparoscopic cholecystectomy should be offered as definitive treatment with close attention paid to preoperative optimization of comorbidities [57, 62].

Overall, acute pancreatitis has a low incidence in the elderly population with biliary causes being the most likely culprit. Older patients are more likely to suffer from multiple organ dysfunction and failure due to acute pancreatitis. However, this is due to exacerbation of comorbidities and systemic symptoms rather than local complications from the acute pancreatitis. Supportive care with early endoscopic intervention for clearance of the bile ducts is indicated. This should be followed by laparoscopic cholecystectomy during the same hospital admission to prevent further and more serious episodes of acute pancreatitis in the elderly population.

Chronic

Chronic pancreatitis is defined the irreversible sclerosis of the pancreatic gland leading to destruction of the ductal exocrine parenchyma and distortion of the ductal system [76]. Chronic pancreatitis is less common in the elderly compared to younger patients. Alcohol is the most common etiology of chronic pancreatitis regardless of age accounting for about 70% of cases. Idiopathic, obstructive, and biliary causes remain less likely but possible etiologies. Autoimmune pancreatitis with elevated serum levels of gamma globulin has also been diagnosed in the elderly population [76].

These patients typically present with recurrent abdominal pain associated with long-standing alcohol abuse which is also accompanied by smoking in most cases. Pending the duration of chronic pancreatitis, symptoms tend to evolve from abdominal pain to symptoms of pancreatic insufficiency. Elderly patients with chronic pancreatitis can also present with obstructive jaundice due to ductal strictures that developed over time. However, occult malignancy needs to be ruled out.

Cross-sectional imaging of chronic pancreatitis reveals calcifications and atrophy of the parenchyma. Ductal changes include irregular dilation and narrowing of the PD and a tapering of the CBD which can also be seen on ERCP. Acute on chronic exacerbations of pancreatitis might show focal enlargement of the gland with obliteration of the peripancreatic fat. Complications from chronic pancreatitis that might be apparent on imaging include pancreatic pseudocysts, pseudoaneurysms, and splenic vein thrombosis.

Treatment of chronic pancreatitis in the elderly population remains supportive with endoscopic or surgical intervention in refractory patients. While pancreatic operations are being performed more often in the elderly population, chronic pancreatitis as an indication for surgery is decreasing while surgery for cystic tumors is increasing [77].

Chronic pancreatitis is considered a low-risk diagnosis when undergoing a pancreaticoduodenectomy compared to bile duct, duodenal, or ampullary neoplasms after review of the ACS NSQIP [78]. Elderly patients undergoing elective pancreaticoduodenectomy have an expected mortality of <5% suggesting radical pancreatic resection in an elderly population has no increased mortality compared to younger patients [78, 80]. Pancreatic resection can be safely performed utilizing a minimally invasive, robot-assisted technique without increased mortality or morbidity in comparison with a younger population [81].

Postoperative morbidity after pancreatic resection remains high regardless of operative indication, and increased age and preoperative morbidity are independent prognostic indicators of postoperative morbidity [78–80]. Overall, elderly age does not preclude pancreatic resection although there is significant morbidity with poor long-term survival in those patients >80 years which is most likely due to preoperative comorbidities [82, 83].

Conclusions

Overall, benign diseases of both the gallbladder and pancreas occur in the elderly population with biliary disease more common and pancreatic disease less common compared to the general population. However, many of the diagnosis modalities and treatment algorithms essentially remain the same as endoscopic, percutaneous, and surgical interventions are safe and feasible in the elderly.

It is most important to account for and optimize the comorbidities of these patients as exacerbation of coinciding medical conditions is what leads to unfavorable outcomes. A multidisciplinary team approach to a focused, comprehensive geriatric assessment should be a high priority in order to identify risk factors preoperatively and manage them postoperatively to improve outcomes.

Conclusion

Gallstones have an increased incidence in the elderly population with acute cholecystitis as a common presentation. Pancreatitis is less common in the elderly compared to younger patients, and gallstones are the most common etiology followed by unknown or idiopathic causes. Elderly patients are more likely to present with nonspecific, constitutional symptoms. ERCP, percutaneous cholecystostomy tube, and laparoscopic cholecystectomy are safe and feasible procedures in elderly patients. The higher risk of morbidity and mortality with biliary or pancreatic disease is due to decreased reserve and exacerbation of comorbidities.

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54 Elderly Donors in Transplantation

Brian Gilmore and Andrew Barbas

Contents

Abstract

The disparity between supply and demand of donor organs remains a major limitation in the field of transplantation. Increased utilization of organs from older donors has significant potential to expand the pool of donor organs; however, utilization of such organs has been limited both in the United States and internationally. Accumulating evidence demonstrates that the use of organs from well-selected older donors produces acceptable patient and graft survival. As donor and recipient selection

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criteria are refined, it appears likely that outcomes will continue to improve with time.

Keywords
Organ transplantation · Extended criteria donor · Elderly · Kidney transplantation · Liver transplantation

Cases for Contemplation

1. Kidney donor profile: a 63-year-old male, donation after cardiac death (DCD), history of hypertension, and terminal creatinine of 1.5 with 100 ml/h of urine output prior to death. What additional criteria would help inform the decision to accept a kidney from this donor for transplant? What type of recipient would you prioritize for such a graft?
2. Liver donor profile: an 80-year-old male, no significant past medical history, brain death due to cerebrovascular accident, normal liver function tests, and liver biopsy. What additional criteria would help inform the decision whether to accept the liver from this donor for transplant? What type of recipient would you prioritize for such a graft?

Introduction

Although outcomes of solid organ transplantation are excellent in the modern era, the scarcity of donor organs relative to patients on the waiting list has remained a limitation of the field. The critical organ shortage has led to the increased use of organs from extended criteria donors – particularly organs from older donors.

The effects of aging on organ function are organ specific and highly variable, depending on the severity of comorbid conditions. Although age-dependent dysfunction of an organ must be considered carefully, the majority of available data suggests that appropriately selected older donors can be used routinely with acceptable transplant outcomes.

Demographics

Approximately 100,000 patients in the United States are currently on the kidney transplant waiting list, organized through the United Network for Organ Sharing (UNOS). The average wait time has increased, with 15.7% of patients now having a wait time of more than 5 years, compared to 11.4% in 2005 [1]. This is a continuation of a previous trend, with average wait times increasing from 2.7 to 4.2 years from 1998 to 2008 [2]. In parallel, the age of patients on the waiting list has also increased, with 22.0% of patients being greater than 65 years of age in 2015, compared with 14.5% in 2005. As noted by Hart et al., the number of kidney transplant candidates aged 65 or older is projected to surpass those aged 35–49 years by 2020 [1]. Despite the aging of the recipient population, the use of kidneys from older donors has remained relatively stagnant. In 2005, 5.1% of donors in the United States were older than 65, and this has increased slightly to 7.8% in 2015 [3]. Of these donors older than 65, 66% were deceased donors, and 34% were living donors.

The demographics of the liver transplant waiting list in the United States share some similarities with the kidney transplant waiting list. Approximately 15,000 patients are currently on the waiting list in the United States [4, 5]. The wait time for transplant recipients increased between 2005 and 2015, with 17.2% of patients waiting greater than 1 year in 2005, compared to 21.9% in 2015. The proportion of elderly patients on the waiting list has also increased, with 22.2% of patients being greater than 65 years of age in 2015 compared to 11.7% in 2005. In terms of utilization of older donors, trends appear to be divergent between Europe and the United States. The European Liver Transplant Registry (ELTR) has noted a significant increase in utilization of livers from donors older than 65, from 15% in 1999 up to 29% in 2009 [5–7]. In the United States, however, the utilization of older donors has actually decreased, with only 7.7% of donors being over 65 in 2015 compared with 10.2% in 2005.

Broadly speaking, the increasing wait times for listed individuals and the relatively stagnant utilization of elderly donor organs suggest that the elderly represent an underutilized resource to combat the scarcity of organs.

Renal Transplantation

The binary classification of donor kidneys as either "standard criteria donor" (SCD) or "expanded criteria donor" (ECD) was introduced in 2002 in an effort to identify factors that influence graft failure (Table 1) [8, 9]. By definition, all kidneys from patients 60 years of age and older were categorized as ECD kidneys, despite a wide spectrum of graft outcomes within that heterogeneous cohort. The use of ECD kidneys has increased over time due to a significant literature demonstrating superior outcomes compared to patients who remain on the waiting list [10–14]. This is particularly true in older transplant recipients, where despite comorbidities and advanced age, transplantation has been shown to improve life expectancy relative to remaining on the waiting list. One study of transplant recipients in the UNOS database demonstrated 58% 5-year and 24% 10-year survival among recipients older than 70 [15]. Importantly, despite the increasing use of ECD kidneys, evidence suggests that the most common cause of graft loss in older kidney transplant recipients is recipient death with a functioning graft rather than graft failure [16].

Table 1 Definition of extended criteria donor: Kidney transplantation

Donor characteristic	ECD donor
Age (years)	≥60 or ≥50 plus two risk factors below
Cause of death	CVA
Past medical history	Hypertension
	Cr >1.5 mg/dL

Adapted from Mendizabal, Hsu, and Shaked *Principles and Practice of Geriatric Surgery*, 2011
CVA cerebrovascular accident, *Cr* creatinine

The dichotomous ECD/SCD classification has since been replaced in 2014 with the more granular kidney donor profile index (KDPI), which combines a variety of donor factors to calculate a single number that summarizes the risk of graft failure for a given donor [17]. The KDPI is based on ten donor factors, including donor age, height, weight, race, history of hypertension, history of diabetes, cause of death, serum creatinine, hepatitis C status, and donation after cardiac death (DCD) status. The KDPI ranges from 0% to 100%, with a lower number signifying increased donor quality; it represents the percentile of quality for a given donor kidney in relation to all other deceased donor kidneys recovered in the past year. The overlap between ECD/SCD status and KDPI is significant but not complete, and the transition to KDPI was motivated by a desire to improve prognostication of graft survival beyond the rather crude ECD/SCD designation [17]. The expected half-life of a particular kidney graft strongly correlates with KDPI; for example, kidneys of the highest quality (KDPI of 0–20%) have an estimated half-life of 11.4 years, compared to kidneys of the lowest quality (KDPI >85%), which have an estimated half-life of 5.6 years [18]. The optimal strategy for allocating high KDPI donor kidneys (KDPI >85%) is still under investigation, but most transplant programs favor their use in older recipients who have less life expectancy compared to younger recipients.

Age-Dependent Changes in Kidney Function

The kidney, like most organs, undergoes a progressive decline in function with advancing age. This is distinct from, but can be exacerbated by, the accumulated damage caused by concomitant nephropathy from hypertension, diabetes, and other comorbid conditions [19, 20].

Macroscopically, the kidney undergoes a progressive decrease in overall renal mass [21, 22]. This is predominantly due to a loss of cortical volume with an associated decrease in the number of nephrons. This process is partly compensated until age 50 by an increase in medullary volume which can blunt the overall decrease in renal volume despite declining nephron number [23]. Atherosclerosis, another common finding with aging kidneys, has been shown to accelerate this process [24]. Older kidneys are also known to accumulate both benign cysts and parenchymal scars [19, 25].

Microscopically, kidneys undergo progressive diffuse glomerulosclerosis. This is thought to be due to parenchymal ischemia resulting from arteriosclerosis of the microvasculature [19]. This process results in a decrease in the number of functioning nephrons, producing the gross changes in organ volume described above, and often leads to hypertrophy of the remaining nephrons.

Unlike other organs, kidney function is readily quantified by calculating the estimated glomerular filtration rate (eGFR), a measure of the filtration capacity of the kidney. Although the eGFR for a given individual is variable, there is a predictable decline in eGFR with increasing age [26–28]. This decline is clinically important; even in the absence of diagnosed CKD, the decreased functional reserve significantly increases susceptibility to physiologic insults. Interestingly, the decrease in eGFR seen with aging is not necessarily concordant with the aforementioned macroscopic or microscopic structural changes.

Deceased Donor

The majority of transplanted kidneys continue to come from deceased donors. Indeed, in 2015, 61.8% of the 14,744 kidney transplants done in the United States were deceased donor kidney transplants (DDKT) [3]. Despite the ongoing organ scarcity and large number of patients on the waiting list, it has been estimated that up to 60% of available kidneys from donors older than 65 in the United States are being discarded [13].

Although the use of SCD kidneys is preferred, several studies have demonstrated superior survival among patients receiving ECD kidneys compared with patients who remained on the waiting list, particularly for patients older than 40 years of age [11, 29]. These findings have been confirmed in the setting of high KDPI kidneys where the use of high-risk organs produced the greatest benefit in patients older than 50 years [12].

These observations have significantly impacted allocation policy. In 1999, the Eurotransplant region adopted the Eurotransplant Senior Policy (ESP), in which kidneys from older donors were matched to older recipients [30]. Early data from the ESP found that there was no significant difference in patient survival among older recipients receiving older rather than younger kidneys [31, 32]. More recent data have demonstrated that although outcomes with older grafts are inferior compared to younger grafts, older recipients do derive benefit from early transplantation with older grafts [14]. Comparable outcomes were demonstrated in a 2014 study comparing data from the ESP and the United States [13]. In both Europe and the United States, early transplantation with an ECD graft resulted in improved survival compared with delayed transplantation with a non-ECD kidney. It is noteworthy that many patients in this study, particularly in the United States, died with functioning grafts having never required additional dialysis.

In 2014, the United States adopted the new kidney allocation system (KAS), which requires broader sharing of kidneys with a low KPDI (optimal kidneys) as part of an effort to improve matching of optimal donor organs and recipients with longer life expectancy [33]. The combination of KDPI and the KAS has streamlined the organ allocation process and decision-making regarding the use of what were previously classified as ECD organs. Importantly, the KAS has resulted in a decreased rate of significantly age-mismatched kidney transplantation but has also appeared to decrease utilization of kidneys from donors older than 65 and transplantation in recipients older than 65 [34, 35].

Living Donor

The use of a living donor is favored when possible, as living donor kidney transplantation (LDKT) has superior outcomes in comparison to

DDKT [36–38]. LDKT can also significantly decrease time on the waiting list and eliminate or minimize time on dialysis, which is particularly important for elderly recipients [39]. The percentage of older living donors has been increasing, and this trend can be expected to continue as the general population continues to age [40].

Several single institution studies have found similar patient and graft survival rates between recipients receiving grafts from older and younger living donors [41–43]. In contrast, subsequent studies utilizing large national databases demonstrated somewhat inferior outcomes in patients receiving kidneys from older living donors [44–46]. Despite this observation, additional studies demonstrated that the use of older organs for LDKT was associated with improved outcomes relative to the use of ECD organs for DDKT and similar outcomes to SCD organ use for DDKT [40, 47].

Choice of Older Donors for LDKT

The prospect of LDKT requires careful consideration of the perioperative risks for the older living donor. Although older individuals are generally assumed to have an increased risk of perioperative complications, there are reports of successful living donation from patients as old as 90 years [37, 48]. As such, there are no standardized inclusion/exclusion criteria, although individual institutions have specific internal protocols. However, broadly speaking, an older candidate for kidney donation must have adequate renal function to minimize the risk of renal dysfunction post-nephrectomy and relatively few cardiovascular comorbidities, which could portend serious perioperative complications.

One study of 80,347 living donors found no increase in perioperative mortality among older donors compared to younger donors [49]. Although this study did demonstrate increased long-term mortality among older donors, this cohort had equivalent mortality compared to age-matched non-donors. Additional studies have also demonstrated that perioperative morbidity is not increased in older donors [50, 51]. A 2012 study from a single center in the United Kingdom demonstrated no difference in perioperative complication rates with older patients and similar rates of post-nephrectomy decline in GFR compared with younger patients [50]. Similarly, a 2004 study comparing laparoscopic donor nephrectomy in younger patients and patients older than 60 years found no increase in either perioperative complications or rate of rise in serum creatinine following donor nephrectomy [51].

Encouraging Older Patients to Become Donors

The popularity and feasibility of LDKT are influenced by cultural and economic factors, as well as specific allocation policies [52–54]. Addressing the disparities both within and between countries remains an area of significant research interest, with particular attention being paid to increasing the utilization of paired kidney donation and altruistic kidney donation [55, 56]. Although the optimal policies for facilitating donation from older living donors remain unclear, improved counseling of both potential recipients and potential donors with regard to expected outcomes will ideally increase participation of older donors [57].

Summary

Kidneys from older donors provide significant improvements in mortality and quality of life for patients with end-stage renal disease. Although there is some expected decline in graft survival with utilization of older organs, this is largely outweighed by the benefits of earlier transplantation. In addition, the use of older living donors can significantly improve recipient outcomes with minimal added risk to donors compared with younger candidates.

Liver Transplantation

The first successful liver transplant was performed in 1963 [58]. In the nearly 55 years since that landmark operation, the procedure has become increasingly routine with excellent short- and long-term outcomes. The scarcity of donor organs has motivated attempts to expand the available donor pool, including split liver transplants, living donor liver transplantation, and greater consideration of extended criteria donors, including those from elderly donors. The importance of expanding the number of available organs is of particular importance with regard to liver disease due to the inability to provide life-sustaining organ replacement therapy.

Age-Dependent Changes in Liver Function

In contrast to kidney transplantation, the decision to use elderly livers is confounded by the inability to reliably quantify age-dependent decline in liver function. The biochemical markers used as "liver function tests" such as bilirubin, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) do not consistently change with increasing age [59]. More generally, the decline in liver function and regenerative capacity is difficult to determine and incompletely understood.

The liver appears to be relatively spared from the significant age-dependent structural and functional changes seen with other organs. There is evidence that the liver sustains measurable decreases in both organ volume and effective blood flow in the elderly [60]. Similarly, both hepatic uptake of radioisotopes and elimination of galactose have been found to decrease in older individuals [61, 62]. While these have been interpreted as proxies for regenerative capacity and metabolic ability, there is no clear correlation of these findings with clinically relevant changes [63].

Histologic and electron microscopic examination of rat livers has demonstrated that although hepatocytes increase in size with aging, they decrease in number and sustain a decrease in smooth endoplasmic reticulum content and impaired lysosomal function [64]. There is also evidence that glutathione reductase, a key component of the antioxidant pathways in the liver, is decreased in older organs [65]. Similarly, the hepatocyte content of cytochrome P450 declines substantially in the elderly [66]. Studies have demonstrated that older livers have a decrease in cell cycle activity as well as an increase in autophagy, suggesting that the impairment stems from an inability for the normally quiescent hepatocytes to reenter the cell cycle and proliferate [67]. There is evidence that this impairment is driven by age-dependent shortening of telomeres and decreased numbers of hepatocyte precursor cells [68–72]. Regardless of the underlying mechanism, no currently available clinical tests have been validated for the purpose of assessing the age-related decline in liver function, and there is little evidence demonstrating a clinically relevant deterioration [73–75].

Deceased Donor Liver Transplantation

A number of multi-institutional and international registries have produced high-powered studies evaluating the impact of donor and recipient age. The European Liver Transplant Registry (ELTR), which dates back to 1968, captures approximately 95% of all liver transplants done at 145 sites in Europe. As of 2009, this included more than 93,000 transplants. A 2003 analysis of this registry demonstrated a significantly lower rate of graft survival with the use of livers from donors over 65 compared to those younger than 55 (52% vs. 63% at 5 years) but similar overall patient survival rates [6]. A second analysis of this registry published in 2012 confirmed this difference in graft survival (57% vs. 65% at 5 years), although the rate of graft survival improved for each group over the preceding 10 year period [7]. This study also provided evidence that utilization of organs from octogenarian donors is feasible, though associated with significantly lower 5-year (50% vs. 65%) and 10-year survival (45% vs. 55%).

The decrease in graft survival noted in the ELTR has been corroborated by data from several additional studies. Both a 2006 analysis of 20,023 transplants performed in the United States and a 2015 study examining 20,288 transplants performed in Spain found decreased graft survival with increasing age [76, 77]. An additional retrospective study of 44,756 patients in the OPTN database suggested that this age-dependent decline in graft survival was potentiated by prolonged cold ischemia time [78].

In parallel to the larger studies discussed above, a number of smaller series have been conducted which suggest that neither graft nor patient survival is significantly influenced by donor age, if appropriate recipient selection criteria are applied [79–81]. Although there appears to be an expected decrement in graft survival, the bulk of the available evidence supports the routine use of livers from elderly deceased donors, including organs from octogenarian donors, in appropriately selected patients.

Living Donor Liver Transplantation

Living donor liver transplantation using elderly donors must account for the effects of advanced age on both graft function and the capacity of the remaining liver to regenerate in the donor. With these considerations in mind, the use of an elderly living donor remains an attractive option as it can significantly reduce recipient waitlist time and facilitates an elective procedure for which the recipient can be medically optimized.

In comparison to deceased donor liver transplantation, the majority of studies on living donor liver transplantation come from to a relatively small number of institutions. In 2014, Han et al. published an analysis of the largest patient cohort to date, detailing the outcomes from 604 living donor liver transplants performed in South Korea from 1999 to 2012 [82]. Of the 604 cases, 26 received organs from donors older than 55. This cohort was observed to have a significant decrease in mean graft survival (31.2 months vs. 51.4 months), although 5-year patient survival was not different between groups (79.5% vs. 81.5%) and no patients suffered primary graft nonfunction.

The remainder of the existing literature on outcomes from elderly living donor liver transplant has been inconsistent, with some studies suggesting impaired survival and others demonstrating no difference [74, 83–85]. It does appear that the rate of small-for-size syndrome is increased with the use of older living donor grafts [86, 87]. This finding has been supported by imaging data suggesting slower regeneration of the liver graft in the first month following transplant [72]. In the absence of prospective, large-scale studies, it appears that the use of older living donors is acceptable, provided careful consideration is given during selection of both the donor and recipient.

Prognostic Scoring of Donor Organs

In contrast to kidney transplantation, in liver transplantation, there is no universally accepted definition of “extended criteria donor.” Generally, the term extended criteria donor is used in reference to livers donated after cardiac death, donor livers with significant steatosis, and livers from older donors. Despite the limitations in current knowledge about the effects of aging on the liver, several attempts have been made to develop prognostic scoring systems to guide organ use. In 2010, Feng et al. utilized data from 20,033 transplants performed in the United States to develop a donor risk index (DRI) encompassing eight variables: donor age, donor race, donor height, donor cause of death, donation after cardiac death, partial or split liver graft, geographic allocation, and cold ischemia time [76], Table 2. Of these individual criteria, donor age was most significantly associated with poor outcomes. DRI was found to be predictive of graft survival out to 3 years (81.2% vs. 60.0% for DRI <1 and >2, respectively). In 2012, the DRI was adapted specifically for use in the Eurotransplant region as the Eurotransplant-DRI (ET-DRI) by replacing donor race, donor height, organ location, and cold ischemia time with latest serum gamma-glutamyl transpeptidase, geographic allocation, and rescue allocation [88].

Several additional models have been generated to incorporate both donor and recipient characteristics. One of these is D-MELD, calculated as the product of the donor age and the recipient preoperative MELD (Model for End-Stage Liver Disease) score [89]. Data from the United States

Table 2 Donor risk index: Liver transplantation

Donor factor	Reference donor
Age	<40
<40	
40–50	
50–60	
60–70	
>70	
Cause of death	Trauma
Anoxia	
CVA	
Other	
Race	White
White	
Black	
Other	
DCD donor	No
Partial/split graft	No
Height (cm)	170 cm
Location	Local
Local	
Regional	
National	
Cold time (h)	8 h
Donor risk index	1.0

CVA cerebrovascular accident, *DCD* donation after cardiac death

OPTN suggests worse outcomes with a D-MELD of greater than 1,600, whereas an analysis of patients in the Andalusian Transplant Registry found a preferred cutoff to be a D-MELD of 1,500 [90]. Regardless of the predictive scoring system used, donor age remains one of the dominant factors in predicting outcomes.

Summary

The use of livers from older donors is associated with a higher risk of graft failure, although overall patient survival appears to be similar. Care must be taken during selection of both donors and recipients when considering livers from older donors. In light of a significant ongoing organ shortage, increasing the use of elderly donors appears to be an effective strategy for expanding the donor pool and reducing waitlist morbidity and mortality in liver transplantation.

Improving Utilization of Organs from Older Donors

When compared to organs from younger donors, both kidney and liver grafts are more sensitive to cold ischemia time. A 2004 European study of nearly 3,400 renal transplants found that prolonged cold ischemia time in organs from donors older than 60 was associated with both an increased risk of delayed graft function and ultimately graft loss [91]. Similarly, prolonged cold ischemia time has been associated with both graft nonfunction and diminished recipient survival in livers from older donors [92–94]. Together, these findings strongly support the minimization of cold ischemia time as a strategy to improve recipient outcomes when utilizing organs from older donors. There is no specific cold ischemia threshold for kidney transplantation, while for liver transplantation, a cold ischemia time of greater than 12–15 h is strongly associated with impaired graft and patient outcomes [95, 96].

A novel organ preservation approach that may facilitate the use of organs from older donors is normothermic machine perfusion (NMP). Rather than static storage of organs on ice, in NMP, organs are perfused with an oxygenated nutrient solution at physiologic temperature. This intervention holds promise not just as a method of improving organ preservation but as a platform for rehabilitating organs prior to transplantation. Several recent studies investigating the use of NMP in liver transplantation for organs considered suboptimal due to donor age, graft steatosis, or donation after cardiac death have demonstrated promising results [97, 98].

Current Organ Allocation Policies

Organ transplantation in the United States is governed by the United Network for Organ Sharing (UNOS), which was first established in 1984 as a nonprofit organization to standardize organ allocation. The guiding principle of UNOS is summarized in the “Final Rule,” established by the US Department of Health and Human Services in 2000, which calls for “the equitable allocation of deceased donor organs among potential recipients" [99, 100].

Prior to the implementation of the KAS in 2014, kidney allocation was driven by a combination of recipient waiting time, panel-reactive antibody level (PRA), and degree of HLA matching [99]. The weight given to specific criteria has changed over time, as has the methodology for evaluating donor organs. Notably the designation of donor grafts as either SCD or ECD was replaced following the development of the more granular KPDI system [17]. The introduction of the kidney allocation system in 2014 shifted emphasis to expected life years after transplant in an effort to improve efficiency of utilization of available organs. Although the kidney allocation system has decreased the incidence of significantly age-mismatched transplants, it has also led to an overall decline in utilization of older grafts [34, 35].

Liver allocation in the United States is based on recipient MELD score, which is well validated and has been in use since 2002. However, there is wide geographic disparity in organ availability across the United States [101]. The disparities in organ availability between regions have led to the development of policies such as Share35, which prioritizes sharing of grafts for suitable recipients with a MELD of greater than 35 [102].

Conclusion

Organ scarcity remains an enormous problem for the transplant community. The use of organs from older donors should be routinely considered as data accumulates to demonstrate safety and efficacy in expanding the donor pool. Challenges remain in identifying specific criteria that inform organ performance, and more research is necessary to further elucidate this in elderly donors.

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Malignant Diseases of the Gallbladder and Bile Ducts

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Contents

Abstract

Malignant diseases of the gallbladder and biliary tree are challenging cancers in the elderly, often presenting late with poor prognosis. As surgery affords the only cure for gallbladder and biliary cancer, the appropriate selection of patients who may benefit and application of current and disease-specific surgical procedures are paramount. Gallbladder cancer tends to be either an incidental finding after laparoscopic cholecystectomy or an advanced and metastatic cancer with dismal outlook. Gallbladder polyps and porcelain gallbladder

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are two particular conditions that warrant attention because of malignant risk. Cholangiocarcinomas include intrahepatic tumors, treated akin to primary hepatic malignancy; Klatskin tumors at or near the bifurcation which require special consideration; and distal bile duct tumors which act as periampullary cancer. Management of each will be elucidated with detailed attention to diagnostic work up and discriminatory testing to guide treatment decisions for the clinician.

Keywords
Gallbladder cancer · Porcelain gallbladder · Gallbladder polyps · Cholangiocarcinoma · Klatskin tumor · Elderly

Introduction

Case Study Gallbladder Adenocarcinoma

Background

A 69-year-old male with past medical history of hypertension presented with abdominal discomfort and bloating. Laboratory values were unremarkable; however, a right upper quadrant ultrasound was performed revealing a ~2.5 cm lesion suspicious for malignancy. A subsequent cross-sectional computed tomography scan was performed for further evaluation and staging. A diagnosis of gallbladder adenocarcinoma was made based on imaging without confirmatory biopsy.

Management

No additional treatment or imaging was obtained and the patient was taken to the operating suite for resection. Due to concern for possible extension beyond the lamina propria an open approach to cholecystectomy was selected. On frozen section while the margins were negative, suspicion of invasion beyond the muscular layer was confirmed and thus wedge resection of the liver bed was performed. Final pathology revealed a stage T2 N0 M0: 2.6 cm gallbladder adenocarcinoma. The patient had an uneventful stay and was discharged to home on day 6. The patient elected for close observation and did not receive initial adjuvant therapy. Unfortunately, a metastatic lesion was appreciated in the left hepatic lobe at 1 year on routine surveillance imaging. A gemcitabine based regimen was initiated; however, disease progression continued leading to biliary obstruction eventually requiring palliative stenting. Ultimately, the patient succumbed to his disease 2 years following initial diagnosis.

Case Study Perihilar Cholangiocarcinoma

Background

A 76-year-old male without any past medical history presented to urgent care with report of gradual onset dark urine that was not accompanied by pain. Subsequent evaluation demonstrated an elevated bilirubin of 9.3, CA 19–9 of 2241, and a presumed perihilar cholangiocarcinoma extending to segment 5 of the liver on CT imaging. An ERCP with sphincterotomy was performed and adenocarcinoma diagnosis confirmed with brushings and biopsy.

Management

Surgical options were discussed and due to hepatic parenchymal extension a hepatectomy would be necessary. Liver volumetrics suggested 28% volume of the potential remnant thus right portal vein embolization was performed preoperatively. Three weeks later, the patient was taken to the operating suite for resection. An initial diagnostic laparoscopy did not find evidence of metastatic disease and a right trisegmentectomy, bile duct resection, portal lymphadenectomy, cholecystectomy, and Roux-en-Y hepaticojejunostomy reconstruction was performed. Intraoperative frozen sections of the bile duct margins were found to be negative. Final pathology revealed a stage T2b N0 M0: 2.2 cm bile duct adenocarcinoma extending into the liver parenchyma. All margins were negative, no vascular invasion was appreciated, and all lymph nodes were negative for metastatic tumor. The patient went to the ICU for recovery, had an uneventful stay, and was discharged to home on day 7. Close observation versus adjuvant chemotherapy was discussed, and ultimately the patient decided to undergo 2 months of gemcitabine plus oxaliplatin therapy. Adjuvant treatment was tolerated well and at 6 months no evidence of recurrent disease was appreciated on surveillance imaging.

Gallbladder Malignancy

Malignancy of the gallbladder is rare and historically recognized to have a bad prognosis often. Disproportionately impacting elderly patients, females, and particular ethnic groups, gallbladder cancer (GBC) is a challenging disease for the surgeon as it traditionally presents at late stage, is aggressive, and often unresectable. However, with the increased utilization of laparoscopic cholecystectomy for gallstones the incidental diagnoses of early stage cancer have increased. In order to develop a rational treatment strategy, it is imperative to appreciate the risks of radical surgical resection, the limitations of surgical intervention in advanced disease, and the poor efficacy of adjuvant and palliative therapies.

Incidence

Cancer of the gallbladder was first described in 1777 and since that time, survival has not changed appreciably [1]. Despite its rarity, gallbladder adenocarcinoma is the most common malignancy of the biliary tract. It follows a bimodal presentation pattern – either presenting incidentally at the time of laparoscopic cholecystectomy for presumed benign conditions or presenting at late stages with disseminated or invasive disease. Global and national incidence varies greatly by geographic region, gender, and race. For instance, the highest global incidence of GBC is in Chile, where the associated mortality ranges regionally from 8.2 to 12.4 per 100,000 inhabitants. It is the number one cause of cancer-related death in Chilean women, ahead of breast, colon, and lung cancers [2]. Due to this disproportionate incidence, Chile employs an aggressive screening policy recommending sonography yearly from age 35–49 with low threshold for cholecystectomy. Comparatively, the United States has a much lower yearly incidence with 1.4 cases and 0.7 deaths per 100,000 women and 0.8 cases and 0.5 deaths per 100,000 men [3].

In the United States, we note a racial distribution with a 3x higher incidence in American Indian/Alaskan Natives compared to non-Hispanic whites. Across all genders and ethnicities, GBC is a disease of the elderly with a peaked incidence in the 6th decade [4].

Etiology

The etiology of gallbladder adenocarcinoma is not well understood. Several theories center around chronic inflammation caused by gallstones, chronic bacterial infection, or subacute mechanical obstruction of bile outflow. There is a well-known association with primary sclerosing cholangitis (PSC), although the risk of GBC in patients with this disease is only 2% [5]. Historically, infection with typhoid was an important consideration; however, currently the incidence of this infection in the USA is very small and therefore not responsible for many cases. This may be, however, one of the more important associated factors worldwide.

Gallstones are thought to be an underlying concern, with 75–90% of GBC cases occurring concomitantly with cholelithiasis. Clearly, however, few patients with gallstones ever develop malignancy with an estimated rate of only 0.3–3% [4]. On routine examination of pathology specimens following cholecystectomy, Jain et al. reports the incidence of epithelial dysplasia to be 15.7% and carcinoma in situ at 0.6% [6].

A well-defined radiologic finding associated with GBC is the "porcelain gallbladder," referring to calcification in the wall of the gallbladder caused by long-term inflammation (Fig. 1). Recent studies find that patients with porcelain

Fig. 1 Cross-sectional CT scan demonstrates calcification of the gallbladder wall often described as a "porcelain gallbladder"

gallbladder have a 10–15% risk of harboring cancer [7], which is much lower than previously believed. Cholecystectomy is recommended for all medically fit patients.

Pathology and Staging

Adenocarcinoma comprises an overwhelming majority of GBCs (90%), while 4% are squamous/adenosquamous, 3% are neuroendocrine, and 3% other types [8]. It is believed over time that epithelial tissue develops dysplasia which progresses to carcinoma in situ and then invasive cancer [6]. Contrary to popular believe, polyps are rarely part of this dysplastic progression and typically have a negligible chance of malignant transformation [9].

The characteristic appearance of GBC is a thickened gallbladder wall with diffuse inflammation. When advanced in the neck region, obstruction, hydrops of the gallbladder, and invasion into portal vascular and ductal structures may be observed mimicking cholangiocarcinoma [10]. GBC can be separated into infiltrative, nodular, and papillary subtypes, or combinations thereof. Most tumors have at least some infiltrative component, causing wall thickening and induration. Papillary tumors have frond-like projections into the gallbladder lumen. They can become very large, but often have a better prognosis because they are less invasive into the gallbladder wall and liver bed [9]. Regardless of subtype, once the tumor metastasizes, they have the same dismal prognosis. The currently agreed upon staging system is established by the American Joint Committee on Cancer (AJCC) (Table 1).

GBC spreads along lymphatic tracts, hematogenously, with peritoneal implantation, and also through direct invasion (Table 2). The gallbladder is not completely covered in peritoneum. The posterior wall has a fibrous layer of attachment to the liver known as the "cystic plate." This plane of dissection during cholecystectomy is of anatomical importance; surgeons can appreciate the increased ease of direct invasion of the liver without the peritoneal barrier. This route for disease spread is the underlying reason that a simple cholecystectomy is inadequate for most GBCs, particularly those that extend beyond the muscularis layer. The lymphatic drainage pathway of the gallbladder is from cystic to pericholedochal nodes, to retroportal nodes, and ultimately pancreaticoduodenal nodes before reaching the celiac and caval regions. Notably, GBC is not known to ascend to the lymphatics of the proximal porta hepatis.

Presentation and Diagnosis

Clinical Presentation

The classic presentation of symptomatic GBC is an elderly person complaining of right upper quadrant (RUQ) pain, weight loss, anorexia, and in a third of patients, jaundice. The later finding is predictive of more advanced disease (median survival 6 months vs. 16 months in those without jaundice) [11]. Physical exam may demonstrate RUQ tenderness or palpable mass, although this is rare in the absence of advanced disease or concomitant cholelithiasis/cholecystitis. There are no laboratory tumor markers that are very sensitive and specific of GBC; however, CEA and CA 19–9 are often measured and can be trended if elevated.

Although the overall incidence of GBC on a presumed benign cholecystectomy is <1%, nearly half of GBCs are identified in this incidental

Table 1 American Joint Committee of Cancer 7th edition staging system for gallbladder cancer (Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is Edge SB, et al.: AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer Science and Business Media LLC)

	Staging system
T	Tis = Carcinoma in situ T1 = Tumor invades lamina propria (T1a) or muscle layer (T1b) T2 = Tumor invades perimuscular connective tissue T3 = Tumor perforates serosa and/or invades the liver and/or one adjacent organs T4 = Tumor invades main portal vein or hepatic artery, or multiple extrahepatic organs
N	N0 = No regional nodal metastases N1 = Metastases to nodes along cystic duct, common bile duct, hepatic artery, and/or portal vein N2 = Metastases to periaortic, pericaval, superior mesenteric artery, and/or celiac artery nodes
M	M0 = No distant metastases M1 = Distant metastases

Staging groups

	T	N	M
0	Tis	N0	M0
I	T1	N0	M0
II	T2	N0	M0
IIIA	T3	N0	M0
IIIB	T1–3	N1	M0
IVA	T4	N0–1	M0
IVB	Any T	N2	M0
	Any T	Any N	M1

Table 2 Patterns of gallbladder malignancy invasion (Data from Boerma EJ, 1994: Towards an oncological resection of gall bladder cancer. Eur J Surg Oncol 20 (5):537–544)

Pathologic finding	Relative incidence (%)
Confined to gallbladder wall	10
Liver invasion	59
Common bile duct infiltration	35
Lymphatic invasion and regional lymphatic metastases	45
Portal vein or hepatic artery invasion	15
Adjacent organ invasion (excluding liver)	40
Perineural invasion	42
Liver metastasis	34
Distant metastasis (excluding liver)	20

fashion after the specimen has been sent to pathology [8]. Some are discovered and noted intraoperatively, allowing the surgeon to change the course of the operation as indicated. Those that are suspected preoperatively tend to be locally advanced (53% of the time) and are found to be disseminated in more than 1/3 of cases [12].

Radiological Evaluation

Ultrasonography is an excellent modality for gallbladder imaging as it is ubiquitous and inexpensive, and several key findings can alert the astute radiologist to the potential presence of malignancy. Discontinuous mucosa, submucosal echo-lucency or heterogeneity, and abnormalities of blood flow in the mucosa help to differentiate benign and malignant disease. Common ultrasonographic findings include a heterogeneous mass replacing all or part of the gallbladder (40–65% of cases), or diffuse thickening of the gallbladder wall (20–30% of cases) [13] (Fig. 2).

Cross-sectional computed tomography (CT) scan can aid in the evaluation of an inconclusive ultrasound exam and is valuable in staging if a malignancy is suspected. Gallbladder carcinoma can be hypodense, hypervascular, and irregular, and this asymmetry and marked enhancement help differentiate malignant from benign processes. In a retrospective analysis of patients at Johns Hopkins Hospital, 66% of patients were

Fig. 2 Coronal view of CT scan reveals a gallbladder mass (circle) later confirmed as stage IIb biliary adenocarcinoma

diagnosed with the correct stage preoperatively on CT scan, which is reflective of prior studies in the literature [14].

On magnetic resonance imaging (MRI), GBC is routinely hypo- to isointense on T1 phase and moderately hyperintense on T2 sequences. It is currently unclear whether MRI can add value to results obtained on CT scan; however, magnetic resonance cholangiopancreatography (MRCP) can be valuable to create a reconstruction of the biliary tree. This is particularly useful in cases that involve the gallbladder infundibulum with invasion into the surrounding cystic duct, common bile duct, or directly into the liver. PET imaging is of limited use in primary diagnosis, as benign inflammation can be interpreted as a false positive [13]. However, PET can be very useful in evaluation for nodal or distant metastasis in later stage disease or disease recurrence. One study found that PET imaging changed the pathway of surgical treatment in 23% of patients who were being preoperatively staged for an initial resection or preparing for a reoperation after incidental cancer was encountered during a laparoscopic resection previously [15].

Treatment

Incidental Discovery

Adenocarcinoma is encountered incidentally in <1% of cholecystectomy specimens on pathologic examination. Nearly 50% are stage T1 in this circumstance [16]. For tumors invading only the lamina propria (T1a), a simple laparoscopic cholecystectomy is sufficient for cure and repeat operation with hepatic wedge-resection is not required. However, for tumors extending into the muscular layer (T1b), the literature has reported a wide range of survival: as low as 50% at 1 year and as high as 75% at 5 years [17]. To err on the side of caution, re-resection of the gallbladder fossa of the liver bed, along with lymph node dissection, is recommended. If there is an intraoperative suspicion of malignancy (palpable, nonmobile mass noted on specimen extraction, enlarged regional nodes), the specimen should be sent for frozen section and the surgeon should prepare for a liver resection and posterior pancreatic nodal dissection if conclusive evidence of cancer is found. If the surgeon does not feel confident performing these maneuvers, data show that closure and referral to a hepatobiliary center for re-operation does not significantly affect survival [18]. Staging workup is recommended postoperatively for all known cases of GBC, regardless of TNM stage.

Single Polyp

Gallbladder polyps are occasionally identified on incidental imaging or cholecystectomy specimens. Unlike polyps of the colon, these are not frequently considered to be precancerous lesions and are most commonly benign cholesterol polyps [9] (Fig. 3). The prevalence of adenocarcinoma is only 0.08% in polypoid lesions and for polyps ≤0.5 cm, no strict follow-up regimen is required. However, in patients with PSC or polyps >1 cm in size, the risk of malignant transformation is elevated particularly in elderly patients and a

Fig. 3 Ultrasound image demonstrates a gallbladder polyp (*arrow*)

cholecystectomy should be performed [9]. In cases where the polyp is between 0.6–1 cm, serial ultrasound imaging can be utilized for follow-up.

A laparoscopic approach is appropriate if the surgeon feels confident in removing the specimen intact, but preoperative consent for liver resection should be obtained if more advanced disease is discovered intraoperatively.

Resection of T2 + Disease

Diagnosed preoperatively on imaging or intraoperatively, tumors stage T2 or T3 (without evidence of distant metastasis) necessitate open cholecystectomy, en-bloc liver resection of segments IVb/V, and regional lymphadenectomy. This aggressive resection increases median survival to 17 months from 9 months [19]. Particular attention should be paid to the cystic duct margin on frozen section, as a positive margin necessitates biliary resection to negative margins. Smaller liver wedge resection is adequate if margins of 1–2 cm are obtained and no radiologic findings were appreciated preoperatively [20]. Studies have failed to demonstrate benefit of more aggressive anatomic liver resection when negative margins are achieved [21].

The benefits of lymphadenectomy have not been clearly demonstrated; however, prognostication is improved with knowledge of nodal status. Regional lymphadenectomy has been a topic of debate in prior years, with most considering dissection of cystic, pericholedochal and hepatoduodenal nodes to be adequate. Yet, the anatomical lymphatic drainage of the gallbladder includes the posterior pancreaticoduodenal nodes and retroportal nodes. Studies of recurrence patterns after surgery support the dissection of these nodal basins, with a goal of harvesting at least 6 nodes to improve prognostication [22, 23]. Unfortunately, evaluation of the SEER database reveals that this is rarely the case with only 5–7% of patients undergoing resection of ≥ 3 nodes [24].

If advanced disease is suspected, staging laparoscopy can be performed to rule out unresectable disease, avoiding laparotomy. Extensive resections for tumors invading the hepatic inflow have not been shown to increase survival, and certainly in the elderly have an increase in morbidity and mortality [25]. If nonregional lymph node or distal metastases are present, palliative resection is not indicated. Additionally, presence of a port-site recurrence following laparoscopic resection is known to be a marker of aggressive disease and overall peritoneal involvement. Despite the previously common practice of resecting port-sites at time of hepatic resection and lymphadenectomy, this is no longer recommended, as there has not been a demonstrable benefit in survival.

Outcomes

GBC has an overall dismal prognosis for nearly every stage with a median survival of 16 months and overall 5-year survival of 20% for patients with *resectable* disease [26]. No significant changes in survival have been noted from 1991 to 2005 [26]. For *unresectable* patients or those who are untreated, median survival is only 2–6 months [27] (Fig. 4). The 5-year survival based on AJCC stage drops precipitously (Table 3).

Adjuvant Therapy

Effective options for chemotherapy and radiotherapy are unfortunately lacking. As 85% of recurrences include distant sites, development of a systemic therapy would greatly improve survival

[26]. A postoperative regimen of mitomycin C and 5-fluorouracil has shown modest improvement of disease-free survival [to 20.3% at 5 years, compared to 11.6% at 5 years with surgery alone ($p = 0.02$)] [28]. Specifically targeting unresectable patients, gemcitabine increased survival to 9.5 months compared to 5-FU (4.5 months) or supportive care (4 months) in a triple-arm randomized controlled trial [29]. Radiotherapy has shown slight improvements in short-term survival, but not at 5 years [30]. This may be attributable to the fact that the disease spreads via multiple avenues, and locoregional radiation does not address distant sites of spread.

Fig. 4 Cross-sectional CT scan reveals invasive stage IV gallbladder malignancy with distant hepatic metastases

Palliation

As GBC is an aggressive disease of the elderly with poor outcomes with or without surgery, palliative care is an important consideration. Proper patient selection for operative management is of concern, as liver resections are not well tolerated by frail patients, and the survival benefit must outweigh the risks of treatment. For symptomatic patients, jaundice caused by obstructive or compressive masses can be managed using biliary stents via ERCP or percutaneous approaches.

Cholangiocarcinoma

Cholangiocarcinoma is a rare group of malignancies arising from the biliary tract epithelium, consisting of three distinct subclasses determined by the location at which they arise in the bile duct: intrahepatic, extrahepatic perihilar, and distal extrahepatic. These three phenotypes have distinct presentations and management. Similar to GBC, outcomes for cholangiocarcinoma have been universally dismal due to its aggressive nature and diagnostic challenges leading to advanced disease on initial presentation. Most patients with unresectable disease live less than a year after diagnosis, dying of disease progression, biliary sepsis, or liver failure. Surgical excision

Table 3 Staging, treatment, and survival for gallbladder malignancy (Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is Edge SB, et al.: AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer Science and Business Media LLC)

Stage	AJCC/TNM (7th ed)	Recommended treatment	5 year survival
0	Carcinoma in situ (Tis), N0, M0	Simple cholecystectomy	80–100%
I	Invasion of lamina propria (T1a) or muscular layer (T1b), N0, M0	Simple cholecystectomy (T1a) vs. Cholecystectomy with wedge resection of liver to 1–2 cm margins (T1b)	50–100%
II	Invasion of perimuscular connective tissue without extension beyond serosa (T2), N0, M0	Open en-bloc resection of gallbladder, segments IVb/V, lymphadenectomy	28%
III	Tumor through serosa or into liver or adjacent organs (T3), N0, M0 [IIIA]; or T1–3 with N1 LN [IIIB]	Open en-bloc resection of gallbladder, segments IVb/V, lymphadenectomy, adjuvant chemotherapy considered	8%
IV	Invasion of portal vein or hepatic artery, or two or more extrahepatic organs (T4), N0–1, M0 [IVA]; any N2 LN or metastases [IVB]	Unresectable, adjuvant chemotherapy optional	2–4%

with curative intent is the most effective form of therapy; however, outcomes remain poor.

Incidence

Hepatic and biliary malignancies represent the third most prevalent gastrointestinal malignancy in the United States behind colon and pancreatic cancer [31]. Of these, cholangiocarcinoma represents <3% of all malignant liver tumors [32]. In the United States, cholangiocarcinoma occurs with an average incidence of 1 to 2 cases per 100,000 people with a slight male predominance (1.5:1). Cholangiocarcinoma most frequently presents in the geriatric population with a peak age of diagnosis in the eighth decade of life [33]. Perihilar extrahepatic, or Klatskin tumors (after Klatskin's description in 1965 [34]), are the most prevalent with intrahepatic the least common. Prevalence shows significant variation based on geography with incidences as high as 113 per 100,000 men and 50 per 100,000 women in Asia likely reflecting regional differences in risk factors [35].

Etiology

The etiology of cholangiocarcinoma remains undetermined, although long standing inflammation, biliary stasis, and infection are suggested to play a role. The majority of cholangiocarcinoma is sporadic. There are several established risk factors including advanced age, congenital biliary cystic disease, hepatolithiasis, thorotrast radiographic contrast, and the parasitic hepatobiliary flukes *Clonorchis sinensis* and *Opisthorchis viverini* that inhabit bile ducts predominately in Southeast Asia [35]. The autoimmune disease primary sclerosing cholangitis (PSC) strongly predisposes for cholangiocarcinoma. The lifetime incidence for cholangiocarcinoma among PSC patients ranges from 6% to 36% with most presenting within 2.5 years of their PSC diagnosis [35, 36]. PSC leads to chronic inflammation, proliferation of biliary epithelium, and bile stasis. The risks of inflammatory bowel disease, choledocholithiasis, alcohol abuse, smoking, chronic viral hepatitis, and cirrhosis are less well established [35].

Pathology and Staging

More than 90% of biliary tract cancers are adenocarcinoma with the remainder being squamous cell tumors [36]. Grossly, cholangiocarcinoma is divided into three pathologic classifications: sclerosing, nodular, and papillary. Sclerosing cholangiocarcinoma is the most common pathologic subtype comprising up to 70% of cholangiocarcinomas [33]. They are frequently found at the hilum and grow diffusely along the biliary wall with a corresponding dense desmoplastic reaction and radial tumor infiltration. This allows for perineural and lymphatic spread making local extension into regional lymph nodes and vasculature including hepatic artery, veins, and porta hepatis quite common. Nodular subtypes have firm irregular projections into the lumen of the bile duct. Papillary subtypes, representing less than 10% of cholangiocarcinoma, have a less invasive growth pattern arising from a well-defined stalk and are more often resectable with a more favorable prognosis [36].

Klatskin and Distal Extrahepatic Cholangiocarcinoma

The AJCC staging system for cholangiocarcinoma divides the disease to its locational subtypes accounting for extension of disease, nodal involvement, and distal metastases (Tables 4, 5, and 6). Alternative staging systems, including the Bismuth-Corlette system and Memorial Sloan Kettering Cancer Center classification, can further assist in predicting local resectability and need for hepatic resection. The Bismuth-Corlette system provides anatomic classification based on tumor location and duct infiltration: Type I are confined to the common hepatic duct below the level of bifurcation. Type II involve the hepatic duct confluence without involvement of secondary intrahepatic ducts. Type IIIa and IIIb involve the bifurcation but also extend into the right and left secondary intrahepatic ducts, respectively. Type IV tumors

Table 4 American Joint Committee of Cancer 7th edition staging system for perihilar cholangiocarcinoma (Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is Edge SB, et al.: AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer Science and Business Media LLC)

	Staging system
T	Tis = Carcinoma in situ T1 = Tumor confined to bile duct histologically T2a = Tumor beyond the wall of bile duct into adjacent fat T2b = Tumor beyond the wall of bile duct into liver parenchyma T3 = Tumor invades ipsilateral portal vein (R or L) or hepatic artery (R or L) T4 = Tumor invades Main portal vein or its branches bilaterally or Common hepatic artery or The second-order biliary radicals bilaterally or Unilateral second-order biliary radicals with contralateral portal vein or hepatic artery involvement
N	N0 = No regional nodal metastases N1 = Regional lymph node metastases including nodes along the cystic duct, common bile duct, hepatic artery, and portal vein N2 = metastasis to periaortic, pericaval, superior mesenteric artery, and/or celiac artery lymph nodes
M	M0 = No distant metastases M1 = Distant metastases

Staging groups

	T	N	M
0	Tis	N0	M0
I	T1	N0	M0
II	T2	N0	M0
IIIA	T3	N0	M0
IIIB	T1–3	N1	M0
IVA	T4	N0	M0
IVB	Any T	N2	M0
	Any T	Any N	M1

involve both the right and left secondary intrahepatic ducts [37]. The Memorial Sloan Kettering Cancer Center (MSKCC) classification for hilar cholangiocarcinoma similarly assesses local tumor extent while also assessing portal vein and hepatic lobar atrophy [38].

Intrahepatic Cholangiocarcinoma

Staging for intrahepatic cholangiocarcinoma in the AJCC is based on the number of intrahepatic lesions, presence or absence of vascular invasion, lymph node, and distal metastases (Table 6). The overall median 3- and 5-year survival is 31% and 18%, respectively. In the absence of nodal involvement or distant intrahepatic metastases, 3- and 5-year survival is somewhat better at 40% and 25% [39, 40].

Presentation and Diagnosis

Klatskin and Distal Extrahepatic Cholangiocarcinoma

The most common presentation for extrahepatic cholangiocarcinoma is painless jaundice due to biliary obstruction. Pruritus, abdominal pain, anorexia, fatigue, acholic stools, dark urine, and weight loss may also be present. Apart from potential jaundice, the physical exam is predominately normal. In uncommon cases a palpable gallbladder, Courvoisier's sign may be appreciated. Laboratory evidence of biliary obstruction such as elevated alkaline phosphatase, elevated g-glutamyl transferase, hyperbilirubinemia, or bilirubinuria may also be present. Tumor markers such as CA125, CA19–9, and CEA can be

Table 5 American Joint Committee of Cancer 7th edition staging system for distal cholangiocarcinoma (Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is Edge SB, et al.: AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer Science and Business Media LLC)

	Staging system
T	Tis = Carcinoma in situ T1 = Tumor confined to bile duct histologically T2 = Tumor beyond the wall of bile duct T3 = Tumor invades liver, gallbladder, pancreas but no involvement of celiac axis or the superior mesenteric artery T4 = Tumor involves the celiac axis or superior mesenteric artery
N	N0 = No regional nodal metastases N1 = Regional lymph node metastases including hilar, celiac, superior mesenteric, periduodenal, and peripancreatic
M	M0 = No distant metastases M1 = Distant metastases

Staging groups

	T	N	M
0	Tis	N0	M0
IA	T1	N0	M0
IB	T2	N0	M0
IIA	T3	N0	M0
IIB	T1–3	N1	M0
III	T4	Any N	M0
IV	Any T	Any N	M1

elevated in cholangiocarcinoma, and higher levels are associated with advanced tumor stage predicting a worse overall survival [36]. These markers, however, are nonspecific as they also increase with other gastrointestinal and gynecologic neoplasms, as well as in benign extrahepatic obstruction [32].

Ultrasonography can identify large hilar tumors but is not the optimal form of imaging for operative planning and has low sensitivity in identifying metastases. CT allows for better understanding of the extent of the disease process; it can demonstrate the level of biliary obstruction or the presence or absence of local vascular invasion or lymph node involvement, and can show distal metastasis that would preclude resection. Klatskin tumors cause biliary dilation of the intrahepatic tree, while distal biliary disease has dilatation of both intrahepatic and extrahepatic ducts as well as the gallbladder (Fig. 5).

Magnetic resonance cholangiopancreatography (MRCP) best defines biliary anatomy. MRCP allows noninvasive three-dimensional reconstruction of ductal anatomy and can accurately identify the level and cause of biliary obstruction while also assessing the extent of bile duct invasion, vessel encasement, and adjacent liver extension [41]. Contrast enhancement is imperative for operative planning in both MRCP and CT to asses both vascular invasion as well as possible anomalous hepatic flow. Endoscopic retrograde cholangiography (ERCP) is an invasive approach that allows visualization of ductal anatomy with the ability to obtain brushing or biopsy specimen. However, ERCP should be used selectively due to risks of pancreatitis and cholangitis. Endoscopic ultrasound scan (EUS) is becoming more commonly utilized due to the ability to evaluate the biliary tract without instrumentation thus avoiding the potential for biliary sepsis. EUS can also assess the level of obstruction, vascular involvement, or regional lymph nodes and provides the ability to sample nodes with fine needle aspiration (FNA) or core needle biopsy. Needle biopsy can often be nondiagnostic due to the desmoplastic nature of this disease and technical challenges of tissue sampling.

Table 6 American Joint Committee of Cancer 7th edition staging system for intrahepatic cholangiocarcinoma (Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is Edge SB, et al.: AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer Science and Business Media LLC)

	Staging system
T	Tis = Carcinoma in situ T1 = Solitary tumor without vascular invasion T2a = Solitary tumor with vascular invasion T2b = Multiple tumors, with or without vascular invasion T3 = Tumors perforating the visceral peritoneum OR involving local hepatic structures by direct invasion T4 = Tumor with periductal invasion
N	N0 = No regional nodal metastases N1 = Regional lymph node metastases present
M	M0 = No distant metastases M1 = Distant metastases

Staging groups

	T	N	M
0	Tis	N0	M0
I	T1	N0	M0
II	T2	N0	M0
IIIA	T3	N0	M0
IVA	T4	N0	M0
	Any T	N1	M0
IVB	Any T	Any N	M1

Fig. 5 Endoscopic retrograde cholangiopancreatography imaging demonstrates filling of proximal biliary tree with narrowed common bile duct secondary to compressive distal cholangiocarcinoma

Intrahepatic Cholangiocarcinoma

Intrahepatic cholangiocarcinoma typically presents as an incidental hepatic lesion (Fig. 6). Obstructive jaundice is rare and the majority of patients are asymptomatic. Liver function changes may be present as well as weight loss, early satiety, and anorexia. Contrast enhanced CT or MRI imaging is necessary to determine the extent of disease spread, the size, number and location of lesions, vascular invasion, and anatomy. Imaging also can assess for cirrhosis, portal hypertension, and ascites that may affect treatment decision-making.

Treatment

Margin negative resection for cholangiocarcinoma is the only treatment strategy with a potential for cure. Preoperative evaluation is critical to review patient performance status, extent of comorbidities, nutrition status, and hepatic function. The patient presenting with biliary sepsis should undergo biliary stenting to relieve cholestasis. Stenting can also be utilized in cases of marked hyperbilirubinemia and jaundice as a temporizing drainage maneuver while awaiting scheduled surgery. However, biliary instrumentation and manipulation can predispose to infection

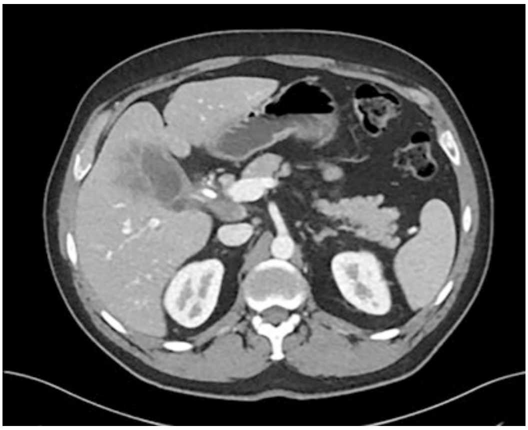

Fig. 6 Cross-sectional CT scan image demonstrates intrahepatic cholangiocarcinoma involving segment 4 of the liver

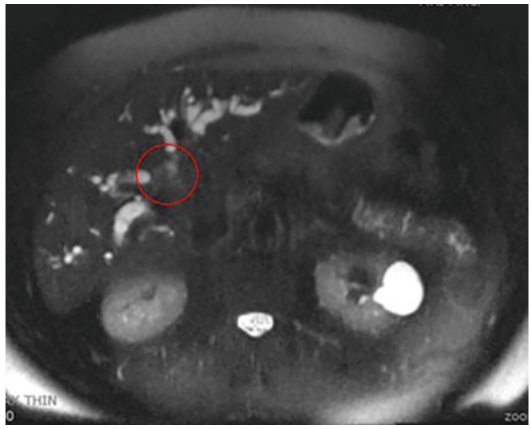

Fig. 7 T2 weighted MRI imaging demonstrates a Klatskin's tumor (*circle*) at the hepatic duct confluence

and prolonged postoperative hospitalization. Additionally, localized inflammatory effects of stenting can feasibly complicate the determination of tumor extent at the time of resection. Therefore, it is preferable, when feasible, to go directly to surgery avoiding stenting in operative candidates.

Patients without locally unresectable disease or metastasis should undergo surgical exploration. Unfortunately, more than half of such patients explored are found to have peritoneal implants, hepatic metastasis, or locally advanced disease precluding a complete resection. Due to the poor predictive value of preoperative staging for surgical resectability, diagnostic laparoscopy, which can identify two third of radiographically occult metastasis, can be utilized to spare laparotomy [42].

Surgical Resection of Klatskin Tumor

The extent of surgical resection for Klatskin is dictated by the location and local extension of disease (Fig. 7). Outcomes have improved with the adoption of more aggressive surgical approaches including extended hepatectomy and portal vein resection. Portal vein embolization (PVE) may be used as an adjunct measure. Preoperative imaging and staging are imperative for surgical planning. Perihilar tumors involving the proximal common duct without proximal involvement of the intrahepatic ducts (Bismuth type I and II) nor vascular involvement are candidates for local tumor excision. The distal bile duct is isolated to the level of the pancreas and divided with intraoperative frozen section to ensure negative margins. The duct is then dissected from hepatic artery medially and portal vein posteriorly with portal caval lymphatics also removed en bloc. At this point a top down approach cholecystectomy is performed. Proximal hilar exposure is accomplished with individual dissection of the right and left bile ducts. Extent of tumor extension is identified and ducts are ligated proximal to the tumor individually with frozen sections to ensure negative margins. A Roux-en-Y reconstruction is performed with individual anastomoses to each duct. If tumor involves the right or left intrahepatic ducts (Bismuth type IIIa or IIIb), respective right or left hepatic lobectomy should also be performed. Frequently, caudate lobectomy is required due to direct extension into the caudate. Tumor invasion of the contralateral or bilateral hepatic arteries, secondary biliary radicals, or extensive portal vein involvement prevents successful resection [43]. The remnant liver following resection must have adequate arterial inflow and venous drainage in at least two contiguous hepatic segments.

Surgical Resection of Distal Extrahepatic Cholangiocarcinoma

Distal bile duct tumors are more often resectable than the perihilar and intrahepatic counterparts. Pancreaticodudoenectomy is required, removing the pancreatic head, proximal duodenum, gallbladder, and bile duct. Identification of tumor extent is imperative and frozen margin of the proximal bile duct should be assessed. Bile duct excision alone is not recommended due to worse lymph node clearance, a lower likelihood of having curative margins, and poorer survival [44].

Surgical Resection of Intrahepatic Cholangiocarcinoma

As with Klatskin's tumors, successful hepatectomy for intrahepatic cholangiocarcinoma must maintain functionally adequate remnant liver. Therefore, initial preoperative assessment must address general liver function. Chronic liver disease or portal hypertension precludes resection. Selective ipsilateral PVE can enable more extensive resections than possible previously by inducing compensatory hypertrophy of the future remnant and should be considered if remnant volume is expected to be less than 30% [45]. Furthermore, PVE is pertinent for patients in which an extended right hepatectomy is anticipated due to the frequent inadequacy of remaining left lateral and caudate volumes [46]. In cirrhotic patients, a larger remnant is essential. Additional criteria for unresectability include tumor extension to bilateral secondary branches of hilar structures, portal vein, hepatic artery, and bile ducts.

Transplantation

In highly selected patients, orthotopic liver transplant (OLT) may be considered for unresectable cholangiocarcinoma. The rates of long-term survival for cholangiocarcinoma associated with PSC are dismal, even following surgical resection, due to frequently multicentric disease and underlying liver dysfunction. Thus, OLT has been pursued particularly for this cohort. The Mayo Clinic has developed a neoadjuvant chemotherapy followed by transplantation protocol for unresectable hilar cholangiocarcinoma or hilar cholangiocarcinoma with PSC. Eligibility criteria include a tissue diagnosis of cholangiocarcinoma, disease above the level of the cystic duct, radial dimension of <3 cm without intrahepatic or extrahepatic metastasis, and absence of prior radiation therapy. Patients must also have adequate performance status. A regimen of 5 fluorouracil, external beam radiation, and iridium 192 brachytherapy is given with Capecitabine added for 2 of every 3 weeks until the day of transplantation. With this protocol, 5-year survival rates of approximately 70% have been reported [47]. Despite these promising results, transplantation remains recommended only in selected patients in specialized centers.

Chemoradiation Therapy

Radiation in the adjuvant setting may provide local disease control and slow overall disease progression. Prospective data are limited although survival benefits have been suggested with utilization in the adjuvant setting compared to controls. Outcomes for unresectable disease treated with radiation have remained poor, with little improvement in disease-free survival. The data for chemotherapy utilization in cholangiocarcinoma are similarly limited. Systemic chemotherapy regimens most commonly consist of a combination of gemcitabine with a platinum agent with modest improvements reported in survival and quality of life compared with best supportive care [46].

Outcomes

Murakami et al. reported a series of 127 patients with cholangiocarcinoma (21 intrahepatic, 50 perihilar and 56 distal) who underwent surgical resection. Overall 1-, 3-, and 5-year survival rates for the entire cohort were 80%, 51%, and 40%, respectively [48]. Complete R0 surgical extirpation remains the best chance for long-term survival, with positive margins associated with a 13% 5-year survival compared to 49% following R0 resection [48]. An additional large single institution series reported median survivals following R0 resected intrahepatic, perihilar, and distal tumors of 80, 30, and 25 months with 5-year survivals of 63%, 30%, and 27%, respectively [44]. Concomitant hepatic resection, histologically negative margins, lymph node status, and well-differentiated tumor histology are all associated with improved outcome after resection.

Operative mortality for perihilar and intrahepatic cholangiocarcinoma is not insignificant and reported at rates of 6–8% with morbidity as high as 70% [36, 44, 49]. The greatest risk factors for recurrence are positive margins and lymph node metastasis [49]. Unfortunately, most cholangiocarcinomas present as unresectable disease. Untreated, survival of these patients is short with a median survival between 3 and 8 months, with patients most frequently succumbing to hepatic failure and cholangitis [32].

Unresectable Disease/Palliation

Less than half of cholangiocarcinomas are resectable on presentation and of patients proceeding to the operating room, 40–50% are found to be unresectable [36]. Palliative biliary drainage may be the only therapeutic possibility. Surgical bypass for patients deemed unresectable preoperatively should not be pursued due to lack of survival benefit and the associated surgical morbidity and mortality. For these patients, percutaneous placement of expandable metal stents or drainage catheters for proximal disease and endoscopic placement for distal can be provided. Stent occlusion is not uncommon and thus self-expanding metal stents are preferred. If determined to be unresectable intraoperatively, however, surgical bypass by Roux-en-Y hepaticojejunostomy has been associated with fewer episodes of cholangitis and improved patency compared to stenting [50].

Palliative chemotherapy treatment can be offered to unresectable individuals, but response rates are disappointing with median survival remaining only 6–12 months [32, 51]. Gemcitabine and cisplatin has shown benefit over 5FU-based chemotherapy or supportive care alone [46]. No randomized data are available to assess the benefit of adding radiation to palliative chemotherapy.

Unresectable cholangiocarcinoma without evidence of metastatic disease in patients who are not candidates for liver transplantation may benefit from photodynamic therapy (PDT). PDT utilizes an intravenous photosensitizing agent which accumulates in tumor cells and is activated during cholangiography by induction of a specific wavelength of light that activates the accumulated agent leading to formation of oxygen free radicals and tumor cell destruction [46]. PDT may lead to marginal improvements in cholestasis and quality of life [46].

Conclusion

GBC and cholangiocarcinoma are uncommon and aggressive malignancies predominately affecting the elderly. Complete surgical extirpation by resection or rarely transplantation remains the only current potential curative treatment; however, outcomes remain dismal and palliation may be the goal of therapy. At present, our armamentarium against this condition is predominantly limited to wide resection. With the advent of molecular medicine and immunotherapeutic approaches to cancer, we hope to see improvements in disease-free and overall survival in the future.

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Benign Colorectal Disease in the Elderly

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Walter E. Pofahl and Mark L. Manwaring

Contents

Abstract

Benign colorectal diseases are a cause of many quality of life impairments for patients. With aging of the population, physicians are likely to encounter more affected patients in the years to come. Constipation, especially prevalent among older patients, has many downstream effects and, with these, may create significant morbidity and expense for patients. Chronic straining and pelvic floor weakness may result in rectal prolapse that usually can be corrected with an appropriate surgical intervention. With antibiotic use, there is risk of *Clostridium difficile* infection which may complicate recovery from a host of conditions seen in elderly patients. Only in fulminant cases is surgery typically required. Colonic volvulus is an unusual cause of large bowel obstruction in the United States; however, its frequency too increases with patient age. Mortality may result from incorrect diagnosis or failure to intervene promptly. Fecal incontinence is disabling for a

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large cohort of elderly patients, and although not always reversible, the impact on quality of life can be minimized with a number of strategies.

Keywords
Rectal prolapse · Volvulus · Elderly · Pelvic floor dysfunction · Clostridium difficile infection

Case Study

Background

A 59-year-old female with chronic straining constipation since her teen years presents with a bulge in the anal area for the past 6 weeks. She has a small amount of blood on the toilet paper, mucous discharge, and has noted difficulty getting clean after bowel movements. She does not have pain but does note a “pressure” sensation at the times she has prolapse with an intermittent urge to defecate, but when she toilets, she finds there is only some mucus to pass. For many years, her constipation was untreated but she has begun taking stool softeners and occasional milk of magnesia. Her past medical history is significant for basal cell skin carcinoma, excised last year, and thyroid cancer treated with resection and hypercholesterolemia. Her past surgical history is significant for a laparoscopic total abdominal hysterectomy for dysfunctional uterine bleeding at age 39. She is gravida 3, para 3. Her current medications include Synthroid and lovastatin.

On physical exam, she is a healthy-appearing overweight, middle-aged woman. Abdominal exam is benign. There is a well-healed small Pfannenstiel incision. On digital rectal examination, she has normal anal tone, and there is a broad-based rectocele that is prominent on Valsalva. A mass is palpable against the tip of the examining finger. Proctosigmoidoscopic examination shows infolding of the rectal wall anteriorly with ulceration along the fold. There is some hard stool in her rectal vault. Examination while sitting on the commode shows full-thickness prolapse upon straining on the toilet.

Management

Anal physiology (including anal manometry, EMG, and transrectal ultrasound) is not needed for evaluation of the patient’s condition. Left untreated, full-thickness rectal prolapse would likely progress and dilate the anal sphincters resulting in compromised continence. Chronic constipation and loss of supporting tissue integrity have allowed for folding of the rectal wall, and ulceration sometimes progresses from recurrent trauma as in solitary rectal ulcer syndrome. Defecography or dynamic MRI may be done to confirm the degree of internal intussusception and to evaluate the size/severity of the rectocele, presence of an enterocele, or vaginal prolapse. Colonic transit time using a sitz marker test can be used to categorize her chronic constipation though this would probably not change the management given her age and her limited use of osmotic laxatives. Since rectopexy alone may worsen the patient’s constipation, a laparoscopic (or robotic) rectopexy with sigmoid resection would be the treatment of choice. Properly done, this will correct the internal and early external prolapse and prevent sequela of sphincter dysfunction while avoiding constipation exacerbation. Were the patient to be without constipation symptoms, a rectopexy alone with suture or mesh may be preferred. Though there is interest in anterior mesh approaches for rectal prolapse as this may avoid the denervation of the rectum resulting from lateral stalk division, posterior rectopexy with mesh or suture are most commonly employed. Vaginal/uterine prolapse if present can be treated with cooperation of urogynecologist by sacral colpopexy or other needed intervention.

Introduction

The incidence of benign medical and surgical diseases of the colon and rectum increases with age [1]. Although constipation, fecal incontinence, and several other associated benign conditions increase in frequency with aging, a paucity of information exists regarding the normal aging effect on gastrointestinal pathophysiology. Studies documenting anatomic, physiologic, and pathologic changes that occur in the aging colon have not been definitive, and many studies have reported conflicting results. Mucosal atrophy, atrophy of circular muscles, thickening of longitudinal muscles (taeniae coli), increased elastin deposition, and atherosclerosis are several of the changes seen in the aging bowel [3]. These changes may factor into the development of several disease states (i.e., diverticular disease and angiodysplasia). Medications affect gastrointestinal function, and many have constipation as a side effect. Preexisting diseases (cardiac, pulmonary, renal, neurologic, psychiatric) may affect colonic motility directly or secondarily. Advanced age is a risk factor for the development of infectious processes such as *Clostridium difficile* infection. Comorbidities and age limit physiologic reserve in the elderly, making operative risks higher. These differences make early diagnosis and treatment crucial to good outcomes. In this chapter, we address benign colorectal diseases frequently encountered in the elderly patient and which may increase as the population ages. Diseases equally common to both young and old persons, such as hemorrhoids and fissures, are not discussed.

Constipation and Pelvic Floor Dysfunction

Difficult or infrequent passage of stool and other bowel symptoms that define constipation are common complaints in the United States (Table 1). The frequency of constipation increases with age, and it is more common in women, blacks, and persons of lower socioeconomic status and family educational status [4–6]. The overall prevalence of reported constipation in the elderly Western population is probably 20–33% but differs according to the source of the sample [5, 7–9]. The incidence of constipation is approximately 12% in the ambulatory geriatric population vs. 41% in acute-care facilities and more than 80% in geriatric nursing homes and extended-care facilities (compared to about 16% in the general population). Elderly women are about 50% more likely to report symptoms of constipation than elderly men [7, 8]. Further, studies indicate large variation in bowel habits and frequent use of laxatives in as many as 30–50% of the elderly population [10–12]. Subjective complaints of constipation and laxative use increase with age, but true epidemiologic data suggest that clinical constipation does not [13]. Although complaints of constipation increase in those over age 65, about 80–90% of subjects over age 60 report at least one bowel movement per day [10, 11]. Although there may be normal physiologic aging of the colon and rectum, asymptomatic geriatric patients do not seem to differ significantly from their younger cohorts.

Table 1 Rome III criteria for functional constipation (Adapted from: Shih DQ, Kwan LY. All Roads Lead to Rome: Update on Rome III Criteria and New Treatment Options)

At least two or more of (during at least 25% of defecations)	And
Straining	Loose stools are rarely present without the use of laxatives
Lumpy or hard stools	Insufficient criteria for irritable bowel syndrome
Sensation of incomplete evacuation	
Sensation of anorectal obstruction/blockage	
Manual maneuvers to facilitate defecations	
Fewer than three defecations per week	

Stool transit through the colon is affected by stool consistency and by underlying large bowel motility. Both of these characteristics can be altered both positively and negatively by medications. Stool content and therefore its physical properties are altered by dietary factors – primarily fluid and fiber. Inadequate fluid intake may decrease the fecal bulk causing decreased intraluminal pressures in the colon, which in turn may decrease the number of propagating motor complexes generated [13]. The role of fiber has been debated, but current aggregate data suggests wheat fiber does increase stool weight and frequency and decreases transit times [14].

Polypharmacy, common in the elderly, places this group at particular risk for compromised colonic motility [15]. Anticholinergics, tricyclic antidepressants, beta-blockers, and calcium channel blockers are commonly implicated. Over-the-counter medications, such as aluminum and calcium antacids and laxatives, may also contribute to patients' symptoms. Chronic medical diseases such as hypothyroidism, diabetes, scleroderma, multiple sclerosis, and Parkinson's disease can result in decreased colonic motility. Psychiatric conditions (depression and dementia) have been associated with constipation, which may be behaviorally related [4]. Inability to ambulate to the restroom because of arthritis, for example, or ignoring the call to defecate because of dementia may contribute to symptoms of fecal impaction, constipation, and the development of a megarectum [4, 11]. Constipation is probably not a normal consequence of aging but is associated with and possibly caused by the immobility, chronic illnesses, and increased neuropsychiatric problems of the elderly population.

Patients with constipation can be separated into three groups: The first and by far the largest group of patients are those with normal transit or functional constipation. These patients complain of hard, dry stools that are difficult to evacuate and should be treated with lifestyle manipulation: increased fiber, increased fluid, and exercise or with osmotic laxatives for refractory symptoms. The second group, more likely to present at younger ages, are patients who have slow transit or colonic inertia. These patients have minimal to no motility of their colon and rarely have spontaneous bowel movements. Many of these patients report going for days and occasionally weeks without bowel function. Patients with colonic inertia commonly report a long history of laxative use and abuse. Chronic laxative use, particularly with the anthracene laxatives, can cause degeneration of the myoneural chains and may impede motility irreversibly over time [16]. The final group are the patients with anorectal dysfunction or pelvic floor abnormalities that prevent evacuation and result in clinical constipation. The pelvic floor abnormality can be identified with colonic transit marker studies, cinedefecography, and dynamic MRI. These patients have normal transit to the sigmoid colon but are unable to evacuate their rectums easily, even if they have a soft stool. Within this group are patients with rectal intussusception, pelvic organ prolapse, rectocele, and obstructed defecation (nonrelaxing puborectalis or anismus). In rectal intussusception, the rectum folds in onto itself and may act as a valve that prevents normal emptying. Symptoms vary from mild constipation with rectal pressure to severe constipation with rectal pain and a "plugging" sensation. Incomplete evacuation and discharge of mucus and blood per rectum are frequent complaints. Rectal intussusception may be identified as a component of pelvic organ prolapse. The etiology of outlet obstruction is unclear, although dysfunction and discoordination of the pelvic floor muscles are the most common explanation. In patients with chronic fecal impaction, the rectal capacity increases over time and rectal sensation becomes blunted. These patients cannot feel the urge to defecate until a fecal bolus is too large to pass. These patients often report the need to use digital maneuvers, suppositories, or enemas to evacuate to their satisfaction.

Patients with complaints of severe constipation should be completely evaluated. Initially, a history and physical examination are performed. A detailed medication list, including all over-the-counter medications, is imperative. A diet and defecation diary is helpful to attempt to define the extent of the problem. The American Gastroenterological Association consensus guideline recommends that most patients with severe constipation have a complete blood count, serum glucose, calcium and creatinine, and thyroid-stimulating hormone levels checked [17].

A digital rectal examination should be done to exclude low rectal carcinomas, anal strictures, and other anorectal abnormalities. Contrast studies or colonoscopy should be performed to rule out obstructing colonic lesions, particularly if the symptoms of constipation are recent or associated with bleeding, mucus, or altered stool caliber.

Table 2 Traditional obstructive defecation treatment algorithm (Adapted from Schwartz [107])

Presenting symptoms:				
Constipation, incomplete evacuation, rectal pressure, need for digital maneuvers				
Workup: defecography, sitz marker study, balloon expulsion test				
Defecography	Nonrelaxing PR	Nonrelaxing PR	Internal intussusception	Internal intussusception
Colonic transit	Normal	+ Outlet obstruction	+ Outlet obstruction	+ Outlet obstruction
Balloon expulsion	Normal	Unable to expel	Normal	Unable to expel
Treatment	**Bulking agents**	**Psychological evaluation**	**Fiber/stool liquification if mild, consider rectopexy**	**Psychological evaluation**
	Stool softeners	**Biofeedback**		**Biofeedback**

Defecography, endoscopy, sitz marker testing, and/or manometry can help guide the clinician in determining cause and treatment. (Table 2) On proctosigmoidoscopic examination, the typical patient with significant intussusception often has an erythematous anterior rectal wall approximately 5–8 cm from the mucocutaneous junction. Patients with solitary rectal ulcer syndrome frequently have more severe symptoms of straining, passage of bloody mucus per rectum, and incomplete evacuation, and the rectal ulcer appears as a heaped-up lesion in the anterior midline 5–8 cm from the mucocutaneous junction. This lesion is often palpable and may be mistaken for a rectal carcinoma. Biopsy is important to exclude malignancy and reveals cystic proliferation of fibroblasts and muscle hypertrophy in the lamina propria, epithelial hyperplasia, colitis cystica profunda, or excess mucosal collagen [18].

Several tests are available for assessment of constipation and can aid in creating a strategy for management although it is not uncommon that patient's complaints and concerns do not correlate well with colonic and anorectal physiologic tests. Colonic transit time is a simple radiographic test which helps assess the bowel motility and can identify patients with colonic inertia or outlet obstruction. Patients are placed on a high-fiber diet and taken off all laxatives and enemas for several days prior to testing. A capsule with 24 radiopaque markers is given to the patient to take orally on day 0. A plain radiograph is obtained on the third and fifth days. The markers are counted, and their location should be noted. The presence of more than 10% of the markers on the fifth day is considered to be an abnormal study. It is important to ensure that the patient took the capsule, did not take laxatives, and did not have abnormal bowel function (i.e., diarrhea) during the study period, as these possibilities may give a false normal examination. Patients with colonic inertia have markers scattered diffusely throughout the colon that remain through the fifth day. In patients with rectal intussusception or outlet obstruction, the markers move through the colon and are held up in the rectosigmoid region. Total colonic transit times in healthy asymptomatic elderly subjects show no change with aging but are prolonged in healthy elderly subjects who report symptoms of constipation [19, 20].

There are clearly cause and effect relationships in both directions between pelvic floor disorders and constipation. Commonly chronic straining behavior results in structural changes over time of the anorectal anatomic relationships. Often, however, anatomic alterations can exacerbate difficulties with evacuation. Physical examination, though important, is of limited value in evaluation of the pelvic floor as it misses a significant number of rectoceles, enteroceles, sigmoidoceles, and cystoceles [21]. Cinedefecography may identify patients with severe rectal intussusception or rectal prolapse and can identify patients with significant rectoceles and enteroceles if vaginal contrast is used. This test is done by placing a thickened barium paste in the rectosigmoid to simulate a bowel movement. The patient is then placed on a commode and asked to evacuate the paste while radiographs are obtained. In a normal test, the rectosigmoid remains stable along the presacral space, and the puborectalis is seen to relax as the patient passes the contrast bolus. With an abnormal test, the rectosigmoid may fall away from its attachments to the presacral space, and the proximal rectum is seen to infold (intussuscept). Internal intussusception of the rectum can block the rectal outlet, resulting in incomplete evacuation of the rectal contrast. With severe straining, the intussusception may worsen, and occasionally the entire rectum is seen prolapsing through the anorectal ring (Fig. 1).

One of the shortcomings of defecography is the utilization of ionizing radiation. MRI is noninvasive, does not use ionizing radiation, has a larger field of view, has improved soft tissue contrast, and has multiplanar capability. Dynamic MR imaging has been used to assess the complex pelvic anatomy and changes in these structures during attempts at evacuation. Older methods had long acquisition times (6–12 s) which did not allow for real-time evaluation. Newer techniques have near real-time continuous imaging and can be performed in less than 2 min [22, 23]. Dynamic radiologic examinations of the endopelvis may reveal multicompartmental dysfunction [24]. Segregation of the pelvic floor into posterior, middle, and anterior compartments, however, is artificial because these structures are closely interrelated [25]. Pelvic organ prolapse can be detected and characterized using dynamic MR imaging but cinedefecography is more sensitive in detecting parietal alterations [26].

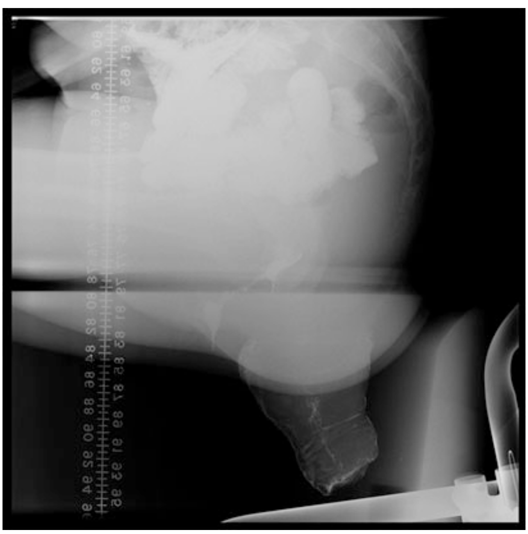

Fig. 1 Defecography showing full-thickness prolapse (Image provided by Manwaring ML)

Anal manometry has limited value in the workup of constipation in the elderly. In select cases, anal manometry, rectal anal inhibitory reflex, minimal sensory rectal volume, and balloon expulsion may identify patients with megarectum and patients with nonrelaxing puborectalis muscle. These tests require specialized manometric instruments and can be done utilizing a capillary perfusion system or microballoon system. These systems measure the pressures within the anal canal and test the function of the anal sphincter mechanism. Anal sensation is tested by inserting a rectal balloon just above the anal sphincter and insufflating increasing amounts of air until the patient notes sensation. Patients with megarectums require large amounts of distension before any sensation is noted. The rectoanal inhibitory reflex is absent in patients with megarectum who require large volumes to induce the inhibitory reflex. A rectal examination performed on an "unprepped" patient with megarectum may reveal a rectum full of stool. The inability to expel the rectal balloon is tested by asking the patient to evacuate a rectal balloon filled with 60 cc of air in the privacy of the bathroom. If patients have an outlet obstruction and the puborectalis muscle does not relax properly, they have difficulty doing this simple task. The inability to relax the puborectalis muscle and evacuate the contrast on cinedefecography helps confirm the diagnosis.

Treatment of constipation in the younger population is generally medical, and treatment of the elderly constipated patient is no different. A trial of dietary fiber and increased fluid intake should be initially instituted once a malignancy has been ruled out. The daily recommended fiber intake is 20–35 g daily, even in the elderly [27]. By adding approximately 5 g of fiber per week until the goal is met, the excessive gas and bloating that occurs with high-fiber diets can be minimized [28]. A bowel evacuation routine is often helpful for those patients with outlet obstruction. The patient is instructed to take bulk-forming agents daily and to use a glycerin suppository or tap water enema at the same time daily. To maximize the effect of the gastrocolic reflex, patients are encouraged to perform this evacuation routine upon wakening in the morning and approximately 15–20 min after drinking a warm beverage. Biofeedback has had some success in the treatment of pelvic floor outlet obstruction but requires a motivated patient [29, 30]. Surgical intervention is rarely indicated for older patients with constipation. A total colectomy with ileorectal anastomosis has been successful in the treatment of severe colonic inertia without small bowel dysmotility if there is no element of outlet obstruction. However, this operation should be reserved for the younger, medically stable patient. Other patients with colonic inertia are probably best treated by accepting the need for continuous laxative use.

Treatment of patients with rectal intussusception is primarily medical. Surgery should be limited to patients who are incapacitated because of the pressure or who have a persistent solitary rectal ulcer after intensive medical therapy. Surgery involves low anterior resection or retrorectal sacral fixation of the mobile rectum. Many patients have persistent postoperative symptoms of constipation and difficulty emptying. Patients with symptoms of nonrelaxing puborectalis or colonic inertia must have these symptoms addressed and treated preoperatively to have a successful surgical result [31]. Patients with pelvic organ prolapse, enterocele, and cystocele combined with intussusception (Fig. 1) may benefit from a combined procedure. Women with severe symptomatic rectal intussusception and pelvic organ prolapse may benefit from a multidisciplinary approach including urology and gynecology. The decision for surgical intervention for pelvic organ prolapse should not be determined by age alone [32] (Fig. 2).

Rectal Prolapse

The most severe abnormality of the pelvic floor is rectal prolapse. Rectal prolapse can be partial thickness (mucosal) or full thickness (complete extrusion of the rectum through the anal canal) (Fig. 3). Patients with these conditions often complain of rectal pressure, mucous discharge, and rectal bleeding. Most patients also report fecal incontinence, while a lesser number have chronic constipation [33]. The prevalence of this condition increases with age and is associated with female gender and neurologic or psychiatric comorbidities [34, 35]. Given that other significant medical comorbidities also increase in incidence with age, patients with rectal prolapse often have other medical problems [36, 37]. Once the

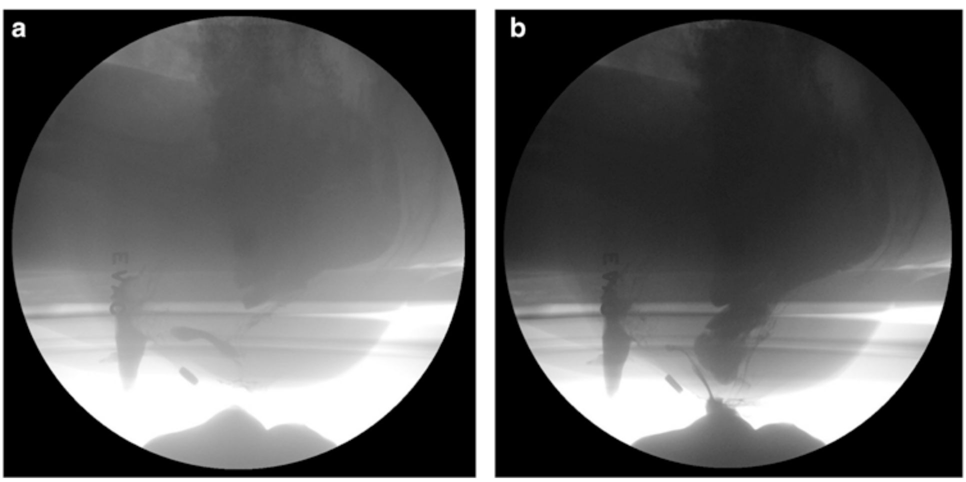

Fig. 2 (**a**) Rectal intussusception at beginning of defecation. (**b**) With push, enterocele drops down into the pouch of Douglas and enters the intussusceptum (Image provided by Liliana Bordeianou, MD)

Fig. 3 Full-thickness rectal prolapse

prolapse begins to occur, patients complain more of the incontinence and rectal bleeding than of constipation [38]. Often patients attribute their anorectal findings to prolapsing hemorrhoids, but direct questioning often confirms that the patient's rectum protrudes with bowel movements (especially with straining) and occasionally when assuming an upright position. Manual reduction of the prolapsed tissue by the patient or their caretakers is common. The symptoms of prolapse can be quite debilitating and at times render a frail patient to remain in bed to avoid prolapse.

Examination typically reveals a lax anal sphincter and prolapsing rectum. Circumferentially oriented folds are seen on the mucosal surface of full-thickness rectal prolapse, whereas radial grooves are common in prolapsing hemorrhoids and may be seen in mucosal prolapse. Incarceration or strangulation of the prolapsed rectum is uncommon but can occur if there is preserved anal sphincter tone or if the prolapsed segment has become extremely edematous. Proctosigmoidoscopy classically demonstrates an erythematous, edematous circumferential region (the "leading edge") approximately 5–8 cm from the dentate line. Asking patients to strain to evacuation their rectum may allow visualization of the prolapse by the examiner. Reproduction of the prolapse sometimes necessitates a patient sitting on a commode and recreating the force used to defecate and is often unsuccessful in lateral or prone positions. If the prolapse cannot be demonstrated in the office setting, defecography or dynamic MRI may be done to demonstrate the redundant internal prolapsing rectum.

A complete evaluation is best performed with colonoscopy to rule out a tumor as a lead point of the rectal prolapse. A solitary rectal ulcer, discussed in the previous section, is seen at the leading edge of the prolapsing rectum in 10–15% of cases [39]. Biopsy of the ulcer should be done to provide a definitive diagnosis. Although not always necessary, rectal prolapse may be demonstrated on defecography as well (Fig. 1). These ancillary studies have the advantage of demonstrating associated pathology such as cystocele, enterocele, and/or vaginal prolapse. The anal sphincter may be assessed using anal manometry and electromyography although the results typically show extremely low rest and squeeze effort. However, with a clearly established diagnosis of rectal prolapse, these studies rarely change the treatment approach [39]. Unilateral and bilateral neurogenic injury may result from chronic stretching of the pudendal nerve. Stretch injury may also be a direct result of repeated trauma to the anal sphincter by the prolapsing rectum. Preoperative motility studies with colonic transit times should be done in patients with complaints of severe constipation to identify a group of patients with colonic inertia and prolapse who may require more extensive resection [40].

Although more than 100 operations have been cited as forms of treatment for rectal prolapse, the two general approaches are transabdominal or perineal. Abdominal rectopexy with or without sigmoid resection is the procedure of choice in patients who have an acceptable surgical risk [39, 41] and can usually be completed using a minimally invasive approach. The American Society of Colon and Rectal Surgeons has developed practice parameters for the management of rectal prolapse as summarized in Table 3 [39]. The rectum can be anchored to the sacrum in two ways – with direct suture or prosthetic mesh placement. Complete encirclement of the rectum with a band of mesh (Ripstein procedure) has been largely abandoned due to problems with stenosis and obstruction at the level of the mesh and mesh erosion. This has been modified to leave the anterior bowel

Table 3 Practice parameters for the management of rectal prolapse (Adapted from: Varma et al. [39] (Table 3: summary of ASCRS practice parameters for treatment of rectal prolapse)

Recommendation	Evidence
The initial evaluation of a patient with rectal prolapse should include a complete history and physical examination	+++
Additional tests such as defecography, colonoscopy, barium enema, and urodynamics can be used selectively to define the diagnosis and identify other important pathology	++++
Physiologic testing may be useful to assess functional disorders associated with rectal prolapse, such as constipation or fecal incontinence	+
Although many patients who present with rectal prolapse are older and have multiple comorbidities, there is little nonoperative treatment available for symptomatic rectal prolapse	+
In patients with acceptable risk, procedures incorporating transabdominal rectal fixation are typically the treatment of choice for the treatment of rectal prolapse	+++
Rectopexy is a key component in the abdominal approach to rectal prolapse	+++
Sigmoid resection may be added to rectopexy in patients with prolapse and preoperative constipation, but it is not necessary in those without constipation	++++
Division of the lateral stalks during rectal dissection may worsen symptoms of constipation postoperatively, but it is associated with decreased recurrence rates	++
The Ripstein procedure with fixation of mesh from the anterior rectal wall to the sacral promontory after posterior mobilization may be used for treatment of rectal prolapse, but it is associated with higher morbidity	+++
A modified Wells procedure using a variety of foreign materials for posterior fixation of the rectum may be used for treatment of rectal prolapse	++
The ventral mesh rectopexy reduces constipation by avoiding posterolateral mobilization of the rectum and produces results similar to other abdominal approaches	++
The use of anterior resection alone to treat rectal prolapse is associated with high recurrence rates and significant operative and postoperative morbidity; it should not be considered as a first-line treatment	++++
A minimally invasive approach to rectal prolapse by experienced surgeons compares favorably with an open repair	++++
Patients with a short, full-thickness rectal prolapse can be treated with mucosal sleeve resection; but for longer prolapse, it is associated with a higher recurrence rate compared with abdominal approaches	+++
Patients with a full-thickness rectal prolapse who are not candidates for an abdominal operation may be treated with a perineal rectosigmoidectomy but are susceptible to higher recurrence rates in comparison with abdominal approaches	+++

+ Weak recommendation based on low-quality evidence
++ Weak recommendation based on moderate-quality evidence
+++ Strong recommendation based on low-quality evidence
++++ Strong recommendation based on moderate-quality evidence

wall free [42, 43], a posterior mesh rectopexy in the manner of Wells [44], which can be done laparoscopically having a low recurrence rate but does impart a risk of constipation. Mesorectum is largely interposed between the rectum and mesh, minimizing mesh contact with the bowel wall itself and leaving the anterior rectum free to expand avoiding obstruction problems.

Low anterior resection may improve the bowel habits of patients who complain of preoperative constipation in whom a markedly redundant distal colon is found [40, 45] but without rectopexy is associated with recurrent prolapse; therefore, suture rectopexy should be performed at the same operation [39] if a resection is being performed. Resection rectopexy is the best treatment for patients with preexisting constipation as it may improve the constipation symptoms and nonresection procedures typically worsen constipation (Fig. 4). Placement of prosthetic mesh is avoided in conjunction with resection because of the risk and morbidities of mesh infection. Anterior mesh rectopexy is the newest approach and is likely associated with less postoperative constipation. There are limited long-term data, and mesh in the rectovaginal septum can be problematic.

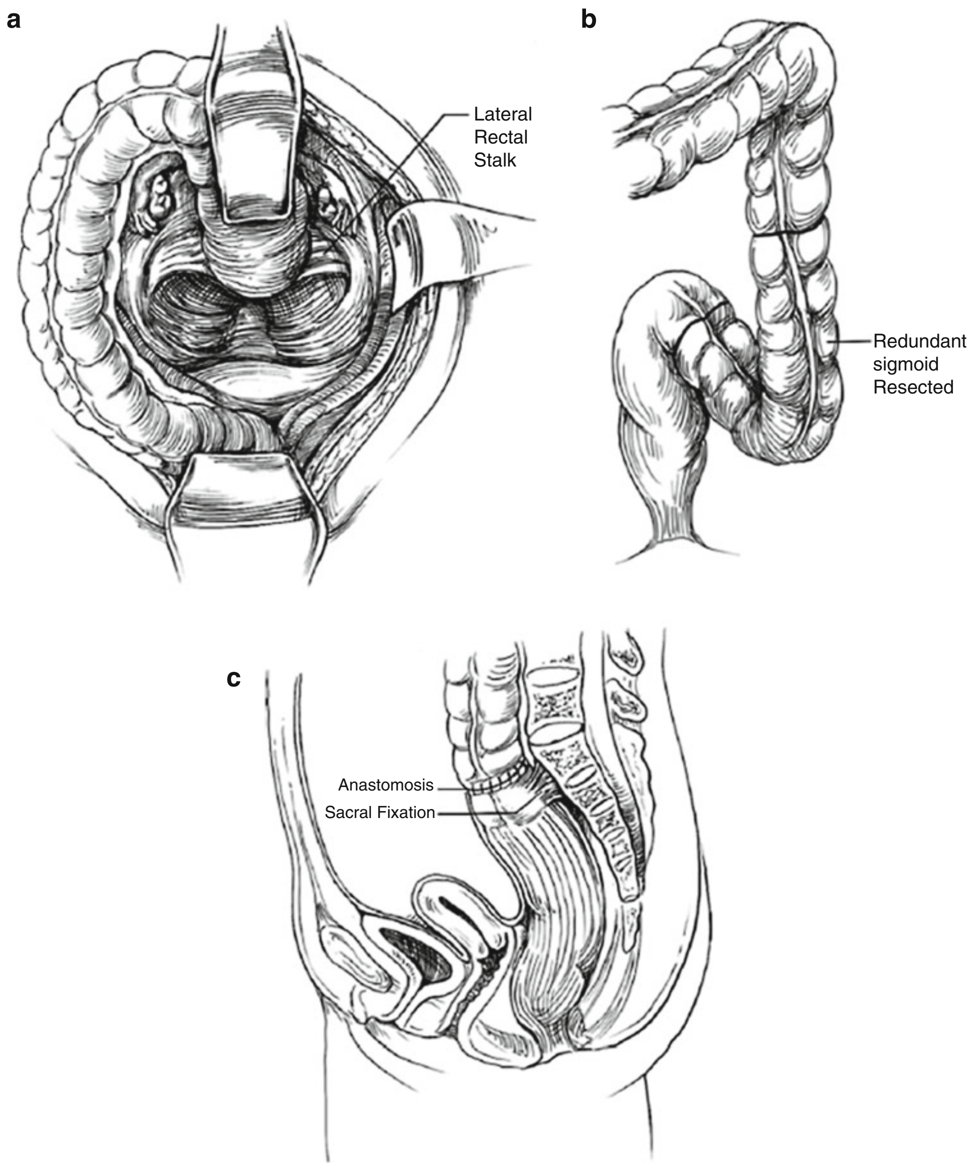

Fig. 4 Resection rectopexy [2]

Whether or not this procedure can be used in full-thickness external prolapse has not yet been determined.

Laparoscopic and robotic approaches have been developed for all the transabdominal procedures for rectal prolapse [39]. The functional and recurrence rates are similar to analogous procedures done open [46–52]. The benefits of minimally invasive approaches are reduced hospital stay, lower narcotic pain requirements, earlier return of bowel function, and reduced wound complications [33, 39, 41], and they have become the standard approach in many practices. Robotic approaches add cost and operative time but allow for enhanced visualization and facilitate suturing deep in the pelvis [53].

Perineal operations are generally reserved for patients who require a regional anesthetic approach or have unfavorable abdominal conditions that increase the risk of an abdominal approach. Postoperative complication rates may be slightly higher for abdominal procedures; long-term results are more favorable (recurrence rate and functional outcome). Laparoscopic recurrence rates increase over time with both the perineal and abdominal approaches [35, 54]. Thiersch wire or other synthetic material is used to encircle the anal canal to prevent rectal prolapse. The encircling material prevents the rectum from prolapsing through the anal canal. The anal encirclement procedures do not treat the underlying condition, and the symptoms of rectal intussusception persist in most patients. It is not uncommon for patients to require laxatives and enemas for fecal evacuation after anal encirclement, as the synthetic material acts as an obstruction to defecation. Because wire erosion, breakage, infection, and fecal impaction complications are common, anal encirclement as a primary treatment for rectal prolapse is generally reserved for moribund patients with limited life expectancy. This procedure is mostly of historic interest and is now rarely performed given the minimal morbidity of both laparoscopic rectopexy and perineal proctosigmoidectomy. However, this procedure with a biological material as an adjunct to perineal proctosigmoidectomy has recently been reported [55].

A mucosal sleeve resection, also called Delorme procedure, can also be used in short, full-thickness rectal prolapse [39] and for mucosal prolapse. This procedure is not a full-thickness rectal resection, but rather the redundant rectal mucosa is stripped circumferentially. The remaining, redundant outer rectal wall is then plicated with a series of circumferential sutures which then allows the mucosal edges to be reapproximated. Although there are concerns for recurrence [56] based on the, limitations of mucosectomy with imbrication of the rectal wall alone, a recent study found that the Delorme procedure could be done with minimal morbidity, a short hospital stay, and a recurrence rate of only 14.5% at a mean of 31 months. The authors found that the recurrence rate was relatively low in patients under 50 (8%) and felt that this procedure may be reasonably be offered to younger patients [38].

Perineal proctosigmoidectomy, first described in 1889 by Mikulicz [57], has been modified and popularized by others [36, 58] (Fig. 5). It can be performed under regional anesthesia in either prone jackknife or lithotomy position. The redundant rectum and portion of sigmoid colon can be easily removed via the anal incision. Resection and anastomosis can be performed with sutures or surgical staplers. Addition of a posterior levator repair described by Prasad et al. re-creates the anatomic anorectal angle and may help patients gain fecal control postoperatively [58]. Minimal pain and little physiologic alteration are associated with this procedure, and most patients can be discharged from the hospital within 24–48 h. The recurrence rate of a perineal proctosigmoidectomy is related to the length of follow-up and ranges from 0% to 22% [36, 37, 39, 58–61].

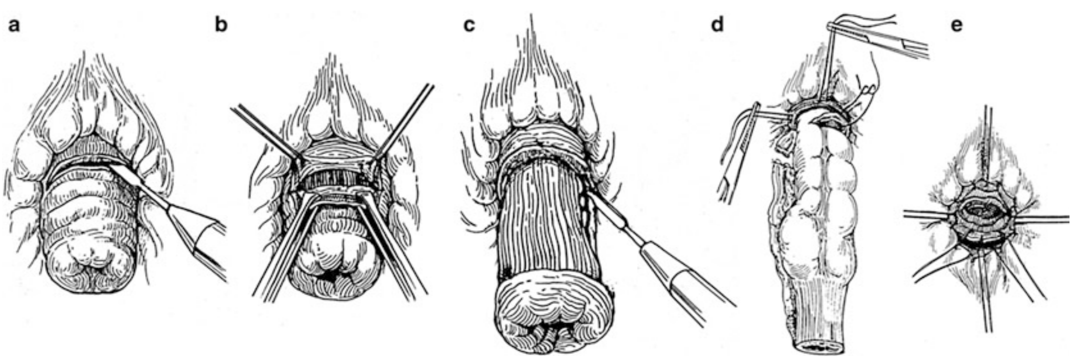

Fig. 5 Perineal proctosigmoidectomy (The ASCRS textbook of colon and rectal surgery, publisher Springer 2007, Chap. 47, Fig. 47.3)

Colonic Pseudo-obstruction

Colonic pseudo-obstruction (CPO) is relatively rare with an annual incidence estimated at 100 cases per 100,000 inpatient hospitalizations per year. It occurs in patients with a mean age of about 65 years but is rare in young patients [62]. It generally follows an inciting event of trauma, surgery, or other medical illness and results in colonic distention without mechanical obstruction [62]. Altered parasympathetic activity, dysregulation of stretch receptors, and compromised smooth muscle activity in the colonic wall have been implicated as causative factors [63–65] resulting in progressive dilation of the colonic wall. When the cecum reaches 10–12 cm in diameter, risk of ischemia and perforation increases, and decompressive treatment is generally recommended [66]. Without decompression, progression to necrosis and perforation may occur with tension increasing proportionally to the radius according to the law of Laplace. Medical therapy initially is directed at eliminating physiologic stress from the inciting event while maintaining decompression. Acetylcholinesterase inhibitors such as neostigmine can be used as treatment of the distention, but this is less effective than endoscopic therapy [67]. Although colectomy with ileostomy should be performed promptly when there is colonic necrosis, surgically treated patients have significantly more morbidity and mortality than medically managed cohorts. This is likely related to the fact that CPO often occurs in comorbid elderly patients who tolerate operative intervention poorly.

Stercoral Ulceration and Perforation

Stercoral perforation is caused by pressure necrosis from fecal mass effect on the wall of the colon and primarily affects the left colon and rectum. Though constipation is present as a chronic condition in a majority of patients suffering from the condition, it is a relatively uncommon but serious complication. Stercoral perforation accounts for just 3% of colonic perforations. The median age of patients suffering from this condition has been reported to be 62 years of age [68]. Diagnostic features include an antimesenteric round or ovoid defect in the colon more than 1 cm in size associated with fecalomas present protruding through the bowel wall. Microscopic findings include chronic inflammation and pressure necrosis or ulceration [68]. Use of NSAIDs, narcotics, sedative medications, and other medications such as aluminum hydroxide containing antacids has been reported in patients suffering these conditions [69]. Treatment should be preventative with osmotic laxatives to avoid fecal impaction, but when presenting with perforation, patients are treated with resection and diverting colostomy.

Clostridium difficile Infection

Clostridium difficile infection (CDI) is caused by a gram-negative, spore-forming bacteria that are frequently a normal intestinal luminal inhabitant. Alterations in gut microflora, typically through antibiotic use, can lead to clostridium overgrowth [70–72]. The production of two exotoxins (A and B) leads to the clinical illness associated with CDI. *Clostridium difficile* infection is an increasing source of community and healthcare-associated infection. It is estimated that there were 450,000 *Clostridium difficile* infections and 29,000 resultant deaths in 2011 alone [73], an incidence more than double that in 2000 [72, 74, 75]. Community-associated infections account for one-third of cases; healthcare-associated infections are evenly divided among community onset, nursing home onset, and hospital onset infections [74]. The mortality associated with CDI is 2.5–5 times greater than expected [72, 76]. Risk factors for CDI include advanced age, antibiotic use, hospitalization, or residence in a skilled nursing facility [70, 72, 75, 77]. CDI results in a significant healthcare and economic burden. The cost associated with this infection is estimated to range from $8900 to $30,000 for hospitalized patients [78]. This is an annual economic burden of $1.5–$3 billion per year [75, 79].

The diagnosis and treatment of CDI are outlined in a set of practice parameters published by the American Society of Colon and Rectal Surgeons [71] (Table 4). Diagnosis is based on

Table 4 Practice parameters for the management of *Clostridium difficile* infection (Adapted from Steele et al. [71]). (Table 4: summary of ASCRS practice parameters for management of *C. difficile* infection)

Recommendation	Evidence
In a patient in whom CDI is suspected, a disease-specific history should be performed, emphasizing symptoms, risk factors, underlying comorbidities, and signs of advanced disease	+++
Patients should be thoroughly evaluated to determine the severity of CDI, such as the presence of peritonitis and/or multisystem organ failure	+++
Endoscopic and radiologic evaluation may be performed to help determine the diagnosis and extent of disease	++
Diagnosis of CDI typically includes laboratory testing	+++++
Infection control measures should be implemented for hospitalized patients with *C. difficile* colitis	+++
Once CDI is diagnosed, the associated antibiotics should be stopped as soon as possible, as clinically indicated	+++
Metronidazole and vancomycin are acceptable first-line agents for an initial bout of CDI, with selection normally based on severity	++++
Surgery for *C. difficile* colitis should typically be reserved for patients with severe colitis that fails to improve with medical therapy, for generalized peritonitis, or for rare cases of colonic perforation	+++
Subtotal colectomy with ileostomy is typically the operative procedure of choice for *C. difficile* colitis	+++
Diverting loop ileostomy with colonic lavage may be an alternative to total abdominal colectomy for treatment of severe *C. difficile* colitis	+

+ Weak recommendation based on low-quality evidence
++ Weak recommendation based on moderate-quality evidence
+++ Strong recommendation based on low-quality evidence
++++ Strong recommendation based on moderate-quality evidence
+++++ Strong recommendation based on high-quality evidence
CDI Clostridium difficile infection

testing to document CDI in symptomatic patients. The gold standard is toxigenic culture of *C. difficile* organism followed by cell cytotoxicity assay [79, 80]. Unfortunately, this is time-consuming and difficult to perform. Nuclear acid amplification testing for *C. difficile* toxin genes using polymerase chain reaction or loop-mediated isothermal amplification now provides accurate, rapid diagnosis in symptomatic patients [70, 71, 79, 80]. However, the sensitivity of these assays can result in false positives in asymptomatic patients. Once the diagnosis is established, infection control measures should be implemented and inciting antibiotics discontinued. Treatment with oral metronidazole or oral vancomycin should be instituted. A 10–14-day treatment course will cure CDI in greater than 90% of patients with mild to moderate CDI [70–72, 77, 79]. Vancomycin is more effective in the treatment of severe disease with cure rates of 90% or greater [70–72, 77, 79]. Vancomycin can also be administered as an enema in patients unable to tolerate oral intake or as an adjunct.

Fulminant CDI does not have a clear definition, and only a small proportion of patients with CDI require operation [71]. In the absence of perforation, other indications for colectomy may include underlying inflammatory bowel disease, need for vasoactive agents, ongoing sepsis, and multisystem organ failure. Although there has been interest in lesser procedures, the procedure of choice remains total abdominal colectomy with ileostomy [71, 81, 82]. A large meta-analysis of 31 series documented a 30-day mortality rate of 40% following emergency colectomy [82]. This has prompted a reexamination of the traditional surgical approach. There has been interest in diverting loop ileostomy with distal lavage as an alternative to total abdominal colectomy [71, 83]. However, results of this initial trial have not been replicated. Recurrent CDI refractory to antibiotic therapy is effectively treated with fecal transplant.

In summary, CDI in elderly should be promptly treated with medical therapy outlined above. Of particular importance for frail patients, the decision to perform a colectomy and ileostomy is ideally made early, before sequelae of fulminant sepsis and multisystem organ failure have occurred. Limited reserve in this subgroup of patients makes them especially prone to morbidity and mortality.

Volvulus

Colonic volvulus occurs when an air-filled segment of colon twists about its mesentery. In the United States, colonic volvulus is an unusual cause of intestinal obstruction and accounts for approximately <5% of colonic obstructions [84]. In contrast, the rate of colonic volvulus as a source of large bowel obstruction is reported to be as high as 50% in Africa, the Middle East, and South America [85]. The high incidence of sigmoid volvulus has been attributed to the high-fiber diets in those regions. Chagas' disease, which causes megacolon, may play a role in the development of sigmoid volvulus, particularly in countries where the disease is common [86]. In North America, the incidence increases over the age of 50 years. Sigmoid volvulus and cecal volvulus account for the vast majority of cases of large bowel volvulus [84, 87, 88] [84]. Sigmoid volvulus (Fig. 6) is more common in elderly males, African Americans, nursing home residents, and patients with chronic constipation, diabetes, and neuropsychiatric disorders [84, 87, 88]. Patients with cecal volvulus tend to be younger and have a female predominance [84, 89]. The American Society of Colon and Rectal Surgeons has developed clinical practice guidelines that are summarized in Table 5 [89].

Fig. 6 Abdominal X-ray film of sigmoid volvulus, ASCRS Textbook of Colon and Rectal Surgery, 2011 [2]

Patients with volvulus usually present with abdominal distention, obstipation, and pain. Peritoneal irritation on physical examination, fever, or an elevated white blood cell count indicates ischemic or gangrenous bowel. Plain abdominal radiographs may show an inverted, U-shaped, air-filled bowel loop ("bent inner tube"), with a dense line running toward the point of torsion (Fig. 7a). This radiologic finding is highly suggestive of sigmoid volvulus. Conventional radiographs are less accurate in the diagnosis of cecal volvulus [88–90]. Although water-soluble contrast studies can assist with establishing the diagnosis (Fig. 7b), contrast-enhanced computed tomography is the diagnostic study of choice when plain radiographs do not establish the diagnosis [89]. When used in conjunction with plain radiographs, computed tomography is accurate in >90% cases in establishing the diagnosis of cecal and sigmoid volvulus [90, 91].

In patients with suspected sigmoid volvulus, if peritonitis is not present, sigmoidoscopy (flexible or rigid) should be performed to the point of obstruction. The volvulus can often be reduced by traversing the point of obstruction with the endoscope. A release of gas and liquid follows successful detorsion. A soft tube should be left in place traversing the area for several days to allow for decompression prior to definitive management. The success rate with this technique is good, and reduction of the volvulus can be expected with approximately 75% of attempts [89]. Endoscopy also allows for examination of the mucosa to inspect for ischemic changes. Evidence of mucosal ischemia, bloody discharge, or unsuccessful detorsion indicates strangulation and possibly gangrene. If the patient has signs of peritonitis or if gangrene is suspected, contrast study and tube decompression should not be attempted, and the patient should undergo emergency exploration. When cecal volvulus is suspected, attempts at endoscopic reduction are not recommended; these patients should undergo abdominal exploration and surgical treatment [88, 89].

Following endoscopic reduction, sigmoid colectomy is indicated to prevent recurrence.

Table 5 Summary of clinical practice guidelines for management of colonic volvulus (Adapted from Vogel et al. [89]). (Table 5: summary of ASCRS practice parameters for management of colonic volvulus)

Recommendation	Evidence
Initial evaluation should include a focused history and physical examination, complete blood cell count, serum electrolytes, and renal function assessment	+++
Diagnostic imaging is initial plain abdominal radiographs and often includes confirmatory imaging with contrast enema or CT imaging	+++
Rigid or flexible endoscopy should be performed to assess sigmoid colon viability and to allow initial detorsion and decompression of the colon	+++
Urgent sigmoid resection is generally indicated when endoscopic detorsion of the sigmoid colon is not possible and in cases of nonviable or perforated colon	+++
Sigmoid colectomy should be considered after resolution of the acute phase of sigmoid volvulus to prevent recurrent volvulus	+++
Nonresectional operative procedures, including detorsion alone, sigmoidoplasty, and mesosigmoidoplasty, are inferior to sigmoid colectomy for the prevention of recurrent volvulus	+
Endoscopic fixation of the sigmoid colon may be considered in select patients in whom operative interventions present a prohibitive risk	+
Attempts at endoscopic reduction of cecal volvulus are generally not recommended	+++
In patients with cecal volvulus, resection is required in patients with nonviable or perforated bowel. Resection is also appropriate first-line intervention for patients with viable bowel who are good operative candidates	+++
For cecal volvulus with viable bowel, nonresectional operative procedures may be a suitable alternative to resection	+

+ Weak recommendation based on low-quality evidence
++ Weak recommendation based on moderate-quality evidence
+++ Strong recommendation based on low- or very low-quality evidence
++++ Strong recommendation based on moderate-quality evidence
+++++ Strong recommendation based on high-quality evidence

Recurrence rates after endoscopic reduction have been reported to be as high as 50–60% [88, 92]. Once the volvulus is reduced, medically stable patients should undergo bowel preparation and elective resection. The choice of operation depends on the ability to detorse the sigmoid volvulus preoperatively, the adequacy of the bowel preparation, and the viability of the colon. Emergent of urgent operation due to presence of peritonitis, the inability to endoscopically reduce the sigmoid volvulus, or the presence of ischemia or gangrenous bowel is an indication for resection and colostomy (Hartmann procedure). In cases of cecal volvulus, resection has the lowest risk of recurrence. Unfortunately, there are little data on whether resection with ileostomy is superior to resection with anastomosis in the presence of nonviable bowel [89]. Nonresectional surgical therapy has been described for treatment of sigmoid and cecal volvulus. In general, results are inferior to resectional therapy with little improvement in postoperative death and complication rates [89]. Endoscopic fixation (percutaneous endoscopic colostomy (PEC)) is an option for treating patients with sigmoid volvulus who have prohibitive operative risks [89, 93].

Operative mortality rates for sigmoid volvulus depend upon the urgency of the operation, the presence of gangrene and peritonitis, and presence of comorbidities [84, 94]. For elective resection, death and complication rates of zero and 12%, respectively, have been reported [94]. In contrast, emergency operation was associated with a complication rate of 35% and death rate of 16%. Elderly patients receive particular benefit from minimally invasive approaches to colorectal diseases [95].

Fecal Incontinence

Fecal incontinence is a disabling problem in the elderly and in institutionalized patients [96]. A community-based prevalence study estimated that fecal incontinence affects 2.2% of the general population although the incidence and prevalence are probably underestimated [97]. More than 60% of patients who complain of fecal incontinence are

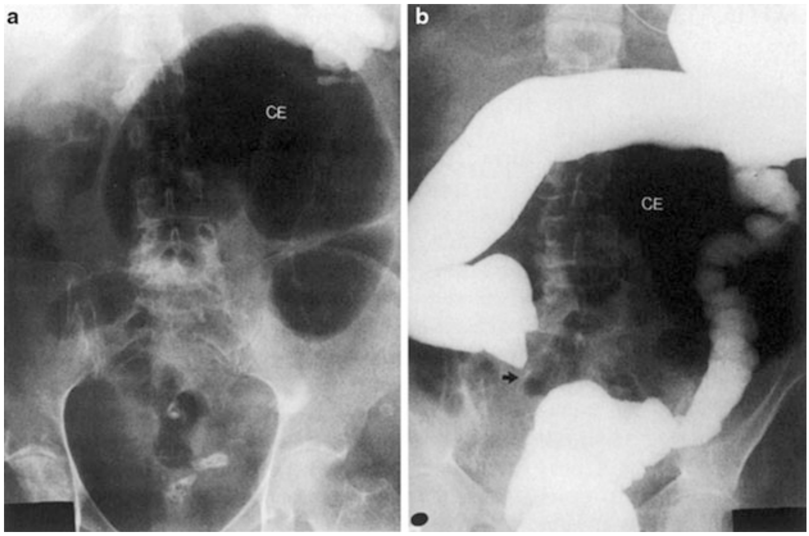

Fig. 7 (**a**) Cecal volvulus, plain radiograph, *CE* cecum. (**b**) Barium enema. *Arrow* indicates the point of obstruction, *CE* cecum [1]

women [97]. In community-based women older than 60, it is estimated that the prevalence varies from 12% to 33% depending on the definition used [98].

Incontinence may be neurogenic, mechanical, mixed, or secondary to other medical conditions. Anal sphincter injuries are the leading cause of mechanical incontinence and are most commonly the result of a midline episiotomy. Fecal incontinence may not occur immediately after the injury, but rather the presentation may be delayed for years. The majority of women with late-onset fecal incontinence have an anatomic sphincter defect [99]. Neurogenic incontinence may be due to central or peripheral denervation of the puborectalis muscle or external anal sphincter. Rectal prolapse or descending perineum syndrome may denervate the sphincter by a stretch injury to the pudendal nerve. Injury to the sphincter mechanism, traumatic or surgical, may lead to fecal incontinence immediately after the injury or during the ensuing years. Decreased anorectal sensation caused by radiotherapy or diabetes mellitus may lead to incontinence as well. Certain physiologic factors have been shown to occur with aging: decreased rectal tone and weakening of the anal sphincter mechanism [100, 101]. The anal sphincter may decrease in strength secondary to loss of muscle mass or neuropathy. These differences are more pronounced in elderly women. It may be due to weakening of connective tissues, possibly from decreased estrogen secretion. Physical limitations and poor general health are other predisposing factors that contribute to fecal incontinence [96, 97]. A common cause of fecal incontinence in the elderly, however, is fecal impaction with overflow incontinence [97]. Systemic diseases such as scleroderma, polymyositis, multiple sclerosis, and diabetes mellitus can be associated with fecal incontinence. Colorectal carcinoma, colonic ischemia, and inflammatory bowel disease may cause symptoms of fecal urgency, and incontinence may be a result of the patient's inability to respond quickly.

On initial evaluation, constipation with overflow incontinence must be ruled out by history and digital rectal examination. A complete colonic evaluation with colonoscopy or contrast enema should be done especially if the symptoms of fecal incontinence have a short history. The anal physiology laboratory can objectively evaluate the anal sphincter mechanism to determine the cause of fecal incontinence and direct treatment. Anal manometry, electromyography, and transrectal ultrasonography can help differentiate neurogenic from mechanical injury to the anal sphincter. Anal manometry assesses the rest and squeeze pressures generated by the anal sphincter. The sphincter length can be determined, and some systems can identify the specific quadrant involved in a sphincter defect. The minimal sensory rectal volume is useful for identifying patients with a very large rectum who do not sense the presence of a large bolus of fecal material in their rectum. Electromyography is used to evaluate the pudendal nerve terminal motor latency. The pudendal nerve innervates the external anal sphincter and the puborectalis muscle. Both muscles are involved in maintaining fecal continence; and denervation of these muscles, represented by prolonged pudendal nerve terminal motor latency, may cause neurogenic incontinence. Transrectal endoluminal ultrasonography has replaced needle electromyography as the preferred method for evaluating the anal sphincter for defects. Using this modality, the puborectalis muscle and the external and internal anal sphincters can be thoroughly evaluated for defects.

Initial treatment may be as simple as dietary alteration (avoidance of milk products and food with high fat content) and a bowel evacuation regimen (bulk-forming agents and glycerin suppositories) [101]. Biofeedback has had some success in patients but requires the understanding and cooperation of the patient [102]. Combined pharmacologic and physical therapy may be more beneficial when combined in appropriate patients [103]. Sacral nerve stimulation (SNS) which was FDA approved for use in the treatment of fecal incontinence in the United States in 2011 has become the most prevalent treatment strategy for fecal incontinence. Implanted electrodes are placed percutaneously adjacent to the S3 nerve root and a generator implanted after a test phase. Pooled data suggests that over three-fourths of patients have at least a 50% improvement in their fecal incontinence symptoms [104]. Application is not precluded by age alone, and though some studies show elderly patients derive a lower success from SNS [105], it is currently the best surgical option available. Anterior sphincter reconstructions with direct muscle repair have had success in the elderly population [106]. Older women undergoing pelvic floor surgery can expect similar results and outcomes as younger patients [32]. A diverting colostomy is rarely necessary for control of the fecal stream in the elderly population. If the rectum is severely damaged by radiation injury, a diverting colostomy is probably the best treatment option for severely incontinent patients.

Conclusion

Benign colorectal conditions are frequently encountered in elderly patients and are usually treatable. A good history and physical examination including office proctoscopy or anoscopy can usually point the clinician to the appropriate needed tests. Directed workup can confirm the diagnosis, and thoughtful intervention usually leads to marked symptom improvement. Though not all conditions can be corrected surgically, an accurate diagnosis with associated counseling directed at minimizing the impact on patient quality of life can ameliorate patient concern and suffering.

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Diverticulitis and Appendicitis in the Elderly

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Abstract

This chapter deals with diverticular disease and appendicitis in the elderly. Diverticular disease increases in incidence with age and also appears to present with diffuse peritonitis more frequently in the older population. Appendicitis in the elderly accounts for 5–10% of all appendicitis. There is good evidence that the elderly present more frequently in an atypical fashion with both of these diseases compared with their younger counterparts. Furthermore, emergency operations in the elderly are associated with higher mortality and morbidity rates. Appendicitis and diverticulitis have much in common and may share etiologies. High fiber diet and poor hygiene have protective effects on both diseases. Historically, both have been described as starting with local inflammation, having the potential to progress, untreated, to perforating disease. Most nonperforating diverticulitis and appendicitis do not evolve to perforating disease. The incidence of uncomplicated presentation in both diseases is increasing while perforating disease rates remain steady. Uncomplicated appendicitis can be treated nonoperatively with similar success rates as uncomplicated diverticulitis, with similar recurrence rates after nonoperative treatment as well. The major difference is that operative treatment of appendicitis carries significantly lower complication and mortality rates, thus leading surgeons to suggest operation more easily with appendix disease. This chapter attempts to explain these findings.

Keywords

Diverticulitis · Appendicitis · Nonoperative management · Abscess

Introduction

This chapter deals with diverticular disease and appendicitis in the elderly. Diverticular disease increases in incidence with age and also appears to present with diffuse peritonitis more frequently in old than in young patients. Acute appendicitis in the elderly accounts for 5–10% of all appendicitis, and old patients tend to present more frequently with advanced disease than do young groups. There is good evidence that the elderly present more frequently in an atypical fashion with both of these diseases compared with their younger counterparts. Abdominal pain may be absent or not greatly perceived in older patients. Physiologic responses to stress and infection are also blunted in the elderly. Older patients are burdened with more comorbid conditions and less mental and physical reserves compared with their younger counterparts. Furthermore, it is well known that emergency operations in the elderly are associated with significantly higher mortality and morbidity rates than similar operations on younger patients. Thus, old patients present atypically often with more advanced disease and have higher complication and death rates than the young. Interestingly, appendicitis and diverticulitis have much in common and may share etiologies. A low fiber diet has been implicated with both diseases. Poor hygiene seems to have a protective effect on both diseases. Elevated pressures have been implicated in both diseases, but without definitive studies showing cause. Historically, both have been described as starting with local inflammation, having the potential to progress, untreated, to perforating disease. Over time, many studies have concluded that most nonperforating diverticulitis as well as appendicitis will not evolve to perforating disease. The incidence of uncomplicated presentation in both diseases is increasing (presumably due to increased diagnosis of minimal to moderate disease by CT) while perforating disease rates remain steady. This fact suggests that prior to CT, a significant number of patients with both diseases resolved without medical help or were misdiagnosed and not treated with hospitalization. There is mounting evidence that uncomplicated appendicitis can be treated nonoperatively with similar success rates as uncomplicated diverticulitis. In fact, recurrence rates after nonoperative treatment are similar in both diseases as well. The major difference is that operative treatment of appendicitis carries significantly lower complication and mortality rates, thus leading surgeons to suggest operation more easily with appendix disease. This chapter attempts to explain these findings.

Diverticular Disease

Case Study

MS is a 90-year-old woman with no significant comorbidities who lives by herself at home. She was hospitalized five times over 4 months with unrelenting ischemic colitis of the descending colon diagnosed by multiple CT scans and with endoscopic confirmation. Despite antibiotics and enteral supplementation, she had slow and progressive weight loss and increasing inability to eat. Indication for operation was failure to progress with medical therapy and inability to eat. Her albumin was 2.0 and her prealbumin was 9 and her initial weight was 92 pounds. She underwent a left colectomy with primary anastomosis and protective loop ileostomy. Operative finding, confirmed by pathologic examination, was retroperotineal perforated diverticulitis with contained abscess. Her postoperative course was complicated by ileostomy dysfunction resulting in watery diarrhea which caused dehydration and electrolyte imbalance. She developed a lower extremity deep venous thrombosis and was started on Warfarin after a vena cava filter was placed. After a single 5 mg dose of Warfarin, her INR rose to 10 and she had a spontaneous intra-abdominal bleed requiring transfusion. She was unable to eat due to newly diagnosed, severe esophagitis. This was treated medically and a PEG was placed for enteral nutrition. She was ultimately discharged to an extended care facility 1 month after surgery. She maintained mental acuity throughout her illness and is anxiously awaiting the reversal of her ostomy.

Background

Etiology

Diverticular disease is the fifth most costly digestive disease in the United States [1]. The cause of diverticulosis is unknown. Colonic diverticula are mucosal (and submucosal) herniations through the muscle wall of the colon. The sigmoid colon is affected in 96% of patients, with this area being the only site of diverticulosis in two-thirds of patients [2]. Acute diverticulitis can occur anywhere in the colon and has been reported in the rectum [3, 4]. Diverticula occur at the points of weakness where the blood supply to the mucosa penetrates the bowel wall. Most commonly, they occur between the mesenteric and antimesenteric teniae coli. Less commonly, they occur between the two antimesenteric teniae. Strong epidemiologic evidence suggests that a low fiber diet has a substantial etiologic role in the development of diverticulosis [5–7]. In the United States, the incidence of diverticular disease has increased with decreasing fiber intake [8]. Vegetarians have been found to have a lower incidence of diverticular disease than nonvegetarians [9]. Other studies have confirmed these findings [10–14].

The current speculation is that a diet low in fiber decreases stool bulk. This in turn causes narrowing of the colonic lumen, prolongs intestinal transit time, and increases intraluminal pressures. Painter et al. [15] combined manometry and cineradiography and found that the increased intraluminal pressure may be due to simultaneous contractions of circular muscular bands causing occlusion of short segments of bowel. Contraction rings are thus formed in the sigmoid colon, which produces “segmentation” of these short segments of bowel. Contraction of the muscle wall of these sections can result in intraluminal pressures of 90 mg Hg or more. This pulsion pressure may lead to mucosal herniation along the weak points of the bowel wall, resulting in diverticula. Others have found that the contractile response to eating is exaggerated in people with diverticulosis [16]. Although consistent with the speculation that elevated pressures are particularly significant in combination with or potentiated by low fiber stools, experimentation with colomyotomy showed that decreased muscular activity did not affect intraluminal pressures [17]. Stool bulk may be related to intraluminal pressure only in that stool bulk increases the radius of the colon, thereby decreasing wall tension. Painter et al. suggested that a low fiber diet causes a narrower colonic lumen, which allows the colon to segment more efficiently, increasing the segmental intraluminal pressures [15]. Low fiber diets in rats have been shown to result in diverticulosis in 45% of subjects compared with only 9% in a group fed the highest fiber diet [18]. Further, a large, longitudinal study of males in the United States revealed a relatively straight line correlation between fiber intake and diverticular symptoms [19]. Exercise may also have a protective effect on the development of symptoms from diverticular disease [20].

Colonic dysmotility may contribute to diverticular disease. Abnormally slow wave patterns have been found in patients with symptomatic diverticular disease [21]. Furthermore, patients with symptomatic diverticular disease return to normal motility patterns with ingestion of bran, whereas those with asymptomatic diverticulosis have no change in motility with bran intake [22]. Others have disputed these findings [23]. Colonic transit times can be decreased by adding bran to the diet [24–26], and water-retaining fiber can decrease intraluminal pressure [27]. These findings lead to dietary modifications in attempts to alleviate diverticular symptoms.

One report [28] implicated localized ischemia as a causative factor for antimesenteric free perforation of the colon from diverticulitis. In patients with multiple bilateral pseudodiverticula arranged in a double row about the antimesenteric teniae, the vascular supply to the middle area of the antimesenteric wall is compromised. Careful histologic studies showed that free perforation associated with diverticulitis has the same histologic characteristics as ischemic bowel perforations. It is well known that microvascular changes predisposing to microvascular ischemia occur in the elderly. The more aggressive disease and higher perforation rates found in the elderly [29–32] may be related to this ischemic process. Perhaps this is the reason the elderly have higher free perforation rates when compared with younger patients.

Investigators have also touched on whether an intrinsic change in bowel wall composition is necessary for the development of diverticula. Young people with collagen vascular diseases such as Marfan’s syndrome [33] have been reported with diverticular disease. Several authors have also documented an association of diverticular disease with degenerative disorders such as varicose veins [34], hiatal hernias [35], and arthritis [36]. The most important element with regard to strength of the colon wall is collagen [37]. Collagen fibrils in the left colon become more numerous but smaller in width with age, and this difference is greater with diverticular disease [38]. Similarly, elastin fibrils increase in number but decrease in quality with age [39]. Pace [39] found that colon wall thickness increases with age and is thickest in the distal colon. These factors combined to result in decreased tensile strength and decreased expandability of the aging colon wall [40]. Electron microscopic examination reveals that there is a two times increase in elastin deposition and normal muscle cells in the muscle layer of diverticular diseased colon. The elastin is in a shortened form which may account for the thickened, foreshortened bowel typically found at surgery [41].

The distal sigmoid is the narrowest portion of the colon, and the distal sigmoid narrows with age [42]. The law of Laplace states that wall tension is directly proportional to the pressure times the diameter. Thus, as contractile pressures remain the same and the diameter is decreased, there is an increase in pressure delivered to the bowel wall. A simple example of Laplace's law is inflating a balloon. It is most difficult when there is no air in the balloon and becomes easier as the diameter increases. Similarly, increased pressures are required in the narrower distal sigmoid to propel stool. As the lumen narrows with age, higher pressures are required. This increased stress further damages the colon, causing decreased elasticity and more loss of tensile strength [40]. Comparison studies show that populations with a low incidence of diverticular disease have stronger, more elastic distal colons than industrialized populations [42] presumably due to years of more bulky stools keeping the lumen diameter large. Furthermore, with increasing wall tension pressures, there must be a concomitant decrease in microvascular perfusion [43], possibly adding further weight to the vascular theory of free perforation of diverticulitis [14]. The resulting increased intraluminal pressure causes long-term changes in the bowel wall, including decreased tensile strength, decreased diameter and vascular changes which predispose to diverticular disease and the more frequent perforation seen in the elderly.

Epidemiology

Diverticulosis is an entity particular to the dietary patterns of Western society. There are linear increases in size, number, incidence, and symptoms of diverticula with age [6, 44]. Diverticulae are commonly 5–10 mm in size and can occasionally be greater than 2 cm. Giant diverticula have been described. Diverticulosis occurs in 2–5% of patients less than age 40 and up to one-third of people over age 45. Two-thirds of people over age 85 have radiographic or pathologic evidence of diverticulosis [45]. Deckman and Cheskin [46] cited prevalence in the United States as high as 33% with similar figures in European countries. In comparison, the prevalence in populations with higher per capita fiber intake is much lower. Diverticulosis is uncommon in developing parts of Africa and Asia with rates as low as 1% in Korea [35]. Low incidences have also been found in other, similar populations [47–52].

Independent of age, prevalence is thought to be similar in men and women. However, in a large single institutional series by Rodkey and Welch [53], when sex and age were examined jointly, women over the age of 70 predominated over men by more than 3:1. The reverse was found in patients less than 50 years of age, with more than twice as many men affected as women. This ratio was also substantiated by Ouriel and Schwartz [54], who found a predominance of men in the under-40 age group.

Nonsteroidal anti-inflammatory drugs (NSAIDs) have also been linked to diverticular disease [55], and others have implicated NSAIDs as a potential cause of acute diverticulitis [56–58]. Steroids have been linked to diverticulitis as well. Steroids also mask symptoms of infection which may cause delays in diagnosis with resulting poor prognosis [59–61].

Pathogenesis

Diverticulitis is the inflammatory process that originates within colonic pseudodiverticula. The particular mechanisms of both the local and systemic infections have not been well characterized. It has been hypothesized that diverticulitis constitutes the same endpoint of localized luminal obstruction found with other intra-abdominal visceral inflammatory processes such as appendicitis and cholecystitis [62–64]. Obstruction of the neck of the diverticula, presumably with inspissated stool, creates a closed microenvironment characterized by fluid sequestration, stasis, and bacterial overgrowth. Deitch [65] showed that even in the absence of perforation, obstruction alone is sufficient for bacterial translocation across the intestinal barrier. As the diameter of the diverticulum expands to accommodate the increased intraluminal pressure venous, arterial pressures are overcome. This results in congestion, ischemic necrosis, and perforation. Others cannot find supporting pathologic evidence and suggest that perforation is likely the result of increased intraluminal pressure [46]. Activation of local and systemic inflammatory mediators, in combination with microscopic or macroscopic perforation and soiling of the peritoneum, leads to the clinical manifestations of the disease. The role of localized ischemia was discussed earlier [28].

Atypical, painful, or chronic diverticular disease is a difficult to describe entity. It is described as chronic, intermittent left lower abdominal pain, not usually associated with typical findings of acute inflammation. Motility patterns may be abnormal in this subset of patients [66]. Pain is usually chronic, intermittent, and not associated with acute symptoms. Narrow stools and other changes in bowel habits may result. Attacks may come and go. Symptoms may be confused with irritable bowel syndrome. The diagnosis is difficult, with barium enema showing only diverticulosis and possibly spasm of the sigmoid colon. CAT scan does not reveal acute inflammation and it does not respond to antibiotics or dietary modification. Endoscopic findings are generally nonspecific, although a tortuous colon may be found. Endoscopy may show edema or associated patchy colitis. Treatment is aimed at relieving symptoms. Bulk agents (psyllium seed) and a high fiber diet are usually helpful. Differentiating between irritable bowel syndrome and painful diverticular disease is difficult as symptoms of bloating, distention, and intermittent nonspecific abdominal pain are common. Fortunately, IBS and painful diverticular disease are treated similarly with high fiber diet and symptom control with moderate success. Uncommonly, sigmoid resection is required to produce relief. Appropriate patient selection is paramount in identifying who may respond to operative intervention and those who will not. When well chosen, sigmoid resection will relieve pain in up to 80% of patients [67].

Symptoms

The spectrum of disease produced by diverticula ranges from completely symptom-free to vascular collapse secondary to systemic sepsis from peritonitis. About 10–25% of patients with diverticulosis progress to diverticulitis [68, 69]. Most of these patients never come to surgical attention [68, 69]. A small number, estimated at fewer than 25% of those with diverticulitis, require inpatient management of their disease [70]. Complicated cases involving sepsis, obstruction, fistula formation, or peritonitis constitute approximately 40% of all those admitted. Older patients present more often with complicated disease. The elderly present with diffuse peritonitis up to twice as frequently as younger patients [29, 32].

Typically, patients with diverticulitis seek medical care owing to mild or moderate peritoneal irritation often accompanied by a change in bowel habits. Crampy left lower quadrant pain is also common. Approximately two-thirds of patients complain of constipation or diarrhea [71]. Other associated symptoms may include a palpable mass, abdominal distension, dysuria, excessive flatus, nausea, and vomiting. About 30–40% of patients have occult blood in their stool [2]. Fever and pain are the most consistent indicators of acute disease, occurring 45% of the time. Septic shock with diffuse peritonitis may be the presenting picture. With the presence of a redundant sigmoid colon, suprapubic or right lower quadrant pain may manifest. Occasionally, the diagnosis of appendicitis is the indication for surgical exploration when a redundant sigmoid colon with diverticulitis is found to be the culprit.

Considerable diagnostic overlap exists between diverticulitis and other acute abdominal processes. The spectrum of differential diagnoses range from relatively common urinary tract infections in the elderly to inflammatory bowel disease, colon cancer, closed loop obstruction, and ischemic bowel. These diagnoses and causes of abdominal pain must always be kept in mind during the initial evaluation. Symptoms of diverticular fistulas may lead to an accurate preoperative diagnosis. Pneumaturia and fecaluria are diagnostic of an enteric–vesicular fistula and in the appropriate patients are highly suggestive of a diverticular origin. Similarly, flatus or stool via the vagina leads to common bowel sources. Thigh abscesses, especially those with foul smelling anaerobic pus, may originate from a diverticular abscess with tracking along the psoas muscle onto the skin.

Many investigators have found atypical presentations of diverticular disease in the elderly [29, 72–76]. Wroblewski and Mikulowski [74] noted the absence of typical manifestation of peritonitis in the elderly to be associated with a poor outcome. They also found an absence of abdominal pain in half of their patients with peritonitis. Intra-abdominal abscesses are the most common cause of fever of unknown origin in the elderly [77]. Others noted that elderly patients with intra-abdominal infections have hypothermic temperatures more frequently than young patients. Similarly, old patients have less nausea, vomiting, diarrhea, and fever compared to the young [72]. Acute abdominal pain is more likely to require surgery in the elderly [78, 79]. France et al. [73] examined 12 elderly patients who died of diverticulitis: 75% did not have symptoms typical of their disease, 3 of the 12 did not have abdominal symptoms, and another's symptoms did not warrant further investigation. Generalized peritonitis occurs in up to one-half of old patients [29, 30]. Old patients require operations more frequently, have free perforation more commonly, and have higher mortality rates than young patients [29–32, 80]. Watters et al. [29] attempted to explain this difference. They found that the mean time from the onset of symptoms to hospitalization for old and young patients with generalized diverticular peritonitis was the same. Thus, old patients have peritonitis and free perforation more frequently than the young do, and it is not due to a delay in seeking medical care. This finding suggests that the severity of disease in the elderly is determined early in its course and is independent of the passage of time. Another possible explanation is that symptoms begin later in the course of the disease in the elderly. The former explanation further supports the theory that ischemia is the cause of the more frequent diffuse peritonitis found in the elderly.

Diagnosis

Diverticulitis is usually diagnosed based completely on clinical grounds. This presents a unique problem in the elderly because, as previously shown, they often present atypically and abdominal pain is minimal or absent. A history of known diverticula seen by barium enema or endoscopy often aids the clinician. However, it is unnecessary to have previous knowledge of diverticula in a particular patient, as more elderly patients have diverticula than do not [45]. Useful serologic and hematologic tests include a complete blood count, serum electrolytes, urinalysis, and in the case of suspected ischemic bowel, arterial blood gas measurement for acid base disturbances. WBC can be normal in almost one-half of older patients [81]. Physical examination usually reveals peritoneal irritation to some extent. Mild left lower quadrant tenderness to generalized peritonitis may be found. Rectal examination may reveal a pelvic abscess.

Several diagnostic modalities are helpful for establishing the diagnosis of diverticular disease and assessing the extent of inflammation. In preceding decades, contrast enema was the test of choice for diagnosis. Previous practice parameters of the American Society of Colon and Rectal Surgeons [82] cite a sensitivity of 94%, an accuracy of 77%, and a false-negative rate of 2–15% with water-soluble enemas. Contrast enemas in the setting of diverticular disease have been shown to be less reliable at identifying neoplastic growth compared with colonoscopy [83]. Radiographic findings include intramural or extramural sinus tracts, filling of the abscess cavity, or inferred extramural compression or spasm of the bowel lumen.

Ultrasonography may also provide useful information in the setting of suspected diverticular disease. Investigators have found it to be 84–98% sensitive [84–86]. Ultrasonography can detect abnormal segments of bowel, those with mural thickening, peridiverticular inflammation and abscess, and linear echogenic foci suggestive of fistulous tracts. Unfortunately, this technique is both operator-dependent and limited by the body habitus of the patient. Zielke et al. [86] found that surgical residents were able to accurately diagnose diverticulitis in 84% of patients, with a 16% false negative rate.

Computed tomography (CT) has emerged as the imaging modality of choice for evaluating suspected diverticulitis [87–92]. Though in some studies it is comparable to contrast enema, other investigators have found a clear advantage regarding diagnostic sensitivity and specificity [92]. Hulnick et al. [91] found that CT not only stages the extent of the inflammatory process more accurately, it better differentiates the varying gradations of pericolic inflammation. Furthermore, CT has the distinct advantage over a contrast enema because of its ability to identify both the intraluminal and extraluminal components of diverticular disease. It is also the diagnostic modality of choice for identifying colovesicle and colovaginal fistulas. Findings suggestive of diverticulitis include inflammation of the pericolic fat, thickening of the sigmoid mesocolon, pericolic phlegmon, visualization of colonic diverticula themselves, and thickening of the colonic wall. CT is helpful for demonstrating the manifestations of intra-abdominal abscess, particularly abscesses amenable to percutaneous drainage [88–92]. Despite these modalities, the diagnosis of diverticulitis can be obscure in the elderly [74].

Endoscopic evaluation is reserved until after the acute phase has resolved; it is used mainly to rule out carcinoma. CT colography is a new modality which noninvasively evaluates the contour of the colon lumen. It is especially helpful in cases where, due to stricture or obstruction, a colonoscope cannot traverse the diseased bowel. Colography can ensure the proximal bowel does not harbor unsuspected neoplastic lesions.

Management

Prevention of Symptoms

High fiber diet has been shown to decrease the formation of diverticula in rats [19]. Examination of population based per capita fiber intake reveals less diverticular disease with high average fiber intake [47, 50, 51]. High fiber intake in American males decreases the risk of diverticular symptoms. There is no evidence that increasing fiber intake can cause diverticulae to regress. It follows that high fiber diet should be suggested to decrease the chance of diverticular symptoms. There is no evidence to support the concept of avoiding food particles which can obstruct the neck of diverticulae. Accordingly, avoidance of seeds, nuts, popcorn, etc., has not been shown to cause acute disease. Most physicians suggest a high fiber diet with bulk-producing supplements (psyllium seed) for patients with asymptomatic diverticulosis [93–95]. Fiber has been shown to decrease intraluminal pressures and colonic transit time [27, 96–98]. It also decreases symptoms attributed to diverticular disease [99, 100]. Antispasmodic medications have not been shown to help.

Uncomplicated Diverticulitis

Most acute diverticulitis is treated by primary physicians on an outpatient basis. Those with only mild tenderness, no clinical peritoneal signs, and the ability to achieve satisfactory pain control and tolerate adequate fluids orally may be treated empirically on an outpatient basis [6]. Treatment consists of oral antibiotics covering anaerobic and gram-negative bacteria for at least 7 days and liquid diet until resolution of symptoms. Significant systemic signs of infection including high fever and leukocytosis suggest the need for hospital treatment. Resolution is common. There is no place for outpatient management in the setting of significant concurrent medical disease, immune compromise or in patients those with altered mental status or patients without appropriate supervision.

Immune-compromised patients have a more aggressive disease path, are more likely to present with perforation, and have higher morbidity and mortality rates [60, 101, 102]. Perkins et al. [101] found a 100% failure rate with conservative treatment of immune-compromised patients. Early surgical management is appropriate in this patient population. Due to the aggressive nature of diverticulitis, some have suggested elective sigmoid resection in patients with a single prior attack when they are candidates for organ transplantation with its attendant long-term immune suppression [102]. Patients on continuous peritoneal dialysis represent a special dilemma. CT scanning is usually nondiagnostic and delay in treatment results in poor outcomes. After treatment, very few are able to remain on peritoneal dialysis [103].

Patients who fail outpatient therapy or who present with significant systemic symptoms should be admitted to the hospital. Hospital treatment consists of complete bowel rest and parenteral broad-spectrum antibiotics to cover anaerobic and gram-negative bacteria. Triple-antibiotic or single-agent therapy are both effective. Nasogastric suction is required only with persistent vomiting or evidence of bowel obstruction. Laboratory evaluation includes a complete blood count and urinalysis. CT should be done to confirm the diagnosis, quantify the extent of inflammation, and identify possible complicated diverticular disease. Conservative treatment of acute uncomplicated diverticulitis leads to resolution of symptoms in 70–100% of cases [46, 47, 53, 87, 104]. Oral intake is resumed with disappearance of symptoms. Following hospital discharge, oral antibiotics should be continued for 7–10 days. With complete resolution of the inflammation, patients should have endoscopic or radiographic evaluation of their colon to rule out carcinoma, and they should be started on long-term fiber supplementation. Psyllium seed or hydrophilic colloids have been shown to reduce recurrence by up to 70% [100]. Old studies suggest that one-fourth of patients who recover from their first attack will have further attacks requiring hospitalization [2, 105]. One study with a median 5 year follow-up revealed less than 2% of patients reported more than mild symptoms [106].

Antibiotic treatment of acute uncomplicated diverticulitis is the standard of care. This is despite lack of controlled study. Recent studies questioned this. Chabok [107] conducted a prospective, randomized trial to evaluate whether antibiotics are necessary to treat hospitalized uncomplicated diverticulitis. CT scans were used to ensure diagnosis. Patients were randomized to receive antibiotics or only IV hydration. A small number of patients were placed on antibiotics due to increasing pain. There was no difference between groups regarding complications or surgical procedures. An equal number of patients from both groups were operated on during the follow-up period. There was no difference in hospital length of stay. A recent Cochrane Collaboration agrees with the conclusion that new evidence suggests that antibiotics have no effect on uncomplicated diverticulitis. The Collaboration suggests that more confirmation from future trials is required before clinical guidelines can be changed safely [108].

The goal of elective sigmoid resection is to reduce the potential for re-presentation with complicated disease requiring emergency colon surgery with its attendant increased complication and mortality rates. Emergent surgery often results in Hartmann's resection with temporary ostomy formation. Ostomies formed during emergency operations are not reversed in a significant minority of patients [109]. Over the last decade, there has been a major shift in decision making regarding elective resection and diverticulitis. The natural history of disease is not well known. Past practice parameters from the American College of Gastroenterology, American Society of Colon and Rectal Surgeons, and the European Association of Endoscopic Surgeons have all supported elective resection after 1–2 attacks, especially in younger patients [110–112].

A population based study of first event hospitalized diverticulitis patients [113] showed that only 5% of older patients who did not require emergency surgery at first presentation ultimately required emergent colectomy/colostomy formation. Some have estimated the risk of colostomy after one attack of mild diverticulitis at one in 2,000 patient years of follow-up [114]. A multicenter Kaiser Permanente study [115] followed 3,165 patients admitted with diverticulitis for a mean of 8.9 years. They found a 13.3% recurrence rate in patients treated nonoperatively, one quarter had re-recurrences. Old age was associated with a lower recurrence rate (12.2%). They also noted an increased risk of further attacks with each additional re-recurrence. They believe no patients had colostomies in this group.

These findings have led to a change in the tradition suggestion that patients undergo elective sigmoid resection after 1–3 documented attacks. The frequency and severity of attacks, crescendo attacks, and the medical comorbidities should be considered when deciding to suggest elective sigmoid resection. The number of attacks should not be a major factor in decisions regarding timing of surgery. Most patients with perforating diverticular disease present with such at their first attack [113–118]. As seen above, very few patients require colostomies after initial successful non-operative management. The number of attacks required to suggest elective resection is in dispute at this time. Salem [116] used a Markov model to evaluate the lifetime risk of death and colostomy as well as care costs and quality of life and elective resection for diverticulitis. They conclude that performing colectomy after a fourth attack in 50-year-old patients would result in 0.5% fewer deaths, 0.7% fewer colostomies, and save over $1,000.00 per patient. Using 35-year-old patients in the model resulted in 0.1% fewer deaths, 2% fewer colostomies, and over $5,400.00 saved per patient. Clearly, delaying elective resection appears beneficial to patients and the cost of health care. The severity of disease, as measured by CAT scan during the first attack, may be a predictor of aggressive disease and the future need for operative intervention [119].

Elective resection for diverticulitis results in acceptable results. Thorn et al. [120] followed 75 consecutive elective sigmoid resections for diverticulitis. They found 13% major perioperative complications. Eight percent had recurrent diverticulitis in the follow-up period. Two-thirds of patients classified their results as good or excellent. IBS type symptoms in the preoperative period predicted less successful outcomes. Elective resection after one attack in patients requiring long-term immunosuppression is appropriate to prevent future sepsis. Elective resection may be required if cancer cannot be ruled out [62].

Surgical Technique for Elective Sigmoid Resection

Elective sigmoid resection after resolution of the acute inflammation should include adequate mobilization of the proximal bowel to provide a tension-free anastomosis. The proximal bowel need not be devoid of diverticulosis, but the bowel must be soft, supple, and free of diverticular thickening. Resection should include all thickened, diseased bowel. Splenic flexure mobilization is occasionally required to achieve these goals. Distal resection must include removal of the entire sigmoid to the rectum to significantly reduce recurrent attacks [121]. No diverticula should be left distal to the anastomosis. The site of distal transection should be at the point where the teniae coli are lost, signifying the beginning of the intraperitoneal rectum.

Laparoscopic techniques have evolved significantly in recent years. Laparoscopy has been used in all types of diverticular resections and to drain abscesses drainage not amenable to percutaneous CAT approaches. Laparoscopic colectomy in the elderly is safe and effective as well [122]. Laparoscopy is safe with complicated diverticulitis as well [123]. Laparoscopic surgery is successful in treating fistula disease as well, with laparoscopic colovesicle and colovaginal fistula operations becoming more common [124, 125]. Many studies have showed that laparoscopic approach to this disease is safe and effective and may confer benefits to patients compared with traditional open surgery. Decreased complications, faster recovery of bowel function, and oral intake have been seen in older patients [126, 127]. Pulmonary function is better preserved and a host of stress measurements show less stress is imparted to laparoscopically treated patients compared with open techniques [128]. These benefits have been shown to be enhanced in older patients compared with younger ones [129]. Older patients also enjoy fewer cardiopulmonary complications with laparoscopy [130]. Laparoscopy has allowed more elderly patients to be discharged home rather than rehab facilities compared with open surgery [125, 131]. Finally, Senagore [132] showed a lower direct cost in elderly patients undergoing laparoscopic resection compared with those having open surgery. Practice Parameters published in 2006 by the American Society of Colon and Rectal Surgeons conclude: When a colectomy for diverticular disease is performed, a laparoscopic approach is appropriate in selected patients [133]. More recent Practice Parameters suggest “when expertise is available, the laparoscopic approach to elective colectomy for diverticulitis is preferred” [134].

Robotic Surgery for Diverticulitis

The application of robotic surgery to the treatment of colorectal pathologies has grown in recent years. Most published studies have examined outcomes for oncologic resections. However, there have been reports of its application in the surgical management of diverticulitis. Most of these studies have looked at the feasibility and safety of the technique. In one small series of 24 consecutive patients, Ragupathi [135] demonstrated robotic surgery for recurrent complicated and uncomplicated diverticular disease could be offered to patients with low complication rates and short hospital stay.

On the other hand, Elliott [136] compared their robotic experience in patients with diverticulitis complicated by fistula to the bladder, vagina, or skin with that of patients undergoing laparoscopic resection for the same indications. They found a higher conversion rate, diverting stoma need and longer length of stay in the robotic group, though the retrospective nature of the study and other confounding factors may have influenced these outcomes. Others have described its use in elective reversal of a colostomy after a Hartmann's resection [137]. Much work is still needed to determine whether the application of robotic surgery for the management of diverticular disease is equivalent or superior to the well-established laparoscopic approach. With the growing experience gained by surgeons using this platform, we anticipate its use in diverticular disease will continue to grow in the near future.

Emergent Surgery for Uncomplicated Diverticulitis

Up to one-third of all patients admitted to the hospital require urgent or emergent surgery [2, 45, 46, 56, 106]. Up to one-half of elderly patients present with generalized peritonitis requiring operative intervention [29]. Similarly, more old patients with diverticulitis require urgent or emergent operations compared with younger patients [30]. Most patients requiring urgent or emergent surgery are undergoing their initial episode of diverticulitis [116]. Hinchey et al. [138] described a grading system for acute diverticulitis. Stage I is confined pericolic abscess. Stage II is distant abscess. Stage III is generalized peritonitis caused by rupture of a pericolic or pelvic abscess, "noncommunicating" with bowel lumen because of obliteration of diverticular neck by inflammation. Stage IV is fecal peritonitis caused by free perforation of a diverticulum ("communication"). Emergent surgical treatment aims to relieve sepsis, remove the diseased bowel, minimize mortality and morbidity, and avoid stomas with their concomitant second operation to restore bowel continuity. Options include resection with proximal colostomy and closure of the distal end (Hartmann's procedure), resection with primary anastomosis, laparoscopy with lavage (dealt with later in this chapter), and diversion with drainage alone. The latter plays only a small role today, with only the most ill and unstable patients unable to tolerate removal of the infectious foci. Diversion alone leaves a column of undrained stool above the perforation that can further contribute to the septic process [139, 140].

Hartmann's procedure has been the standard of care for acute diverticulitis surgery for many decades. It consists of removing the affected bowel with proximal end colostomy and closure of distal rectosigmoid stump. Mobilization of the colon should begin in an unaffected area to facilitate entrance into normal planes of dissection. The retroperitoneal structures (ureters and gonadal vessels) can be swept dorsally, elevating the sigmoid colon. Ureteral catheters can be helpful in selected cases due to inflammation causing difficulty with normal anatomic planes [141].

Hartmann's procedure carries significant complication and mortality rates and requires another operation to reverse the colostomy [142]. This has led to the proposal of resection and primary anastomosis for acute noncomplicated disease [95, 135, 139]. Selection is important and should include minimal local sepsis and well-nourished patients. Adding on table lavage of the bowel is an option in patients with proximal solid stool [143]. Adequate diverticular resection requires removal of the distal sigmoid from the rectum when restoring bowel continuity after Hartmann's procedure. Removing the sigmoid from the rectum decreases recurrences of diverticular disease [121]. Furthermore, using the distal sigmoid instead of rectum for the anastomosis was found to be a risk factor in the development of postoperative colocutaneous fistulas [144].

Complicated Diverticular Disease

Complicating factors associated with diverticular disease include abscess formation, free perforation, fistula formation, obstruction, and bleeding. The presentation of complicated diverticular disease occurs in up to one-third of hospitalized patients [87] and more than 50% of the elderly [28]. Bleeding diverticular disease is discussed elsewhere in this text. The vast majority of perforating diverticulitis occurs during the first attack [145, 146]. The incidence of perforating diverticulitis may be increasing [146]. Complicated diverticulitis is associated with significant morbidity and mortality, and the need for operative intervention should be continually reassessed. Treatment of complicated diverticular disease requires accurate diagnosis and staging. The goal of treatment of complicated diverticular disease is to minimize morbidity and mortality, avoid ostomy formation and the number of subsequent operations. To achieve these goals, nonoperative techniques are used to convert complicated disease to medically manageable disease, thereby allowing future elective resection with primary anastomosis.

Hartmann's procedure is associated with high morbidity and mortality rates [141, 147, 148]. The rate of retained colostomy after Hartmann's operation ranges from 5% to 58% [141, 149]. A large review of Hartmann's procedure [109], where diverticulitis was the indication for almost 60% of operations, found a 14% mortality rate and more than 40% of colostomies were not reversed. In a related study [150], a higher than expected mortality rate was found in older patients undergoing colostomy reversal. And in these older patients, only 30% of colostomies created were reversed! Surgeons operating emergently on the elderly need to ensure proper placement and construction of these temporary ostomies, as many of them are permanent to the patient. Furthermore, colostomy closure is associated with significant complication and death rates, especially in the elderly [149]. Eisenstat [151] recorded a lower mortality rate for complicated diverticular disease treated with elective resection than that treated with staged surgical procedures. Avoiding a stoma with its concomitant second operation is a major goal of operative management for complicated diverticular disease. Accurate preoperative diagnosis is helpful, as up to 25% of patients explored for abscess or fistula have a perforated cancer [152].

Abscess formation is the most common complication of acute diverticulitis, occurring in 32–68% of complicated diverticular cases [88–90, 153]. A wide spectrum of presentations may result: small occult abscesses; scrotal, buttock, or thigh abscess; and sepsis due to a large abscess. Diagnosis is best made with CT [89, 154]. Treatment is aimed at relief of the sepsis and treatment of the diverticulitis. Small peri-colic abscesses or phlegmon may be managed conservatively with bowel rest and broad-spectrum intravenous antibiotics [134]. Elective, single-stage sigmoid resection with primary anastomosis can be done with resolution of symptoms. If symptoms worsen or are not alleviated, repeat CT scan with percutaneous drainage of the abscess should be considered. Exploration is reserved for patients whose abscesses are not amenable to percutaneous drainage or who fail conservative management. Primary anastomosis is possible if the proximal and distal bowel is healthy and the perforation is contained, and if a gentle preoperative mechanical preparation has been done [90, 149]. The patient's underlying medical diseases and acute physiologic status must obviously be considered.

Large abscesses, including more distant pelvic abscesses, and smaller ones that do not respond to conservative treatment should be referred quickly for possible percutaneous drainage under CT guidance [155]. Percutaneous drainage of diverticular abscesses is associated with a success rate of 62–100% [155–159]. Following placement of a drainage catheter and aspiration of the pus, repeat radiologic evaluation should be undertaken to assess not only resolution of the abscess cavity but to identify potential fistulous communications to the small or large bowel. In the setting of appropriate drainage, treatment should then progress as for uncomplicated diverticulitis. The catheter may be removed when the drainage stops or when complete collapse of the abscess cavity has been shown by sinography. At discharge, the catheter may also be left in place and removed during subsequent elective sigmoid resection [88]. The presence of a persistent colocutaneous fistula does not preclude elective resection with primary anastomosis [141]. Such a course of treatment allows complicated disease to be transformed nonoperatively to disease that responds to medical treatment, thereby avoiding emergent surgery with stoma formation. Subsequent elective sigmoid resection with primary anastomosis after resolution of inflammation (in about 6 weeks) becomes the only operative intervention required [159]. This has become the standard treatment for diverticulitis complicated by abscess formation.

Another clinical decision which is evolving concerns what to do with a patient who has successfully had a diverticular abscess nonoperatively drained by interventional radiology. Past standard of care required elective sigmoid resection due to small studies. Stabile et al. [88] followed three patients who refused surgery after catheter drainage for large abscesses. One required resection after a repeat diverticulitis attack 7 months later. The second required permanent catheter drainage for recurrent and persistent abscesses. The third died in hospital of sepsis. Ambrosetti [32] suggested that occasional small mesocolic abscesses can be managed without operation, but they stated that pelvic and abdominal abscesses behave aggressively and require surgical treatment. Kaiser [160] found that 41% of patients managed with percutaneous abscess drainage without surgery developed severe sepsis. Conversely, Broderick-Villa [115] found no increase in recurrence rates after abscesses were percutaneously drained and treated without elective operation compared with uncomplicated diverticulitis followed nonoperatively. Others suggest a conservative approach after drainage is appropriate as well [161]. Another study compared uncomplicated diverticulitis and diverticulitis with abscess formation. There was a high initial success rate of nonoperative treatment in both complicated and uncomplicated cases: 92% versus 97%. Readmission occurred more frequently in complicated disease during the first year: 27% versus 11%. Similarly, surgery was performed twice as often in patients who had abscesses: 48% versus 19% at 2 years. Interestingly, more than one-half of abscess patients avoided surgery, with the most common indication for operation being recurrent disease, not complication [162]. Gaetner [163] followed 32 patients who did not have operations, with a mean abscess size of 4.2 cm. Recurrence was 40%, with increasing recurrence rate if the abscess was greater than 5 cm. Devaraj [164] followed 185 abscesses. Sixty percent had recurrent diverticulitis with 40% of these having multiple attacks. One quarter of these patients required urgent surgery and almost one-half re-presented with higher Hinchey scores. They also noticed that larger abscess increased risk of recurrence. With such conflicting data, expectant, nonoperative management has been supported, but future research is needed to better determine the resection criteria in this group of patients [134].

Pelvic abscesses can be drained transrectally and transvaginally in women as well. These techniques have been replaced by CT-guided drainage but should remain in the surgeon's arsenal. If large abscesses cannot be drained adequately or if sepsis does not resolve, operative exploration is required. Gentle preoperative mechanical bowel preparation can be performed in well-selected patients; and with normal proximal and distal bowel, resection and primary anastomosis can be performed safely [149]. The use of Hartmann's procedure is reserved for most other patients. One should remember that restoring bowel continuity after Hartmann's procedure has high morbidity and mortality rates, and a large percentage of "temporary" stomas become permanent [139, 148–150].

Perforating diverticular disease is the most virulent form of this disease. The vast majority of patients with perforating diverticulitis have no previous history of diverticulitis [114–116]. It is important to consider these patients separately from other complicated diverticulitis patients. Perforating diverticulitis has higher operative mortality (12–21% vs. 0–2.6%) compared with nonperforating complicated diverticulitis [53, 118]. Free perforation of diverticulitis generally presents as acute sepsis or an acute abdominal crisis and some degree of shock. It occurs in approximately 10% of complicated cases [88]. More importantly, up to 50% of elderly patients present with diffuse peritonitis [29]. Rapid hydration with correction of electrolyte abnormalities is necessary. Broad-spectrum antibiotics are administered preoperatively. Immunocompromised patients may not exhibit classic abdominal findings. Physical examination and CT scans generally yield the diagnosis. A large number of old patients with peritonitis lack abdominal pain as a finding [74] so a high index of suspicion is required when treating them. Emergent exploration with aspiration of pus, cleansing of fecal material, resection of the diseased bowel, and proximal end colostomy with oversewing of the distal stump (Hartmann's operation) are performed [165–167]. Only rarely are patients so sick that diversion and drainage without resection is appropriate [166, 168]. In fact, one study [139] found higher mortality among patients treated with diversion only compared to those who underwent resection, despite more steroid use and fecal peritonitis in the resection group. The mortality rate associated with fecal peritonitis is as high as 35% [139, 166, 168].

A few important technical aspects of resection must be emphasized. When possible, care should be taken in the face of peritonitis to avoid opening noninfected tissue planes such as the presacral space and the splenic flexure area. These areas are known to invite abscess formation and are best left intact and free from contamination by the infectious process. Ureteral catheters may be employed, as the inflammatory process may obliterate the normal tissue planes and allow the ureters to be drawn into the inflammatory process [169]. The reader is referred to standard surgical textbooks for other technical aspects of sigmoid resection.

Laparoscopic Lavage

As previously discussed in this chapter, resection with or without primary anastomosis is the most common emergent operation performed for acute diverticulitis [170]. There are numerous reasons to avoid ostomy formation. Up to 35% of patients who undergo a Hartmann's procedure for diverticulitis do not have their ostomies reversed [171]. Moreover, colostomy reversal is associated with significant morbidity, including an anastomotic leak rate of 2–20%, and mortality of up to 5% [172]. Because of these problems, some authors have challenged the need for resection in patients with purulent peritonitis resulting from acute diverticulitis [173]. This originates from the observation that during surgery, the perforation is often noted to have self-sealed. Aspiration of the contamination followed by thorough laparoscopic washout of the peritoneal cavity may be all that is needed, thus negating need for sigmoid resection. This would avoid the risks of major laparotomy, stoma creation, and its subsequent reversal.

The laparoscopic lavage technique involves initial exploration to exclude fecal peritonitis, as this typically precludes good outcomes with its use. Most surgeons prefer to leave the omentum over the perforation intact. A four quadrant washout takes place, with thorough irrigation until the effluent is clear. This usually requires somewhere from 10 to 20 L of saline. Some surgeons prefer to suture the perforation closed if identified and others perform a pneumatic test, though these are not standard practice. Most use one or two intra-abdominal drains, with at least one placed in the pelvis. Antibiotics are generally administered for 7 days.

O'Sullivan [173] first published in 1996 a series of eight patients diagnosed at laparoscopy with generalized peritonitis due to acute diverticular disease, all treated successfully with laparoscopic lavage only. Interestingly, the first patient on this series had developed an arrhythmia intraoperatively, which prompted laparoscopic lavage to control the sepsis in expedited fashion, and later observation that recovery was possible without resection. Multiple studies have tried to determine what patient characteristics make this approach successful. The same authors published the results of a prospective multi-institutional series in 2008 [174]. All patients had evidence of peritonitis on exam and radiologic evidence of colonic perforation on CT or CXR. A total of 92 patients treated with laparoscopic lavage were followed for an average of 36 months (12–84 months). Two patients developed pelvic abscesses requiring percutaneous drainage and one returned to the operating room for Hartmann's resection. Mortality was 3% (3/92) and morbidity very low at 4%. However, most of the attention the study generated was based on the fact that no elective resection was needed in any of these patients in the follow-up period.

In the next few years, data became available from numerous nonrandomized studies, mostly retrospective and nonconsecutive. A systematic review from 2010 that included 13 of these publications concluded that laparoscopic peritoneal lavage for patients with peritonitis caused by perforated diverticulitis was an effective and safe treatment that may be preferable to colonic resection [175]. They found a mean hospital stay of 8.5 days (based on data from 11 articles). Mortality was 1.7%, morbidity 10.4%, and stoma rate 1.7%. Failure to control the acute episode was 4.3%. Thirty-eight percent of patients underwent delayed elective resection. There appeared to be a general consensus, from the data available, that laparoscopic peritoneal lavage should not be used for patients with Hinchey grade IV diverticulitis. Other patients who may not benefit from laparoscopic peritoneal lavage included those with pelvic abscess formation.

Subsequently, many European countries provided higher quality data that has allowed for better decision making. In the Netherlands, patients participating in the **LADIES** trial were randomized to laparoscopic lavage versus resection [176]. Preliminary data showed that in patients in which sepsis was not controlled (7/38), the mortality was dangerously high at 42% (3/7), emphasizing the importance of patient selection.

The **DILALA** trial was another prospective randomized multi-institutional trial involving nine surgical departments in Sweden and Denmark between 2010 and 2014 [177]. Here, patients underwent initial laparoscopy to confirm Hinchey III purulent peritonitis, and then were randomized to either laparoscopic lavage versus open Hartmann's resection. Of the 139 patients who underwent diagnostic laparoscopy, 83 Hinchey III patients were randomized. Laparoscopic lavage appeared feasible and safe in the short term. The study drew criticism due to potential bias in patient selection, given the large amount of patients eligible but not included (52 patients with Hinchey III diverticulitis not included). In a 12 month follow-up published in 2016, only three patients in the laparoscopic group had stoma formation [178].

A multicenter prospective randomized trial with 21 participating institutions in Norway and Sweden took place between 2010 and 2014 (**SCANDIV**) [179]. Laparoscopic lavage was performed in 101 patients (no disruption of adhesions, 2 pelvic drains) and 98 underwent colon resection (either Hartmann's resection or primary resection with anastomosis). Although no difference in mortality was observed, laparoscopic lavage did not reduce severe postoperative complications compared to resection. Moreover, the reoperation rate was significantly higher in the laparoscopic lavage group, including both the need for surgery and percutaneous drainage procedures. In addition, four cancers were missed in the laparoscopic lavage arm. **SCANDIV** did not confirm the findings from previous trials.

Similar to **SCANDIV**, Vennis did not demonstrate superiority of laparoscopic lavage for Hinchey III diverticulitis [180]. This prospective randomized trial (**LOLA**) with 34 participating teaching hospitals throughout Belgium, Italy, and the Netherlands had to be closed early due to an increased event rate in the lavage group. Major morbidity or mortality was higher in the lavage group, 16/46 (35%), when compared to the resection group, 7/40 (18%). However, laparoscopic lavage was successful in 52% of patients in long term. Three quarters of the lavage group never had a stoma and at 1 year, 78% were stoma free compared with 71% in the sigmoidectomy group.

Laparoscopic lavage for Hinchey III diverticulitis certainly allows some patients to be treated successfully without stoma (and perhaps never have resection). Patient selection is important and still not adequately determined. In addition to the risk of persistent intra-abdominal sepsis, there is a potential increase in early re-interventions. The long-term fate of the unresected sigmoid colon is also not adequately resolved at this time. All patients who retain their sigmoid colons require colonoscopy to exclude malignancy. In an attempt to answer some of these questions, the **LapLAND** trial is underway in Ireland (Laparoscopic Lavage for Acute Non-faeculant Diverticulitis) [181]. This will be a multi-institutional randomized controlled trial, with a primary endpoint directed at operative and in-hospital mortality and secondary endpoints addressing in-hospital and post-discharge morbidity, rates of stoma formation, and rates of re-presentation with diverticulitis with or without perforation.

Fistula formation occurs in approximately 2% of diverticulitis cases but accounts for up to 22% of patients requiring surgery [149, 166, 182, 183]. Multiple fistulas are uncommon [183]. Fistulas develop when inflammation or abscesses develop in close proximity to adjacent organs. The inflammatory process invades the adjacent normal organs and causes decompression, which spontaneously converts the acute complicated infectious process to controlled, drained, simple diverticulitis. It is diagnosed often on clinical grounds, after the acute inflammation has resolved. Symptoms are usually related to the invaded organ. Diagnostic tests are used to rule out cancer and other diagnoses. Expensive, complex testing is often unnecessary. In general, single-stage resection with primary anastomosis can be performed as the acute inflammation is usually absent.

The bladder is affected most commonly [184, 185]. Symptoms include pneumaturia and fecaluria. Urosepsis can also occur. Diagnosis is made most commonly by the patient's history. CT scan is most accurate for diagnosis, showing air in the un-instrumented bladder and inflammation of the sigmoid colon and dome of the bladder [166]. Contrast enema or endoscopic evaluation is required to rule out colon cancer. Cystoscopy may be performed to rule out a neoplastic process originating in the bladder. In many patients the fistula cannot be demonstrated. Elective sigmoid resection with primary anastomosis is curative [184]. The fistula is pinched off the bladder. A small bladder defect is best treated by Foley catheter drainage for 7–10 days. Large defects should be closed in two layers with absorbable suture and drained by Foley catheter for a similar length of time. Bladder resection should be reserved for malignant disease [185].

Colovaginal fistulas occur most commonly in women who have had a hysterectomy. Diagnosis is simply made by the history, including flatus or stool per vagina. It is confirmed by transvaginal and transanal endoscopy. Air may be heard exiting from the vagina during sigmoidoscopy. Contrast enema or endoscopic evaluation of the colon is required to rule out neoplastic and inflammatory bowel disorders. Patients generally are not septic at the time of presentation and may undergo elective sigmoid resection with primary anastomosis. The vagina can be left open for drainage or may be closed with absorbable sutures and omentum interposed between the vagina and the anastomosis. Other organs, including the uterus, may be involved with the fistulous process. Hysterectomy may be required if the uterus is involved with the infectious process or if a neoplastic process is suspected [186]. Spontaneous colocutaneous fistulization is uncommon and can be treated with resection and primary anastomosis if sepsis is controlled.

Obstruction complicating diverticulitis occurs uncommonly [187]. Repeated episodes of edema, spasm, and inflammation cause a chronically strictured bowel lumen to become narrowed. Acute inflammation can then complete the luminal obstruction. Gentle water-soluble enema or endoscopy by a skilled endoscopist with minimal air insufflation can confirm the diagnosis and exclude a neoplasm. With proper diagnosis and treatment, the inflammation usually resolves and the obstruction abates. This allows it to be treated as uncomplicated diverticulitis with preoperative bowel preparation followed by elective resection and primary anastomosis after complete resolution of inflammation. Emergency operation for obstruction due to diverticulitis generally requires removing the diseased bowel with creation of an end colostomy. The unprepared and dilated proximal bowel often precludes safe primary anastomosis. On-table lavage has been used more frequently in selected cases to allow primary anastomosis [188]. Colonic obstruction due to narrowing from chronic diverticular disease should be treated as malignant obstruction, usually with Hartmann's procedure.

Right-Sided Diverticulitis

Right-sided diverticulitis has a different etiology and pathophysiology and affects a different patient population group compared with left-sided disease. Right-sided diverticula are true diverticula, with all layers of the bowel wall involved with the out pouching. They most commonly affect Far Eastern populations. Presentation mimics appendicitis with right-sided pain and infectious systems. Preoperative diagnosis is uncommon. X-ray findings often suggest neoplastic diseases. Nonoperative treatment is usually effective if accurate diagnosis is made before surgery. Not infrequently, the diagnosis is in doubt at time of operation and right colon resection is performed with a presumed diagnosis of tumor. Resection, diverticulectomy, and inversion of the diverticulum have been reported.

In conclusion, diverticulitis is common in the elderly. Symptoms may be avoided with a high fiber diet and fiber (psyllium) supplement intake. Older patients frequently present atypically and are difficult to accurately diagnose. Diverticulitis appears to be a more virulent disease at initial presentation in the elderly. More than one-half of patients require emergent operation with many having ostomy formation. Ostomies are commonly permanent in these old patients. Goals of treatment include avoidance of ostomy formation and conversion of surgical intervention from emergency to elective, thus decreasing morbidity and mortality. CAT drainage of abscesses allow for safer, elective resection. Laparoscopic lavage may be helpful as well. Most patients who avoid surgery at initial presentation can be managed without subsequent operation. Laparoscopic approaches allow for decreased morbidity, mortality, lower hospital stays, and more frequent discharge to home, and these advantages are more pronounced in the elderly.

Appendicitis

Case Study

JM is an 86-year-old man who presented with urospesis. He lives alone at home and has moderate cardiac disease. CT scan revealed a right pelvic phlegmon. He responded to intravenous antibiotics. He was discharged with the plan of elective laparoscopic appendectomy in the near future. This was done after preoperative colonoscopy was unremarkable. He recovered and was able to be discharged home. Pathology revealed a small carcinoid tumor which had favorable characteristics and was removed completely. No further therapy was suggested.

Many investigators have tried to assign an immune function to the appendix, as it does secrete immunoglobins, but the appendix is an organ whose function is unknown. Certainly, normal life results after its removal. Inflammation and neoplastic transformation are by far the most common afflictions that affect the human appendix. Infectious diseases (typhoid and tuberculosis), regional enteritis, and congenital defects of the appendix are beyond the scope of this chapter. Similarly, neoplasms of the appendix are not addressed. Appendectomy is one of the most common operations performed, with more than 500,000 appendices removed annually in the United States; 5–10% of acute appendicitis occurs in the elderly. Old patients delay presentation, present atypically, and suffer delay in diagnosis and treatment more often than young patients. Perforation is found more frequently in the elderly. Higher mortality rates and prolonged hospital stays result. The following section attempts to explain these findings.

Background

Etiology

Obstruction of the lumen of the appendix has been thought of as the predominant cause of appendicitis, with fecaliths a common cause of the obstruction. After the lumen is obstructed a closed microenvironment is produced, which allows fluid sequestration, stasis, distension, and bacterial overgrowth. Mucosal secretion and bacterial multiplication increase the distension and intraluminal pressure. As the diameter of the lumen expands to accommodate the increased pressure, venous and then arterial pressures are overcome. Ischemia, necrosis, bacterial translocation, and appendiceal perforation result. Interestingly, humans are one of the few animals able to secrete fluid into the lumen of the appendix at pressures high enough to produce necrosis and perforation [189].

Nonperforating appendicitis may have a different pathophysiology compared with perforating appendicitis. Rivera-Chavez [190] suggests that if infection is the major cause of acute appendicitis, isn't it logical to treat it with antibiotics. Most uncomplicated appendicitis resolves with antibiotics alone. If obstruction causes acute appendicitis, then it would be logical to conclude that untreated patients should routinely progress to perforation. This is clearly not the case. Complicated appendicitis was found to occur at similar rates despite varying time to surgery of greater than 12 h [191]. Arnbjornsson [192] measured the intraluminal pressure in patients with acute appendicitis. It was normal in 14/16 with phlegmonous appendicitis and elevated in all three patients with gangrenous appendicitis. They also suggested that enteric bacteria play an important role in pathogenesis of acute appendicitis and obstruction may play a role in perforation. Further an older large Swedish study [193] showed perforated disease occurred at the same rate over 20 years, and was independent of age, while nonperforating disease decreased over the length of the study and was age dependent. More recent study has found a reversal in this decreasing rate of nonperforating appendicitis when CT scanning became more available, again with stable perforating rates [194]. It follows that some patients with nonperforating appendicitis in the pre-CT era resolved without being operated upon, while their more current cohorts are now having an operation due to more accurate CT diagnosing. An autopsy study found about one-third of cadavers showed a diseased appendix [195]. Perforated disease produces significant symptoms which lead virtually all patients to seek medical care. Nonperforating appendicitis produces a varying severity of symptoms, combined with other factors including gender and age, which combine to lead a majority, but not all patients to seek formal medical care or come to operation.

Perforation may occur due to vascular compromise, causing necrosis, usually on an antimesenteric border. There are thought to be many differences in the elderly appendix that predispose it to obstruction and perforation. The appendiceal lumen is small or obliterated, and the blood supply is decreased, predisposing to necrosis; the mucosa is thinned, and there is fatty infiltration of the wall [196]. These changes may lead to increased rupture rates with decreased pressures, thus altering the natural history of appendicitis in the elderly. NSAIDs have been implicated in appendicitis as well. Campbell and DeBeaux [197] found that 37% of patients over the age of 50, with the diagnosis of acute appendicitis, were on NSAIDs compared with only 11% of a similar age group admitted with other emergencies.

Epidemiology

Appendicitis is the most common acute surgical condition of the abdomen. Six to eight percent of the population will suffer from acute appendicitis in their lifetime [198–200]. Life-table analysis estimates that 12% of males and 23% of females have their appendixes surgically removed [199]. Acute appendicitis occurs at all ages but is most frequent during the teenage year [199, 201]. This age peak is thought to result from the peak in lymph tissue in the appendix during these years. The extra lymph tissue presumably narrows the lumen, predisposing it to obstruction and the resulting appendicitis. Males are more commonly affected in young ages, but during later adult life the male/female ratio equals out [202]. Five to ten percent of all acute appendicitis occurs in the elderly [198, 201, 203, 204], and in fact the incidence of acute appendicitis in the elderly is increasing [196, 202, 203]. It may be due to longer life-spans, as Thorbjarnarson and Loehr [196] found that old patients accounted for only 1% of appendicitis between 1932 and 1937, whereas this percentage increased to 6–8% after 1957. Altogether, 1 of 35 women and 1 of 50 men over age 50 years develop acute appendicitis [200]. Furthermore, appendicitis accounted for 2.5–5.0% of all acute abdominal disease in patients over 60–70 years of age [74, 204].

Acute appendicitis is the third most common cause of abdominal pain in the elderly after gallbladder disease and small bowel obstruction [205, 206]. It is the leading source of intra-abdominal abscess, which in turn is the most common cause of fever of unknown origin in the elderly [77]. About 33–50% of the mortality due to acute appendicitis occurs in the elderly [198, 199, 207]. Lowered immune responses to foreign antigens and decreased production of lymphocytes with advancing age limit the older patients' ability to wall off peritoneal inflammation and fight overall infectious events [208, 209]. It has been postulated that changes occur in the appendix as we age, including atrophy of the intraluminal lymphoid tissue and thinning of the appendiceal wall, which render the appendix more susceptible to inflammation. Atherosclerosis diminishes the blood supply narrowing the lumen. Small changes in intraluminal pressure can produce rapid ischemia, gangrene, and perforation at rates much quicker in older persons than the young [210].

Symptoms and Diagnosis

Abdominal pain, fever, and leukocytosis are the hallmarks of acute appendicitis. Distension of the obstructed appendix stimulates visceral afferent nerve fibers, producing vague, dull, mid-abdominal pain. Pain classically begins in the periumbilical area and migrates to the right lower quadrant within hours [189, 211]. This pain is peritoneal in origin and as such is constant and increases with time. Anorexia is common. Vomiting occurs up to 75% of the time. Protracted vomiting and diarrhea should lead the clinician away from the diagnosis. There are many variations in presentation.

Physical examination reveals the site of peritoneal inflammation. Usually tenderness is found at McBurney's point. Rovsing's sign (pain referred to the right lower quadrant with palpation of the left side) indicates localized peritoneal irritation. The appendix may be found anywhere in the abdomen and thus can cause pain during psoas muscle stretch, obturator muscle stretch, rectal examination, or palpation of any abdominal site [211]. Continued irritation results in rebound and referred peritoneal irritation. Frank peritonitis can ultimately result with perforation. Elevated core temperature is usually not more than 39 °C. The white blood cell (WBC) count is generally between 10,000 and 18,000/mm^3 with a left shift [189]. Higher or lower counts and extreme left shifts are indications of diffuse peritonitis. Acute-phase reactants are being examined in an attempt to increase the accuracy of the preoperative diagnosis. Urinalysis should be done but may be abnormal if the appendix is adjacent to the bladder or ureter.

The presentation and difficulty with diagnosis of acute appendicitis in the elderly deserves special consideration. Most importantly, older patients more frequently delay seeking medical attention for a variety of reasons: difficulty leaving home, fear of hospitalization, decreased ability to appreciate or express symptoms. An elderly patient with a perforated appendicitis who was incorrectly treated for alcohol withdrawal for 5 days prior to being accurately diagnosed has been reported [212]. Burns et al. [213] found that 20% of older patients with acute appendicitis had WBC counts less than 10,000/mm^3 and neutrophil counts less than 75%. Lau et al. [214] found only 43% of old patients with simple appendicitis to have elevated WBC counts. Thorbjarnarson and Loehr [196] recorded an average duration of symptoms prior to admission in patients over age 60 to be 2.5 days. Horattas [215] found that one-third of patients over 60 years of age waited more than 48 h from onset of symptoms before presenting to the hospital. Fewer than two-thirds had “typical” right lower quadrant pain, and one-half had a temperature <37.6 °C. Similarly, Smithy et al. [216] found that only 55% of patients over age 80 had right lower quadrant pain, and 18% did not have abdominal pain. They also noted that only 1 of 13 patients had “typical” periumbilical pain localizing in the right lower quadrant. They hypothesized that because of the smaller lumen diameter of the elderly appendix, which requires less pressure to produce rupture, the old patient does not necessarily experience the prodromal phase of appendicitis with the generalized abdominal pain, anorexia, nausea, and vomiting thought to be caused by visceral distension. Nausea, vomiting, fever, and anorexia were found to be uncommon in old patients by others as well [72, 212]. Burns et al. [213] compared the presentations of young and old patients. They found that twice as many young patients presented “classically,” and old patients were more than two times more likely to delay presentation for more than 72 h after onset of symptoms. Furthermore, in their study old patients were three times as likely to have operation delayed more than 24 h after admission than were the young. Others agree; finding that 13% of patients had their operations delayed more than 48 h after admission [215], further illustrating the difficulty of correctly diagnosing this age group. Sami described a blunted or absent pain response in the elderly [217]. And, perhaps more importantly, some have found that doctors often minimize the importance of the older patient’s pain, attributing it to old age or concomitant diseases [218–220]. Clinicians must be more cognizant of the abdominal complaints in old patients if prompt diagnosis and treatment with resultant decreased morbidity and mortality are to be expected.

The confident diagnosis of acute appendicitis is difficult, and the experienced clinician is wrong 5–25% of the time 201, 221]. Many books and articles have been written describing techniques for diagnosing acute appendicitis [222–224]. The combination of appropriate history, physical examination, and elevated WBC count is thought to be most important for diagnosing appendicitis correctly [225]. Unfortunately, these factors are not often present together [224]. Ultrasonography and focused CT have been used extensively for presurgical evaluation of patients [222, 223, 226]. Despite numerous advances in radiographic techniques, unnecessary explorations occur [223, 227].

C-reactive protein (CRP) has been studied as a tool to aid in the accurate diagnosis of appendicitis [228]. There is a decline in the production of inflammatory mediators and the immune system with aging [208, 229]. CRP is preserved with age. CRP has been found to be consistently elevated only in patients with perforation, perhaps because it first appears in the serum about 8 h after the initial insult and takes 24–48 h to reach peak blood levels [228]. Thus, elevated serum levels are often found only with prolonged symptoms, which correspond to high perforation rates. Obviously, if symptoms progress rapidly, there is no time for serum CRP levels to rise. CRP is not specific for appendicitis: It also increases with any inflammation, surgical trauma, and acute myocardial infarcts [228].

CT scanning has made accurate diagnosis easier. More liberal use of CT scanning can lead to the diagnosis of appendicitis in older patients where this diagnosis was not entertained [230]. Despite this, outcomes including perforation rates and duration of hospitalization may not be affected. Despite advances in preoperative modalities, an accurate diagnosis of acute appendicitis is made in only 30–77% of the elderly on admission and in only 70% preoperatively [212, 216, 221, 231]. Between 14% and 33% of older patients have operations more than 24 h after admission [213–216, 231].

Management

Antibiotics first treatment of acute uncomplicated (nonperforated) appendicitis has been receiving support. Multiple prospective studies and reviews have been published [232–237]. A large retrospective state database study found appendectomy rates of less than 10% over a mean follow-up of over 7 years [238] Others have found somewhat higher rates while still concluding nonoperative management is safe and effective [239]. Six prospective studies evaluated antibiotics first treatment [233–235, 240–242]. Nine percent of patients randomized to antibiotics required surgery during the initial hospitalization, many of whom had misdiagnosed complicated disease at presentation. Another 19% of the remaining patients had recurrence within the first year, for a 29% failure rate at 1 year. These failures did not present with increased risk of complicated appendicitis at surgery. These studies show that antibiotics as a first line of treatment is safe and permits nonoperative intervention in 75% of patients at 1 year. Decreasing initial failure of antibiotics first can be accomplished by more accurately diagnosing complicated appendicitis. Risk of undiagnosed neoplasm has been studied as a reason to avoid antibiotics first treatment in older patients. Wright [243] specifically looked at patients over 40 who were initially treated with appendectomy (suggesting noncomplex disease) and found a neoplasm rate of 0.7%. Of the 62 patients who were treated without initial surgery, presumably due to complicated disease, and then underwent interval appendectomy, 16% had a previously undiagnosed neoplasm. This suggests that uncomplicated appendicitis in adults is probably not associated with increased risk of neoplasm, but complicated appendicitis is. Some authors have suggested antibiotics first treatment of acute uncomplicated appendicitis for high operative risk patients such as those with recent MI, drug eluting stents, etc. Though not specifically studied, perhaps the elderly may fit this suggestion as well. Specific study in the elderly is currently lacking.

Early, aggressive operative treatment, when chosen, is imperative to minimize mortality in the elderly. In fact, Burns [213] suggested that "based on the lack of significant complications in those patients with a false-positive diagnosis and the 65% perforation rate in older patients, we feel an even earlier and more aggressive surgical approach is warranted." Operative treatment for acute appendicitis remains resection of the offending organ. Hydration and correction of electrolyte imbalances prior to urgent operation is prudent. Untoward delay before exploration may allow progression of the disease and ultimately free rupture of the organ with resultant peritonitis. Preoperative broad-spectrum antibiotics are administered intravenously and are continued postoperatively if necrosis or perforation is discovered. All pus should be evacuated, localized abscess cavities irrigated thoroughly, and appropriate closed-suction drains employed if abscess cavities are encountered [213]. The skin should be left open in complicated cases. When a normal appendix is discovered, the abdomen should be systematically examined to search for the origin of the symptoms; resection of the normal appendix is usually appropriate.

Nonoperative management of abdominal abscesses is well known. CT-guided drainage of abscesses allows resolution of the acute septic process followed by elective, internal operative treatment, thereby avoiding emergency surgery with its attendant morbidity [89, 90, 153, 244]. Acute appendicitis with a contained abscess responds well to drainage [219, 245]. Further, nonoperative management of these complex patients results in less complications and re-operations compared with patients who underwent emergent appendectomy [246]. Initial nonoperative treatment is frequently safer than emergent surgery. Many of these patients will recover with their appendixes in place. There is controversy on whether interval appendectomy (AI) should be done on these patients. Factors to consider include cost, chance for recurrent appendicitis, and undiagnosed neoplasm.

Senekjian [247] used mathematical models to determine that interval appendectomy after nonoperative resolution of phlegmonous appendicitis is cost effective until the patient is 33 years old, due to higher recurrence rates with duration of life. Clearly, IA the elderly is probably not cost effective.

Repeat appendicitis has been reported to be as high as 37%. Marin [245] retrospectively looked at a large database and identified 864 out of

32,938 patients who were treated nonoperatively and did not undergo elective IA. Recurrent appendicitis occurred in only 5% of 864 nonoperatively treated cases. The median time to first recurrence was about 1 year. Similarly, concern for repeat appendicitis is not an important indication for IA in the elderly.

Undiagnosed neoplasm after complicated appendicitis treated nonoperatively is a real problem. Multiple studies have examined this problem. Undiagnosed neoplasm occurs much more frequently in complicated appendicitis, when compared with uncomplicated presentation [243, 248, 249]. Age has been shown to be a significant risk factor of neoplasm associated with appendicitis [250, 251]. Carpenter found all patients with noncarcinoid neoplasm presented with complicated appendicitis with perforation or abscess formation [248]. Wright studied over 6,000 consecutive patients [238]. Of the 188 patients who were treated with nonoperative management, 89 subsequently underwent IA. Appendix neoplasm was found in 11 of these, including 6 mucinous neoplasms and one adenocarcinoma. Interestingly, in patients over 40, 16% had some type of neoplasm. Smaller studies have found higher rates [249–251]. Conversely, in these older patients undergoing routine appendectomy, neoplasm was found in only 0.7%. These findings suggest that due to a significant risk of clinically important neoplasm, routine IA should be performed in all elderly patients (with complicated appendicitis) medically stable enough to withstand surgery. Furthermore, elective interval appendectomy lends itself well to the laparoscopic approach, as stressed by Greig and Nixon [252]. Thus, nonoperative first-line treatment of complex appendix disease, with interventional radiologic help allows conversion from acute emergency operation with its attendant increase in complications to elective IA. This path should always be entertained when dealing with complex appendix disease in the elderly.

Ileocecal resection and primary anastomosis are reserved for the markedly inflamed cecum. Rarely, resection cannot be performed safely because of the inflammatory reaction. In these cases, irrigation and drainage are performed, and interval appendectomy is scheduled for 6–12 weeks later. The reader is referred to general surgical textbooks for the detailed operative technique.

Lau et al. [209] found a 38% perforation rate in old patients operated on within 24 h of the onset of symptoms, suggesting aggressive disease. Wolff and Hindman [253] agreed, finding a perforation rate of 41% in old patients with onset of symptoms within 24 h of operation. However, Burns et al. [208] found that one-third of young and old patients operated within 24 h had perforation. Von Tittle [254] also found that roughly one-third of old patients with perforation had symptoms less than 24 h. Older patients present with perforated disease at a much higher rate than the young.

Complicated Appendicitis: Differences Between Young and Old Patients

Luckmann [196] found that only 53% of patients over age 80 in California had their operation on the day of admission, compared to more than 80% of young patients. More impressively, in patients with abscesses, more than 85% of young patients had operations within 1 day of admission, compared to only 57% of those older than 80 years. This further attests to the difficulty accurately diagnosing and treating acute appendicitis in the elderly. One study revealed that 17% of elderly patients were treated without accurate diagnosis prior to being admitted with acute appendicitis [214]. Incorrect diagnosis rates in the elderly are as high as 25% [255].

In-hospital observation has been shown to decrease negative operative rates safely without increasing the perforation rate [255, 256]. This suggests that the out-of-hospital delay is most important for determining the aggressiveness of disease. Lau et al. [209] found a statistically significant increase in perforation rates in elderly patients when surgeons delayed operation for more than 25 h. Klein [216] also found increased perforation and abscess rates in old patients with increasing delays of operation. Because of the difficulty diagnosing old patients, attempting to decrease perforation rates through hospital observation in the elderly is unwise.

Many authors have examined laparoscopic versus open appendectomy [256–261]. One prospective randomized study found that patients used fewer analgesics and returned to full activities sooner compared to those exposed to conventional operative techniques [260]. Some have found fewer wound infections with laparoscopic techniques [262–264]. A large comparative study and a prospective randomized study both found advantages for laparoscopic approach to appendicitis, without increased abdominal abscesses [265, 266]. One obvious advantage of laparoscopic appendectomy is the ability to view the entire abdomen and pelvis in cases where the diagnosis is in question.

Konstantinos [267] examined more than 1,000 consecutive laparoscopic operations for suspected appendicitis. They had a conversion rate of less than 1% and 1.1% wound infection rate with no intra-abdominal abscesses or deaths, despite a 14% ruptured or gangrenous appendix rate and 4% having intra-abdominal abscesses. They also found significantly shorter hospital stays and quicker return of bowel function. Paranjape [268] examined three different time periods and how laparoscopy changed outcomes in the elderly. They found an increased use of CT scanning, fewer patients presenting with classic symptoms, increased correct admission diagnoses, fewer perforations, and fewer complications in the most recently treated group. They also found shorter hospital stays with laparoscopy. Their operative time was similar for both open and laparoscopic approaches.

Laparoscopically treated appendicitis in elderly North Carolina residents has been studied as well [269]. The patients who underwent conventional and laparoscopic operations were comparable with regards to age, gender, and comorbidities. Fifty-five percent presented with perforated appendicitis. There was a steady increase in laparoscopic use over time, rising from 11.9% in 1997 to 26.9% in 2003. Advantages found in the laparoscopic group includes shorter length of stay (4.6 vs. 7.3 days), higher rate of discharge to home (91.4% vs. 78.9%), fewer complications (16.3% vs. 20.8%), and a lower mortality (0.4% vs. 2.1%). As important is overall hospital costs, which shows a trend for lower total costs for the laparoscopic group, $17,031 vs. $19,587.

Conclusion

In conclusion, 10% of all appendicitis occurs in the elderly. Older patients present atypically and often delay seeking medical treatment. Diagnosis is difficult owing to blunted symptoms and response to inflammation. Perforation occurs more frequently and possibly faster than younger patients. High index of suspicion and liberal use of CT scanning can facilitate correct diagnosis. Interval appendectomy should be performed in those treated nonoperatively for perforating disease due to increased risk of neoplasm. Laparoscopic technique decreases complications, shortens hospital stay, increases home discharge, and is not associated with increased hospital costs (Figs. 1, 2, 3, 4, and 5).

Fig. 1 Acute diverticulitis of the sigmoid colon with paracolonic fat stranding

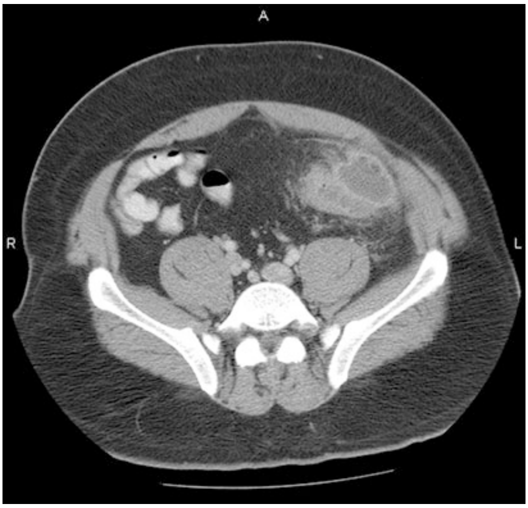

Fig. 2 Diverticular abscess with well-formed, enhancing wall

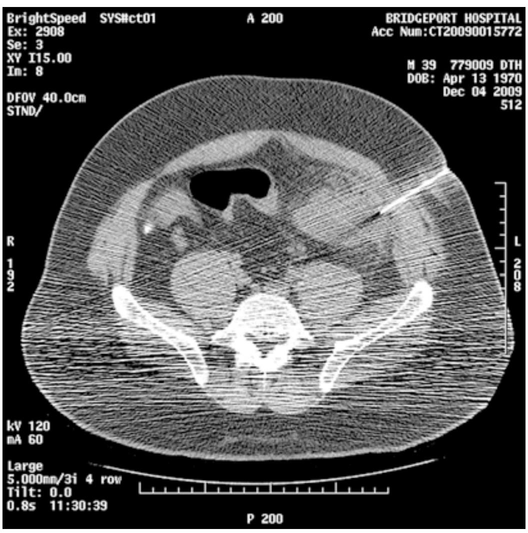

Fig. 3 Percutaneous drainage of the abscess

Fig. 4 Fecalith within an acutely inflamed appendix

Fig. 5 Same patient, coronal view

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Lower Gastrointestinal Bleeding in the Elderly

58

Hadley K. Wesson and Michael E. Zenilman

Contents

Abstract

This chapter will discuss common causes, clinical assessment, and the medical and surgical management of lower gastrointestinal bleeding in the elderly. The chapter will outline how this approach differs from a younger patient population and address the unique needs of the elderly.

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Case Presentation: Diverticular Bleeding

A 75-year-old woman presented to the emergency department with bleeding per rectum. She was tachycardic and hypotensive. She had a past medical history diverticulosis, seen on colonoscopy 10 years earlier. Her rectal exam was negative for any palpable masses, but a large amount of dark blood was noted on her gown and on digital rectal exam. Two large bore IVs were started and infused with normal saline boluses. She responded well and her vital signs normalized. Her hemoglobin was noted to be 8.5 g/dl; as such, she did not require a blood transfusion at this time. An upper gastrointestinal bleed was considered as a source, and she underwent gastric lavage in the emergency department via placement of an NGT. This was negative and her vital signs remained stable. The gastroenterology

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service was consulted for a colonoscopy, but they did not think at the time she would tolerate the prep needed to undergo a colonoscopy. As such, she underwent a CT angiography that showed no evidence of an active bleed. Extensive colonic diverticula were noted on CT. She was admitted for observation, and clinically, she had no additional episodes of lower gastrointestinal bleeding. At the time of her discharge, she was instructed to follow up with gastroenterology for an elective colonoscopy which confirmed diverticulosis.

Case Presentation: Colorectal Malignancy
A 70-year-old man presented to his primary care provider with one episode of bleeding per rectum. His history was remarkable for fatigue and a recent 15 pound weight loss. He had never had a colonoscopy. His rectal exam was unremarkable except for a positive fecal occult blood test. He was hemodynamically stable and his hemoglobin was 9.5 g/dl. He was referred to gastroenterology for a colonoscopy that showed a large fungating mass of the right colon. The mass was biopsied and tattooed during the procedure. It was noted that it was not currently bleeding. Biopsies confirmed adenocarcinoma. He was then referred to surgery who proceeded to stage the malignancy. A CT of the abdomen, pelvis, and chest showed no signs of distant metastasis. Laboratory evaluations, including a CBC, chemistry, and CEA level, were remarkable for anemia and an elevated CEA. He underwent an uneventful laparoscopic right hemicolectomy. Following a review of the patient's pathology that showed T3 N1 adenocarcinoma, he referred to medical oncology to discuss chemotherapy options.

Introduction

Gastrointestinal bleeding is one of the most common causes of hospitalization due to gastrointestinal disease in the United States, of which lower gastrointestinal bleeding accounts for 30 to 40% of all gastrointestinal bleeds. The elderly are more likely to have a lower gastrointestinal bleed than younger adults. In fact, a retrospective review found an 80-year-old is 200 times more likely to have a lower gastrointestinal bleed than a 20-year-old [1]. While mortality from a lower gastrointestinal bleed is relatively low, advanced age is one of the strongest predictors of mortality [2, 3]. For these reasons, it is essential that the operating surgeon has a firm grasp of the causes and management of lower gastrointestinal bleeding in the elderly. In this chapter, we will outline common causes of lower gastrointestinal bleeds and an approach to management. We will also pay particular attention to special considerations that need to be made when caring for the elderly during a lower gastrointestinal bleed.

Causes of Lower Gastrointestinal Bleeding in the Elderly

Historically a lower gastrointestinal bleed was defined as any bleed distal to the ligament of Treitz. However, the American College of Gastroenterology's 2016 Guidelines redefined a lower gastrointestinal bleed as any gastrointestinal bleed isolated to the colon or rectum [4]. The guidelines also distinguish between acute and chronic bleeding. An acute lower gastrointestinal bleed commonly presents with melena or hematochezia and can be accompanied with hemodynamic instability. In contrast, a chronic lower gastrointestinal bleed may result in a positive fecal occult blood test and is associated with iron deficiency [5]. Common causes of lower gastrointestinal bleeding in the elderly are diverticulosis, colonic angioectasias, malignancy, colitis, and anorectal disorders such as hemorrhoids (Table 1).

Table 1 Common causes of lower gastrointestinal bleeding in the elderly

Common causes of lower gastrointestinal bleed
Colonic diverticulosis
Colonic angioectasias
Colorectal malignancy
Inflammatory bowel disease
Ischemic colitis
Anorectal disorders

Diverticulosis

Diverticulosis is common in the elderly: in western populations, up to 50% of people greater than 60 years of age have radiographic evidence of diverticulosis [6]. As people age, the colonic wall weakens. This, along with increased intraluminal pressure, can result in diverticula. These protrusions occur where branches of the vasa recta perforate through the circular muscle fibers. Only the mucosa remains to act as a barrier between the vessel and the bowel lumen (Fig. 1). As the perforating vessels are exposed to chronic insult, the vessels can erode into the mucosa, resulting in bleeding. As much as 20% of elderly adults with diverticula will develop bleeding [7]. The vast majority of bleeding often stops spontaneously, but 5% of patients can experience life-threatening bleeding.

Colonic Angioectasias

Angioectasias are dilated tortuous submucosal veins found throughout the gastrointestinal tract, but most commonly in the cecum and ascending colon [8]. While the etiology is not fully understood, it is thought that these angioectasias develop from chronic, low-grade colonic contractions. This causes congestion and obstruction of the submucosal veins. In turn, the capillaries dilate, resulting in small arteriovenous collaterals and ultimately an arteriovenous malformation (Fig. 2) [8]. This malformation abuts the colonic mucosa and can cause bleeding. While colonic angioectasias can occur at any age, it occurs most frequently in the elderly, manifesting as severe hematochezia. Approximately 90% resolve spontaneously, but rebleeding can occur.

Colorectal Malignancy

Colorectal cancers are the third most common cancer in the United States. They cause 10% of hematochezia in the elderly, resulting from erosions of the surface of the tumor. While bleeding is common in colorectal cancer, occurring in up to 50% of patients, it is often low-volume and associated with anemia. Massive hemorrhage is uncommon in colorectal cancer [9].

Colitis

Lower gastrointestinal bleeding from colitis in the elderly occurs most commonly from inflammatory bowel disease or ischemia [6]. Inflammatory colitis is associated with bloody diarrhea due to the presence of friable, edematous mucosa. Among inflammatory bowel diseases, bleeding from ulcerative colitis is much more common

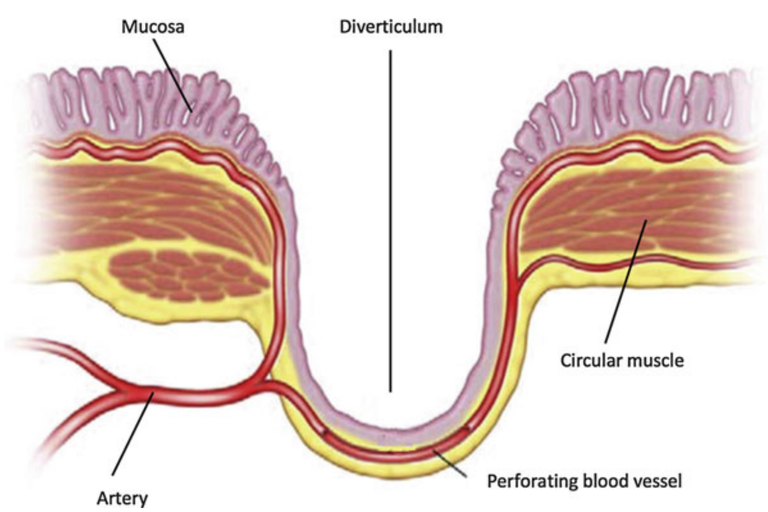

Fig. 1 Exposure of the perforating blood vessel in diverticulosis. (Adapted from [33])

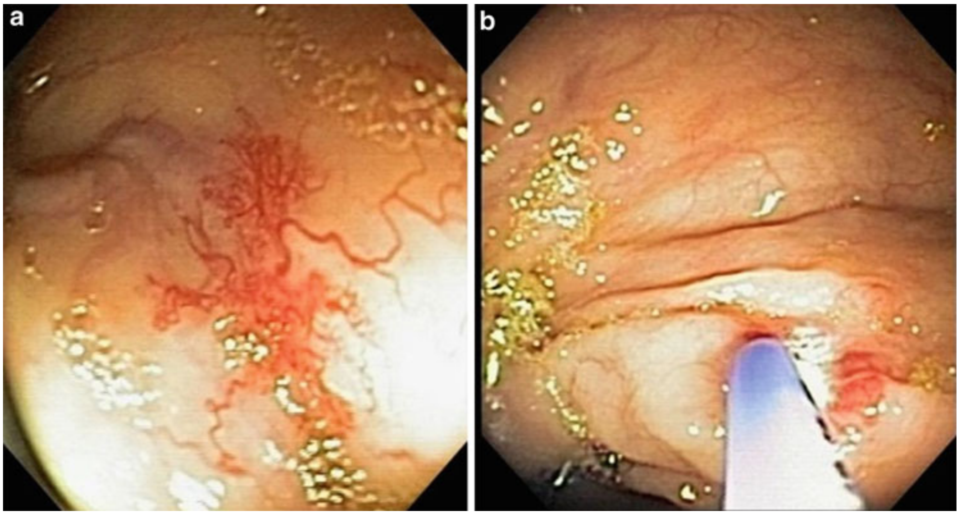

Fig. 2 (**a**) Colonic angioectasias as seen on colonoscopy. (**b**) Colonic angioectasias following argon beam ablation. (Image courtesy of Mahmood Solaiman, MD, Gastro Associates & Central Maryland Endoscopy)

than from Crohn's disease in the elderly. While massive bleeding from inflammatory colitis is thankfully relatively rare, it can result from pancolitis, which may necessitate emergent total abdominal colectomy.

Ischemic colitis can present with acute abdominal pain and bloody diarrhea: ischemia leads to mucosal friability and wall sloughing that can cause blood per rectum. Approximately 90% of colonic ischemia occurs in patients greater than 60 years of age. Comorbidities that increase the risk for either embolic or non-embolic ischemic events, such as arrhythmias or heart failure, also increase the risk of ischemic colitis. The severity of ischemic colitis can vary from mild transient colitis to fulminant gangrenous colitis. Symptoms can vary, but bleeding can occur at any stage of colitis [10].

Anorectal Disease

Benign anorectal disease, such as hemorrhoids and anal fissures, can cause lower gastrointestinal bleeding. The most common reported symptom of internal hemorrhoids is bleeding, typically associated with defecation and almost always painless [11]. Rubber band ligation of internal hemorrhoids can be a simple and effective way to treat hemorrhoidal bleeding. Bleeding from an anal fissure is usually self-limiting and resolves when the fissure can heal through the use of fiber supplementation, increased water intake, and/or topical calcium channel blockers [12]. Significant bleeding from anorectal diseases is rare.

Assessment of Lower Gastrointestinal Bleeding in the Elderly

History, physical examination, and laboratory evaluations are the essential first steps in assessing a patient with a lower gastrointestinal bleed. A history of syncope, signs of tachycardia, hypotension, or orthostatic hypotension are suggestive of a significant blood loss. Any patient, regardless of their age, with hemodynamic instability should be stabilized and resuscitated prior to undergoing any diagnostic testing. Lower gastrointestinal bleeds are usually slower and less severe that upper gastrointestinal bleeds. As such, when treating a patient with shock and blood per rectum, the clinician must consider an upper gastrointestinal bleed as a possible source. In this case, nasogastric lavage and upper endoscopy are useful to identify the cause of the bleed (Fig. 3).

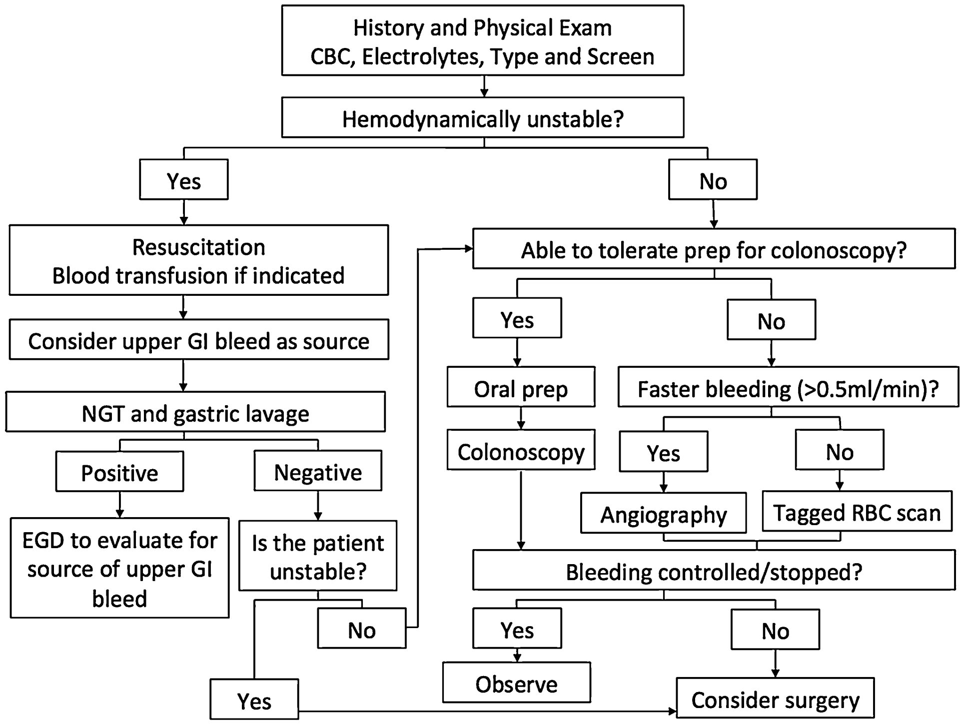

Fig. 3 Approach to a lower gastrointestinal bleed in the elderly

It is important to clarify the nature of the bleeding, such as the color, amount, frequency, and duration to help establish a differential diagnosis [13]. It is equally essential to assess the presence or absence of abdominal pain and have the patient describe the pain. Understandably, this history can be difficult and time-consuming to obtain especially in the elderly but all the more worthwhile if the practitioner can narrow their differential diagnosis to direct management [14]. For example, colorectal malignancy, diverticular bleeding, and angioectasias are typically painless, while abdominal pain with loose bloody stools may be more likely due to colitis.

Obtaining an accurate medical history is never more paramount than in the elderly, as cardiopulmonary, renal, and hepatic dysfunction are associated with an increased risk in mortality and morbidity [15]. Additionally, reviewing and confirming the accuracy of the patient's medications are important steps in the assessment. The practitioner should keep in mind that some medications that are more prevalent in the elderly, such as aspirin, antiplatelet, and anticoagulation agents, can cause or exacerbate a lower gastrointestinal bleed.

An elderly patient may not be able to acutely articulate their history, especially if they are in distress or discomfort. Family members, other advocates, and the patient's primary care provider are essential in contributing to this history. Every effort must be made to contact these individuals to understand not only the context in which the patient has experienced the bleed but also to understand up front the patient's wishes regarding further medical treatment [16].

Once a history has been obtained, a complete physical exam is important, including vital signs. Cardiac and pulmonary exam findings may add to the patient's overall assessment. In the case of the elderly, this may influence their treatment options including their ability to tolerate surgery, should that be deemed necessary. Physical exam findings include an abdominal exam, which may reveal tenderness or distention.

A rectal exam should be performed in all patients presenting with lower gastrointestinal bleed; arguably this part of the exam has been overlooked in recent years with radiographic advancement, leading some to cunningly deem it "a lost art." [17] We argue this part of the exam should not be missed. The rectal exam is an opportunity to assess for hematochezia and anorectal pathology, such as hemorrhoids. Anoscopy may also be of use if the source of the lower gastrointestinal bleed is thought in the lower rectum or anal canal. It is important to note the presence of gross blood, as this is an independent predictor of the severity of the lower gastrointestinal bleed [18]. Given that an elderly patient may have limited mobility, performing a rectal exam may be more difficult and cumbersome for the provider. As such, it is important to ask for assistance from nursing and other healthcare providers to ensure the patient can be safely positioned on their side to allow for an adequate exam.

Laboratory tests should be performed on all patients presenting with lower gastrointestinal bleed and should include a CBC, electrolytes, a clotting profile, and a type and screen. Lactate levels may also be useful in guiding resuscitation for a patient in shock [19].

Management of Lower Gastrointestinal Bleeding in the Elderly

The initial management begins with resuscitation, especially if the patient is hemodynamically unstable. Resuscitation must be implemented with caution in elderly patients who may have cardiac comorbidities and cannot tolerate aggressive intravenous fluid. Blood transfusions are recommended cautiously, keeping in mind current national recommendations regarding when and how to transfuse. One unit of packed red blood cells should be administered when the patient's hemoglobin drops below 7 g/dl. However if significant comorbidities are present, such as cardiovascular disease, current guidelines recommend the threshold to transfuse be increased to 9 g/dl [4].

Once the appropriate resuscitation measures are underway, the next step in management is to determine the source of the bleeding. There are multiple choices in terms of which intervention is most appropriate for the patient, including colonoscopy, computed tomographic angiography, mesenteric angiography, and nuclear scintigraphy. There is a lack of evidence within the literature as to the optimum initial approach to management. As such, most experts agree the physician should be aware of the advantages and disadvantages of each of these choices and make the best decision for the patient based on their presentation at the time of the bleed [20].

Although no one test has emerged as the gold standard in the management of lower gastrointestinal bleed, colonoscopy is often considered the initial procedure of choice [4, 21]. It can be both diagnostic and therapeutic. This should be performed urgently, when the patient is stable and is able to tolerate a bowel prep. Studies show that colonoscopies performed early within the 24 h of admission are associated with higher rates of diagnosis and hemostasis and a decrease in hospital length of stay [20, 22, 23]. Current guidelines recommend a bowel prep consisting of 4–6 L of polyethylene glycol solution over a 4-h period [4].

While colonoscopy is usually well tolerated, elderly patients are at a higher risk for complications than younger adults [12]. Yet despite this, the benefits of a diagnostic and therapeutic colonoscopy appear to outweigh the risks in the setting of a lower gastrointestinal bleed. This is true for even the very elderly patients [24]. Thus it is widely agreed upon that the age of the patient should not prohibit the gastroenterologist from proceeding with the procedure; it should however inform both the gastroenterologist's and the anesthesiologist's approach to the patient [12].

Therapeutically, colonoscopy offers the ability to provide endoscopic hemostasis. These methods include diluted epinephrine injection, thermal coagulation, and mechanical therapy. Thermal coagulation includes bipolar electrocoagulation, heated probe, or argon beam. Mechanical therapies include endoscopic clips or band ligation. Diluted epinephrine injection should be used in combination with thermal or mechanical therapies to minimize the risk of recurrent bleeding [4].

Lower gastrointestinal bleeding caused by diverticulosis and angioectasias is more likely to benefit from endoscopic hemostasis. Mechanical therapy with endoscopic clips is recommended for treatment of diverticular bleeding [25]. Given that the wall of the diverticulum is thin, clips theoretically reduce the risk of bowel perforation compared to thermal coagulation [4]. Argon beam coagulation is the preferred treatment for colonic angioectasias because it is associated with a shorter depth of tissue injury [4]. Approximately 85% of bleeding from colonic angioectasias will resolve with argon beam (Fig. 2) [8]. Coagulation with hot biopsy forceps is currently not recommended for the treatment of colonic angioectasias because it is associated with a high risk of serious complications, including perforation [8]. Patients who experience recurrent bleeding after achieving hemostasis with colonoscopy may be candidates for repeat colonoscopy.

Lower gastrointestinal bleeding from ischemic colitis, ulcerative colitis, and colorectal malignancy are usually not amenable to endoscopic hemostasis, although colonoscopy may help to localize the site of the bleed.

Historically, angiography was reserved for the treatment of upper gastrointestinal bleeding. However, recent advances in the field have enabled transcatheter angiography with super-selective embolization to emerge as the treatment of choice for some cases of lower gastrointestinal bleeds [26]. Angiography is now a preferred modality for patients with brisk bleeding who are not stable enough for colonoscopy or who would not tolerate an adequate bowel prep. Angiography however may be negative and thus of little yield for intermittent or slower bleeds (<0.5 ml/min) [13]. Angiography is also therapeutic: it allows for super-selective embolization of arteries less than 1 mm in diameter with the use of microcoils, absorbable gelatin sponges, cyanoacrylate glue, or ethylene vinyl (Fig. 4) [13].

CT angiography and radionuclide technetium-99 m-labeled red blood cell scintigraphy, also referred to as a tagged red blood cell scan, can be used to diagnose lower gastrointestinal bleeds. While tagged red blood cell scans can detect bleeding rates as low as 0.1 ml per minute, recent studies suggest that CT angiography is also highly sensitive and specific at identifying the site of active bleeding [13, 27, 28]. Although not therapeutic, both studies are important tools to localize the bleed (Fig. 5). If patients fail or cannot tolerate other therapeutic interventions, such as colonoscopy or angiography, and surgery is recommended, it is important that every effort is made preoperatively to localize the bleeding and potentially avoid a subtotal colectomy. In this setting, CT angiography and scintigraphy can be of tremendous benefit.

A surgical consultation is indicated for patients with ongoing lower gastrointestinal bleed who have failed endoscopic or radiographic attempts to stop the bleed. While currently considered a “last resort” option, surgery is required in approximately 10–25% of patients with lower gastrointestinal bleeds [19]. One noted exception is in the case of hemorrhaging colorectal cancer, where surgery may be the most effective and definitive treatment. Other indications for surgery are hemodynamic instability after transfusion of more than six units of blood, slow bleeding requiring more than three units of blood per day, inability to stop bleeding via colonoscopy or endovascular attempts, and recurrent hemorrhagic shock [9].

As previously emphasized, localization of the bleed is essential prior to surgery to prevent a missed lesion or subtotal colectomy. If it is not possible to localize the bleed within the colon or rectum, and an upper gastrointestinal bleed has

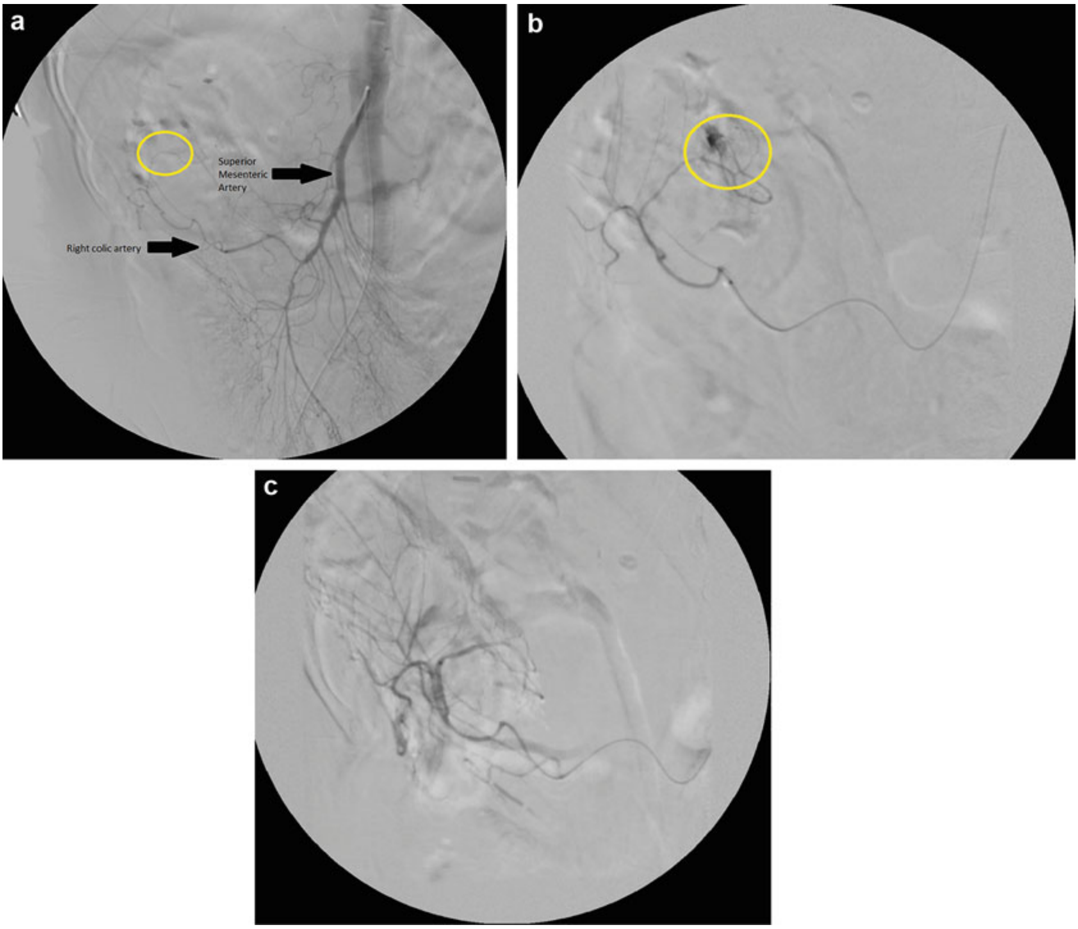

Fig. 4 (**a**) Angiogram in an 83-year-old woman with an acute lower gastrointestinal bleed from right colic artery terminal branches at the hepatic flexure (yellow circle). (**b**) Angiogram in an 83-year-old woman with an acute lower gastrointestinal bleed from right colic artery terminal branches at the hepatic flexure showing blush (yellow circle). (**c**) Completion angiogram in an 83-year-old woman with an acute lower gastrointestinal bleed from right colic artery terminal branches that shows no active bleeding following gelfoam embolization. (Image courtesy of Andrew Morton, MD of American Radiology)

been ruled out, a subtotal colectomy may be indicated. While the operative techniques, whether laparoscopic or open, remain the same regardless of age, the surgeon must take into account the elderly patient's comorbidities and frailty before, during, and after the surgery [29].

Many studies confirm that older populations undergoing urgent surgery have a higher risk of postoperative mortality and morbidity [30]. Efforts should be made before surgery to discuss these risks with patients and their families. This can ensure the patient's goals of care are not only recognized by the medical team but are also met throughout the patient's hospitalization [31]. Prior to emergent or urgent surgery in the elderly, screening tools such as the frailty index score or the Vulnerable Elders Survey may be of benefit to the surgeon in predicting postoperative complications and length of stay [30, 32].

Conclusion

The aging population in the United States will continue to grow, and lower gastrointestinal bleeds will continue to be more prevalent in

Fig. 5 Radionuclide technetium-99 m-labeled red blood cell scintigraphy in an 83-year-old woman that localized an acute lower gastrointestinal bleed to the hepatic flexure. (Image courtesy of Andrew Morton, MD of American Radiology)

our hospitals. When assessing and managing a lower gastrointestinal bleed in the elderly, the approach should be multifaceted involving the gastroenterologist, surgeon, radiologist, geriatrician, family members, and the patient themselves. Through a thoughtful and timely approach, we can strive to provide excellent medical care and ensure we are listening to and meeting the needs of our patients.

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Hip Fracture

59

Simon C. Mears

Contents

Abstract

Hip fracture is a common injury in older adults. Hip fractures are fragility fractures and caused by osteoporosis and a propensity for falls. Classification is according to fracture morphology and the type of fracture guides for surgical treatment. Most patients sustain a low-energy fall and cannot walk after breaking their hip. They are admitted through the emergency department to the hospital. Urgent surgical repair gives the best outcomes and should be performed as soon as feasible. Femoral neck fractures are generally treated with arthroplasty, while intertrochanteric and subtrochanteric fractures are treated with internal fixation. Internal fixation is either with a sliding hip screw and side plate or intramedullary hip screw. A coordinated approach using medical co-management allows for early surgery and reduction in postoperative complications. Standardization of orders reduces errors and prevents the use of unnecessary tests and medicines which harm elderly patients. Patients should be allowed to bear weight as tolerated after surgery and mobilized quickly. Treatment of osteoporosis to prevent further factures is important to prevent future fractures. Mortality

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is high after fractures, and many patients do not return to their preoperative level of function.

Keywords
Hip fracture · Femoral neck fracture · Intertrochanteric fracture · Delirium · Atypical fracture · Osteoporosis · Fragility fracture

Introduction

Hip fracture is a common injury in elderly patients resulting from a low-energy fall. Hip fractures are treated surgically with either repair or replacement. The surgery should be performed urgently to reduce risk of postoperative complications. A coordinated team approach to management between a medical doctor and orthopedic surgeon gives optimal results as patients usually have multiple medical comorbidities. The use of standardized order sets helps to minimize mistakes and medicines that harm elderly patients and reduce the use of unnecessary tests. In the postoperative period delirium, urinary retention and congestive heart failure are common occurrences and should be prevented. Early mobilization with full weight bearing helps to decrease risks of blood clots and pressure ulcers. A rehabilitation stay is common after hip fracture to strengthen patients to get back home. Overall mortality rates are substantial after hip fracture, and many patients do not return to their previous level of function.

Preoperative Care

Hip fracture is a low-energy injury in patients with weak bones. Patients often are frail and have medical comorbidities that increase their risk of falling. Osteoporosis leads to a high risk of fracture with each fall. Injuries are most commonly a fall from standing height and result in an inability to walk. Patients with a hip fracture may be found down and may have been without care for significant periods of time. Most commonly patients are taken to the emergency room. The leg is often rotated externally and shortened and motion of the limb is very painful. Diagnosis is made with

Fig. 1 A magnetic resonance image with T2 weighting is shown of the hip. A stress fracture is seen in the calcar area of the femoral neck

plan radiographs which reveal the fracture in almost all cases. If a fracture is not seen on x-ray, magnetic resonance imaging (MRI) is the next best test to look for occult fracture (Fig. 1) [1]. Other diagnoses in the differential include pelvic fractures, which are also a common fragility fracture.

In some circumstances, geriatric patients in a high-energy trauma also may sustain a hip fracture. These patients are often multiply injured. In this situation, trauma protocols must be followed. Resuscitation must be performed and life-threatening injuries treated. Elderly patients have less reserve and may be more profoundly affected by multi-system trauma. When the patient is stabilized and resuscitated, the hip fracture should be surgically repaired to allow for mobilization.

Standardized order sets are best practice in the emergency room. Lab should be ordered to assess hemoglobin, electrolytes, and prothrombin time. Electrocardiogram should rule out acute coronary syndrome. A full history and physical exam needs to be performed to look for acute medical conditions. Patients often have dementia and may come from a nursing facility. Obtaining records of the patient's medical conditions should be a top priority. Of importance is an accurate medication list to see if the patient is on a blood thinner medication. Patients with a hip fracture are typically dehydrated due to blood loss from the fracture and from the time spent before being found down. Intravenous fluids should be started with normal saline at 150 ml/h [2].

The goal of the preoperative phase is early surgical repair. Early surgery decreases complications and morbidity. Precisely how early surgery should occur is debated. In the United Kingdom, the hip fracture audit has picked 36 h as the goal to surgery. The goal is that the sun should not set twice on a hip fracture [3]. The American Academy of Orthopaedic Surgery guidelines have suggested surgery within 48 h [4]. Preliminary results have shown that ultra-early surgery, within 6 h, may give even better results [5]. Delay does nothing but increase time in pain, increase time in which complications can occur, and increase length of stay in the hospital as well as cost of care. Specific medical problems should be addressed promptly and surgical repair performed urgently.

Testing should be minimized prior to surgical repair. There is very little role for echocardiograms or stress tests. Echocardiograms should be reserved for only patients with suspicion of severe pulmonary hypertension or aortic stenosis. In these cases, knowledge of heart function will change anesthetic management. Specialist consultation should also be avoided. These tests are unlikely to change management and will cause delay [6].

Pain should be managed and not ignored. Initially low doses of narcotic pain medicine should be given to achieve pain relief [7]. The use of nerve blocks has been shown to be very beneficial for hip fracture patients. This can be done in the emergency room to give pain relief without the side effects of narcotic pain medication. Fascia iliaca nerve block can be performed by trained emergency room doctors or anesthesiologists [8]. Patients should be rapidly admitted to the hospital so that they can be on a hospital bed rather than a stretcher [9]. Traction is not helpful and does not improve pain control [7].

Careful attention should be paid to medication review with geriatric principles in mind. The Beers list was developed by the American Geriatrics Society, and this list shows medication that are harmful to elderly patients [10]. Standardized orders will prevent the use of medications such as meperidine or diphenhydramine which are known to promote delirium. Many patients with hip fracture have pre-existing dementia that may or may not be complicated by delirium [11]. A mental status evaluation is important to recognize cognitive impairment. A mini-cog test should be performed to determine if dementia is present. In the hospital, the CAM score can be used by nursing staff to look for delirium. The small things are important to prevent delirium. Hearing aids and glasses are potentially lost in the transfer to the hospital, and without these, many elderly patients cannot see or hear making delirium very likely. Emergency rooms are also loud busy places, and early floor transfer helps to calm patients.

Getting early involvement from family should be started in the emergency room. Patients may not be able to give informed consent for surgical repair on their own. DNR orders may already exist, and these are very important to institute during hospitalization. Discharge planning should begin at hospital admission as most patients with hip fracture cannot go directly home after surgical repair.

The goal of this first phase of care is early surgery. Acute medical conditions such as dehydration need to be rapidly addressed. A problem in 20–30% of hip fracture patients is the use of blood thinning medicines prior to the fall. The use of aspirin and clopidogrel should not delay surgical repair [11]. Warfarin should be rapidly reversed to lower the INR. The precise INR needed for surgical repair is debated. The use of oral and intravenous vitamin K should be given in the emergency room. The INR can then be rechecked. If still elevated, fresh frozen plasma should be given to reverse the anticoagulation [12]. Direct oral anticoagulants (DOAC) are becoming more popular and pose problems for the surgeon as they are not easily reversible. Little data exists about how much time should elapse prior to surgery when a patient is on a DOAC. Probably, surgery should be delayed based on the hall life of the medication, usually in the range of 48 h [13]. This is one of the few recommended delays prior to surgical repair.

Surgical Treatment

Surgical treatment is based on fracture type [14]. The hip can break in three main areas, the femoral neck, the intertrochanteric region, and the subtrochanteric region (Fig. 2). Femoral neck fractures may be nondisplaced or displaced. Nondisplaced fractures can be treated either with screw fixation or arthroplasty. Internal fixation of displaced fracture has a high failure rate, and randomized studies have shown arthroplasty to be superior [15, 16]. Healing potential is limited in the femoral neck. Displaced fractures are best treated with arthroplasty. This may either be partial or total hip replacement (Fig. 3). The type of arthroplasty utilized is based on the activity level of the patient. Active patients have less pain and superior outcomes with total hip arthroplasty [17]. Less active patients do not benefit from total hip arthroplasty and are best treated with hemiarthroplasty. Total hip arthroplasty has a higher rate of dislocation than hemiarthroplasty [18]. It is recommended that a cemented stem be used for hip fracture patients as there is a lower risk of periprosthetic fracture and loosening than if a uncemented stem is used [15, 19]. This is due to the poor bone quality found in hip fracture patients.

Intertrochanteric fractures occur in the metaphysis of the bone that has far superior healing

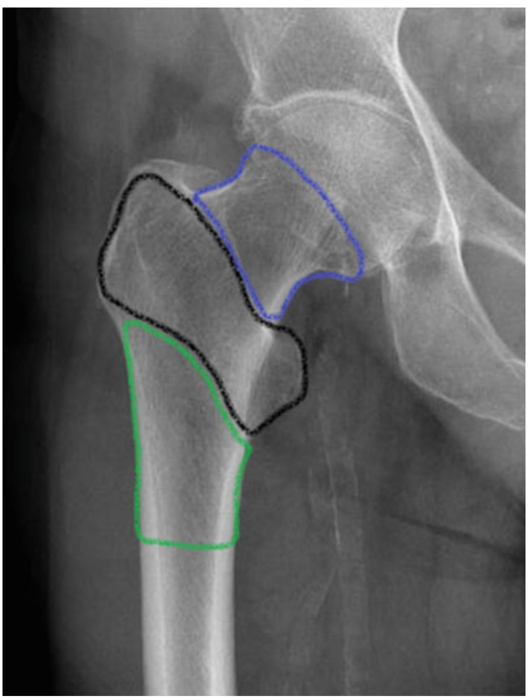

Fig. 2 Typical fracture patterns in the hip: the blue area highlights the femoral neck, the black area is the intertrochanteric and the green area is the subtrochanteric region of the proximal femur

Fig. 3 An AP radiograph of the hip shows a cemented partial hip replacement or hemiarthroplasty. The acetabulum is left unresurfaced, and the metal of the arthroplasty interfaces with articular cartilage

characteristics than the femoral neck. These fractures are treated with internal fixation. This may either be with a sliding hip screw and side plate (Fig. 4) or an intramedullary hip screw (Fig. 5). Depending on the amount of fracture fragments and the direction of the fracture, some intertrochanteric fractures are more innately stable than others. The stable fractures are best treated with the sliding hip screw and side plate. Unstable fractures, especially reverse oblique fractures, are best treated with an intramedullary hip screw [20]. Technique is important when hip screws are used. Fracture reduction should be obtained first prior to screw insertion. The screw should be inserted centrally and deep in the head to prevent screw cutout [21].

Subtrochanteric fractures are below the level of the lesser trochanter and should be treated with intramedullary hip screw. One type of subtrochanteric fracture pattern is the atypical fracture. These fractures develop from long term (>5 years) of bisphosphonate therapy [22]. Bone turnover is turned off, and an area of brittle bone forms usually in the subtrochanteric femur. A stress fracture then develops and the femur breaks. In these cases, intramedullary hip screw is used

Fig. 4 A sliding hip screw with side plate is pictured in an AP image radiograph of the hip. This device is used to treat stable intertrochanteric fractures that have an intact lateral buttress to allow the device to have an end point to sliding. The screw is a separate piece from the side plate. The screw slides within the barrel of the side plate to allow fracture compression with weight bearing

Fig. 5 An AP radiograph of the hip shows an intramedullary hip screw. This device is used for unstable devices. The intramedullary nail acts as the lateral buttress to provide an end point for the sliding hip screw

for treatment. Medical treatment of the frozen bone is critical. Bone turnover markers should be assessed and bisphosphonates stopped. A metabolic bone consultation is needed to follow this long term. These fractures take longer to heal than routine subtrochanteric fractures [23].

The type of anesthesia for hip fracture has been debated. Overall no differences have been seen between spinal and general anesthesia in outcomes or delirium rates [24].

Postoperative Care

Early mobilization is critical after hip fracture repair. All patients should be allowed to weight bear as tolerated [25]. If the surgeon does not feel that the repair is adequate to allow for this, then the wrong surgical technique was chosen. Patients should be mobilized out of bed to chair the day of surgery and should eat all meals in a chair. Physical therapy evaluation is necessary, and a walker should be used for ambulation. Patients may have pre-existing mobility problems prior to the fracture. In some cases, the robust patient with a hip fracture may be able to be discharge directly home from the hospital. In most cases, further post discharge rehabilitation is required. In the United States, this is either an acute rehabilitation center or a subacute nursing facility. These facilities should develop a plan for the patient to continue mobilization and strengthening and hopefully allow for discharge back to the pre-fracture environment. At 1-year follow-up after hip fracture, there is a mortality rate of about 20–30%. About half of patients returned to their pre-existing activity levels, and the other half require more ambulatory aids.

Thromboprophylaxis is important for hip fracture patients. Without treatment, rates of deep vein thrombosis or pulmonary embolism are high. Early surgical repair and mobilization are important factors in prevention. Mechanical compression devices should be started in the emergency department. After repair, some type of thromboprophylaxis should be utilized for a minimum of 3 weeks. Current guidelines recommend warfarin, low molecular weight heparin, or direct thrombin inhibitors [26].

Postsurgical medical care is best with co-management. In this model of care, both a medical physician and a surgeon manage the patient and can write orders. Communication and organization are very important so that each team knows what they are responsible for. Co-management allows for the medical physician to become a true peri-surgical specialist, able to expect routine postoperative problems such as congestive heart failure or urinary tract infection and to prevent and treat these promptly [27].

Fracture prevention is critical and should be started at the time of hip fracture. Hip fracture patients have osteoporosis and are at high risk for future fractures. Osteoporosis workup and treatment should be started at admission. Vitamin D levels should be checked and repletion given. Coordination after discharge for osteoporosis care is difficult, and a system must be organized. The best situation is a fracture liaison service with osteoporosis clinic [28]. In this situation, follow-up with the surgeon and the osteoporosis clinic happens at the same place and visit. The importance of osteoporosis care can be stressed with the patient and family. Bisphosphonates play a large role in initial treatment of osteoporosis [29]. Another aspect to fracture prevention is a fall prevention screening. This is best performed when the patient is to be discharged home and should involve a home visit to remove rugs and prepare the dwelling to minimize the risk of future falls [30].

System Improvements

The use of an organized hip fracture service has led to both improved care and less expensive care [31]. The idea of value is very important. By decreasing costs and improving results, value is created. The use of basic principles of a hip fracture service has been shown to improve value. This includes standardization of order sets, co-management, and early surgery. By standardizing the process, errors can be reduced or eliminated. For the hip fracture patient, this is by elimination of unnecessary tests and consults as well as elimination of medications that can harm the elderly patient. Standardization of osteoporosis care will lead to fracture prevention. Co-management allows for experts to care for these complex patents. Complications can be avoided. Early surgery helps to reduce length of stay and reduce the risk of iatrogenic mistakes. Patients are mobilized faster, take less opioid medications, and are at less risk for delirium and other complications.

Other models for care internationally have also been shown to improve care. The approach in the United Kingdom has been to develop nationally mandated rules for hip fracture care that are checked with live time observation. The National Hip Fracture Audit examines time in the emergency department, time to surgery, and use of geriatric co-management. These are reported and posted on a nationally available website. Hospitals falling below the standards are fined. A hip fracture database accompanies the audit to examine outcomes. This approach has led to a nationwide significant decrease in 1-month hip fracture mortality [32]. This type of reduction has not been seen with any other approaches. Clearly the development of national standards that are guided by payment is effective in improving care.

Scandinavian hospitals have led the world in providing high-quality randomized controlled studies and the use of hip fracture registries to guide our treatment decisions. Studies have shown that arthroplasty is better than internal fixation for displaced fractures and that total hip arthroplasty is better than hemiarthroplasty in active patients [16, 33–35]. The Trondheim hip study has examined the role of geriatric care and found that geriatric management with aggressive rehabilitation gives better results than management by the orthopedic surgeon [36].

In the United States, bundled payments are changing hip fracture care. Currently the mandated CCJR bundle involves all hip fracture patients who are treated with arthroplasty. Payments are the same as those who get elective total hip replacement. Fracture patients are clearly different and cannot be maximized before surgery. They also often need post discharge in patient care. These factures make bundling of hip fracture patients difficult [37]. The bundled movement is increasing with the start of SHFFT which will bundle care for the remaining femur fracture patients and is to start in 2018 [38]. This approach gives hospitals a set amount of money and allows them to spend it on patients as wisely as possible. This approach will strongly support the use of early surgery and co-management to lessen complications. It will really focus on post discharge care to minimize the time in a rehab unit and to maximize the return to home life [39].

Clinical Vignettes

Femoral Neck Fracture

An 88-year-old lady with a history of hypertension, previous breast cancer, and a previous stroke with some left-sided weakness fell onto her left hip. She lives at home with her husband and ambulates within the house with a walker. On exam, her leg is shortened and rotated, and motion

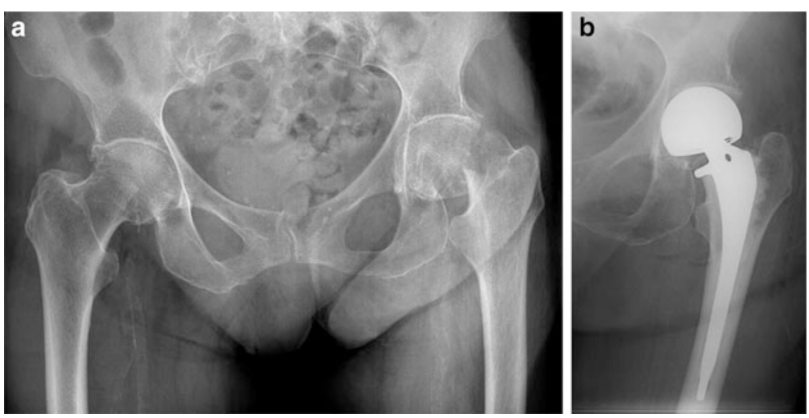

Fig. 6 Vignette 1 – femoral neck fracture. (**a**) AP radiograph at the time of injury of the hip shows a displaced femoral neck fracture. (**b**) AP radiograph of the hip shows a cemented hemiarthroplasty. The ball of the implant seems to be correctly sized, and the stem appears well cemented

of the hip is very painful. The left leg does have weakness as residual from the previous stroke. She does not take any medications for osteoporosis. Plan radiographs reveal a displaced femoral neck fracture (Fig. 6a). Options were discussed. With her poor bone quality, internal fixation is a poor option due to the very high rate of a second surgery. With her relative low function, hemiarthroplasty is a better option than total hip arthroplasty. The benefits of hemiarthroplasty are higher joint stability with lower dislocation risk. The downside is possibly higher rate of subsequent pain in the hip. In low-activity patients, this risk is minimized. She underwent a cemented hemiarthroplasty without complication (Fig. 6b). She left the hospital for a subacute nursing facility and went home 3 weeks later where she continues to use the walker for ambulation. Previous stroke is set up for weaker bone due to disuse osteopenia and higher rates of falls due to muscle weakness and poor balance. The patient was referred for metabolic bone evaluation for vitamin D repletion and bisphosphonate treatment.

Intertrochanteric Fracture

An 88-year-old lady who lives with her son at home fell and had a hip fracture. She had previous coronary bypass surgery in the distant past. She was admitted to the hospital and that evening underwent fracture fixation. She had a stable two-part intertrochanteric fracture (Fig. 7a), and a sliding hip screw with side plate was used for fracture fixation (Fig. 7b). She was started on immediate full weight bearing. Two days after surgery, she was discharged home with her family. She was doing well but developed pneumonia and was rehospitalized. She had a subsequently second rehospitalization for congestive heart failure. At the 6-week point, she was home and doing well with ambulation. She was having no pain in the hip. She was started on vitamin D and calcium. This case illustrates the complex medical condition of elderly patients with hip fracture. Two readmissions occurred after her fracture fixation for medical problems.

Atypical Hip Fracture

A 65-year-old lady was walking and felt her hip snap. She fell and was found to have a hip fracture. She has a history of ibandronate use for 10 years. She has a history of hypertension and rheumatoid arthritis and takes methotrexate and prednisone. She was found to have a displaced subtrochanteric femur fracture

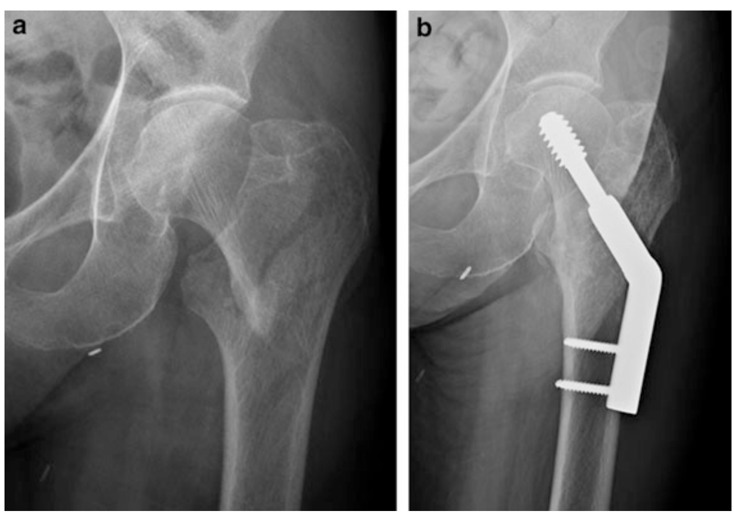

Fig. 7 Vignette 2 – intertrochanteric fracture. (**a**) Shows the injury radiograph with a two-part intertrochanteric hip fracture. (**b**) The radiograph shows the fracture fixation with sliding hip screw and side plate

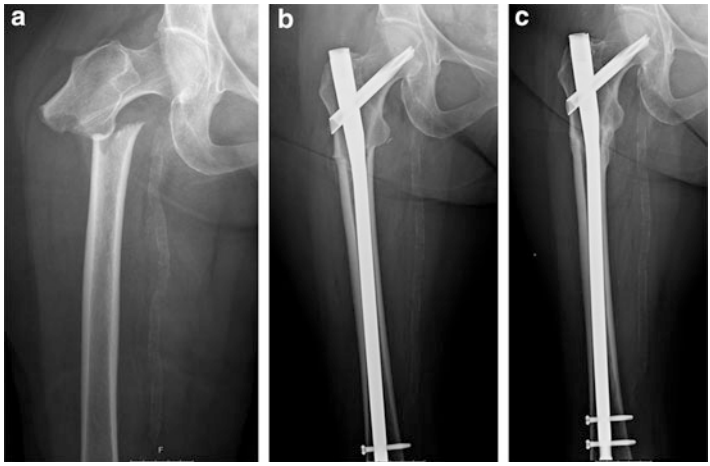

Fig. 8 Vignette 3 – atypical hip fracture. (**a**) Injury radiograph shows a displaced subtrochanteric hip fracture. The fracture line is horizontal in direction. (**b**) AP radiograph shows the intramedullary hip screw used for fracture fixation. The fracture is well aligned. (**c**) One-year postfracture radiographs show healing of the fracture with no change in rod position

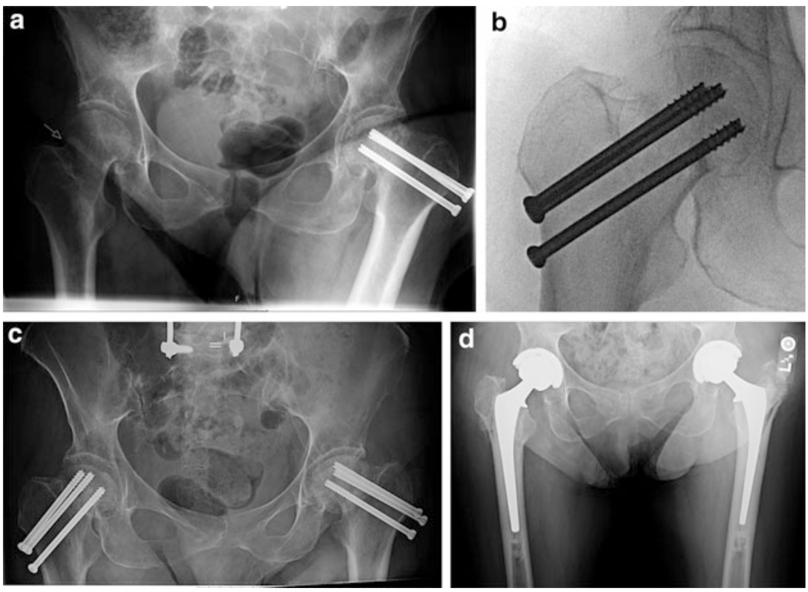

Fig. 9 Vignette 4 – failed screw fixation. (**a**) This AP radiograph shows an acute femoral neck fracture on the right hip. The arrow points to an impacted minimally displaced fracture. The left hip has cannulated screw fixation from previous fracture with a healed shortened fracture. (**b**) Intraoperative fluoroscopy shows the fracture fixation with three cannulated screws in good position. (**c**) Follow-up radiographs show that the right hip has also collapsed and is markedly short with screw back out. (**d**) Both hips were treated with total hip replacement in sequential fashion. This AP radiograph shows the total hip replacements with uncemented acetabular components and cemented femoral components

(Fig. 8a). In hind sight, previous x-ray showed evidence of a thickening of the lateral cortex of the subtrochanteric area with impending fracture (Fig. 8b). The patient had an atypical femur fracture from bisphosphonate use. She was treated with intramedullary nailing and subsequent follow-up with the metabolic bone service (Fig. 8c). Her bone turnover markers were extremely low, and she was taken off of the bisphosphonates. Her fracture years have gone on to complete healing, and she has no pain in the hip (Fig. 8d).

Failed Screw Fixation

A 72-year-old lady with a medical history significant for coronary artery disease and peripheral vascular disease had previous bilateral hip fractures treated with screw fixation about a year ago (Fig. 9a, b). She has had progressive pain of both hips with shortening of the legs since her surgeries. Both hips are quite painful and very stiff, and she is now very limited in her activities of daily living. She is mostly in a wheelchair and can barely walk. She would like to get back to ambulation. She lives with her husband at home. Her x-rays showed evidence of collapse and shortening of both femoral necks with evidence of now posttraumatic osteoarthritis (Fig. 9c). On both sides, the screws have backed out significantly and are prominent. She had a malunion of the fracture on the left and a nonunion on the right. After discussing options, she proceeded with sequential bilateral conversion to total hip replacement. Cemented stems were used due to her poor bone quality and high risk of periprosthetic fracture (Fig. 9d). Subsequently, she has done very well. At latest follow-up she is walking with a cane and is living at home and is pain-free and very pleased with results.

Conclusion

Hip fracture is a common and life-threatening injury in older patient. Fractures occur due to low-energy falls, and patients often have multiple medical comorbidities. Treatment is surgical with fracture repair that depends on the exact fracture type. Femoral neck fractures are treated with arthroplasty, while intertrochanteric fractures are treated with internal fixation. Early surgery and prevention of complications are crucial to success. This is best achieved with standardized order sets, streamlined care, and medical co-management. Despite best efforts, mortality is high and loss of function common.

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Total Joint Replacement

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Contents

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Abstract

Total joint replacement has developed over the past 50 years into a reliable surgical procedure. Arthritic joints are routinely excised and metal implants placed. Joint replacement is used to treat osteoarthritis, inflammatory arthritis,

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osteonecrosis, and posttraumatic arthritis. Implants are attached with or without bone cement. The articulation, or bearing surface, has improved markedly with time. Early bearing surfaces were softer than current ones and polyethylene wear was very common. Wear particles activated macrophages and a subsequent cascade of events produced osteolysis, bone loss, and implant loosening. The advent of highly crossing polyethylene has led to the expectation of lifelong use in most patients. Modern anesthetic and rehabilitation techniques have allowed for short hospital length of stay or even outpatient joint replacement surgery. Patient-recorded outcomes of joint replacements are excellent after surgery. Healthcare reform has led to the use of bundled payments for joint replacement. In response to bundled payments, new protocols to maximize patient's health prior to surgery have been developed, improving results and outcomes of this already very successful surgery.

Keywords
Hip · Knee · Joint replacement · Osteoarthritis · Inflammatory arthritis · Osteonecrosis · Bearing surfaces

Introduction

Replacement of joints with artificial surfaces has become common in the human body. Orthopedic surgeons currently replace joints in the fingers, wrist, elbow, shoulder, spine, hip, knee, ankle, and feet. The most commonly replaced joints are the knee and hip. Starting in the 1960s, hip replacement was markedly improved and is now an extremely reliable procedure. Knee replacement also is markedly improved with very good results. Osteoarthritis, inflammatory arthropathies, osteonecrosis, and posttraumatic arthritis are the most common reasons for joint replacement. Replacements typically use metal parts that are attached to the bone either with or without bone cement. The implants have an articulation which is the moving part within the replacement. With the advent of modern bearing surfaces, wear rates of implants have markedly decreased. The most common complications of joint replacement are infection, loosening, pain, fracture, and dislocation. With the increase in the elderly population, the numbers of joint replacements are increasing. Improvements in anesthetic and rehabilitation techniques have led to the introduction of outpatient joint replacement. In the United States, healthcare reform has led to a payment mechanism for doctors and hospitals termed bundled payments. Bundled payments are radically changing joint replacement surgery. Within this system, all fees of all providers and all hospitals and care within 90 days of surgery are paid for with one lump sum. This fee includes costs of any complications or readmissions. Bundled payments have led surgeons to maximize patient's health before surgery to try as best as possible to assure a quick and smooth recovery.

Total Hip Replacement

History

While types of hip replacements existed in the early twentieth century, the field was really started with vigor by John Charnley, an English surgeon. He developed a regimented approach to total hip replacement based around strict surgical protocol and infection prophylaxis. His initial surgeries utilized an acrylic bearing surface and all failed. Despite this dramatic failure, Charnley continued his efforts at hip replacement and began to use polyethylene as the bearing surface. He approached the hip by removing the greater trochanter. The osteotomy was repaired at the end of the case with wires. He used cemented implants and a 22 mm head size to minimize the wear of the plastic acetabular component. His method became very successful, and his teachings were spread to the United States and throughout the world [1].

In the 1970s, the use of uncemented implants was developed by several surgeons. To install these implants, reamers are used on the acetabular side and the metal component is impacted and attached with screws. The reamer used is 1–3 mm smaller in diameter than the cup allowing for a press fit. A polyethylene liner is then inserted inside the metal cup. On the femoral side, broaches and reamers are used to mill the inside of the femur. The implants have a rough coating and are wedged into the bone. Modular implants were developed to allow better restoration of length, offset, and stability of the hip. The femoral stem has a trunnion with a Morse taper, and the head ball is impacted onto the trunnion. Modularity allows for different lengths and diameters of head size to let surgeons obtain correct leg length and adequate soft tissue tension. The surgical technique has been further refined and is now performed routinely throughout the world [2]. In the United States alone, over 300,000 hip replacements are performed each year.

Indications

Hip replacement is performed for a variety of indications. Osteoarthritis of the hip is the most common. Other indications are inflammatory arthropathies such as rheumatoid arthritis, osteonecrosis, hip dysplasia, hip impingement, or arthritis from trauma or infection. Plain radiographs are the first modality used to diagnose arthritis of the hip. Patients with arthritis present with pain that is typically in the groin or buttock. Pain is often worse with activity and is better with rest. Patients may notice that the hip is getting stiffer and that they have trouble reaching down to put on socks or tie their shoes. They may have trouble cutting their toenails. The patient may notice that the leg is shorter than the other side from the wear of the hip.

On physical examination, hip motion will be limited when compared to the other side. In particular, flexion and internal rotation will reproduce the symptoms, and the patient will hurt in the groin region. On physical exam it is important to rule out other causes of pain around the hip, such as pain from the lumbar spine with radiculopathy down the leg. Pain can also be in the soft tissues around the lateral aspect of the hip. Pain around the iliotibial band and greater trochanter is called trochanteric bursitis. The patient may have more than one of these problems around the hip region.

Fig. 1 AP radiograph of the hip shows osteoarthritis of the hip. There is joint space narrowing and osteophytes on the edge of the acetabulum and the femoral head

If physical exam points toward the hip as the source of pain, plain radiographs should be taken. The radiographs should be examined for signs of joint space narrowing (Fig. 1). Other signs of osteoarthritis include osteophytosis, joint line sclerosis, and periacetabular cyst formation. Patients with osteonecrosis may have a normal hip x-ray. If the x-ray is normal and it seems that the patient has hip pain on exam, the next study should be an MRI scan. This will show evidence of other pathology in the hip such as a labral tear or femoral acetabular impingement. MRI is also an excellent test to look for osteonecrosis of the femoral head (Fig. 2).

Patients diagnosed with osteoarthritis of the hip are first treated nonoperatively [3]. Activity modification should reduce high-impact activities, and the patient may require the use of a cane or walker. Anti-inflammatory medication should be prescribed if there are no contraindications. Acetaminophen is also helpful for pain. Glucosamine chondroitin has not been found to be helpful for osteoarthritis. Opioid medication should be avoided if possible. Another option for

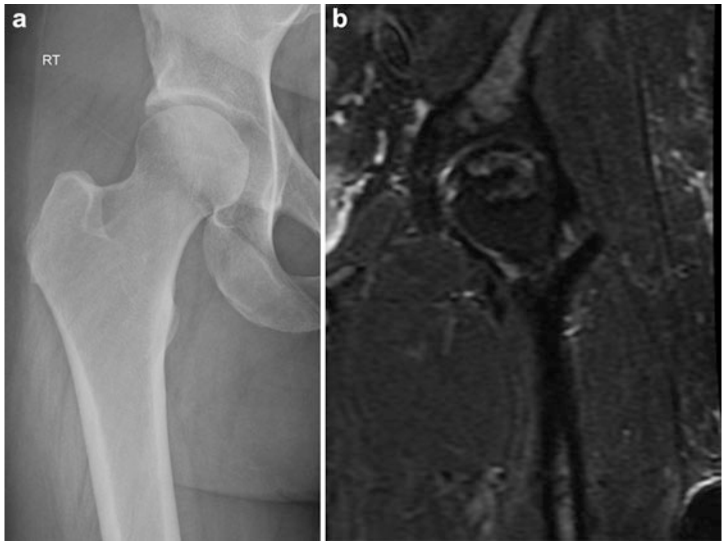

Fig. 2 Imaging osteonecrosis of the femoral head. (**a**) AP radiograph of a patient with osteonecrosis and hip pain. The radiographs do not show the lesion. (**b**) T2-weighted MRI scan shows the lesion within the weight-bearing region of the femoral head

treatment of pain is an intra-articular cortisone injection. For the hip, this requires either fluoroscopic or ultrasonic guidance. Injection is a temporary treatment option. Weight loss and physical therapy may also help hip pain from arthritis.

The decision for surgery should be based around the failure of these treatment options and continued worsening pain. The patient should have severe enough pain that it is affecting his or her activities of daily living. The patient should reveal that they cannot do things that they would like to do in life. If this is true and the radiograph reveals osteoarthritis, total hip replacement is an excellent option. In the past, other procedures such as partial or hemiarthroplasty and resurfacing arthroplasty have been performed with poor results, and these procedures should be avoided [4].

Surgical Technique

There are three main surgical approaches to hip replacement. These include the anterolateral, anterior, and posterior approaches to the hip (Table 1). Each of these approaches uses a different muscular interval to access the hip joint. The optimal approach has been debated for 40 years, and each of the approaches has pluses and minuses [5]. The anterolateral approach comes from the side of the hip and involves taking off a portion of the gluteus medius and minimus tendons. This gives excellent access and exposure to the hip joint. Hip replacements are very stable after an anterolateral approach and have low rates of dislocation. However, by approaching through the gluteus medius, there is a low rate of problems with the tendon after surgery. If this fails to heal, the patient may develop a symptomatic limp called a Trendelenburg gait [6].

The anterior approach comes through the front of the hip in the interval between the tensor fascia lata and sartorius muscles. The hip is very stable to posterior dislocation as the posterior structures are not damaged. Patients may feel more weak in the front of the hip. The anterior approach has been made popular recently with the intraoperative use of fluoroscopy and special surgical table [7]. However, the approach itself is not new and has been used for over 40 years with excellent results. The anterior approach has a higher rate of femoral fracture and loosening [8]. Fixation of femoral fractures is also more difficult with this approach and may require another incision.

The third main approach to the hip is the most commonly used in the United States and is the posterior approach. With this approach, the external rotators are taken off, and the hip is dislocated posteriorly. This is an excellent approach affording wide exposure. The posterior approach is perhaps the easiest approach to extend if any

Table 1 Approaches to hip arthroplasty

Approach	Interval	Pros	Cons
Anterior	Between tensor fascia lata and sartorius	Theoretically muscle sparing	Higher rate of femoral fracture and loosening Difficult to extend
Anterolateral	Through the gluteus media	Lowest dislocation rate	Abductor damage with Trendelenburg gait
Posterolateral	Through external rotators	Most easily extensile	Higher dislocation rate

intraoperative problems happen or if revision arthroplasty is needed. The negative with this approach is that there is a slightly higher risk of posterior dislocation. This is improved with careful soft tissue closure of the capsule at the end of the case. While these approaches have been debated for years, there is no clear winner, and the experience of the surgeon performing the surgery is the most important aspect of picking which approach should be used [9].

With all approaches, after the hip is exposed, the femoral head is cut and removed (Fig. 3). The acetabulum is then exposed and the soft tissues including the labrum and the tissues in the fovea are removed to give good visualization. Hemispherical reamers are then used to shape the acetabulum so that the acetabular component can be impacted (Fig. 4). Most typically, uncemented acetabular components are used, although cemented components also have good results, particularly in elderly patients. If using an uncemented acetabular component, supplemental screws may be utilized. At this point in the procedure, a trial liner is placed into the shell (Fig. 5).

The surgeon then exposes and prepares the femur. The canal is opened, and depending on the system to be used, sequential reamers and broaches are used (Fig. 6). The femoral component may be inserted with or without bone cement. If an uncemented component is used, this must have an excellent press fit and be wedged into the femur. Several designs of uncemented femoral implants exist. These are shaped differently and have coating either on the top portion of the implant or extending all the way to the end of the prosthesis. Many designs exist that have shown excellent clinical results [10]. It is critical that the coating allows ingrowth to extend circumferentially around the implant. After placing the femoral component, a trial head ball is placed. An intraoperative x-ray is taken to assess size, positioning, and leg length. The hip is tested though range of motion to make sure that it is stable. The real liner and head ball are placed, and the incisions are closed.

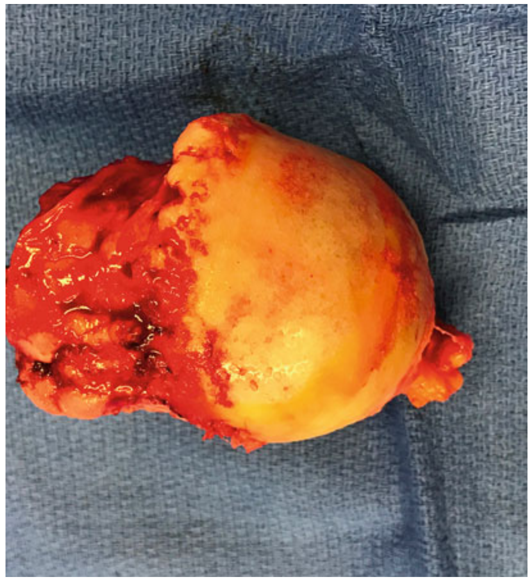

Fig. 3 A photograph of an arthritic femoral head that has been removed for arthroplasty. The head is not round, and the cartilage is worn away exposing eburnated bone

Implant Design

Design of hip replacement implants have changed over the years [11]. The acetabular component may be cemented or uncemented. Uncemented components have a rough coating to allow for bony ingrowth. The size of the finish or coating has been found to be important. Bone ingrowth is best with a pore size of 100–150 microns [12]. Initial fixation must be stable with micromotion of less than 150 microns to allow for bone ingrowth [13]. The bone must subsequently grow into the

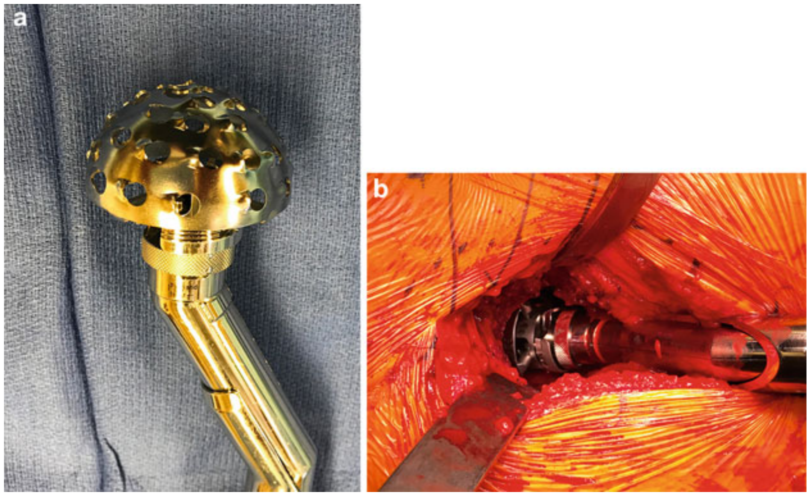

Fig. 4 Acetabular reamers are used to shape the acetabular bone for implant insertion. (**a**) The reamer is hemispherical in shape with a cheese grater-like surface. (**b**) The reamers are used in increasing sizes until a diameter 1–3 mm smaller than the implant to allow for a press fit

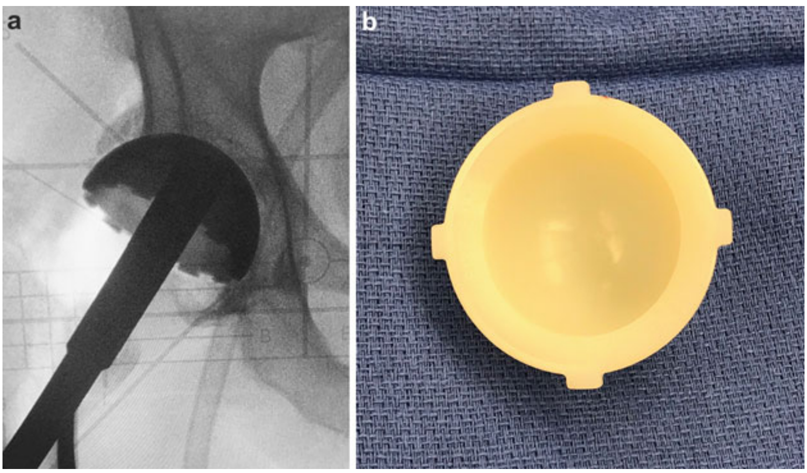

Fig. 5 The acetabular component has a rough surface for bone ingrowth. A locking mechanism inside the cup allows for insertion of a modular polyethylene liner that serves as the bearing surface for the hip. (**a**) This intraoperative fluoroscopy picture shows the acetabular component being driven into the acetabulum. (**b**) The liner is pictured which is made of highly cross-linked polyethylene. It has a locking mechanism to fit into the cup and a smooth inner surface

implant so that the implant becomes osteointegrated. Many finishes exist that are successful, some with hydroxy-apatite coatings.

There are different bearing surfaces, or liner and head ball combinations, that are used for hip arthroplasty. In the past, a polyethylene liner was most typical. About 15 years ago, methods were found to make the plastic harder with a process called highly cross-linking. Changes in how liners are packaged have also led to a decrease in free radicals and subsequent liner oxidation and degradation [14]. Initial polyethylene liners would wear, and if the wear was over 0.1 mm per year, the patient typically became symptomatic. The polyethylene wear would cause small polyethylene microscopic particles to develop in the hip. The particles stimulate macrophages and activate the receptor activator of nuclear factor kappa-B ligand pathway to stimulate osteoclast to resorb bone around the implant [15]. Over time this could become catastrophic. The newer highly cross-linked polyethylene liners have been

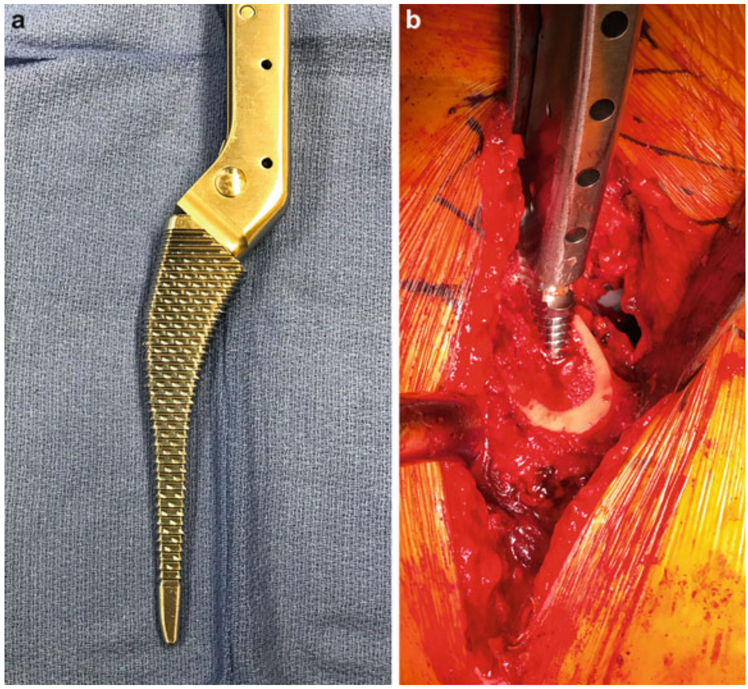

Fig. 6 Broach used to shape the femoral canal has cutting surfaces. (**a**) A broach is pictured. The broach mirrors the shape of the implant. (**b**) An intraoperative photograph showing a broach within the femoral canal. Increasingly larger sizes of broach are impacted until a stable fit is obtained

very successful. Wear rates at 13 years out from implantation are less than 0.01 mm per year [16, 17]. The most common head ball material used is highly polished cobalt-chrome steel.

Other bearing surfaces have been developed including metal-on-metal, ceramic-on-plastic, or ceramic-on-ceramic articulations. Metal-on-metal articulations have led to complications. These were initially made popular with the hope that a very large head ball size could be used. A large femoral head would lessen dislocation rates. At the same time, it was felt that wear of this surface would be better than with a polyethylene liner. However, this has not been the case. In many cases catastrophic metallosis has developed with allergic reactions and a macrophage-induced process with soft tissue and bone destruction. Failure of metal-on-metal implant led to the recall of the Depuy ASR metal-on-metal articulation and many revision surgeries. These can be catastrophic as the metal debris can work into the musculature and the bone around the hip [18].

Ceramic bearings have been used with success. Ceramic head balls are now commonly used with highly cross-linked polyethylene liners. Ceramic-on-ceramic has been a successful articulation but is harder to install than a polyethylene liner. The ceramic liner must be precisely placed into the cup, and if it is off just slightly, problems can occur. There is a low but real rate of squeaking that can be audible with ceramic-on-ceramic articulations [19]. With the medium-term success of highly cross-linked polyethylene liners, surgeons are hopeful that this will be the uniform articulation of choice in the future.

There are many designs of femoral implants. Cemented designs such as the original Charnley design have been incredibly effective, and subsequent cemented implants using a dual taper geometry have also met with excellent success. Uncemented implants of many designs are also successful. These include designs to wedge the implant into the top part of the metaphysis of the femur in different ways. Uncemented designs also may use the diaphysis of the femur for fixation. Uncemented designs do have higher rates of periprosthetic fracture than cemented designs, particularly in osteoporotic bones. These fractures may occur during surgery or years later from a fall. Uncemented designs also have a low rate of pain due to mismatch of the modulus of elasticity of the implant to bone. This is more common with diaphyseal fixation than with metaphyseal fixation [20].

Outcomes

The use of patient-reported outcomes (PROs) is becoming more important to accurately assess the outcome of total hip replacement [21]. Several scores now exist that can be quick and easy to use. The most common of these are the Hip dysfunction and Osteoarthritis Outcome Score (HOOS) or the Patient-Reported Outcomes Measurement Information System (PROMIS) developed by the National Institute for Health. These scores supplant previously used scores, such as the Harris Hip Score, that were collected by observers (typically the surgeon). Currently there is a push to move to collection of routine outcomes using PROs. Current medical record systems are poor, and often surgeons must buy separate software systems for collection of data. Hopefully the future will allow routine collection of data as mandated by healthcare reform laws. The use of registries has improved care worldwide and allowed surgeons to quickly find implant designs that are less successful and remove these from the market [22]. Excellent registries exist in Australia and Scandinavia. The American Joint Replacement Registry is relatively new and behind that of other countries. This registry is growing and hopefully will allow for prompt recognition of inferior implants in the future.

Complications

Complications after hip replacement may be major or minor. Major complications include mortality, thromboembolic events, loosening, dislocation, fracture, infection, and damage to nerves, blood vessels, and tendons. Mortality rates after total joint surgery are low and are less than 0.1% 30 days out of surgery [23].

Thromboembolic events include deep vein thrombosis and pulmonary emboli. Prophylaxis used by surgeons includes medication and mechanical means. Early mobilization is now commonly employed. In the past, patients would not move and would be at bed rest after surgery. Now, patients mobilize the same day of surgery and often go home the next day. Compression devices are utilized to decrease rates of deep vein thrombosis and are either foot pumps or sequential compressive devices. Thromboprophylaxis includes aspirin, low-molecular weight heparins, warfarin, or direct thrombin inhibitors. It is debated what the best option is, and this is currently unknown. Recommendations for joint replacement have been standardized between the American Association for Hip and Knee Surgeons and the American College of Chest Physicians [24].

Wear of the polyethylene liner is another complication of hip replacement. This may lead to osteolysis and loosening of the implant. It is possible for the head ball to wear through the liner and through the metal cup, creating vast amounts of metal debris and damage to the bone and musculature (Fig. 7). Wear rates have decreased with modern highly cross-linked liner.

Aseptic loosening may happen after hip replacement on either the femoral or acetabular

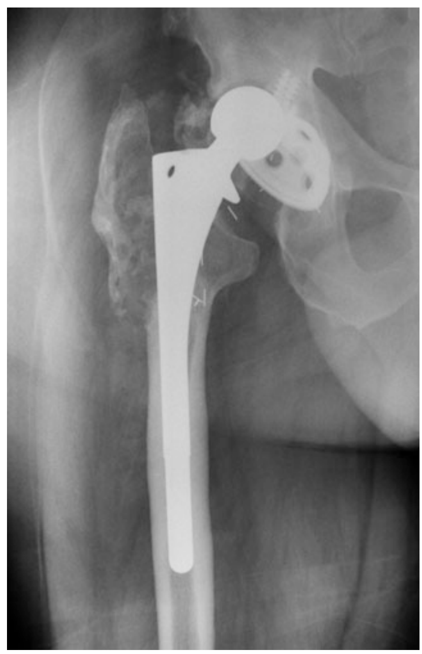

Fig. 7 An AP radiograph of a hip replacement where the head has worn through the metal socket of the acetabular implant. This was more common with older polyethylene liners with poor wear characteristic. This leads to metallosis, an extensive infiltration of pericapsular tissues with black metal debris

side. The etiology of this is an unstable implant at the time of implantation. Aseptic loosening is typically diagnosed with pain with weight-bearing and with radiographs which reveal lucencies around the implants. Loosening of cemented implants may also occur and typically develop over time. Aseptic loosening, if symptomatic, can really only be treated by revision surgery to put a stable implant in place. Revision implants are typically longer and engage more bone on the femoral side. On the acetabular side, these may require augments and multiple screws to get solid fixation.

Dislocation is an unfortunate complication of hip replacement. This may occur in the immediate postoperative period or many years after surgery. Late dislocations typically occur because of wear of the plastic liner and require revision surgery. First-time dislocations are generally treated with closed reduction under anesthesia. After reduction of the hip, a brace may be placed to try and prevent the hip from dislocating. If dislocation occurs several times, revision surgery is required to fix the problem. This may involve changing the position of the implants, the use of a larger head ball, or the use of a constrained liner.

Periprosthetic fracture is an increasing complication of hip replacements, especially as patient's age and become more osteoporotic. This is most common around the femoral implant due to a fall. Periprosthetic fractures generally require surgery. This may either be with plate fixation if the implant is stable or with revision surgery if the implant is loose.

Infection of implants occurs in about 1–2% of patients. About half of infections occur immediately after surgery and the other half may occur years later. Acute infections usually are due to intraoperative contamination. Later infections may be from hematogenous spread of other infections in the body such as sepsis, urinary tract infections, or dental infections. The most common organism to infect a joint replacement is staphylococcus. Bacteria form a layer, called a biofilm, on the metal implants. This allows the bacteria to become very difficult to eradicate with retention of implants. Approaches to prosthetic joint infection with antibiotics alone do not succeed. Antibiotic suppression may be used in ill patients who would not tolerate surgery. Washout of the joint with retention of implants and subsequent antibiotics may be successful in acute infections that are diagnosed within 3 weeks of the infecting event. More commonly, infections are chronic and implants must be totally removed and the bone surgically debrided to eradicate infection. The implants may be replaced immediately using a one- or two-stage approach. In a one-stage approach, implants are removed and permanent revision implants placed during one surgery. In a two-stage approach, after removal of implants, a spacer is placed to allow local drug delivery, and the infection is treated with 6 weeks intravenous antibiotics. Subsequently, the spacer may be removed and revision implants placed. Overall, about 80–90% of infections are thought to be cured with this approach. Success depends on the health of the host, on their ability to fight infection, and on the precise type of bacterial infection. Hip infections are serious events with high rates of morbidity and mortality [25].

Leg length differences are a common problem after hip replacement surgery. Most typically the arthritic hip is shorter than the nonarthritic hip due to wear of the cartilage and bone. With surgery, the hip is lengthened to equal leg lengths. It is possible for the leg to be overlengthened during surgery. This may be done by the surgeon in an attempt to make the hip as stable as possible to reduce the possibility of dislocation. Sometimes the leg length difference may be due to weakness of the hip muscles, producing a pelvic tilt. In this case the actual leg length is equal, but the patient perceives the leg to be longer. Usually this improves with strengthening. True leg length differences are treated with a lift in the contralateral shoe.

Damage to the sciatic or femoral nerves may occur after hip replacement. Usually these result from stretching of the nerves due to retractor placement. Sciatic nerve palsy may also occur from overlengthening of the leg. Nerve palsies are more common in patients with dysplasia. About 50% of cases have return of function.

Total Knee Replacement

History

Initial knee replacements utilized hinged devices and were developed in the 1960s. These devices did not perform well. In the early 1970s, Dr. John Insall pioneered the cemented condylar knee replacement. In this design, the femur and tibia are resurfaced, and a plastic liner is placed that locks into the tibial component. The collateral knee ligaments give stability to the device. This was a much-improved design from the initial hinged knee and led to wide acceptance of knee replacement. Subsequently the condylar knee has been modified and improved into the current modern designs of implants. One of the main improvements have been better tools to reproducibly install the device in the correct alignment.

Fig. 8 An AP radiograph of the knee showing osteonecrosis of the medial femoral condyle due to protease inhibitor therapy. The large lesion within the bone causes pain and may collapse leading to articular damage and wear. Complete fragmentation and collapse is seen in this image

Indications

The primary indication for total knee replacement is osteoarthritis of the knee. Other indications are inflammatory arthritis and posttraumatic arthritis. Osteonecrosis is less common in the knee than in the hip (Fig. 8). Osteoarthritis is a common condition leading to wear of the articular cartilage and tears of the primary shock absorbers in the knee, the menisci. There are three main compartments, or anatomic areas, within the knee. These include the medial, lateral, and patellofemoral compartments. Arthritis may affect one or multiple compartments of the knee (Fig. 9). In the United States, osteoarthritis of the knee is about twice as common as in the hip. Obesity is directly related to rates of knee arthritis.

Treatment of osteoarthritis of the knee includes the use of nonsteroidal anti-inflammatory medications, acetaminophen, braces, ice, heat, gels and creams, physical therapy, and activity modification. More severe pain can be treated with injection therapy. Cortisone injections help for a limited period of time. Evidence is uncertain whether hyaluronic acid injections help symptoms. AAOS Guidelines do not recommend the use of hyaluronic acid injections [26]. These injections do not build up cartilage in the knee and are more expensive than cortisone therapy. If these treatments fail to give pain relief and if the patient has disability from the knee and loss of function, then knee replacement may be a good option.

Patients with knee arthritis typically develop stiffness of the knee and may develop deformity from wear of the cartilage and bones. Deformity may be in a valgus, or knock-kneed, alignment when the wear is in the lateral compartment or varus, or bow-legged, deformity when the wear is more in the medial compartment. If only one compartment is affected, a partial knee replacement may be considered [27]. Most often, more than one compartment is involved, and a total knee is performed.

Diagnosis of knee arthritis is done with history, physical exam, and plain radiographs. Radiographs will show joint space narrowing, joint line sclerosis, and osteophytosis. In the case of normal x-rays, MRI may be considered to

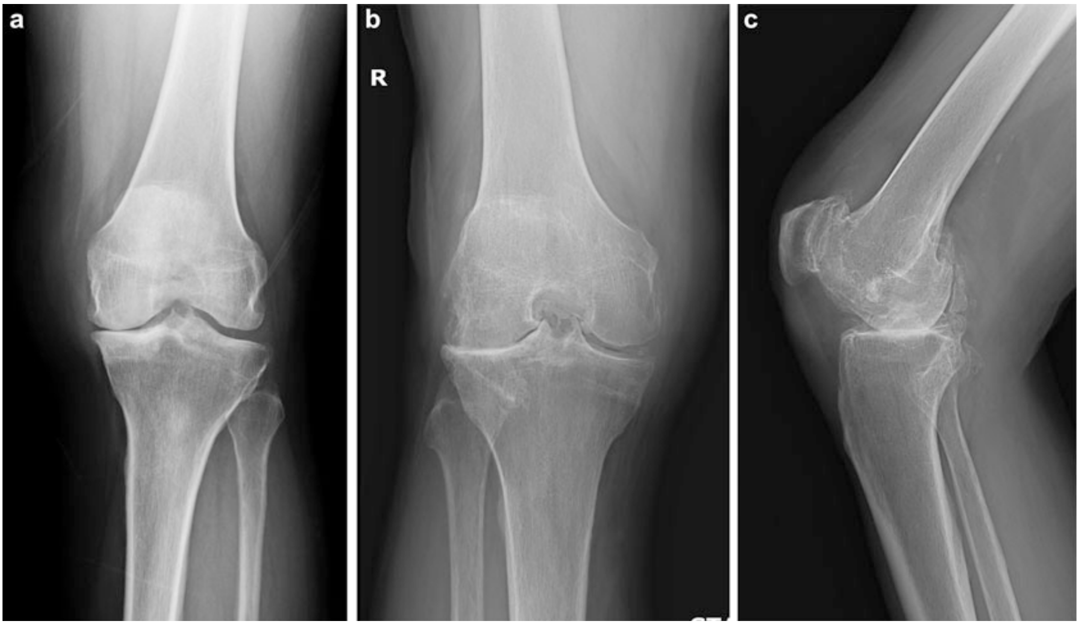

Fig. 9 AP radiographs of the knee showing different patterns of wear caused by osteoarthritis. (**a**) The medial compartment is worn creating a bow-legged or varus deformity of the leg. (**b**) The lateral compartment is worn creating a knock-kneed or valgus deformity of the leg. (**c**) A lateral radiograph shows wear in the patellofemoral compartment of the knee

examine the menisci, ligaments, and cartilage in the knee.

Surgical Technique

Total knee replacement is performed through an arthrotomy on the medial side of the knee. The knee is exposed and osteophytes removed. Cutting blocks are then used to make the cuts to align the prosthesis. Most commonly the tibial cut is made at 90° to the shaft of the tibia. The femoral component is aligned at between 5 and 7° of varus. This allows for restoration of correct alignment of the limb. This method of cuts is termed classical alignment. Another type of alignment is called anatomic [28]. In this alignment, the tibia is placed in 3° of varus and the femoral component at about 9° of varus. Both of these give the same overall alignment of the limb (Fig. 10). Little difference has been found between these methods as long as overall alignment is achieved [29]. Precise cutting jigs are used to allow for sizing of the components and correct alignment (Fig. 11). Alignment must be checked in three planes: the coronal plane, the sagittal plane, and the rotation of the implants. Rotation is very important to allow for proper patellar tracking (Fig. 12). In general, the femoral and tibial components must be placed in slight external rotation. Internal rotation will cause patellar maltracking.

The position and rotation of the femoral component can be performed through two general methods. One is called gap balancing, and the other is called measured resection. Basically these methods depend on whether the bony cuts are made first and ligament balancing is performed second or whether ligament balancing is performed first and then the cuts are made. Results of these two methods of placing the implants are comparable [30]. After the cuts are made, the ends of the bones are prepared. Most total knee replacements are implanted using cemented technique (Fig. 13), although some uncemented designs have been successful. Overall cemented designs have better results than uncemented designs [31].

Fig. 10 A long-standing x-ray shows coronal alignment of the knee. When aligned correctly the line drawn from the center of the femoral head to the center of the ankle should pass through the center of the knee. On the right side, the leg has a varus deformity from deformity of the femur. The line from the center of the femoral head to the ankle is medial to the center of the knee

A polyethylene liner attaches to the tibial component and articulates with the femoral component. A variety of different styles of liner exist. The patella may be left unresurfaced or be resurfaced. Results do not greatly differ, and this is an area of controversy [32]. After the implants are placed, the arthrotomy and skin are closed.

Implant Design

The most common type of bearing surface for a knee arthroplasty is a cobalt-chrome femur on a polyethylene liner. The polyethylene may be highly cross-linked to potentially obtain better wear. The wear process is different mechanically in the knee when compared to the hip. In the knee, there are also rolling, sliding, and rotation motions at the joint surface, which can lead to delamination, pitting, and fatigue failure of the polyethylene [33]. While highly cross-linked polyethylene is thought to be an improvement in the knee, the improvement is more modest than in the hip due to these other biomechanical forces on the plastic. Ceramics and coated metals such as zirconium exist on the femoral side although ceramics may be more prone to implant fracture.

There are different designs of knee replacements that reflect different levels of constraint of the implants. The least-constrained design is

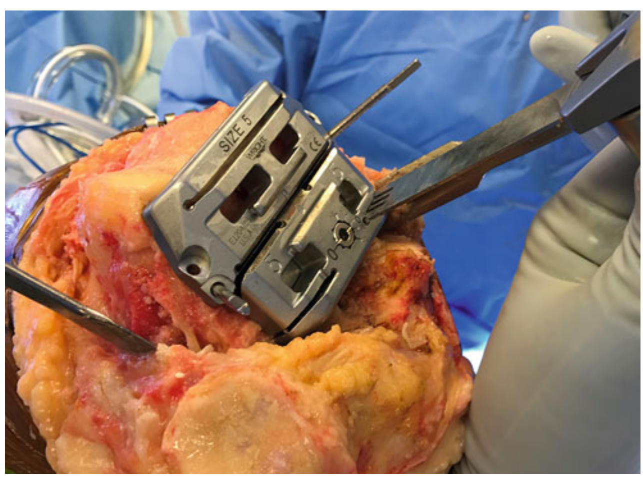

Fig. 11 Intraoperative photograph showing a cutting block placed on the distal femur. Slots in the blot allow for the saw to make precise cuts

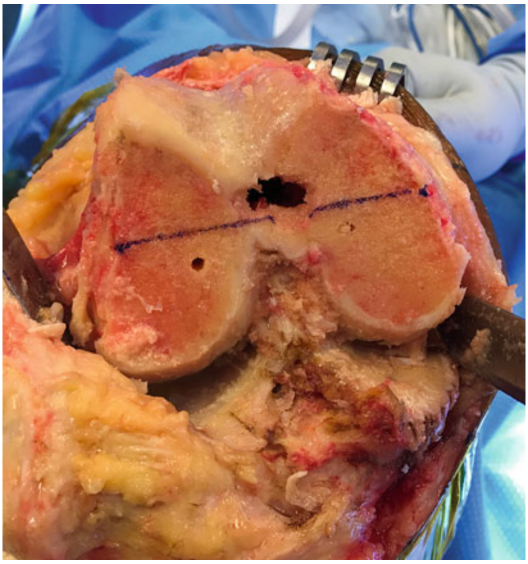

Fig. 12 An intraoperative photograph showing correct rotation of the femoral implant. The implant should not be internally rotated and should be aligned with the epicondyle axis of the femur, which is marked

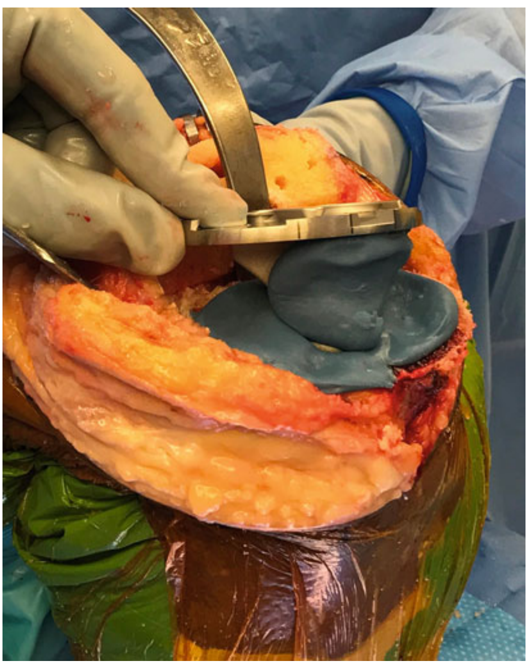

Fig. 13 Intraoperative photograph showing bone cement placed on the tibia. The implant is then impacted, and the bone cement interdigitates into the cancellous bone. This particular type of cement has a blue dye so that it can be identified later for removal

called a cruciate-retaining total knee replacement. In this design the anterior cruciate ligament (ACL) is resected, and the posterior cruciate ligament (PCL) is left intact. The bearing surface has a flat design that is unconstrained (Fig. 14). There are modifications of this with more lipped liners that may provide more constraint. Another commonly used design is termed the posterior cruciate-sacrificing knee. In a traditional PCL-sacrificing design, the femoral implant has a box, and the tibial liner has a peg, which limits posterior translation of the implant like the PCL. In revision designs more constraint is necessary, and the peg may be much larger, or a rotating hinge may exist. Despite the many designs of primary knees, there have been no outcome differences seen between PCL retaining or sacrificing designs [34].

Outcomes

Results of knee replacements are not as good as total hip replacements. More patients with a total hip feel they have a natural feeling hip in place. Patients with a knee replacement often have some type of click or pop to the knee. Overall, about 81% of patients are satisfied with total knee replacement [35]. About 10 or 15% have pain that is difficult to understand. It's hard to know whether these patients had less severe arthritis to start or whether there is some complex biomechanical factor that is not adequately replaced by the replacement. This is a subject of great interest and research.

Much recent focus is in on the use of better outcomes scoring systems after knee replacement. As in the hip, initial outcome scores were doctor-collected. Now, patient-recorded outcome scores, performance-based measures, and registries are being used [36].

Complications

Complications of total knee replacement include stiffness; pain; fracture; infection; damage to nerves, blood vessels, or tendons; thromboembolic events; and mortality. Stiffness is very

Fig. 14 A cruciate-retaining liner is shown. The liner does not have a central peg

common in knee replacements [37]. In general, the more motion a patient has before surgery, the more they will have after surgery. It is difficult to regain more motion in a patient with a stiff knee. Physical therapy is thought to be beneficial after total knee replacement in order to get the knee moving. It hurts the patient to move the knee, and thus they will want to get stiff if left to their own efforts. If adequate knee motion is not restored, the knee may be manipulated under anesthesia to try and get more motion. This should be done within 3 months of surgery [38]. To walk upstairs reciprocally, a patient needs 90° of motion of the knee. 110 degrees is needed to achieve most activities of daily living. Full extension is necessary to walk with an even gait. Significant flexion contracture is quite debilitating. Patients with hip and spine disease are particularly prone to flexion contracture. Marked stiffness can be treated with revision surgery. In most cases a full revision is needed to try to improve motion.

Pain that is difficult to understand occurs after knee replacement. A thorough workup should be taken to look for malposition of implants, stiffness, infection, or aseptic loosening [39]. Aseptic loosening is more common in patients who are obese or very large. These patients are susceptible to tibial subsidence, and a tibial component with an additional stem should be considered in these patients. Loosening is diagnosed with x-ray and is treated with revision surgery.

Periprosthetic fracture is a complication on the rise after knee replacement. This may occur right after surgery or later in time. This is more common in patients with osteoporosis. Fixation of periprosthetic fractures depends on fixation of the total replacement. If the implant is well fixed to the bone and sufficient bone remains, then plate fixation works well. If the replacement is loose or not attached to the bone, this must be revised and the bone fixed [40].

Infection is rapidly becoming the most serious complication after knee replacement. Treatment is similar to prosthetic joint replacements in the hip. Chronic infection should be treated with implant removal and either one- or two-stage revision and antibiotics. Recurrent infections are treated with knee fusion or above knee amputation.

Flexion instability may occur if an implant is not balanced correctly [41]. In this situation the knee is looser in flexion than in extension. This may lead to pain, chronic effusions, or instability. This is treated first with bracing and quadriceps strengthening. If this fails, revision surgery may be necessary.

Damage to nerves and blood vessels is rare but can be catastrophic. Stretch of the peroneal nerve is more common in patients with severe valgus deformity, where the nerve is stretched with realignment of the knee. Vascular injury occurs in about one in 10,000 cases. It is difficult to diagnose and if not picked up very quickly will often lead to amputation. If found rapidly a vascular surgeon can bypass the knee. Diagnosis of vascular injury is often delayed by subsequent development of compartment syndrome.

Minimally Invasive Surgery, Bundled Payments, and Changes in Joint Replacement

Over the past 20 years, many improvements in total hip and knee replacement have occurred. These include improvements in implant fixation, materials, and bearing surfaces. The surgical procedure has been streamlined, and recovery time has been shortened. Faster recovery has long been a goal of surgeons. Initially in the early years of joint replacement, patients were in the hospital for a long period of time and weight-bearing restrictions were used. Over the past 20 years, smaller incisions, termed minimally invasive surgery, have been popularized. Initial waves of enthusiasm met this practice and direct-to-patient marketing made minimally invasive techniques very popular. Subsequent research has shown that it is not the length of the incision but more the techniques used for pain control, anesthesia, and rehabilitation that have made the difference in patient recovery.

Pain control with the use of periarticular injections and regional techniques has led to decreased use of narcotics after surgery. This has decreased the side effects of narcotics including nausea and confusion. Immediate weight-bearing is now routinely employed after replacement surgery. This allows patients to mobilize the day of surgery. Another huge advance in joint replacement has been in blood conservation policies. The use of tranexamic acid to limit bleeding during surgery combined with the elimination of allogenic blood transfusion and lower transfusion thresholds has dramatically reduced blood transfusions after surgery. Ten years ago the rate of blood transfusion after a joint replacement was approximately 40% nationally. With the use of modern blood conservation policies, this rate has been reduced to approximately 1–2% [42]. As the use of blood transfusion is thought to be related to prosthetic joint infection, this will hopefully improve infection rates.

While these changes have gradually occurred, over the past 5 years, bundled payments have been adopted by payers, including Medicare, to try to reduce the amount of healthcare expenditure on joint replacement surgery. Bundled payments were first introduced as a voluntary program of Medicare called the Bundled Payments for Care Improvement Initiative (BPCI). Hospitals or physicians could voluntarily apply to participate. In a bundled payment, one payment is given for all care given within 90 days of surgery. This includes the surgery, the hospital stay, all doctor's fees, and all rehabilitation and post-discharge care. The payment also includes any readmissions or other care that occurs in the 90-day period. Bundled payments put the provider or hospital financially at risk for poor outcomes or expensive care. BPCI was felt to be successful and to improve care while decreasing costs [43]. The Comprehensive Care for Joint Replacement Model (CCJR) is now mandatory in 65 geographic regions in the United States [44].

The use of bundled payments has changed surgeons' thoughts about joint replacement. The hospital or doctor group is now at risk for the outcomes of the patient. If any complications occur, these are taken out of the overall payment to the group or hospital. This system puts a lot of emphasis on proper screening of patients and proper maximization of patients prior to surgery. The term that has been used is modifiable risk factors [45]. These risk factors include obesity, cigarette smoking, dental condition, opioid use, uncontrolled diabetes, and other uncontrolled medical problems. All of these conditions can be improved upon prior to surgery and have been shown to lead to more complications after surgery. Obesity, for instance, is a major factor in predicting infection after joint replacement. Patients with a body mass index over 40 have significantly higher risk of infection and other complications. This is true with poor dental condition, cigarette smoking, and uncontrolled diabetes. This has led surgeons to develop programs to maximize patients. Surgeons now require patients to go to smoking cessation classes or weight reduction programs prior to surgery. The use of chronic opioid medications before surgery has also been shown to lead to poor results after joint replacement [46]. In one study, it was shown that reducing the amount of preoperative opioids in half improves results after surgery [47]. To achieve success in a bundled payment model, it is necessary to improve modifiable risk factors so that patients can do better after surgery. One infection can financially cause great harm if the patient is readmitted in a bundled payment system. In a fee-for-service model, this is not true.

Preoperative education is also important to properly educate patients prior to surgery. Education helps in allowing for early discharge and in reducing readmissions after surgery. The preoperative joint class is best shown to improve results when required by patients and their families. This should be a formal program that involves therapists and discharge planners.

The postsurgical protocol of surgeons has also changed with the introduction of bundled payments. Most patients now spend one night in the hospital after routine hip or knee replacement. In some cases the surgery is performed as an outpatient procedure. Patients are now routinely mobilized the day of surgery.

In a bundled payment system, the biggest influence on overall cost of care is the rate of complications after surgery, readmissions of the patient, and the use of post-admission services. These include home care, home health, home physical therapy, outpatient therapy, or admission to a nursing home or rehabilitation center. In the past, a 2- to 3-week stay in a rehabilitation center or nursing home was almost routine after joint replacement. However, patients that are discharged to home instead of a nursing home and use no home health services have lower readmission rates. Patients who are stratified for medical comorbidities have a higher rate of readmission if admitted to a nursing home rather than going home [48].

It has recently been shown that physical therapy may not give any advantage after total hip replacements [49]. A self-guided exercise plan seems to give the same results. This is probably not as true after knee replacement where stiffness is such a great problem. In this case patients can now be immediately referred to outpatient physical therapy after surgery. This approach has several advantages. Mobilization is a good thing for patients. Outpatient physical therapy requires them to leave the house and walk just to get to the therapy site. It also means they need to have thought about who is going to take them to therapy after surgery. This level of organization and support really helps after a joint replacement. Education prior to surgery is important. Most centers have education classes with required attendance prior to surgery. By requiring this ahead of time, many problems can be avoided. There are still some patients where a nursing home stay cannot be avoided. These would include those with several arthritic joints or those with absolutely no social help. An example may be an elderly patient who has no family and is also caring for their spouse.

In bundled payment models, it is very important that excellent follow-up be achieved. Follow-up phone calls are a necessity. Access of the physician day or night by the patient is very important so that patients can be directed to follow up in clinic rather than in the emergency room where they are likely to be readmitted [50]. Follow-up at 2 weeks in the office helps to avoid problems and assure the patient is on the right track. In terms of recovery, most patients are doing well 4–6 weeks after surgery. They continue to improve in mobility and strength all the way up to a year.

Clinical Vignettes

Vignette 1: Routine Total Hip Replacement

A healthy 53-year-old man presents with progressive right hip pain especially in the groin area. His leg feels shorter than the other side. He is having trouble timing issues and walking distances. The pain is a little better with anti-inflammatory medication. On physical exam, his hip is stiff with range of motion, and extremes reproduce his symptoms. Plain x-rays show advanced osteoarthritis with joint space narrowing and osteophytes (Fig. 15a). Options were discussed, and he was felt to have maximized nonoperative treatment. He elected to undergo total hip replacement. This was performed

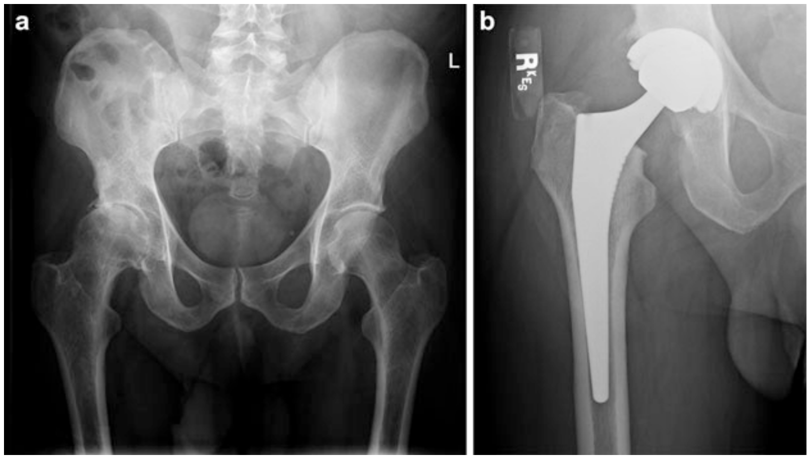

Fig. 15 Vignette 1: Routine total hip replacement. (**a**) AP pelvis radiograph showing a severely arthritis right hip. There is marked joint space narrowing with complete loss of articular cartilage. (**b**) AP hip radiograph showing the uncemented total hip replacement with good position of implants

with an uncemented device, and he was discharged home the next day. He performed a self-directed therapy program and did not require blood transfusion. He has done very well after surgery and at 6 weeks was pain-free and back to his normal activities of daily living. His implants appear to be stable on radiographs (Fig. 15b).

Vignette 2: Complex Total Hip Replacement

A 43-year-old woman was in a motor vehicle accident and sustained a right acetabular fracture and dislocation of the hip (Fig. 16a). Medically she has a kidney transplant that has performed well for 20 years. She was treated with closed reduction and subsequent internal fixation with partial hip resurfacing (Fig. 16b). She was morbidly obese at the time. Over the past 2 years, she has developed worsening hip pain in the groin with any activity. Physical exam show a stiff painful hip. Radiographs show broken hardware and marked joint space narrowing with post-traumatic arthritis of the hip (Fig. 16c). She presented with a BMI of 48, and weight loss was counseled to improve on this modifiable risk factor. She has been successful at losing weight, and her BMI is now 39. She would like to undergo conversion to total hip replacement. The screws and hardware were removed, and hip replacement was performed with uncemented components (Fig. 16d). She has done very well since surgery and is pain-free and mobilized. Often total hip replacements are more complicated than a standard procedure. Hardware may have to be removed and bone defects reconstructed.

Vignette 3: Loose Total Hip Replacement

A 49-year-old man underwent total hip arthroplasty 9 months previously. He had had progressive pain in his hip. This has not gotten better and is worse with walking and weight-bearing. It is sharp and in the proximal femur region. His x-ray shows evidence that his uncemented hip stem has not ingrown. There is lucency around the femoral implant on the x-ray (Fig. 17a). He had a negative workup for infection and was treated with revision surgery with a long uncemented stem that gets fixation in the bone of the femur diaphysis. He did very well with this and is pain-free at 1 year (Fig. 17b).

Vignette 4: Primary Total Knee Replacement

An 87-year-old man is referred to orthopedic clinic with left knee pain. He states that it has

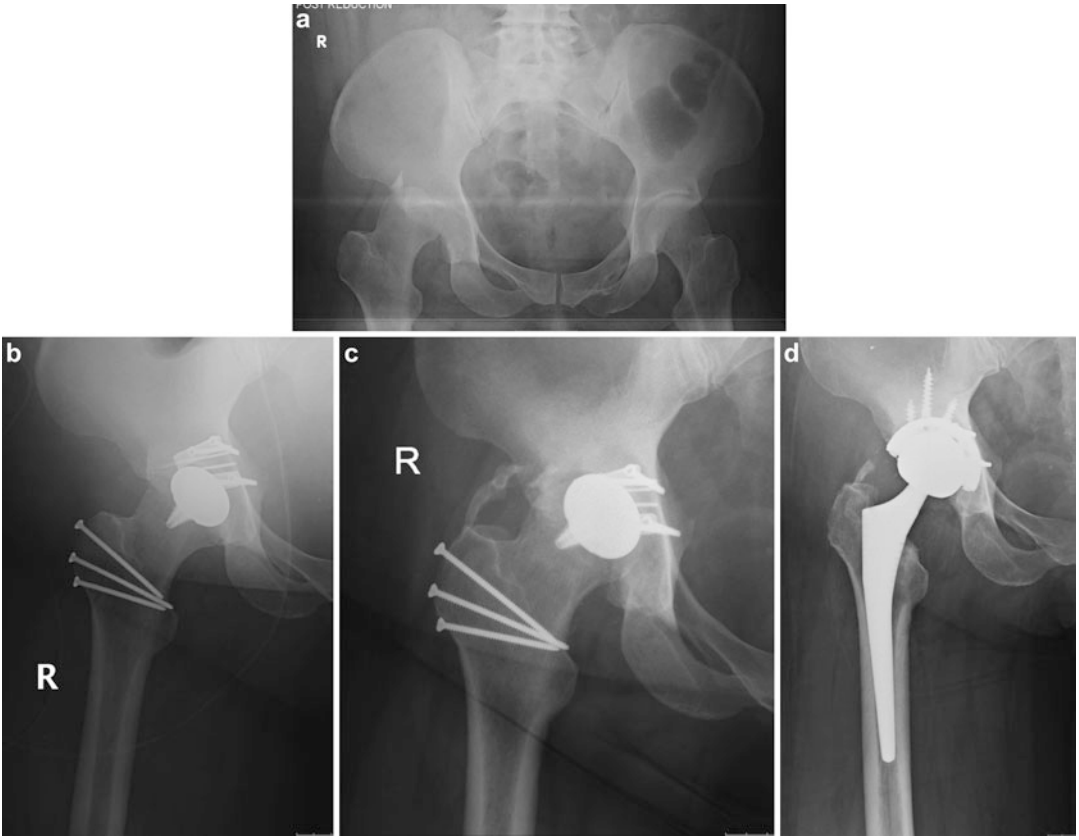

Fig. 16 Vignette 2: Complex total hip replacement. (**a**) Injury AP radiograph showing a dislocated right hip with acetabular fracture (**b**) Postoperative AP radiograph showing acetabular fixation and partial hip resurfacing (**c**) AP hip radiograph showing decreased joint space and post-traumatic arthritis (**d**) Postoperative radiograph showing an uncemented hip replacement. The screws were left in the acetabular region to avoid damage to the sciatic nerve

been present for many years but has started to bother him more over the past several months. His primary care doctor injected his knee about 1 year ago, but he did not get any relief from this. He is starting to have trouble walking long distances and walking downstairs and hills. He has to walk downstairs backward. He has been using a cane for the last 2 weeks after he sustained a fall and hyperflexed his knee. The patient is very healthy for his age but underwent bypass surgery many years ago and is still followed by cardiology. On exam, his knee range of motion has crepitus but is quite good from 3 to 100°. He has a slight varus deformity that is worse with standing. X-rays show severe osteoarthritis of the knee, primarily in the medial and compartment (Fig. 18a). He feels like he has maximized non-operative treatment and NSAIDS and acetaminophen are not helpful. He would like to plan for knee replacement.

He underwent a cemented total knee replacement with patella resurfacing. He was discharged the following day and completed 4 weeks of outpatient physical therapy. At 3 months, he feels the knee pain is gone. His knee range of motion is 0–100°. He is walking well without ambulatory aid. His x-rays show his implants to be in good position (Fig. 18b, c).

Vignette 5: Infected Total Knee Replacement

A 79-year-old man had a total knee replacement 10 years ago, and this has been well functioning (Fig. 19a). His medical history includes atrial

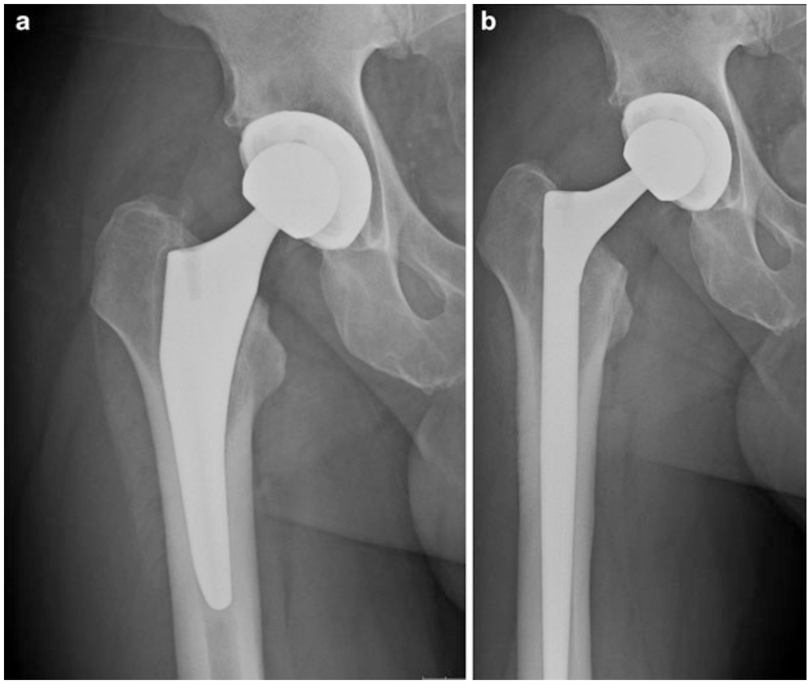

Fig. 17 Vignette 3: Loose total hip replacement. (**a**) AP radiograph of a painful hip replacement. The femoral component has a lucency around the implant in the proximal ingrowth area of the prosthesis. The implant is not ingrown and is loose. (**b**) AP radiograph of a revision total hip with a long fluted conical stem. The stem is wedged into the femoral shaft to give fixation and appears stable and ingrown

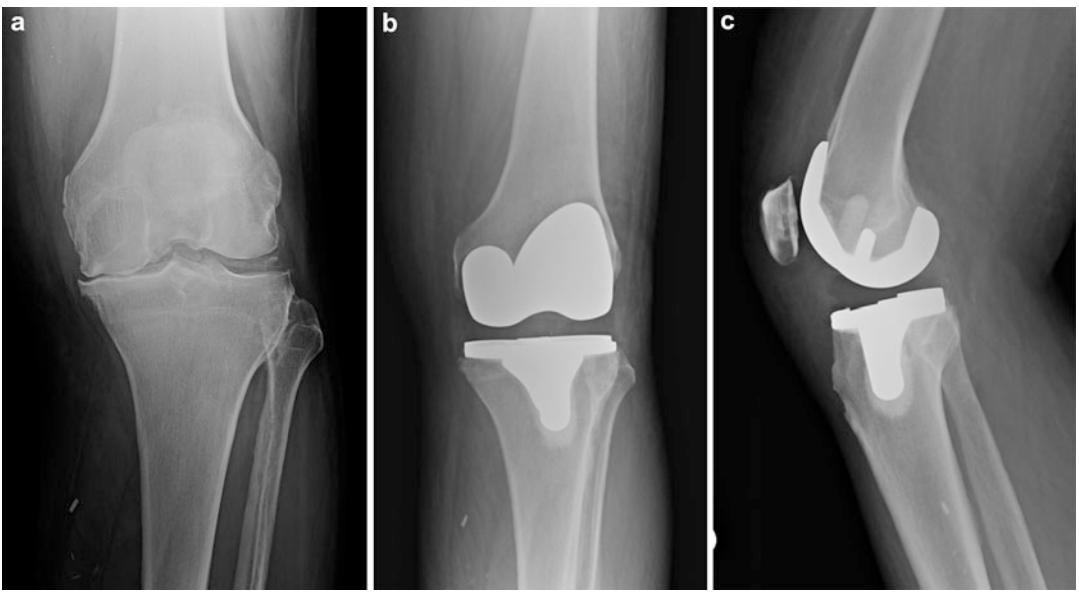

Fig. 18 Vignette 4: Primary total knee replacement. (**a**) AP radiograph of the knee showing joint space narrowing and irregularity in the medial compartment. Calcification of the lateral meniscus is visualized. (**b**) AP radiograph showing a cemented total knee replacement. (**c**) Lateral radiograph of the total knee replacement

fibrillation and a pacemaker with chronic warfarin therapy. He developed 5 days of acute pain in the knee. The knee was markedly swollen with painful and limited range of motion. Aspiration of the knee was positive for infection. Because of the acute onset of symptoms, he was treated with a washout and liner exchange with intravenous antibiotics. After treatment and the end of antibiotics,

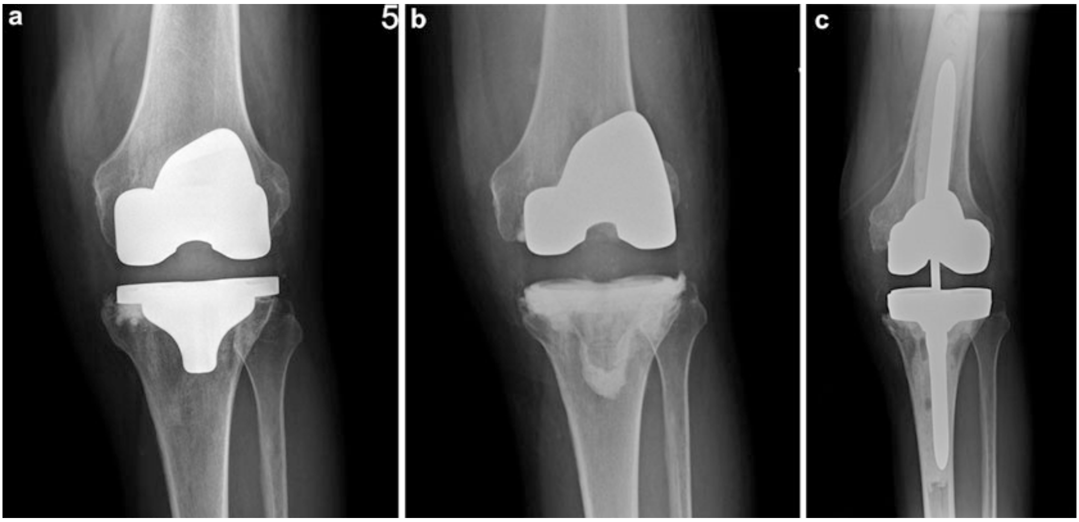

Fig. 19 Vignette 5: Infected total knee replacement. (**a**) AP radiograph showing a cemented total knee replacement that is infected. A lucency is seen under the cement on the lateral side of the tibial tray. (**b**) AP radiograph showing an articulating spacer with antibiotic laden cement. (**c**) AP radiograph showing the final revision total knee replacement with cemented stemmed implants

he developed worsening pain and swelling and was again found to have a positive aspiration. He was subsequently treated with removal of the knee replacement. Bone stock was sufficient for an articulating spacer (Fig. 19b). His cultures grew *Staphylococcus caprae,* and he was treated with ceftriaxone and vancomycin for 6 weeks per infectious disease consultation. He subsequently had reimplantation surgery with cemented stemmed revision implants (Fig. 19c). He has done well and at 6 months, has had no recurrence of infection, and has gotten back to playing golf. Infected joint replacement is a severe problem and often results in multiple surgeries. The patients are often unwell with complex medical issues. In this case, an articulating spacer was able to be used so that the patient could weight bear and be mobilized. In many cases, bone loss or soft tissue coverage is too severe, and a static spacer is used, so the patient cannot weight bear.

Conclusion

Total joint replacement is an extremely valuable procedure. Both total hip and knee replacement have been shown to give excellent long-term results with the reduction in pain and improved function. Joint replacements are primarily used for osteoarthritis of the joints, but other conditions such as inflammatory arthritis, posttraumatic arthritis, and osteonecrosis also respond well to total joint replacement. Improvements in anesthetic and recovery protocols have led to outpatient joint replacement. Modern bearing surfaces using highly cross-linked polyethylene have markedly reduced wear rates. Most patients undergoing primary total joint replacement should not require any further surgical intervention. Recent developments in bundled payment models have led to emphasis on prevention of complications and rapid recovery after surgery.

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Burns in the Older Adult

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Mile Stanojcic and Marc G. Jeschke

Contents

Abstract

Today, there are approximately 40 million people in the United States over the age of 65. As the population ages, this figure is projected to drastically increase to nearly 90 million by the year 2050. With this in mind, as the elderly population increases, it is expected that the incidence of elderly burn victims will as well. This chapter provides insight into the epidemiology, prognosis, and physical considerations in the management and treatment of elderly burn patients. Furthermore, it will explore the acute phase response after burn injury, infections and sepsis, and long-term outcomes. Thermal injuries have a unique manifestation relative to other forms of trauma, and the following sections will demonstrate that this creates further difficulties in older adults. The

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growing body of literature in elderly burn patients in the last decade reflects the inherent challenges when treating and also sheds light on the demand for improved therapeutic regimes for this growing population.

Keywords
Elderly · Burns · Mortality · Outcomes · Sepsis

Introduction

Burns are a major global health burden with a greater incidence in developing countries than developed. Unlike other forms of trauma, burn injuries affect nearly every major organ system. Acutely, the nature of a burn injury results in patients being vulnerable to open wounds, infections, complications, and death. Upon discharge, they further endure economical, psychological, and emotional difficulties with extensive rehabilitation and reconstruction. The complex nature of a burn injury requires medical expertise from a variety of backgrounds, and since the introduction of specialized burn centers, this has significantly improved the care provided to these patients. Despite being extremely effective, it also results in significant costs and financial burden on healthcare. A comprehensive review of 156 studies found that the average cost per burn patient in high-income countries was $88,218 [1]. A single-center retrospective study in Australia found similar results with their average costs totaling AU$71,056 (US$73,532) per patient [2]. The most significant components of cost are hospital length of stay, staffing, operating costs, and dressings, all of which increases with increasing % TBSA (total body surface area) burned.

Today, there are approximately 40 million people in the United States over the age of 65. As the population ages, this figure is projected to drastically increase to nearly 90 million people by the year 2050 [3]. With this in mind, as the elderly population increases, it is expected that the incidence of elderly burn victims will as well. This chapter provides insight into the epidemiology, prognosis, and physical considerations in the management and treatment of elderly burn patients. Furthermore, it will explore the acute phase response after burn injury, infections and sepsis, and long-term outcomes. Thermal injuries have a unique manifestation relative to other forms of trauma, and the following sections will demonstrate that this creates further difficulties in older adults. The growing body of literature in elderly burn patients in the last decade reflects the inherent challenges when treating and also sheds light on the demand for improved therapeutic regimes for this growing population.

Epidemiology

Burn injury is a devastating form of trauma and occurs when cells of the skin or other tissues are destroyed by flames, hot liquids (scald burn), or hot solids (contact burn) [4]. It is estimated globally that 11 million cases of burns require medical attention and account for approximately 300,000 deaths [4]. In the United States, nonfatal burn injuries requiring medical attention are attributed to nearly 500,000 cases annually [5]. Although the treatment of severely burned patients has been continuously improving, death from such injuries is still a primary concern and accounts for more than 4,500 per one million annually in the United States [6]. Primary factors known to determine mortality in burn patients include age, burn size, inhalation injury, and sepsis [6]. Despite 90% of burns being preventable, burns are a neglected form of trauma that has tremendous financial impact on healthcare.

Elderly burn patients represent 13–20% of burn center admission, yet they comprise the highest death rate among the overall burn population [7]. Older adults are more vulnerable to burn injuries due to declining physical, motor, sensory, and cognitive performance [8]. As a result, elderly have burns that are greater in severity, deeper, and increased likelihood of inhalation injury [9]. The majority of thermal injuries in elderly occur within the kitchen and bathroom [10]. A review of 23,180 patients from the American Burn Association National Burn Repository revealed that the injury characteristics in elderly include flame

(41%), scald (24%), contact (5%), chemical (1%), and electrical (1%) [11]. The majority of these injuries occurred at home (56%), and inhalation injuries were present in 10–13% of cases. Despite adult burn victims reflecting a predominantly male population, however in elderly, there is a progressive increase in female victims with increasing age.

It was previously reported that burns in elderly were the fourth leading cause of death, and they are the second population at greatest risk for death due to residential fires [12, 13]. In addition, older adults do not tolerate burns as well as children and adults. Alden and colleagues previously reported that even small scald burns (7% total body surface area) resulted in 22% mortality [14]. In fact, the LA_{50} (percentage of total body surface area that is required to be burned for 50% mortality) in children is above 90%, whereas in patients >70 years old, it is less than 40%, and in patients over 80, it is under 20% [4]. Despite a declining prevalence of burn injuries globally and key advances in therapeutic strategies to improve patient outcome, they still cause significant morbidity and mortality in patients [4].

Prognosis

Determining outcomes and predicting survival is a vital part of guiding the course of burn care [15]. One of these predictors that are most commonly used is the Baux score. The Baux score was originally described as a method to predict mortality in burn patients by simply adding the age and % TBSA, with scores >75 resulting in poor outcomes [16]. Since its introduction in the early to late 1970s, numerous models have been extensively studied and validated to guide burn care providers when determining treatments [17, 18]. Specifically in elderly, Wibbenmeyer and colleagues showed that the Baux score was successfully able to predict mortality in 87% of patients [19]. Another approach that was pioneered at the Birmingham Burn Centre is probit analysis. Using age and severity of injury as standardizing factors, the probit technique determines the percentage of mortality that is inclusive of the entire dataset (both survivors and non-survivors) [20]. The most widely used extension of this work that is used today would be the LA_{50}. The LA_{50} (lethal area 50%) represents the severity of burn injury of a given population that results in 50% mortality. This was later extended by Zawacki et al. to include the influence of inhalation injury to predict mortality [21]. Prediction of elderly mortality is not an easy task which is due to the biological differences of elderly. Mobility, socioeconomic activity, and medical history can vary greatly and affect outcomes of burn elderly.

Despite significant improvements in outcomes of burn patients in part due to improved critical care bundles and protocolized burn care, the best outcomes possible can still be found in children followed by adults than elderly [22]. When comparing elderly burn patients to children and adults, older adults have unfortunately not benefitted from the same advances in mortality improvements [6]. In fact, elderly burn patients have an LA_{50} that has remained unchanged for decades and further indicates this neglected cohort [23, 24]. In 1949, Bull and Squire showed that the LA_{50} was approximately 40% for a 40-year-old and nearly 10% in a 70-year-old [20]. With the modernization of burn care and technological advances, recent reports have consistently shown that adults LA_{50} is between 70% and 80%. Unfortunately, these advances in burn care have not been as effective in elderly who have an LA_{50} of 30–35%. When exclusively considering adults over the age of 70, this proportion decreases to 28% [24, 25].

Along with the increased incidence of mortality, elderly burn patients are at greater risk for complications during acute hospitalization. These complications include pulmonary edema, pneumonia, and congestive heart failure [24]. During hospitalization, it has been shown that elderly burn patients have slower recoveries and longer lengths of admission [26]. Alterations in the dermal layers with age result in deeper injury wounds and delayed/prolonged wound healing [10]. As a widely accepted hallmark of post-burn manifestation, elderly patients have a dampened immune and metabolic responsiveness that drive these aforementioned negative consequences, which will be discussed in later sections.

Taken together, little improvements have occurred in the past decades to increase the survival of elderly burn patients. They continue to face an uphill battle to survive both the burn injury itself and complications while hospitalized. As one recent report suggested, perhaps outstanding questions need to be addressed in order to achieve these outcomes. These include the following: should early excision or elapsed surgeries take place to improve wound healing, what criteria should be used to monitor fluid resuscitation, and, lastly, will early mobilization improve rehabilitation [27]?

Table 1 Clinical frailty scale

Score	Classification	Description
1	Very fit	Robust, active, energetic, and motivated
2	Well	No active disease symptoms, often exercise/occasionally fit
3	Managing well	Well controlled medical problems, not regularly active
4	Vulnerable	Not dependent on others, symptoms limit activity
5	Mildly frail	More evident slowing, limited dependence on others
6	Moderately frail	Help needed with all outside activities and daily living
7	Severely frail	Completely dependent on personal care

Adapted from Ref. [30]

Frailty

As adults age, there is a progressive reduction in protective mechanisms such as thinning of the skin (vascularity and cellularity) and overall sensitivity, which contribute to the higher risk of burn injuries. Along the same lines, elderly also have impaired vision, decreased coordination, poor mobility, and reduced reaction time to get out of harm's way. This is likely responsible for the higher prevalence of inhalation injuries [28]. Another term associated with old age that is used to describe vulnerability to abnormal homeostasis and stress response is frailty [29].

Put simply, frailty is assessed by taking into consideration an individuals' physical activity and nutritional status [29]. As introduced in the previous section, regardless of the approach used, outcome prediction relies extensively on the age of the patient. However, chronological age does not always reflect the physiological or metabolic characteristics. With this in mind, the frailty score was recently shown to be a valid and improved predictor of outcomes in elderly burn patients [30, 31]. As shown in Table 1, the Canadian Study of Health and Aging created a frailty scoring based on clinical judgment. Upon assessment of physical activity level and ability to perform daily living tasks, it consists of 7-point scale from fit and independent to completely dependent on personal care.

In 2013, a study conducted by Masud et al. assessed 42 burn patients frailty scores based on the initial assessment from admission records [30]. They found that patients with better frailty scores or pre-morbid capacity were more likely to survive the burn insult and treatment. They also had significantly more individuals who underwent and survived surgical debridement. Another noteworthy study conducted by Romanowski et al. investigated the relationship between frailty score and clinical outcomes. They found that a higher admission frailty score was associated with non-survivorship and increased likelihood of being discharged to a nursing facility versus home [31]. Thus, frailty scoring has consistently shown to be associated with predicting outcomes in elderly burn patients, and subsequent studies are warranted to determine whether it may also extend to complications or benefit of surgery.

Acute Phase Response

Arguably, the profound hyperinflammatory and hypermetabolic response that occurs after burn injury are the main characteristics that distinguish itself from other forms of trauma. In fact, greater burn injury severity has been shown to result in an increased pro-inflammatory response that contributes to muscle catabolism [32]. Thus, in order to understand the complexity of the post-burn

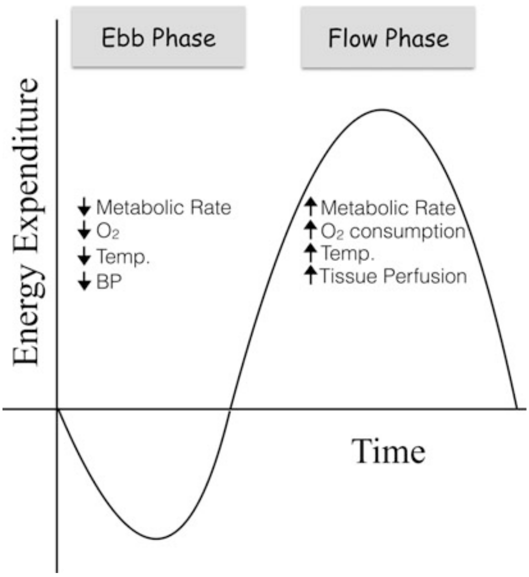

Fig. 1 Posttraumatic metabolic alterations – ebb and flow phases. (Adapted from Ref. [33])

response, both immune and metabolic alterations need to be considered. In the early 1940s, nutritional scientist Cuthbertson introduced the "ebb" and "flow" phases after injury to describe metabolic changes occurring after major trauma (Fig. 1) [33]. First, the "ebb" or shock phase is characterized by reduced total metabolism and diminished peripheral blood volume in circulation. The "flow" or traumatic inflammation phase begins 3–5 days after injury with increases in metabolic activity and various aspects of circulation (hyperemia, exudation, leucocytic migration, etc.) to collectively stimulate a repair process. Although numerous studies have demonstrated the immune and metabolic alterations after injury, elderly burn patients have proven to follow a different course.

Various cytokines, such as IL-1, IL-6, and TNF, have been utilized as markers related to the severity of burn injury. Some of the early markers associated with the initial inflammatory (acute phase) response include IL-6, IL-8, IL-10, TNF-α, and IL-1β [34]. There are varying levels of these cytokines in patients that can be used to distinguish survivors and non-survivors. Specific markers of non-survivors include the elevated expression of IL-6 and IL-8, as well as granulocyte-colony stimulating factor (G-CSF) and monocyte chemotactic protein 1 (MCP-1) [34]. Previous work on a large prospective study of 242 burn patients showed that the entire inflammatory response was profoundly altered up to 2–3 years post-burn [35]. Pro-inflammatory cytokine synthesis or "cytokine storm" is a systemic response to manage deleterious effects of thermal injury in an attempt to restore homeostasis. However, when this response is prolonged post-trauma, it can result in stress-induced hyperglycemia, insulin resistance, hypermetabolism, and catabolism, which are precursors to organ dysfunction and lead to increased risks of infection, sepsis, and death [34]. The prevention of excessive inflammation is a key component of post-burn treatment because of its dynamic relationship with the hypermetabolism and impaired glucose metabolism that are also occurring.

A recent study conducted by Jeschke et al. elucidated the pathophysiological response in elderly burn patients. They demonstrated that even 4 weeks after injury, elderly burn patients are still hypermetabolic with a resting energy expenditure as high as 150% of normal. This aberrant metabolic response was further supported by decreased expression of metabolic markers C-peptide, glucagon-like peptide-1, pancreatic polypeptide, and peptide YY. Consistent with the notion of non-responsiveness, elderly burn patients also had reduced ER stress in adipose tissue. Immunologically, older adults had reduced neutrophil infiltration and macrophage proportion in adipose tissue from the site of injury. Lastly, they showed that systemic inflammation had an acute hypo-inflammatory response preceded by a late surge in inflammation, which will be discussed further below [36].

Inflamm-Aging/Immunosenescence

Inflamm-aging has been increasingly used to describe elderly patients and suggests that there is a global reduction in the ability to cope with stressors with an overall progressive increase in the pro-inflammatory state. Cytokines such as IL-6, IL-1β, and TNF-α are deregulated, and the presence of a chronic inflammatory state impairs the ability to fight off future complications, all of which have shown to be increased in elderly burn patients [37, 38]. Another principle used to describe the elderly immune response is immunosenescence. Immunosenescence is described as the progressive deterioration of the immune system brought on by aging and hinders the host response to pathogens and insult. In healthy elderly, this includes macrophage alterations and reduced antigen-presenting capacity and impairments in natural killer cell, neutrophil, and T-cell activity [39, 40].

A recent study demonstrated the immunosenescence in elderly burn patients by comparing the temporal changes in immune trajectories [41]. The authors observed that during the acute phase (<7 days post-burn), there was a dampened or hypo-responsiveness of pro-inflammatory, chemokine, and immune mediator cytokines in elderly patients. Interestingly, after 14-day post injury, there was a late surge and elevated expression. Beyond 30 days after burn, a dramatic decline occurred which the authors propose is consistent with immune exhaustion. These findings were consistent when comparing non-sepsis and sepsis elderly patients where there was a lack of acute surge in inflammation, which was evident in adults. When elderly patients were stratified based on survivorship, it was observed that there were no differences between the groups and further supports the difficulty in identifying susceptibility to negative outcomes. Thus, elderly burn patients support a "failure to launch" immune characteristic. Collectively, these recent studies demonstrate the aberrant metabolic and immune responses that occur in elderly burn patients. Furthermore, they introduce this systemic hypo-responsiveness to insult that is believed to be the underlying factor for their greater susceptibility to infections and sepsis.

Infection and Sepsis

In the past, patients were most likely to succumb to their injuries due to uncontrollable factors such as age, severity of burn, and inhalation injury. Presently the paradigm has shifted as resuscitation improved, and now sepsis is the leading causes of death in severely burned patients. This in part is attributed to the loss of the skin barrier after injury that results in a heightened risk of wound infections. Sepsis continues to challenge burn-trauma patients in part due to difficulty detecting, defining, and treating.

Infections

It is estimated that between 50% and 75% of burn-related deaths are a direct result of infections and related complications [42]. With the excision of the skin's natural protective barrier, burn wounds are vulnerable portals of microbe infiltration. Unfortunately, any form of infiltration can lead to serious infection due to the ability of a burn injury to suppress the immune system. These infections can leak into the bloodstream and spread throughout the circulatory system, causing bacteremia as well as septic shock. Burn wound infections are a primary concern during the course of treatment due to their potential to create serious complications that will increase the risk of mortality [42]. Bacteria like *Pseudomonas aeruginosa*, which may come from endogenous flora or the environment, are capable of forming biofilms at the wound site that enable the formation of persister-type cells [43]. *Staphylococcus aureus* is another common opportunistic bacteria of concern in post-burn patients due to its ability to generate many virulence factors that allow it to thrive [44]. Bacteria can invade the tissue and make it more difficult to heal or treat the actual burn. Furthermore, the burn wound may become infected after surgery if a donor graft or the excised host tissue is not epithelized properly. New treatment methods allow earlier detection of possible infections, which means they can be addressed before serious complications ensue.

Infections in elderly burn patients are a major concern and frequent occurrence relative to their adult counterparts. It is estimated that 30% of elderly burn patients have burn wound infections and remain an ongoing challenge for burn care providers [36]. This in part is a result of the inflamm-aging and immunosenescence discussed in the previous section. Heightened cytokine production and low-grade inflammation result in an increased severity and prevalence of infection [38]. Elderly burn patients are more susceptible to wound infections (i.e., bacterial) due to the large surface area creating optimal conditions for colonization [45]. Despite origins in the burn wound, these infections can quickly cause bacterial pneumonia, systemic infections, and sepsis [45]. Numerous preventative measures have been reported to avert infection in elderly burn patients including aggressive and early excision of deep burn wounds, early skin grafting, and presence of malnutrition [9]. Collectively, this increased incidence of infections serves as the precursors for subsequent complications and sepsis.

Sepsis

The greatest threat with burn injuries is septic shock or organ dysfunction, which is the leading cause of death [42]. Burn sepsis is usually caused by invasion of the wound site that may result in infection, which spreads systemically to other areas of the body. Sepsis is accompanied by a multitude of symptoms including hyperglycemia, hypotension, and either hypothermia or hyperthermia [42]. Opportunistic pathogens thrive in an immunosuppressed host (i.e., elderly burn patients) and are frequently the source of sepsis.

Elderly burn patients are at greater risk for developing infections and sepsis due to the dysregulated immune response. If untreated, these complications can quickly persist and develop into multiple organ failure and death [10]. A recent study investigating the immune trajectory of adult and elderly patients after burn injury revealed that unlike adults, older adults have a dampened or non-responsive immune response after insult [41]. Stanojcic et al. found that elderly burn patients lacked an acute surge of immune-responsiveness to insult relative to adult counterparts. Interestingly, when elderly patients were stratified based on occurrence of septicemia, it was shown that the majority of inflammatory cytokines and chemokines were unable to distinguish the non-sepsis and sepsis groups. The majority of surge in inflammation in septic elderly occurred late (>30 days post injury). When extending this analysis to the onset of sepsis, elderly burn patients with late onset had significantly reduced proportion of cytokines relative to both adults and elderly with early-onset sepsis. The most striking finding was unlike early-onset septic patients that had a survival of 80%, late-onset sepsis in elderly resulted in 30% survival. Collectively, this study demonstrated the inherent difficulty in distinguishing the susceptibility to sepsis in elderly burn patients and further supports the difficulty in treating these patients with inept immune function. Extending this notion of a “late fight” phenotype in septic elderly, a recent study also demonstrated surges in CD14+/HLA-DR+ monocytes (hallmark of immunosuppression in burn injury) occurring beyond 30-day post-burn [36].

A visual representation of the immune response in adult and elderly patients during sepsis can be found in Fig. 2. As shown in Panel A (adult sepsis), when presented with pathogen or bacterial challenge, this will result in an acute immune response that includes the recruitment of various cell types including monocytes, macrophages, neutrophils, and extensive cytokine secretion. Comparing this to the response in septic elderly (Panel B), the same challenge is met with a dampened immune response with less immune cells recruited and decreased activity. Overtime, adult septic patients will clear the threatening pathogens (in most cases) and will conclude the immune response where innate immune cells undergo cell death (Panel C). Unlike adults, elderly septic patients’ insufficient response will result in not all pathogens and bacteria being cleared, the immune cells will exhaust, and the refractory period or recovery will ensue (Panel D). Upon doing so, this places the elderly at the greatest risk for unresolved infection to spread and induce multiple organ failure and death (Panel D).

Treatment options for trauma patients with burn-induced injuries are regularly improved as research reveals new methods of diagnosing and preventing infection or sepsis. Despite providing

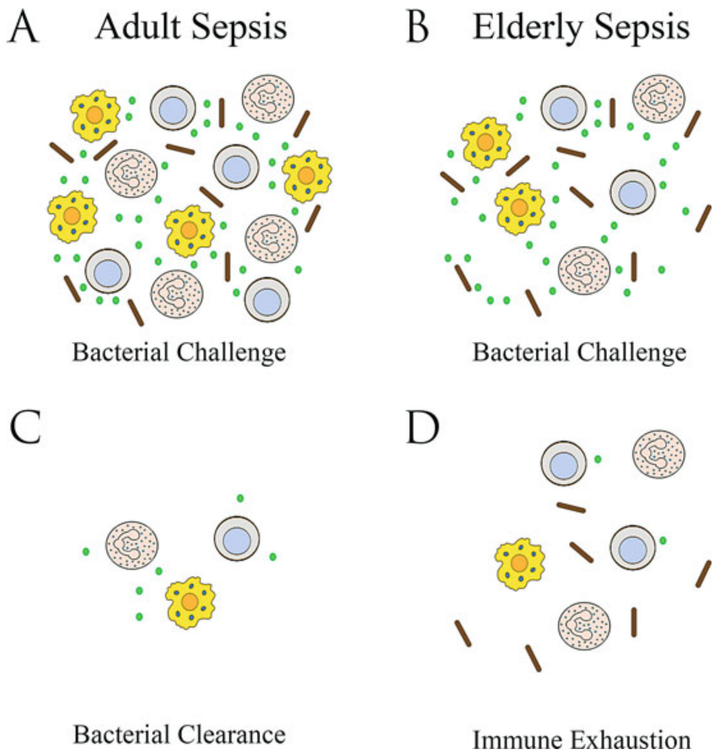

Fig. 2 Comparing the immune response to pathogenic challenge in adult and elderly septic patients

the best critical care possible to patients, a gray zone still exists of what additionally can be done to avoid sepsis. Unlike sepsis, currently there are various approaches to alleviate the hypermetabolic response and support immune function, the most well-established being beta-blocker treatment using propranolol, [46]. Outside of burn trauma, sepsis therapy in critically ill patients focuses on supporting organ function and perfusion. However, there is no globally accepted therapeutic intervention to prevent or predict sepsis, thus making it very challenging to present therapeutic ideas and vision to treat something that will inevitably occur. The ability to prevent sepsis would be a monumental medical advancement for burn patients as the majority of the post-burn complications are sepsis-related.

Long-Term Outcomes

Elderly burn patients have significantly worse outcomes than adult and children counterparts. As demonstrated by minimal increase in the LA_{50}, little progress has been made toward improvements. Numerous factors have been proposed that contribute to this increase in poor outcomes including previous medical conditions, thinning of the skin, increasing susceptibility to complications, inflamm-aging, and immunosenescence that inhibit the ability to mount an adequate immune response, infections and sepsis, frailty score, and nutrition [30, 31, 37, 38, 41]. When comparing genders, it has been suggested that the premenopausal hormone effects (greater hormonal secretion and reduced inflammation) result in poor outcomes in adult females. However, in elderly females there is no apparent increase in mortality due to gender [47]. When comparing hospital admissions, elderly burn patients remain in hospital for longer than adults with similar injuries [48]. Upon discharge, elderly burn patients continue to have both functional outcome and psychosocial impairments for up to 1-year post injury [49]. Extending the notion of long-term impairments, elderly burn patients discharged to skilled nursing facilities die more often than those who went home [50]. In fact, elderly burn patients discharged home were 5.9 times more likely to survive. Elderly burn patients face a high probability and multitude of negative outcomes post-burn, and the subsequent section will introduce a newer approach to delineate geriatric patients at risk for mortality.

Recently, a series of studies proposed and validated the Geriatric Trauma Outcome Score (GTOS) used to determine the probability of mortality in severely injured geriatric patients [51]. Using logistical regression modeling in 3,841 geriatric patients, it was shown that age, injury severity score, and performance of a blood transfusion had a high discriminate ability to predict inpatient mortality. The trauma scores range from 50 to 300 and reflect the increased probability of mortality (1–99%). By incorporating variables in the model that are known at the time of admission, the strength in the GTOS comes from being able to have a quick method of determining negative outcomes, a priori. A subsequent multicenter external validation study was conducted using the GTOS [age + (ISS x 2.5) + 22 (if given PRBC by 24 h)]. Using data provided within 24 h after injury, the authors confirmed that the GTOS accurately predicts in-hospital mortality for injured elderly [52]. Future studies are still required in exclusively elderly burn patients in order to determine its efficacy in this population and determine if the same validity in predicting outcomes is upheld.

Conclusion

Elderly burn patients have poor outcomes, and unfortunately despite advances in burn care, this is not reflected in burned elderly. Elderly have a significantly greater mortality after burn when compared to adults with like-size burns. Newer studies recently identified several pathophysiologic responses that are associated with the detrimental outcomes. It appears that elderly are at higher risk to develop multi-organ failure, are unable to decrease their metabolic needs over time, express profound alterations in glucose and fat metabolism, have an impaired and reversed immune-response with the inability to adequately respond to stress, and, lastly, have a significantly impaired capacity for dermal and epidermal regeneration due to a decreased stem cell pool and dysfunctional stem cells. All of these contributors are pieces of a complex clinical picture, and the next steps are now to further extract these pathophysiological pathways to elucidate more cellular responses and mechanisms in order to develop novel interventions improving the outcomes of severely burned elderly. Another key element that has yet to be addressed is the question about long-term outcomes. Currently, it is unknown what the quality of life and long-term survival of elderly is after burn, and others and we feel that this is an important aspect that requires further investigation.

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