Tomas Lindor Griebling
Editor

Geriatric Urology

Springer

Geriatric Urology

Tomas Lindor Griebling
Editor

Geriatric Urology

Springer

Editor
Tomas Lindor Griebling, M.D., M.P.H., F.A.C.S., F.G.S.A., A.G.S.F.
Department of Urology and The Landon Center on Aging
University of Kansas School of Medicine
Kansas City, KS, USA

ISBN 978-1-4614-9046-3 ISBN 978-1-4614-9047-0 (eBook)
DOI 10.1007/978-1-4614-9047-0
Springer New York Heidelberg Dordrecht London

Library of Congress Control Number: 2013957067

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

This book is dedicated to the memory of my parents, Wilma Arlene Griebling and James W. Griebling, for their constant love and support.

Acknowledgment

"The character of a civilization is reflected in the way it treats its elders."

Arnold J. Toynbee (1889–1975)

I am grateful to have had the opportunity to create and publish this textbook, *Geriatric Urology*. My interest in the field of aging, geriatrics, and gerontology is long-standing, and it has been such a pleasure to incorporate this focus in my career as an academic urologic surgeon, researcher, and educator.

I am indebted to numerous people who have been actively involved in the development of this work. First, I offer a heartfelt thank you to all of the authors who contributed chapters to this book. Your time and expertise are reflected in the excellent information presented in this volume which truly covers the spectrum of modern geriatric care in urology. Over the years, many of you have been and continue to serve as my teachers and mentors. I am honored to have you as my colleagues and friends.

Thank you to my associates at Springer, Kevin Wright (Development Editor), Richard Hruska (Senior Editor), and the entire production team for your patient guidance and help in overseeing the production of this book from the initial concepts to final publication. Thank you also to Annette Hinze from the Springer office in Heidelberg, Germany, for your inspiration.

I sincerely appreciate the countless patients and their families and friends who have served as some of my finest teachers during my medical education and career.

Finally, to my partner, Michael A. Miklovic, for his gentle and humble encouragement throughout this project. Your humor, generosity, and unflagging support saw me through many long evenings and weekends spent in front of my computer writing and editing. I could never have done it without you… thanks so much Scooter!

Kansas City, KS, USA — Tomas Lindor Griebling

Contents

Contributors

Robert Abouassaly, M.D., M.Sc., F.R.C.S.C. Urologic Institute, University Hospitals Case Medical Center, Cleveland, OH, USA

Heather S. Anderson, M.D. Department of Neurology, University of Kansas Medical Center, Kansas City, KS, USA

Karl-Erik Andersson, M.D., Ph.D. Department of Urology, Wake Forest Institute for Regenerative Medicine, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, NC, USA

Christine A. Arenson, M.D. Department of Family Medicine, Thomas Jefferson University Medical School, Philadelphia, PA, USA

Gregory Bales, M.D. Section of Urology, The University of Chicago School of Medicine, Chicago, IL, USA

Katie Ballert, M.D. Department of Surgery, University of Kentucky College of Medicine, Lexington, KY, USA

John M. Barry, M.D. Department of Urology, Oregon Health and Science University, Portland, OR, USA

Joseph W. Basler, M.D. Department of Urology, University of Texas Health Science Center at San Antonio, San Antonio, TX, USA

Christine Bradway, Ph.D., R.N. Department of Biobehavioral Health Sciences, University of Pennsylvania School of Nursing, Philadelphia, PA, USA

Joshua A. Broghammer, M.D., F.A.C.S. Department of Urology, University of Kansas Medical Center, Kansas City, KS, USA

James T. Birch Jr., M.D., M.S.P.H. Family Medicine, University of Kansas Hospital, Kansas City, KS, USA

Kathryn L. Burgio, Ph.D. Department of Medicine, Division of Gerontology, Geriatrics and Palliative Care, University of Alabama at Birmingham, Birmingham, AL, USA

Department of Veterans Affairs Medical Center, Birmingham/Atlanta Geriatric Research, Education, and Clinical Center (GRECC); VA Medical Center, Birmingham, AL, USA

Omer Onur Cakir, M.D. Department of Urology, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Steven C. Campbell, M.D., Ph.D. Department of Urology, Cleveland Clinic, Cleveland, OH, USA

Lysanne Campeau, M.D., C.M., Ph.D., F.R.C.S.C. Wake Forest Institute for Regenerative Medicine, Wake Forest University School of Medicine, Winston-Salem, NC, USA

Ronni Chernoff, Ph.D., R.D., L.D., C.S.G., F.A.D.A. Geriatric Research Education and Clinical Center, Central Arkansas Veterans Healthcare System, Little Rock, AR, USA

Doreen Chung, M.D., F.R.C.S.C. Section of Urology, The University of Chicago School of Medicine, Chicago, IL, USA

Ananias C. Diokno, M.D., F.A.C.S. Beaumont Medical Office Building, Royal Oak, MI, USA

Roger Dmochowski, M.D., F.A.C.S. Department of Urologic Surgery, Vanderbilt University Medical Center, Nashville, TN, USA

George W. Drach, M.D. Department of Urology and Surgery, University of Pennsylvania, Philadelphia, PA, USA

David A. Duchene, M.D. University of Kansas Medical Center, Kansas City, KS, USA

James M. Dupree, M.D., M.P.H. Department of Urology, Northwestern University, Feinberg School of Medicine, Chicago, IL, USA

Sean P. Elliott, M.D., M.S., F.A.C.S. Department of Urology, University of Minnesota Medical Center, Fairview, Minneapolis, MN, USA

Marty L. Eng, PharmD, C.G.P., B.C.P.P., C.D.P., F.A.S.C.P. Department of Pharmacy Practice, Cedarville University School of Pharmacy, Cedarville, OH, USA

Stephanie Fleegle, M.D. Department of Family Medicine, Thomas Jefferson University Medical School, Philadelphia, PA, USA

Mary Ann Forciea, M.D. Department of Geriatric Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Patricia S. Goode, M.S.N., M.D. Department of Medicine, Division of Gerontology, Geriatrics and Palliative Care, University of Alabama at Birmingham, Birmingham, AL, USA

Department of Veterans Affairs Medical Center, Birmingham/Atlanta Geriatric Research, Education, and Clinical Center (GRECC); VA Medical Center, Birmingham, AL, USA

Christopher M. Gonzalez, M.D., M.B.A., F.A.C.S. Department of Urology, Northwestern University, Feinberg School of Medicine, Chicago, IL, USA

Tomas Lindor Griebling, M.D., M.P.H., F.A.C.S., F.G.S.A., A.G.S.F. Department of Urology and The Landon Center on Aging, University of Kansas School of Medicine, Kansas City, KS, USA

Joshua Griffin, M.D. Department of Urology, University of Kansas Medical Center, Kansas City, KS, USA

Jeffrey M. Holzbeierlein, M.D. Department of Urology, The University of Kansas Hopsital, Kansas City, KS, USA

Christine Hsieh, M.D. Department of Family Medicine, Jefferson University School of Medicine, Philadelphia, PA, USA

Theodore M. Johnson II, M.D., M.P.H. Emory Division of General Medicine and Geriatrics, Department of Medicine, Atlanta VA Medical Center, Decatur, GA, USA

Sathish Kasina, Ph.D. Department of Urology, The University of Massachusetts, Boston, MA, USA

Melissa Kaufman, M.D. Department of Urologic Surgery, Vanderbilt University Medical Center, Nashville, TN, USA

Badrinath Konety, M.D. Department of Urology, University of Minnesota, Minneapolis, MN, USA

Stephen R. Kraus, M.D., F.A.C.S. Department of Urology, University of Texas Health Science Center at San Antonio, San Antonio, Dallas, TX, USA

Karl J. Kreder, M.D., M.B.A. Department of Urology, University of Iowa, Iowa City, IA, USA

Michelle J. Lajiness, M.S., F.N.P-B.C. Beaumont Medical Office Building, Royal Oak, MI, USA

Daniel J. Lee, M.D. Department of Urology, University of Iowa Hospitals, Iowa City, IA, USA

Jill A. Macoska, Ph.D. Department of Urology, The University of Massachusetts, Boston, MA, USA

Alayne D. Markland, D.O., M.Sc. Department of Medicine, Division of Gerontology, Geriatrics and Palliative Care, University of Alabama at Birmingham, Birmingham, AL, USA

Department of Veterans Affairs Medical Center, Birmingham/Atlanta Geriatric Research, Education, and Clinical Center (GRECC); VA Medical Center, Birmingham, AL, USA

Niels D. Martin, M.D., F.A.C.S. Traumatology, Surgical Critical Care and Emergency Surgery, Hospital of the University of Pennsylvania, Philadelphia, PA, USA

Mary McDonald, M.D. Department of Community and Family Medicine, Howard University College of Medicine, Washington, DC, USA

Kevin T. McVary, M.D., F.A.C.S. Division of Urology, Department of Surgery, Southern Illinois University School of Medicine, St. John's Pavilion, Springfield, IL, USA

Moben Mirza, M.D. Department of Urology, University of Kansas Hospitals and Clinics, Kansas City, KS, USA

Diane K. Newman, D.N.P., F.A.A.N., B.C.B.-P.M.D. Division of Urology, Department of Surgery, University of Pennsylvania Medical Center, Philadelphia, PA, USA

Susan H. Noorily, M.D. Department of Anesthesiology, University of Texas Health Science Center at San Antonio, San Antonio, TX, USA

David James Osborn, M.D. Department of Urologic Surgery, Vanderbilt University Medical Center, Nashville, TN, USA

Priya Padmanabhan, M.P.H., M.D. Department of Urology, University of Kansas Medical Center, Kansas City, KS, USA

Margaret S. Pearle, M.D., Ph.D. UT Southwestern Medical Center, Dallas, TX, USA

Daniel Ramirez, M.D. Department of Urology, UT Southwestern Health Science Center, Dallas, TX, USA

David W. Rittenhouse, M.D. Department of Surgery, Jefferson Medical College of Thomas Jefferson University, Philadelphia, PA, USA

Vivyenne Roche, M.D. Department of Internal Medicine, UT Southwestern Health Science Center, Dallas, TX, USA

Allen D. Seftel, M.D., F.A.C.S. Division of Urology, Department of Surgery, Cooper University Health Care, Cooper Medical School of Rowan University, Marlton, NJ, USA

Shahrokh Shariat, M.D. Department of Urology, Weill Cornell Medical College, New York, NY, USA

Jeffrey H. Silverstein, M.D., M.S., A.G.S.F. Department of Anesthesiology, Icahn School of Medicine at Mount Sinai, New York, NY, USA

Ashlie R. Stowers, M.D. Department of Anesthesiology, University of Texas Health Science Center at San Antonio, San Antonio, TX, USA

Daniel Su, M.D. Division of Urology, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, USA

Daniel L. Swagerty, M.D., M.P.H., A.G.S.F. Department of Family Medicine and Landon Center on Aging, University of Kansas Medical Center, Kansas City, KS, USA

Elizabeth B. Takacs, M.D. Department of Urology, University of Iowa, Iowa City, IA, USA

Sarah Teymoorian, M.D. Department of Family Medicine, Premier Physicians Medical Group, Stanford, CA, USA

Kari A.O. Tikkinen, M.D., Ph.D. Department of Urology, Helsinki University Central Hospital and University of Helsinki, Helsinki, Finland

Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, ON, Canada

Camille P. Vaughan, M.D., M.S. Department of Veterans Affairs, Birmingham/Atlanta Geriatric Research Education and Clinical Center, Atlanta, GA, USA

Division of General Medicine and Geriatrics, Emory University School of Medicine, Atlanta, GA, USA

Atlanta VA Medical Center, Decatur, GA, USA

Christopher Warlick, M.D., Ph.D. Department of Urology, University of Minnesota, Minneapolis, MN, USA

Christopher Weight, M.D. Department of Urology, University of Minnesota, Minneapolis, MN, USA

Michael S. Weinstein, M.D., F.A.C.S. Division of Acute Care, Department of Surgery, Jefferson Medical College of Thomas Jefferson University, Philadelphia, PA, USA

Jeffrey P. Weiss, M.D., F.A.C.S. Department of Urology, SUNY Downstate College of Medicine, Brooklyn, NY, USA

Tracey Small Wilson, M.D., F.A.C.S. Department of Urology, University of Alabama at Birmingham, Birmingham, AL, USA

Andrew P. Windsperger, M.D. Department of Urology, University of Kansas Medical Center, Kansas City, KS, USA

Daniel Zainfeld, M.D. Department of Urology, University of Kansas Medical Center, Kansas City, KS, USA

Philip T. Zhao, M.D. Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, USA

Philippe Zimmern, M.D. Department of Urology, UT Southwestern Medical Center, Dallas, TX, USA

Geriatric Urology and Aging Societies

1

George W. Drach and Mary Ann Forciea

International Growth in Aging Populations

One of the characteristics of the twenty-first century will be a shift towards older populations in almost every country. One way of illustrating this shift is with a population pyramid: a graphic representation of the ages of a population. Horizontal bars represent cohorts of increasing age, with men traditionally represented on the left and women on the right. Generally, stable populations have resembled pyramids, with larger numbers of younger people underpinning a gradually decreasing population of older citizens. Countries may develop variants of these pyramids at different stages; for instance, rapidly growing countries may bulge near the base of the pyramid (Fig. 1.1, right side for Nigeria), while countries with low birth rates and increasing longevity may become top heavy (Fig. 1.1, left side for the USA) [1].

G.W. Drach, M.D. (✉)
Department of Urology and Surgery,
University of Pennsylvania, West Pavilion,
3rd Floor, 34th Street and Civic Center Boulevard,
Philadelphia, PA, USA
e-mail: drachg@uphs.upen.edu

M.A. Forciea, M.D.
Department of Geriatric Medicine,
University of Pennsylvania School of Medicine,
3615 Chestnut Street, Philadelphia, PA, USA
e-mail: forciea@mail.med.upenn.edu

Another way of expressing changes in life span is with average life expectancy tables which illustrate the average remaining years of life for individuals at any given age. Life expectancy at age 65 is rising for men throughout the developed world, as illustrated in Fig. 1.2, as well as for women [2]. The benefits and challenges of this shift in population age have implications for economics (income generation versus pension support), family structure, and political power to name only a few. The ramifications on health care for countries facing "inverted" pyramids such as China are also manifold (Fig. 1.2). Not only will these countries experience stresses in providing and paying for health care for increasing numbers of retired workers, but the health needs of the population will shift. Patients with multiple chronic diseases will increase. The spectrum of "commonly encountered" disorders in every discipline will shift to those problems seen more often in older patients especially males (Fig. 1.3). More attention to home and community supports for recovery and function will be required in all countries.

Older Americans

Closer study of the older population of the USA gives many useful insights to help prepare healthcare professionals for the needs of their older patients. The numbers of patients older than 65 years in the USA will rise dramatically (Fig. 1.4) [2]. The number of patients older than 85 is rising rapidly within the overall population of older

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_1,

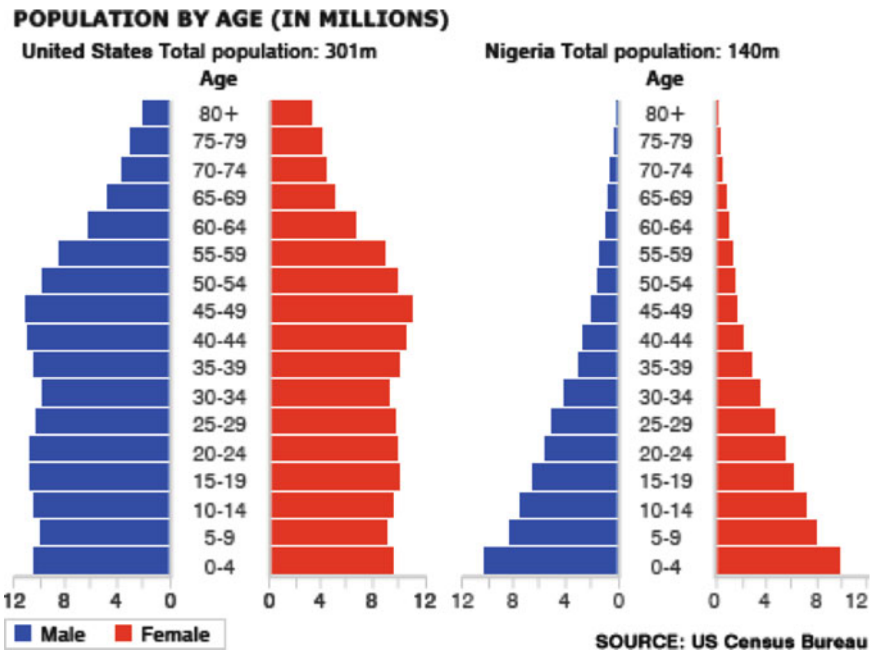


Fig. 1.1 Population pyramids

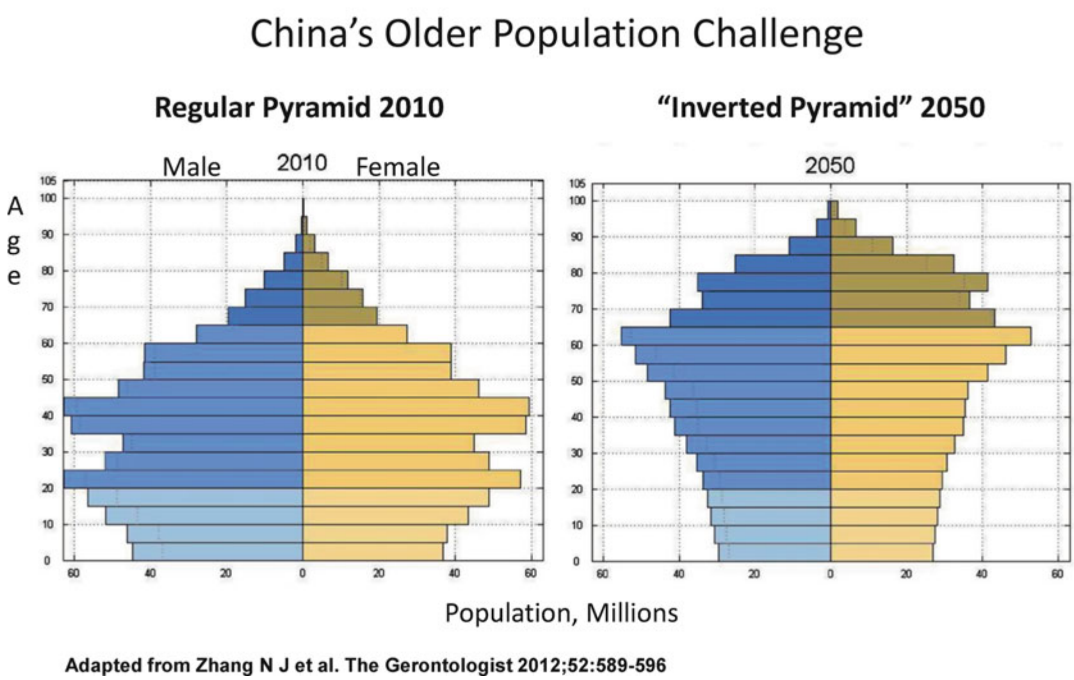


Fig. 1.2 Estimated growth of China's aged population in 40 years: the inverted pyramid

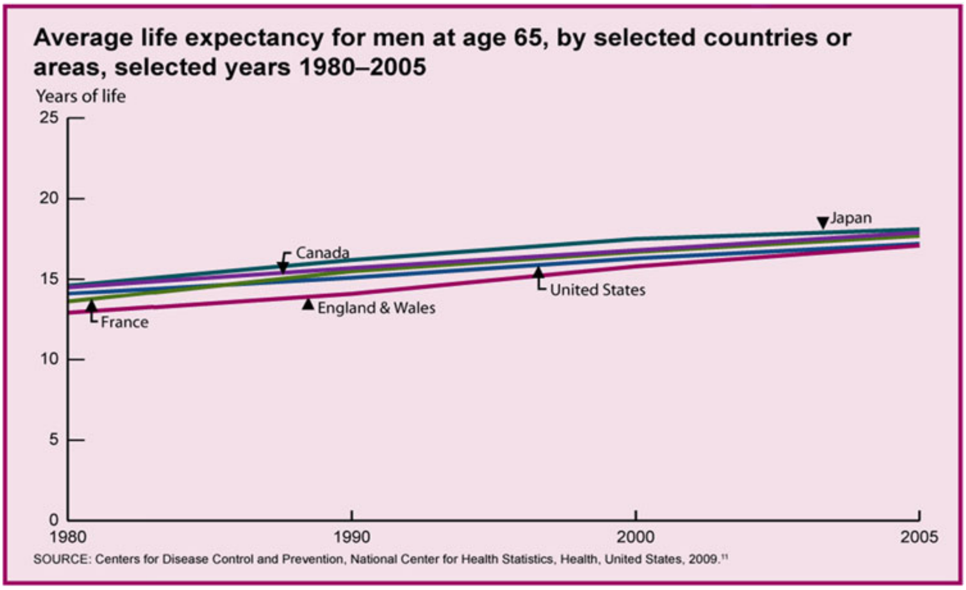


Fig. 1.3 Rising male life expectancy at age 65 in various countries

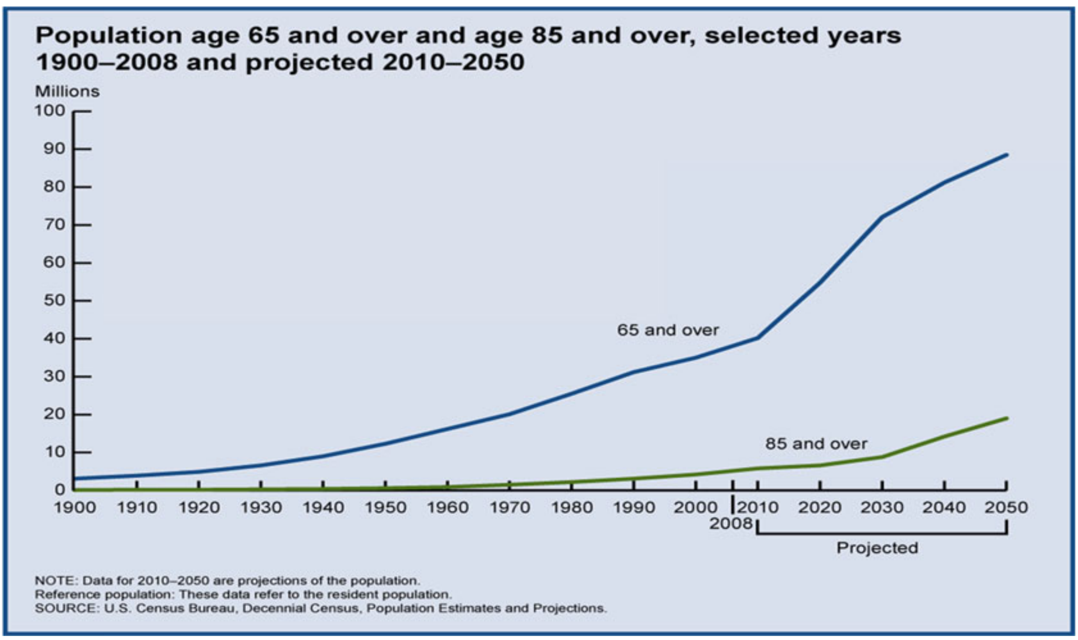


Fig. 1.4 Increases in the population aged 65 and older, as well as 85 years and older

Americans. In fact, this group represents the fastest growing segment of the US population. The increase in the aging population is seen across the country (Fig. 1.5) [2]. As the population ages, the living arrangements of people change: living alone after bereavement becomes more common, especially for older women (Fig. 1.6) [2]. Despite these demographic changes, the overwhelming

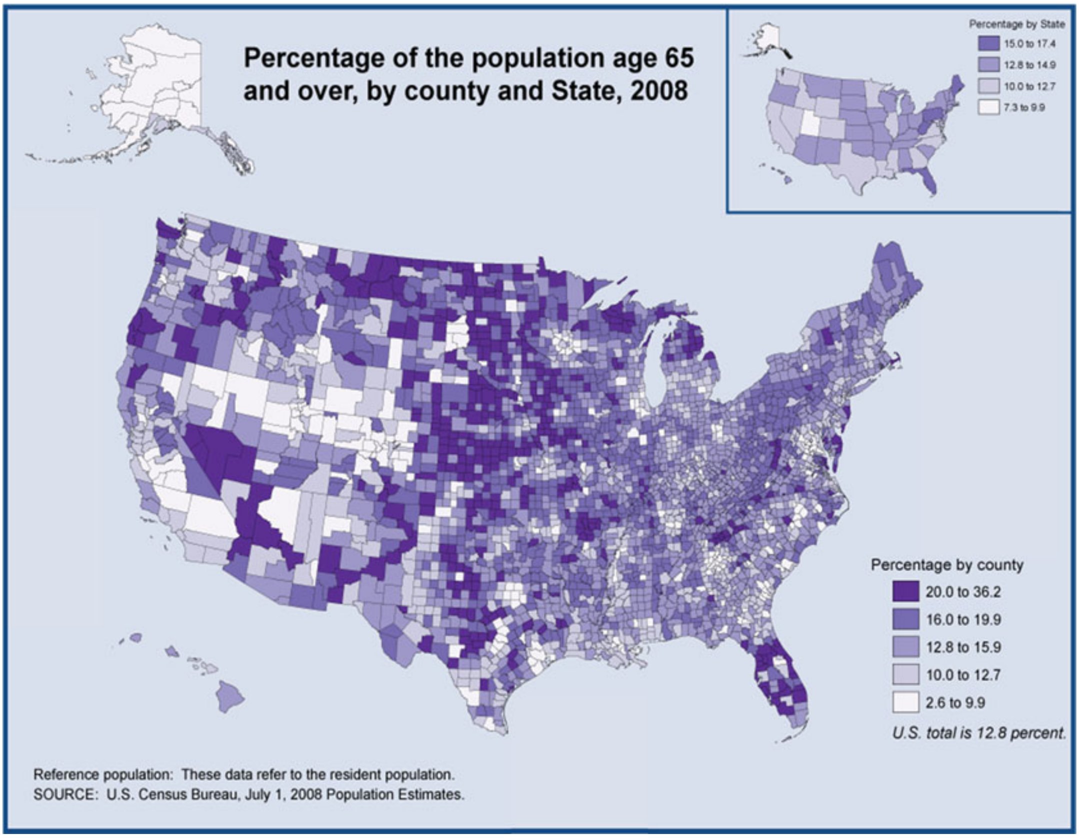


Fig. 1.5 Percentage of the population age 65 and over by county and state, 2008

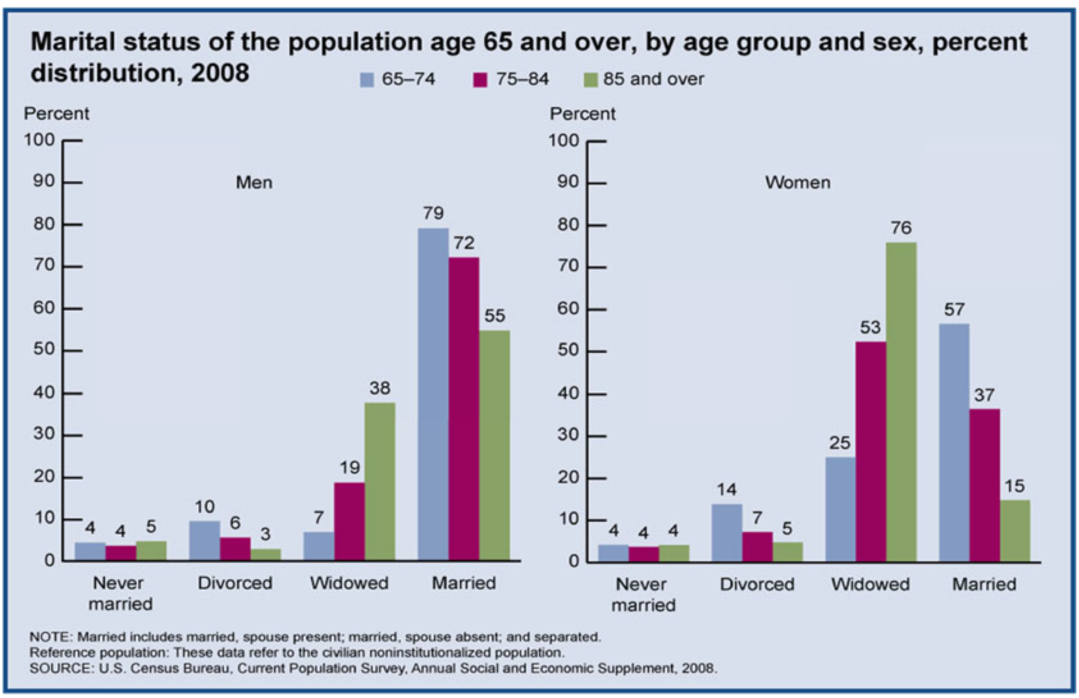


Fig. 1.6 Marital status of older Americans with increasing age

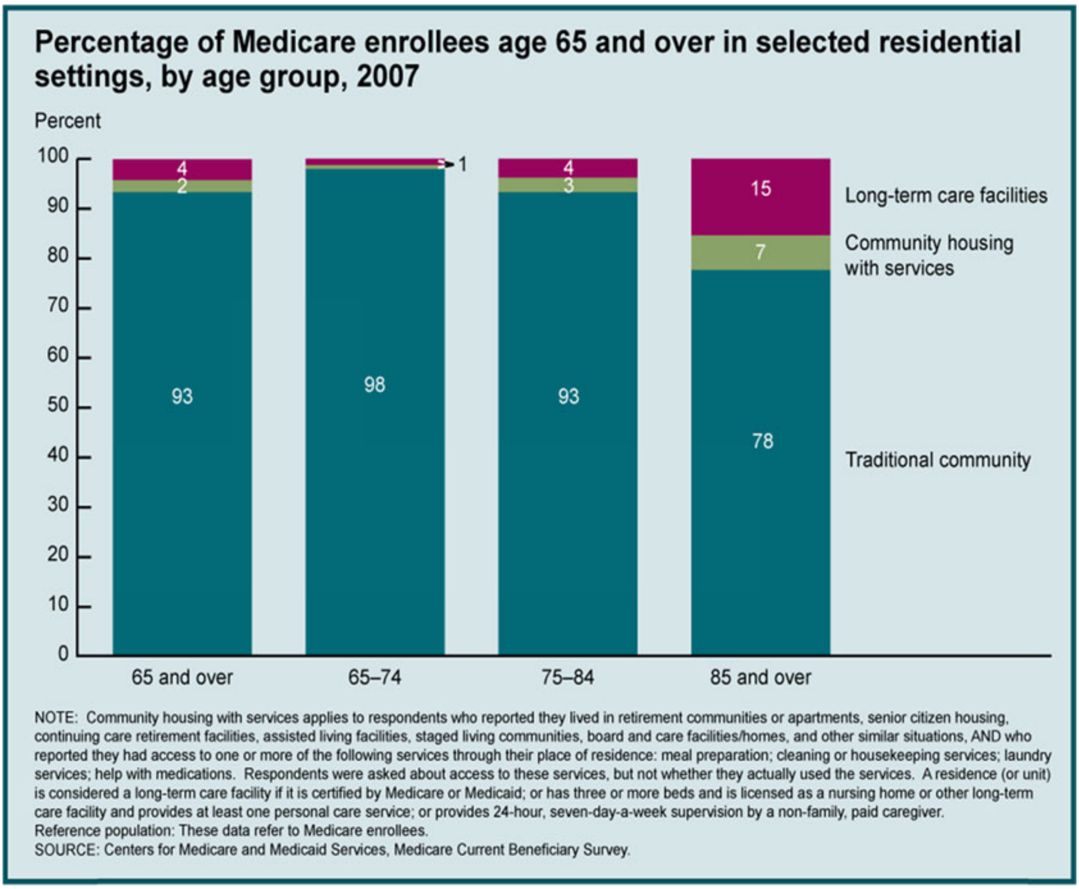


Fig. 1.7 Residential settings of older adults

majority of older patients of all ages still remain in their homes. But an increasing percentage of the oldest old (>85 years of age) reside in institutional settings (Fig. 1.7) [2]. The level of functional limitations seen in older patients is higher in more supported settings such as assisted living facilities and long-term care facilities (Fig. 1.8) [2].

With increasing age, the probability of having chronic disease and multiple comorbidities rises for both individuals and populations. As seen in Fig. 1.9 [2], arthritis and hypertension are the most frequent self-reported health conditions in older patients. The rates of reported cognitive impairment also rise with aging, although widely variable prevalence numbers are reported. The prevalence of dementia in long-term care settings is usually reported at >50 %. Community-based prevalence numbers for cognitive impairment are lower.

These demographic and disease prevalence changes that occur with aging often result in a change in emphasis in the medical encounter. The social situation of the patient becomes increasingly critical to positive healthcare outcomes. Patients with multiple comorbidities often benefit from interdisciplinary team management of their many medical problems, especially around transitions of care from home to hospital to rehabilitative care. The discharge or transfer plan must recognize the functional capacity of the patient and take advantage of informal supports (family members, neighbors) as well as formal supports (visiting nurses, meal services). Structured communication between hospital physicians and primary care physicians or long-term care physicians needs to be built into the system of care for these vulnerable patients.

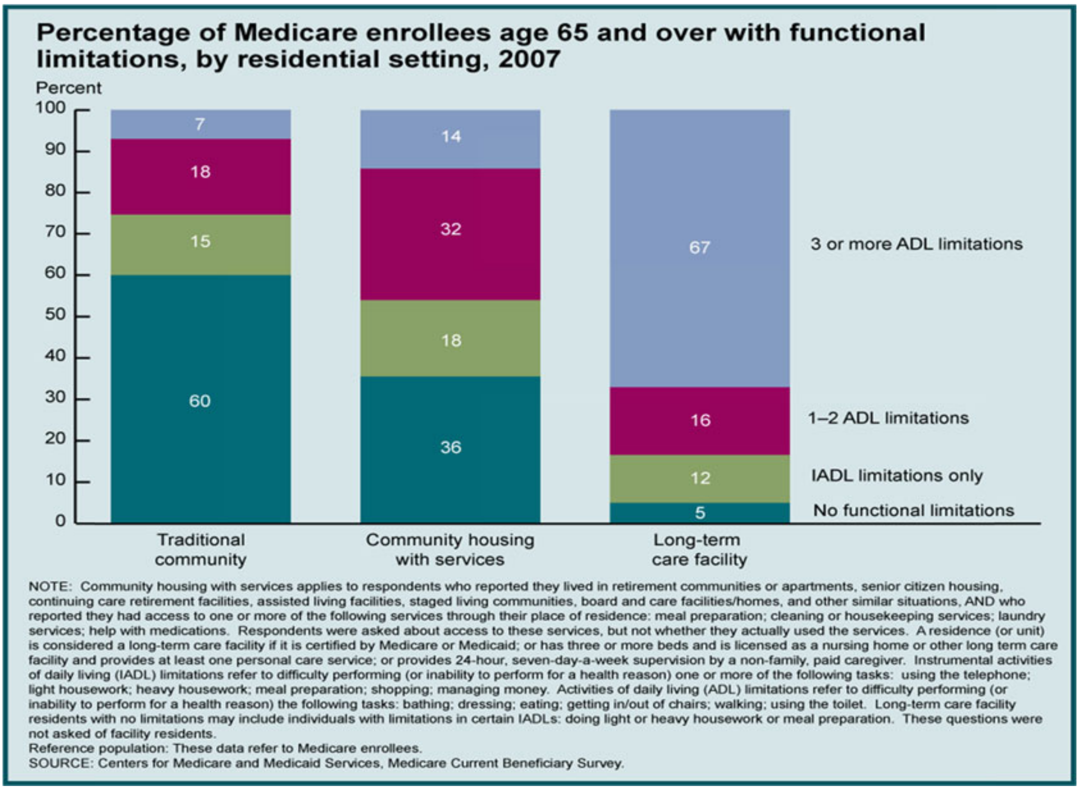


Fig. 1.8 Functional limitations and residential setting

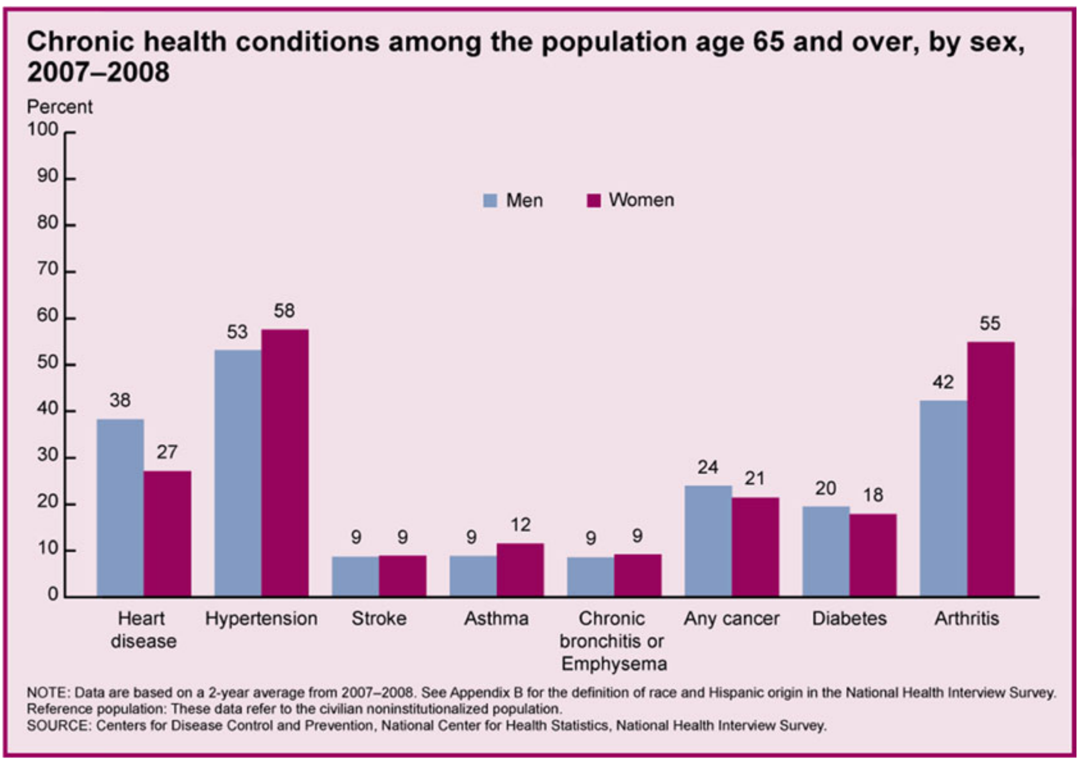


Fig. 1.9 Chronic health conditions self-reported by people age 65 and older

Urologic Diseases Affected by Aging

Urologists will encounter rising numbers of elderly patients who have complaints of the urinary (kidney, ureter, bladder, or urethra) or genital (prostate, testes) systems. Perhaps most important among these is the occurrence of lower urinary tract symptoms (LUTS) associated with benign growth of the prostate, although prostate and bladder cancers gain prominence as the years of age increase. Another complaint of significance relates to all forms of urinary incontinence, whether in females or males.

Benign Prostatic Obstruction

Urology grew rapidly as a specialty after it acquired the ability to perform the procedure "transurethral resection of the prostate" (TURP), primarily used to remove excess prostatic tissue associated with benign prostatic hyperplasia or BPH. This occurred during the early 1930s. Hyperplastic growth of benign prostate tissue occurs gradually in older males, being clinically evident in about 50 % at age 50 and in 80 % at age 80 [3, 4]. About 20–30 % of these men require some type of intervention because of their LUTS [4]. Until the late 1980s, treatment for this condition was mostly surgical and done by TURP. However, in 1985, Medicare put out requests for proposals that would address alternate methods of addressing obstructive BPH. This resulted in the development of numerous medications, such as alpha-blockers and androgen inhibitors and to different ablative methods such as laser destruction, radio-frequency ablation, high-intensity focused ultrasound, microwave thermotherapy, and other transurethral heat applications [5, 6]. As a result, the use of TURP has plummeted from being the second most common surgical procedure of all Medicare patients in 1985 to being below the 110th in 2005. Therapy by medications or alternate procedures has become more prominent, with "Heat Therapy of the Prostate" being now the 106th most common procedure code seen in Medicare in 2005 [7, 8]. In a recent review of studies of treatment with various medications for BPH, 6–16 % of men eventually required some type of surgical or interventional treatment [9].

Cancers of the Genitourinary System

In a recent review, Li et al. summarized the impact of urologic cancers, noting that "Bladder cancer is the fourth most common cancer and the eighth leading cause of cancer-related deaths among US men, and prostate cancer is the most common cancer [in men] and the second leading cause of cancer-related deaths" [10]. They showed that urogenital cancers are found more often in males and in those of African-American race. All three malignancies were significantly more common at age above 49 years and again were more common in men. Kidney cancer also contributed significantly. Using an interesting methodology for analysis, they estimated that deaths from kidney cancer represented 16.5 years of productive life lost (YPLL) per patient, while YPLL for bladder cancer was 12.0 years and that from prostate cancer was 10.1 years. Hence, these three urologic cancers carry a risk of significant loss of economic potential in addition to their extensive costs for treatment.

Prostate Cancer

Prostate cancer treatment contributes about 11 % of the total treatment costs of all cancers in the USA [11]. This disproportionately high cost may or may not be related to the early detection programs using PSA testing. The resulting controversy has led to a recommendation by the United States Preventive Services Task Force (USPSTF) that PSA not be used as a screening test for prostate cancer [12]. This recommendation is Grade D, meaning that it should not be offered to any man. Others have disagreed and indicated that they believe the correct USPSTF Grade should be C, that is, offered when there are circumstances that support providing the service to an individual patient (such as a strong family history) [13]. This will be discussed in more detail in Chap. 17 (Prostate Cancer). Nevertheless, prostate cancer is now the eighth most common diagnosis in all Medicare patients, and its contribution to increased visits to physicians has grown by 58 % in the decade from 1998 to 2008 [14].

Bladder Cancer

Shariat et al. have stated that: "Age is now widely accepted as the greatest single risk factor for developing bladder cancer and bladder cancer is considered as primarily a disease of the elderly" [15]. And although men have a prevalence of bladder cancer that is 3–4 time greater than women, elderly women tend to have more advanced cancer at presentation and poorer overall survival [16]. In addition, design of perioperative management protocols for bladder cancer must consider that many patients requiring extensive treatment will be in the geriatric age group and that their mortality within 90 days of surgery can be greater than those under age 60 [17]. There are few human operative insults greater than radical cystectomy with creation of a neobladder or other form of urinary diversion. Although some articles have chastised the average urologist for undertreating older patients with only local resection rather than radical removal, the survival results after radical cystectomy for a properly chosen elderly candidate can be satisfactory [18–20]. This subject will be discussed more thoroughly in Chap. 18 (Bladder Cancer).

Kidney Cancer

Figure 1.10 presents a dramatic description of the increased incidence of kidney cancer in white and black men and women with increasing age. Martin and Sheaff [21] reviewed the multiple changes in the aging kidney including decreased GFR, decreased renal blood flow, glomerulosclerosis, and decreased glomeruli. They mention that the occurrences of renal tumors "are thought to be

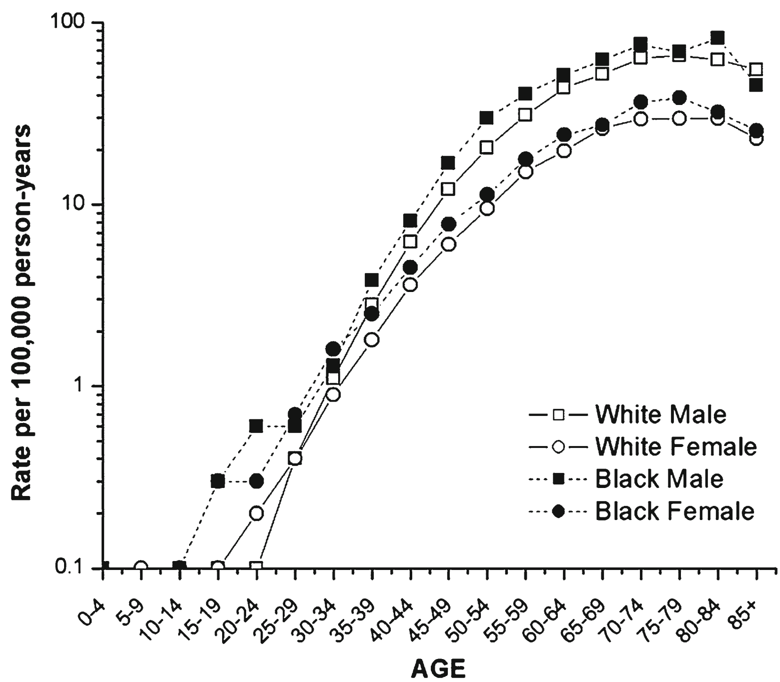


Fig. 1.10 Age-specific incidence of renal cell cancer in the United States by race and sex in 1992–2002 based on SEER data for 13 geographic regions of the United States, including Atlanta, Georgia; Connecticut; Detroit, Michigan; Hawaii; Iowa; Los Angeles County, California; New Mexico; San Francisco/Oakland and San Jose/Monterey, California; Seattle/Puget Sound, Washington; Utah; rural Georgia; and Alaska natives. From J Urol 2006; 176:2353–2358

Table 1.1 Genetic relationships to renal cancer [22]

Renal cancer type	Gene	Mechanism
Hereditary clear cell	VHL	Oxygen sensing
Hereditary clear cell	CHROMOSOME 3	Translocation
Hereditary papillary renal cancer (HPRC)	MET	HPRC gene tyrosine area
Chromophobe	FLCN	Gene deficiency
Hereditary papillary leiomyomatosis cancer	HPLRCC	Fumarate hydrase deficiency

related to the accumulation of genetic damage, with accompanying loss of cell controls." Linehan and his group at the National Cancer Institute [22] have carried these genetic concepts further and have outlined the influence of various genes in the causation of various types of kidney cancer (Table 1.1). Linehan further states that "kidney cancer is a metabolic disease" and that understanding the fundamental aberrations of metabolism may lead to new approaches for therapy.

Most therapy for renal cancer involves surgical removal, either partial or total. In a cost-analysis review of treatment of renal cancers, Hollenbeak et al. [23] determined that higher costs were associated with increasing age, number of comorbidities, and race/ethnicity. In other words, older patients accrued more costs. At the conclusion of 5 years of treatment, about 21 % of their patient group remained alive and had accumulated an average of $59,397 in treatment costs. Patients who received some type of supplemental therapy averaged an additional $13,440 in costs at 5 years [23]. Evaluation and management of kidney cancers in older adults will be discussed in more detail in Chap. 19 (Kidney Cancer).

So these "Big 3" in urologic cancers afflict our elderly population with a greater incidence than younger patients. Successful evaluation and management can be more challenging in this older population, but effective management can be accomplished in many cases.

Other Urologic Diseases Related to Aging

In addition to the LUTS problems associated with BPH noted above, other urologic complaints bring the older patient to the doctor's office including urinary urgency, urinary tract infection, urinary incontinence, pelvic organ prolapse, and nocturia. Again, noting the National Ambulatory Medical Care Survey (NAMCS) reference above regarding prostate cancer [14], we see that the chief complaint of "symptoms involving the urinary system" increased by 139 % during the decade 1998–2008. Possibly the most prominent of these would be related to urinary incontinence, which may be present in 15–30 % of older adults, especially women [24]. And the rising incidence of nocturia becomes important because it causes older patients to arise from bed and proceed to the bathroom in dimly lit rooms with potential hazards (such as loose rugs) that contribute to falls—which then contribute greatly to additional morbidity in geriatric patients [6, 25]. Urinary infections also remain one of the most common reasons for sepsis in older adults [26]. Sexual challenges exist in elderly men and women and complaints in these areas may bring the patient to the internist or geriatrician [27]. Each of these complaints and several others achieve such importance that they deserve full chapters of discussion.

Geriatric Urology and the AUA Core Curriculum of May 2010

In May 2010, the American Urological Association (AUA) announced completion of its Core Curriculum for Urology. Included in this Curriculum is Chap. 42 on "Geriatric Urology." For those with interests in Geriatric Urology, appearance of this Chapter with its nine sections represented new recognition of this topic area as an important component of urology [28]. This electronically published document is an evolving resource available online to members of the AUA and to other individuals or institutions that wish

Table 1.2 Geriatric urology (Chap. 42) sections, AUA core curriculum [28]

1. Demographics/population issues of aging
2. Biology of aging
3. Disease specific aspects
4. Evaluation of the elderly patient
5. Geriatric syndromes
6. Decision-making in elderly patients
7. Geriatric treatment principles
8. Peri-operative Issues
9. Palliative care

to pursue access rights. Most importantly for purposes of this textbook, it provides educational aids and references that may be useful to a person who wishes to improve his or her knowledge of the field of Geriatric Urology. Since the Residency Review Committee (RRC) for Urology and the American Board of Urology (ABU) both now require Geriatric Urology as one of the domains of knowledge required for residency education and Board certification, this Core Curriculum in Geriatric Urology may help those pursuing knowledge necessary in fulfilling this educational requirement. In addition, this present textbook on "Geriatric Urology" will also help individuals in reviewing the related chapters (Table 1.2) within the Geriatric Urology Section of the AUA Urology Core Curriculum.

References

1. US Census Bureau. http://www.census.gov (2012). Accessed 11 Jan 2012.
2. Older Americans 2010: Key Indicators of Well Being. Federal interagency forum on aging related statistics. http://www.agingstats.gov (2012). Accessed 11 Jan 2012.
3. Wei J, Calhoun E, Jacobsen SJ. Urologic diseases in America project: benign prostatic hyperplasia. J Urol. 2005;173:1256–61.
4. Burnett AL, Wein AJ. Benign prostatic hyperplasia in primary care: what you need to know. J Urol. 2006;175:S19–24.
5. McNicholas T, Kirby R. Benign prostatic hyperplasia and male lower urinary tract symptoms (LUTS). Clin Evid (Online). 2011;2011:1801. Accessed 22 Nov 2011.
6. Guzzo TJ, Drach GW. Major urologic problems in geriatrics: assessment and management. Med Clin North Am. 2011;95:253–64.
7. Medicare leading part B procedure codes based on allowed charges, calendar year 2005. http://www.cms.gov 2011. Accessed 23 Apr 2011.
8. Djavan B, Kazzazi A, Bostanci Y. Revival of thermotherapy for benign prostatic hyperplasia. Curr Opin Urol. 2011;22(1):16–21. Accessed 22 Nov 2011.
9. Roehrborn CG. Male lower urinary tract symptoms (LUTS) and benign prostatic hyperplasia (BPH). Med Clin North Am. 2011;95:87–100.
10. Li C, Ekwueme DU, Rim SH, Tangka FK. Years of potential life lost and productivity losses from male urogenital cancer deaths – United States 2004. Urology. 2010;76:528–35.
11. Brown ML, Riley GF, Schussler N, et al. Estimating health care costs related to cancer treatment from SEER-Medicare data. Med Care. 2002;40:IV-104–17.
12. Chou R, Croswell JM, Dana T, et al. Screening for prostate cancer: a review of the evidence for the U.S. Preventive services task force. Ann Intern Med. 2011;155(11):762–71. Accessed 22 Nov 2011.
13. McNaughton-Collins MF, Barry MJ. One man at a time – resolving the PSA controversy. N Engl J Med. 2011;365:1951–3.
14. http://www.cdc.gov/nchs/data/ahcd/namcs_summary/namcssum2008.pdf. Accessed 7 Dec 2011.
15. Shariat SF, Milowsky M, Droller MJ. Bladder cancer in the elderly. Urol Oncol. 2009;27:653–67.
16. Shariat SF, Sfakianos JP, Droller MJ, et al. The effect of age and gender on bladder cancer: a critical review of the literature. BJU Int. 2010;105:300–8.
17. Liberman D, Lughezzani G, Sun M, et al. Perioperative mortality is significantly greater in septuagenarian and octogenarian patients treated with radical cystectomy for urothelial carcinoma of the bladder. Urology. 2011;77:660–6.
18. Chang SS, Alberts G, Cookson MS, et al. Radical cystectomy is safe in elderly patients at high risk. J Urol. 2001;166:938–40.
19. Hollenbeck BK, Miller DC, Taub D, et al. Aggressive treatment for bladder cancer is associated with improved overall survival among patients 80 years old or older. Urology. 2004;64:292–9.
20. Drach GW, Forciea MA. Geriatric patient care: basics for urologists. AUA Update. 2005;24:286–95.
21. Martin JE, Sheaff MT. Renal ageing. J Pathol. 2007;211:198–205.
22. Linehan WM. Genetic basis of kidney cancer: Role of genomics for the development of disease-based therapeutics. Genome Res. 2012;22(11):2089–100. Accessed 31 Oct 2012.
23. Hollenbeak CS, Nikkel LE, Schaefer EW, et al. Determinants of Medicare all-cause costs among elderly patients with renal cell carcinoma. J Manag Care Pharm. 2011;17:610–20.
24. Griebling TL. Urinary incontinence in the elderly. Clin Geriatr Med. 2009;25:445–57.
25. McLaughlin SP, Carson CC. Urinary tract infections in women. Med Clin North Am. 2004;88:417–29.

26. Weiss JP, Blaivas JG, Bliwise DL, et al. The evaluation and treatment of nocturia: a consensus statement. BJU Int. 2011;108:6–21.
27. Ginsberg TB. Aging and sexuality. Med Clin North Am. 2006;90:1025–36.
28. Griebling TL, Drach GW, Pranikoff K, DuBeau CE, Katz P. Geriatric urology – AUA core curriculum. In: Linthicum MD. American Urological Association. May 30, 2010. http://www.auanet.org/eforms/elearning/core/?topic=37. Accessed 12 Jan 2012.

2 The Biology of Aging and the Development of Lower Urinary Tract Dysfunction and Disease

Jill A. Macoska, Sathish Kasina, Lysanne Campeau, and Karl-Erik Andersson

Introduction

Basic and translational research has played a critical role in the understanding of human structure and function and essentially all human diseases. This is certainly true of the aging process. Basic research has advanced our knowledge about anatomic and physiologic alterations that occur naturally as part of aging of the genitourinary tract. In addition, this type of research has led to the development of treatments for a wide spectrum of clinical conditions which predominantly affect older adults. This chapter will focus on basic and translation research related to prostate disease and bladder dysfunction in the elderly population. This includes analysis of benign prostatic hyperplasia (BPH), prostatic fibrosis, and prostate cancer (PCa), and both storage and voiding dysfunction related to the bladder.

J.A. Macoska, Ph.D. (✉) • S. Kasina, Ph.D.
Department of Urology, The University of Massachusetts, 100 Morrissey Blvd., Boston, MA 02125, USA
e-mail: Jill.Macoska@umb.edu; Sathish.Kasina@umb.edu

L. Campeau, M.D., C.M., Ph.D., F.R.C.S.C.
Wake Forest Institute for Regenerative Medicine, Wake Forest University School of Medicine, 391 Technology Way, Winston-Salem, NC 27101, USA
e-mail: lcampeau@wakehealth.edu

K.-E. Andersson, M.D., Ph.D.
Department of Urology, Wake Forest Institute for Regenerative Medicine, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157, USA
e-mail: keanders@wfubmc.edu

Prostate Disorders

Prostatic Enlargement

Benign Prostatic Hyperplasia and Androgens

BPH is a noncancerous enlargement of the prostate and is a common condition associated with aging in men [1–3]. Normal prostate development is dependent on dihydrotestosterone (DHT), which is converted from testosterone by 5α-reductase enzymes. DHT is the major growth factor of adult prostate tissue [4]. In male rodents, castration results in prostatic involution due to massive apoptosis of the luminal epithelium and quiescence of the basal cell population. However, the prostate regenerates in castrate mice supplemented with DHT, showing that the adult prostate is highly sensitive and responsive to androgen [5–7]. Similarly, men who are castrated prior to puberty, have 5α-reductase-type 2 deficiencies, or have naturally occurring or clinically induced hypogonadism, do not develop a fully formed prostate and do not go on to develop BPH later in life [8].

BPH comprises a gradual increase in prostatic volume that occurs over decades of life. Studies have estimated that BPH develops consequent to a low-level, but cumulative, cellular proliferation

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_2,

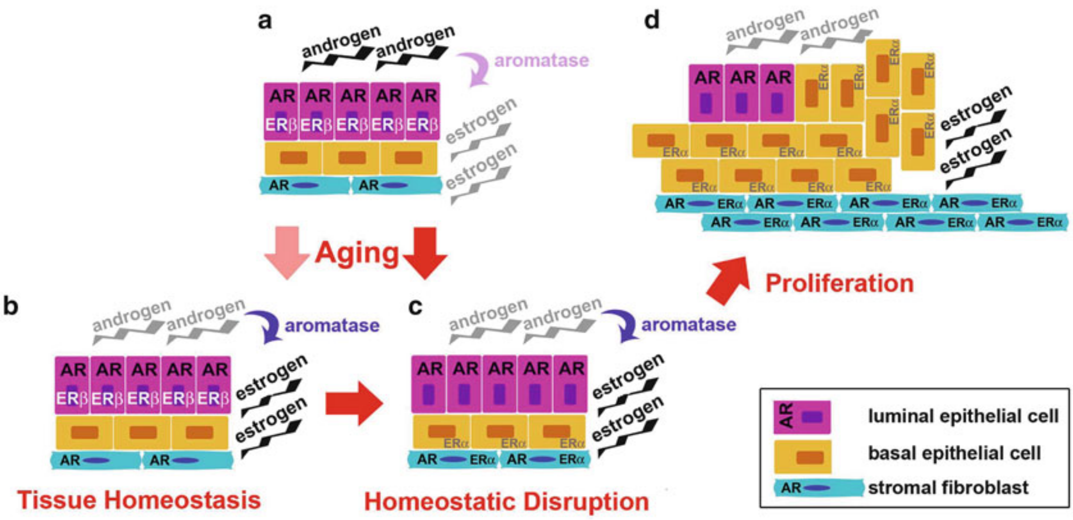


Fig. 2.1 BPH and estrogens. (**a**) High androgen levels and ERβ expression levels in prostate epithelial luminal cells (*pink*) maintain luminal cell differentiation and quiescent basal epithelial (*yellow*) cell proliferation. (**b**) In the aging prostate, androgen levels decrease, aromatase activity increases, and androgens are increasingly converted to estradiols. These events can be countered by normal ERβ function, which helps maintain prostate luminal epithelial cells in a non- or low-proliferative, secretory state by facilitating estrogen-mediated antiproliferative and anti-inflammatory effects. This mechanism maintains tissue and organ homeostasis under normal physiological conditions. (**c**) In the aging prostate, differential methylation of the ERβ and ERα promoters consequent to aging promotes estradiol-stimulated activation of ERα receptors in the basal prostate epithelium (*yellow*) and stromal fibroblast (*blue*) cells and consequent homeostatic disruption. (**d**) Increased expression and activation of ERα receptors in the aging prostate promotes both basal epithelial and stromal fibroblast cellular proliferation, facilitating BPH and prostatic enlargement

that increases post-pubertal prostatic volume by approximately 0.8–1.6 %, equivalent to only 0.2–0.4 mL, per year [9, 10]. Studies both in vivo and in vitro have reported higher proliferative and lower apoptotic rates for epithelial cells from hyperplastic compared to normal prostates, suggesting that some proportion of increased prostate volume with age is attributable to increased epithelial cell densities [11–13]. Work accomplished using rodent and rodent/human in vivo and in vitro models have suggested that paracrine interactions between glandular epithelial cells and adjacent fibroblastic stromal cells play an important role in the development of benign prostatic proliferative diseases [14–19]. These studies show that epithelial–stromal interactions are crucial for the regulation of epithelial cell growth and suggest that changes in such interactions consequent to aging likely contribute to the etiologies of BPH and PCa.

BPH and Estrogens

Serum levels of both total and free testosterone decrease with age as documented in both the Massachusetts Male Aging Study [20] and the Baltimore Longitudinal Study of Aging [21]. Correlative findings show that intraprostatic and/or serum estrogen levels either do not change or are elevated consequent to aging in men [22, 23]. Recent studies have suggested that estrogenic hormones may promote prostatic enlargement in older men in a manner that largely correlates with the expression levels of the two primary estrogen cellular receptors, ERα and ERβ, which are expressed in different cellular compartments of the prostate gland. ERβ is primarily expressed by the prostate epithelium (Fig. 2.1a, b), whereas ERα is primarily expressed (often heterogeneously) by fibroblastic and epithelial prostate stromal cells (Fig. 2.1c). ERβ normally functions to help maintain prostate luminal epithelial cells in a non- or low-proliferative, secretory state by facilitating estrogen-mediated antiproliferative and anti-inflammatory effects. This mechanism maintains tissue and organ homeostasis under normal physiological conditions. However, differential methylation of the ERβ and ERα promoters consequent to processes that are not entirely elucidated (but are likely related to aging) mediates decreased ERβ expression levels in prostate epithelium and increased ERα expression levels, particularly in the prostatic stroma. Thus, compared to normal prostate tissues, BPH tissues exhibit a high stromal ERβ/ERα ratio in association with stromal and epithelial hyperplasia (Fig. 2.1d) and tissue inflammation [8, 24, 25]. In addition, aromatase, the enzyme that converts testosterone to estradiol, is expressed and active in adipose tissue, adrenal glands, the testicles, and prostatic stroma, which suggests that local conversion of androgens to estrogens may promote estrogen signaling within the prostate [26, 27]. Aromatase expression and activity increase with the accumulation of obesity-related adipose tissue, resulting in reduced testosterone concentrations and concurrent increased estradiol production [28]. Obesity itself increases in incidence with age [29], suggesting that aging, obesity, increased aromatase expression and activity, and increased estradiol:testosterone ratios may play complex and intertwined roles in the development of prostatic enlargement and lower urinary tract symptoms (LUTS).

BPH and Nonsteroidal Growth Factors

In addition to androgenic and estrogenic hormones, nonsteroidal growth factors have been identified that promote aging-associated prostatic enlargement. Most of these comprise small, soluble, secreted proteins, including basic fibroblast growth factor (bFGF, FGF-2) [30], insulin growth factors (IGFs) [31], and inflammatory molecules [32, 33].

bFGFs

bFGFs and their receptors are highly expressed in BPH tissues [34, 35], primarily in stromal fibroblasts, smooth muscle, and endothelial cells [36], and promote the proliferation of stromal fibroblasts in vitro [30]. bFGF is also highly expressed by adipose tissues [37], suggesting another avenue through which obesity may promote prostatic enlargement. In vivo studies have shown that targeted transgenic expression of bFGF in the mouse prostate exhibit epithelial hyperplasia and glandular enlargement [38]. Taken together, these studies consistently demonstrate one or more role(s) for bFGF in prostatic enlargement.

IGFs

IGF receptors are expressed in the epithelium [39] and stroma [40] of BPH tissues at elevated levels compared to normal prostate. Expression of the IGF-II gene is biallelic in histologically normal tissues and adjacent malignant glands, but demonstrates an imprinted, paternally imprinted allelic expression in BPH tissues [41]. Mice engineered to overexpress IGF-1 in the mouse prostate exhibit denser, enlarged glands compared to non-transgenic littermates [42]. Interestingly, IGF-1 levels are upregulated by estradiol binding to the ERα receptor [43], suggesting a mechanism whereby increased aromatase activity in the aging prostate (especially in obese individuals) may promote IGF-1 expression and activity.

Inflammatory Molecules

Inflammatory molecules secreted in association with aging tissues that may promote prostatic enlargement include the interleukins and chemokines. The interleukins comprise a large family of related proteins that function to control innate immune responses and as cytokines (growth factors) for many cell types [44]. The primordial interleukins, Interleukin-1α (IL-1α) and Interleukin-1β (IL-1β), accomplish multiple functions in multiple cell types. Of importance to this discussion is that IL-1α and IL-1β activate the powerful NFκB transcription factor which, in turn, promotes the transcription of scores of genes encoding inflammatory proteins, including TNFα, CC-type chemokines, CXC-type chemokines, and interleukins (including IL-1α and IL-1β) [45]. Many of these same inflammatory proteins (especially IL-6 and TNFα) are elevated in older adults, often in conjunction with increased obesity and adiposity and with decreased testosterone in men [46].

A recent study found that stromal fibroblast cells cultured from the prostates of older men (aged 63–81 at the time of prostatectomy) were less able to suppress the proliferation of nonmalignant prostate epithelial cells than those cultured from the prostates of younger men (aged 40–52 years) [47]. Moreover, these studies showed that the transcriptome of aging prostate stroma is characterized by the upregulation of several genes that encode secreted inflammatory mediators, including CXC-type chemokines (CXCL1, CXCL2, CXCL5, CXCL6, CXCL12), interleukins (IL11, IL33), and transcripts with cytokine homology (CYTL1) [47, 48].

Fibroblastic cells cultured from the prostates of older men secreted higher levels of CXCL1, CXCL5, CXCL6, and CXCL12 protein than those cultured from the prostates of younger men [47, 48]. Subsequent studies have confirmed the secretion of CXCL5 , CXCL12 [49], CXCL8 [49, 50], CXCL10, and IL-6 [50] by human prostate stromal fibroblastic cells. Fujita et al. [51] demonstrated >2-fold higher levels of IL-1β, IL-7, CCL2, and IL-6 in the extraprostatic secretions (EPS) of large (>60 g) compared to small (<40 g) prostates and showed that the source of CCL2 secretion was prostate stromal fibroblastic (but not epithelial) cells. High levels of CCL2 secretion by prostate stromal fibroblast cells was also demonstrated by McDowell et al. [49]. Together, these studies suggest that a diverse and robust chemokine "secretome" is expressed by stromal fibroblast cells in the human aging and enlarged prostate.

Mechanisms that Promote the Secretion of Nonsteroidal Growth Factors in the Aging Prostate

With the exception of those cell types that comprise continually renewing tissues originating from particular types of stem cells, many types of mammalian cells become growth-arrested, or senescent, over time. By definition, senescent cells are nonreplicative. Cells may become senescent because they have reached their Hayflick limit, i.e., their chromosomal telomeres are too short to permit further DNA synthesis and cell division. Such cells have effectively reached replicative exhaustion and have entered replicative senescence. Cells may also become senescent because they have become stressed, often resulting in DNA damage and growth arrest. Although these cells have not reached their Hayflick limit, they are, nevertheless, nonreplicative and have entered cellular senescence. Many studies have shown that senescent cells accumulate with age in vivo [52–56]. Senescence is essentially controlled by tumor suppressor genes, including p16, Arf, p53, and RB1, that serve as checkpoints to prevent the proliferation of cells at risk for neoplastic transformation [57, 58] (Fig. 2.2).

Prostatic stromal fibroblasts induced to undergo senescence after achieving replicative exhaustion or after exposure to agents that caused oxidative stress or DNA damage demonstrate similar and significant upregulation of transcripts encoding several inflammatory mediator-type proteins, including the chemokines CXCL1, CXCL8, CXCL12, CCL2, CCL7, CCL11, CCL13, and CCL20 [59]. Fibroblasts induced to undergo replicative exhaustion or irradiation-induced senescence secreted diverse inflammatory mediator proteins, including the interleukins IL-1β, IL-6, IL-7, IL-11, IL-13, and IL-15; the CC-type chemokines CCL2, CCL3, CCL8, CCL13, CCL16, CCL20, and CCL26; and the CXC-type chemokines CXCL1, CXCL2, CXCL3, and CXCL8 [60]. Thus, fibroblastic cells derived from multiple organs, including the prostate, demonstrate senescence-associated secretory profiles (SASPs) that are remarkably similar to each other and to those isolated from aging and/or enlarged human prostates [47, 48, 50, 51]. Moreover, normal human prostate epithelial cells induced to undergo senescence subsequent to ionizing radiation demonstrated a senescence-associated secretome that was very similar to that exhibited by senescent fibroblasts [60]. Taken together, these studies are consistent with the accumulation of senescent stromal fibroblasts as a potential driving force behind inflammatory protein secretion in the aging and enlarged human prostate.

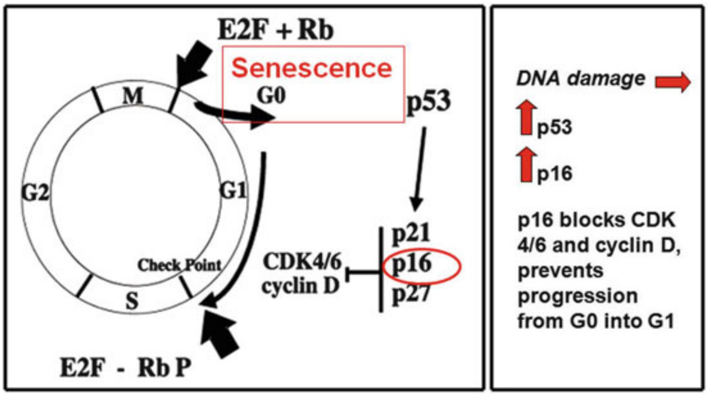


Fig. 2.2 Senescence and the cell cycle. Low-level DNA damage states in the cell include terminal telomere shortening at cellular replicative exhaustion or those produced by exposure to various stresses (oxidative stress, chemical insult, inflammation). Consequently, p53 and p16 protein levels increase, and high p16 levels block progression of the affected cells at G0 in the cell cycle. The cells effectively exit the cell cycle and enter a proliferatively quiescent (but metabolically very active) state of senescence

Mechanisms Through Which Inflammatory Proteins Promote Prostate Cell Proliferation

BPH/LUTS is pathologically characterized by the proliferation of fibroblast/myofibroblast and epithelial cell types within the periurethral, or transitional zone, region of the prostate gland [1, 2, 61]. Previous studies have shown that BPH/LUTS develops consequent to a gradual increase in prostatic volume that occurs over decades of life through a process of low-level, but cumulative, cellular proliferation that increases postpubertal prostatic volume by approximately 0.8–1.6 %, equivalent to only 0.2–0.4 mL, per year [9, 10]. Therefore, the observed low-level secretion of multiple chemokines by prostatic stroma and resident inflammatory cells may promote the concomitant low-level, but cumulative, overproliferation of both stromal fibroblastic and epithelial cell types associated with increased prostate volume in aging men.

In vitro studies have shown that nonmalignant prostate epithelial cells respond proliferatively when cocultured with senescent prostate stromal fibroblasts in vitro [59]. Many of the CC- and CXC-type chemokines identified as secreted by senescent cells have been shown to induce proliferative responses in vitro [47–49, 51, 59, 62] (Fig. 2.3b, c). Transgenic mice engineered to overexpress keratinocyte-derived chemokine (KC), the functional murine homolog of CXCL8, exhibit hyperplastic prostatic epithelium, characterized by age-associated acinar infolding and significant increases in acinar diameter in vivo [63]. Moreover, many of these same CC- and CXC-type chemokines are highly angiogenic and promote tissue vascularization [64]. A small number of studies have demonstrated increased microvessel density (MVD) in BPH/LUTS compared to normal prostate tissue [65] and even in BPH/LUTS compared to malignant tissue [66]. These studies provide some rationale for exploring chemokine-mediated angiogenesis as a contributing factor to BPH/LUTS development and progression.

Prostatic Fibrosis

Fibrosis is an aberrant version of the normal wound healing process and is characterized by myofibroblast accumulation, collagen deposition and extracellular matrix (ECM) remodeling, and increased tissue stiffness [67–70]. Numerous studies have demonstrated that aging- and inflammation-associated fibrotic changes in tissue architecture contribute to dysfunction and disease in multiple organ systems. Examples include pancreatic dysfunction in type 2 diabetes [71, 72],

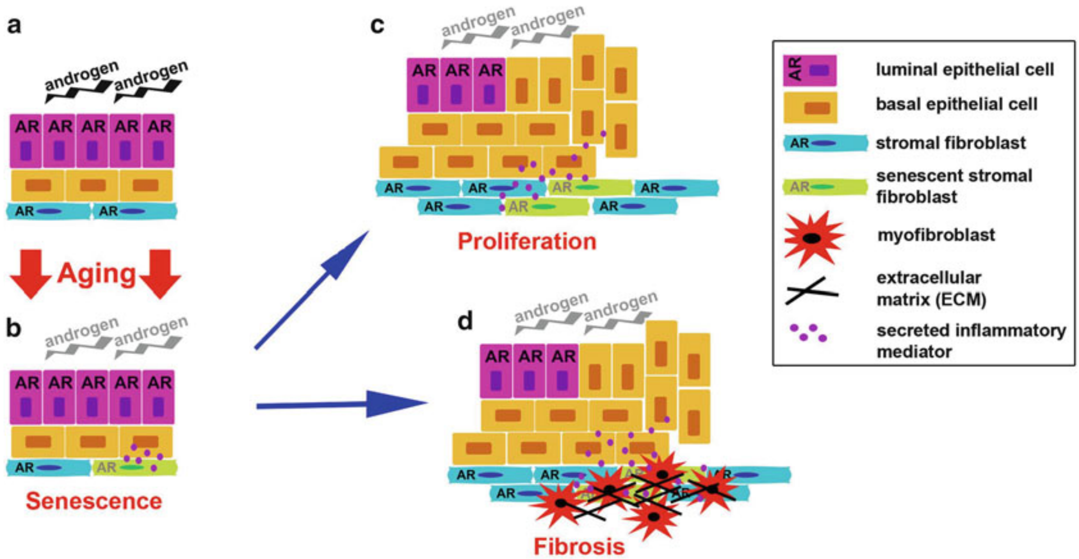


Fig. 2.3 Senescence can promote cellular proliferation and tissue fibrosis. (**a**) High levels of androgen help maintain tissue homeostasis in the prostate. (**b**) Aging-associated replicative exhaustion, exposure to various stresses, and declines in androgen levels induce the senescence of some stromal fibroblasts (*green*) in the prostate. Senescent stromal fibroblasts are secretory cells and produce high levels of inflammatory mediators (*purple dots*). (**c**) Inflammatory mediators secreted by senescent cells may act as cytokines to promote the proliferation of epithelial (*yellow*) as well as fibroblast (*blue*) cells, promoting prostatic enlargement. (**d**) Inflammatory mediators (*purple dots*) secreted by senescent cells (*green*) may also promote resident fibroblast (*blue*) or other (fibrocytes, pericytes) cell types to undergo myofibroblast differentiation (*red stars*). Myofibroblasts accumulate and secrete extracellular matrix (ECM) components such as fibronectin and collagen (*black fibers*). If these changes occur in periurethral tissues, the subsequent increased stiffness may reduce urethral compliance and thereby contribute to obstructive symptoms

chronic obstructive pulmonary diseases [73, 74], cirrhotic nonalcoholic fatty acid liver disease [75, 76], Crohn's Disease, and parts of the spectrum disorder termed inflammatory bowel disease (IBS) [77, 78].

Myofibroblast accumulation and differentiation contributing to tissue fibrosis occurs through a sequence of events initiated by activated TGF-β (primarily TGF-β1; subsequent references to TGF-β are to TGF-β1). Activated TGF-β1 binds to the transmembrane TGF-βRII receptor, which then simultaneously heterodimerizes with and phosphorylates the TGF-βRI receptor, which, in turn, phosphorylates Smad2 or Smad3. Activated Smad2 or Smad3 then translocate as Smad2/Smad3 or Smad3/Smad4 complexes into the nucleus to promote gene transcription. Initial events in myofibroblast differentiation include Smad-mediated expression of the alpha-smooth muscle actin (αSMA) and collagen I (COL1) genes [68, 70].

Myofibroblast accumulation and differentiation have been observed in the prostates of mouse models of BPH/LUTS. Targeted expression of a constitutively active TGF-β1 to the murine prostate gland epithelium promotes fibroplasia and the development of collagenous micronodules in collapsed acini, phenotypes consistent with myofibroblast accumulation, and tissue fibrosis [79]. Similarly, transgenic mice engineered to overexpress keratinocyte-derived chemokine (KC), the functional murine homolog of CXCL8, exhibit hyperplastic prostatic epithelium, characterized by age-associated acinar infolding and significant increases in acinar diameter. Moreover, overexpression of KC was associated with a prototypical reactive stromal phenotype characterized by myofibroblast accumulation [63].

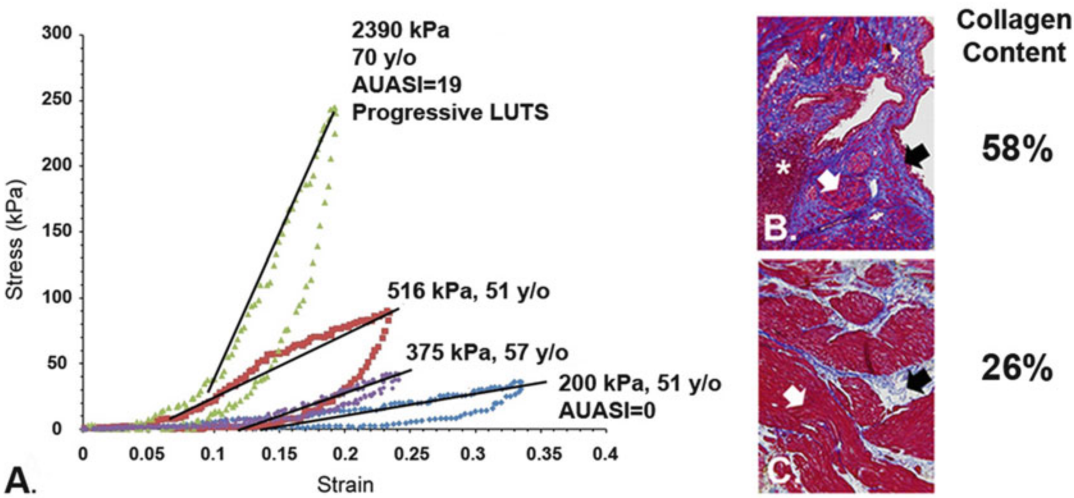


Fig. 2.4 Evaluation of periurethral prostate tissue stiffness and collagen content. (**a**) Stress/strain curves of periurethral prostate tissues from four patients. A high tangent modulus of 2,390 kilopascals (kPa) was obtained for tissue from a 70 year old man with progressive LUTS and self-reporting an American Urological Association Symptom Index (AUASI) score of 19, whereas a low tangent modulus of 200 kPa was obtained for tissue from a 51 year old man self-reporting an AUASI score of 0. (**b**) Masson's Trichrome stained section of tissue tested from the 70 year old man reporting an AUASI score of 19 in (**a**) demonstrates dense collagen fibrils (*blue*) and a total collagen content of 58 %. (**c**) Masson's Trichrome stained section of tissue tested from the 51 year old man in **a**. reporting an AUASI of 0 demonstrates few collagen fibrils (*blue*) and a total collagen content of 26 % (*Reprinted from Ma J, Gharaee-Kermani M, Kunju L, Hollingsworth J, Adler J, Arruda E,* et al. *Prostatic Fibrosis is Associated with Lower Urinary Tract Symptoms. The Journal of Urology. 2012*)

In the human prostate, myofibroblast accumulation and tissue fibrosis were recently shown to be associated with LUTS. Periurethral prostate tissues from men with self-reported high American Urological Association Symptom Index (AUASI) scores in the moderate-severe range were mechanically stiffer and exhibited significantly higher collagen content compared to men with lower AUASI scores in the absent/mild range (Fig. 2.4). Among tissues from 21 patients, measures of tissue stiffness for 9 with AUASI scores in the moderate/severe range were significantly higher than for those tissues from the 12 patients with scores in the absent/mild range ($r = 0.82$). This indicates that higher levels of tissue stiffness are directly correlated with moderate/severe LUTS (Fig. 2.5a) and also with higher levels of collagen content ($r = 0.60$) (Fig. 2.5b). This study clearly demonstrated direct associations between high levels of tissue stiffness, with increased collagen content and fibrosis, and the further association of all of these measures with LUTS [80]. Increased periurethral tissue stiffness consequent to aging likely reduces urethral compliance and thereby contributes to obstructive symptoms.

Prostate Cancer

Prostate Cancer Epidemiology

Prostate cancer is a significant public health issue in the USA. Prostate cancer is the leading cause of newly diagnosed cancers, the second leading cause of cancer-related deaths in American men [81], and is the most commonly diagnosed non-skin cancer. The American Cancer Society estimates that in 2011, approximately 240,890 men were diagnosed with prostate cancer and 33,720 men died of the disease. In Europe, there are about 80,000 deaths a year from PCa, whereas in the USA 27,050 deaths and 218,890 new cases were reported in 2007 (http://www.cancer.gov).

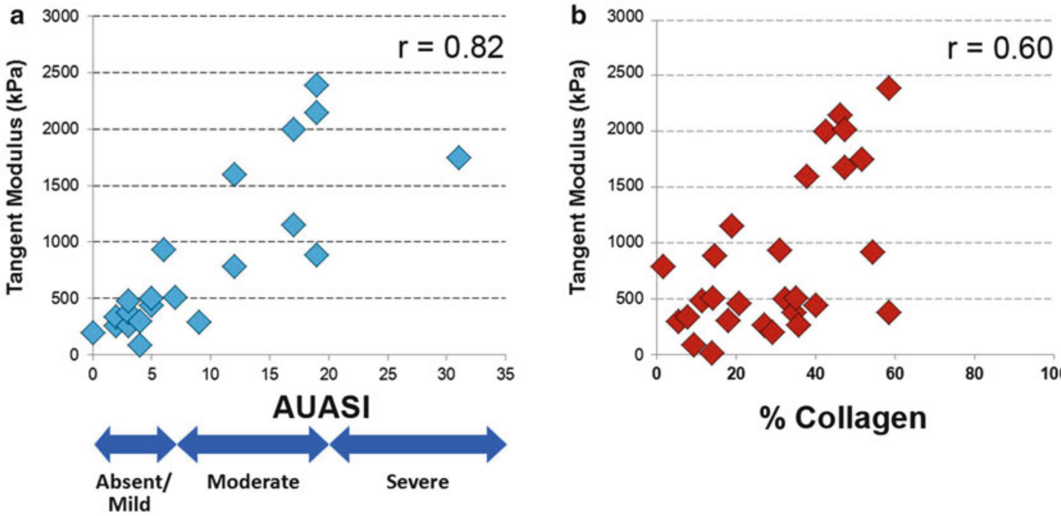


Fig. 2.5 AUASI scores correlate with tissue stiffness and collagen content. (**a**) Among tissues from 21 patient tests, measures of tissue stiffness for 9 with AUASI scores in the moderate/severe range were significantly higher than for those tissues from the 12 patients with scores in the absent/mild range ($r = 0.82$), indicating that higher levels of tissue stiffness directly correlated with moderate/severe LUTS. (**b**) Higher levels of tissue stiffness directly correlated with higher levels of collagen content ($r = 0.60$). These data show that high levels of tissue stiffness correlate with collagen content and fibrosis, and further correlate with LUTS

PCa and Aging

Older age, African American race, and a family history of the disease can all increase the likelihood of a man being diagnosed with prostate cancer. PCa is strongly age dependent. As men increase in age, their risk of developing prostate cancer increases exponentially. Although only 1 in 10,000 under age 40 will be diagnosed, the rate shoots up to 1 in 39 for ages 40–59, and 1 in 14 for ages 60–69. More than 65 % of all prostate cancers are diagnosed in men over the age of 65 (http://www.pcf.org). The relationship between PCa incidence and aging is consistent across ethnic and racial groups.

Androgen/Androgen Receptor (AR) Signaling and Aging

Prostate tumors are initially dependent on androgen signaling and can be successfully controlled by a series of strategies that deplete endogenous androgen expression or interfere with AR-mediated signaling. However, several studies document a progressive decline in the production and tissue levels of the major androgen, testosterone, with age. In contrast, the AR itself is upregulated with age in men and promotes continued proliferation and differentiation of the prostate [82, 83]. Therefore, therapeutic approaches that directly target androgen and/or the AR are only effective for early stage androgen-dependent prostate cancer, as progressive prostate tumors develop alternative strategies to survive and grow despite anti-androgen therapy. Eventually, such tumors develop into lethal, metastatic castration resistant prostate cancers [84] (Fig. 2.6).

Nonsteroidal Growth Factor/AR Signaling and Aging

Despite reduced levels of androgen with aging, the AR is constitutively active and plays an important role in progressive castration resistant disease. Several studies have reported hormone-independent AR signaling in prostate cancer cells by nonsteroidal growth factors such as peptide growth factors [85–90]; neuropeptides, including neurotensin and bombesin [91–94]; inflammatory mediators such as interleukins IL-4 and IL-6 [95–107]; and chemokines CXCL8 [108–111] and CXCL12 [112] (Fig. 2.6). Several of these nonsteroidal growth factors are secreted in excess

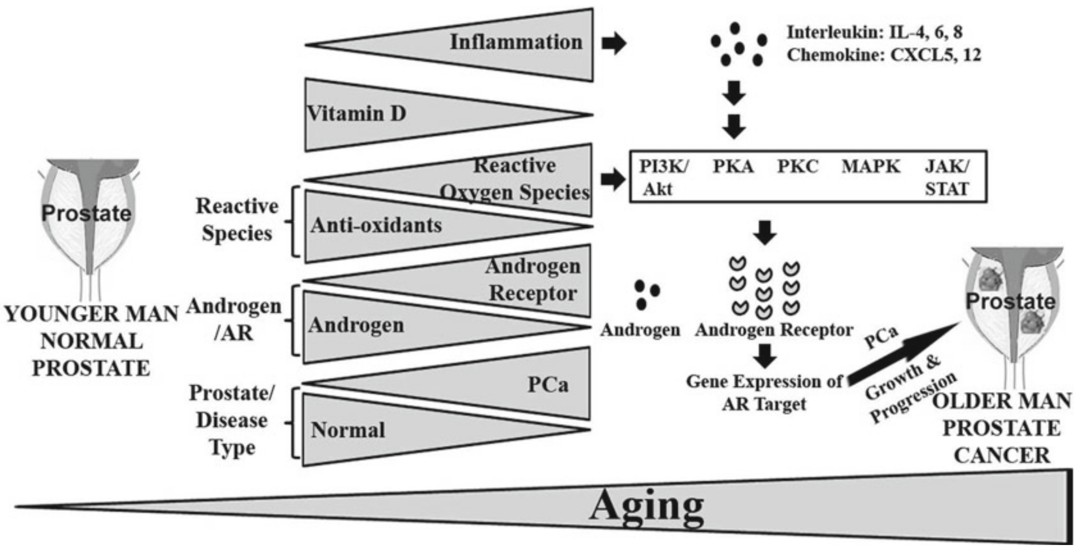


Fig. 2.6 Aging promotes prostate cancer progression. Aging-associated decline in the androgen levels is accompanied by an increase in androgen receptor (AR), reactive oxygen species (ROS) and inflammation, and a decrease in antioxidants and vitamin D. Inflammatory molecules (Interleukins and chemokines) secreted by aged prostate activates different signal transduction pathways, also activated by an increased reactive species (ROS), which then activates the androgen receptor (AR). Activated AR drives the expression of AR target genes and thus promotes the prostate cancer growth and progression

by the aging prostate and promote prostate cancer. As noted earlier in this chapter, CXCL5 and CXCL12 are secreted at high levels by aging prostate stroma [47, 113], and both CXCL5 and CXCL12 have been shown to promote prostate cancer progression [113–115]. Another study has also found that the serum levels of CXCL8 are elevated in aged men with prostate cancer and bone metastasis [116]. These nonsteroidal growth factors activate different signal transduction pathways like PI3K/Akt, MAPK, PKC, PKA, and JAK/STAT (Table 2.1) [93–96, 99, 101, 104–106, 108–110, 112, 117–120], which further activates the AR, drives AR target genes, and promotes PCa growth and progression (Fig. 2.6).

Oxidative Stress and Aging

Aging is also characterized by an increase in intracellular oxidative stress and a decrease in intracellular reactive oxygen species (ROS) scavenging. The increased oxidative stress with aging activates various signal transduction pathways like PI3K/Akt, MAPK, PKA, PKC, and JAK/STAT which activates AR signaling and thus PCa growth and progression (Table 2.1). In addition, increased oxidative damage to cellular macromolecules in the prostate has been observed in aging [121] as well as during the development of prostatic malignancy [122, 123]. Specifically, the increase in oxidative damage to DNA, measured by the accumulation of nuclear 8-hydroxydeoxyguanosine (8-OHdG), has been observed in aging prostate tissues [124]. Glutathione (GSH) is the most abundant antioxidant in cells and tissues, and it plays a primary role in protection against oxidative stress [125]. Depletion of GSH with aging is responsible for increased risk for cancer in older adults [126]. Like glutathione, selenium blood levels decrease with age [127–129]. Selenium is protective against prostate cancer through the reduction of oxidative stress compounds [130, 131]. Clinical chemoprevention trials support the protective role of selenium against cancer development including prostate cancer [132, 133]. A role for oxidative stress in prostate cancer is supported by observations that foods high in antioxidants such as fruits and vegetables are protective [134],

Table 2.1 Non-steroidal growth factors and inflammatory proteins mediate androgen receptor activation in prostate cancer cells

Inflammatory protein	Signal transducing proteins	References
IL-4	Akt, NFkB, p300	[101, 104, 106]
IL-6	STAT3, SRC-1, p300, PI3K/AKT, STAT3, MAPK	[93–96, 99, 105, 117, 120]
CXCL8 (IL-8)	EGFR, Src, Akt, NFkB, ERK, PI3K/Akt, Src	[108–110, 119]
CXCL12 (SDF-1)	SRC-1, MAPK, PI3K/Akt	[112]

and also by clinical studies which indicate that intake of antioxidants, such as selenium, α-tocopherol (vitamin E), and the carotenoid lycopene offers protection against prostate cancer.

Vitamin D and Aging

Vitamin D insufficiency and deficiency are highly prevalent among adult men in the USA [135]. Vitamin D deficiency is associated both with moderate-severe LUTS [135] and with an increase in risk for prostate cancer [136]. Low serum levels of 1,25-D, a vitamin D metabolite, were significantly associated with an increased risk of clinically detected prostate cancer among older men, particularly in men with low levels of 25-dihydroxyvitamin D (25-D) [137]. Therefore, high dose vitamin D alone or in combination with other agents has been shown to be effective in prevention of prostate cancer [138].

Prostate Summary

Aging-associated changes in prostate tissues are promoted by complex biological processes. Transitions in the expression levels and activities of steroidal hormones and nonsteroidal growth factors during the aging process disrupt tissue homeostasis within the prostate and facilitate cellular proliferation, organ enlargement, and malignant growth. The observed low-level secretion of inflammatory proteins within aging prostate tissues promotes the concomitant low-level, but cumulative, overproliferation of both stromal fibroblastic and epithelial cell types. This is associated with increased prostatic volume in aging men and may promote hormone-independent growth of prostate tumors. Many of these same proteins promote other cellular processes in the prostate, including myofibroblast accumulation and tissue fibrosis. This can also contribute to the development and persistence of LUTS in aging men. Though far from complete, a picture is beginning to emerge for how the biology of aging promotes changes in prostatic tissue that contribute to LUTS and malignant growth. These findings may point the way toward development of diagnostic and prognostic tools as well as preventive and therapeutic approaches that will be useful for the detection and treatment of male LUTS and PCa.

Bladder Dysfunction

The prevalence of overactive bladder (OAB) and other LUTS increases with age and has a considerable negative impact on quality of life. The International Continence Society (ICS) has defined OAB as a symptom complex with urinary urgency, with or without urinary incontinence, and nocturia [139]. Detrusor overactivity (DO) is a urodynamic diagnosis associated with demonstration of involuntary bladder contractions during cystometry. Many studies have described the epidemiology and age-dependency of LUTS (Fig. 2.7). The EpiLUTS study surveyed a total of 30,000 women and men in the USA, UK, and Sweden between the age of 40 and 95 years of age, using an Internet-based self-administered data collection. LUTS were found to be highly prevalent in this population study and increased with advancing age in men. Increasing age in women was associated with a higher prevalence of only certain LUTS, such as urgency, urgency with fear of leaking, weak stream, urgency incontinence, and nocturnal enuresis [140]. The National Overactive Bladder Evaluation (NOBLE) specifically assessed the prevalence of overactive bladder (OAB) symptoms in a US adult population over 18 years of age. The prevalence of OAB symptoms was 16.9 % in women and 16.0 % in men and

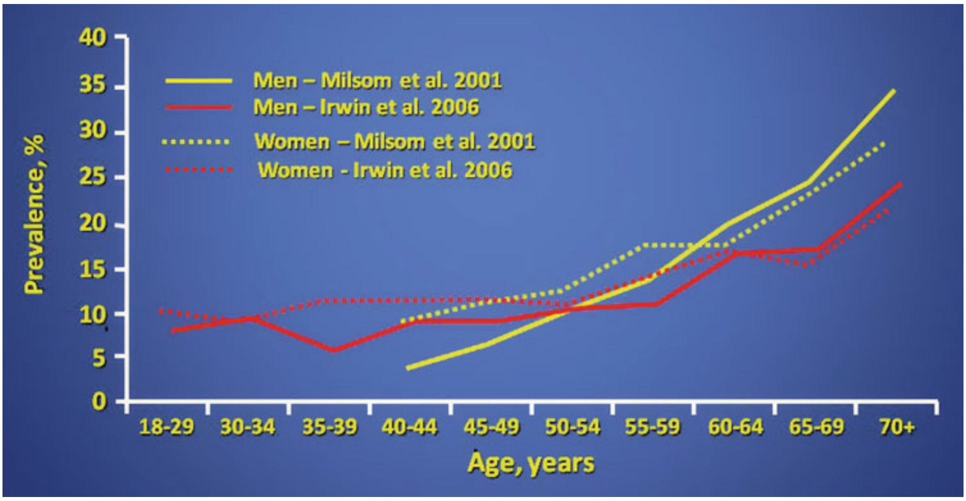


Fig. 2.7 Prevalence of OAB by age. Data from Milsom et al. BJU Int. 2001;87:760–766 and Irwin et al. Eur Urol. 2006 Dec;50(6):1306–14

showed a steep increase with age in women when associated with urgency incontinence. A similar pattern was observed for OAB in men without urgency incontinence, with a threefold increase in individuals more than 55 years of age as compared to those younger than 45 years [141]. OAB symptom prevalence increased with age in both men and women in the EpiLUTS study as well [142]. Wehrberger et al. [143] studied the prevalence of LUTS and UI in a population-based cohort analysis of men and women over 85 years of age in the Vienna Trans-Danube Aging Study (VITA). OAB was reported as 55 % in women and 50 % in men, and UI was found in 35 % of women and 24 % of men. Essentially all epidemiological studies are in accordance and demonstrate that LUTS and overall voiding dysfunction increase with age in both men and women. The proportion of individuals aged 80 years or older is currently the fastest growing sector of the population worldwide [144], and this implies that analysis of age-dependent factors contributing to bladder dysfunction will be urgently needed to develop strategies for managing the problem.

Physiological aging affects lower urinary tract function at all levels of the organism, from changes in the central (CNS) and peripheral (PNS) nervous systems to biochemical and cellular alterations within the detrusor and urothelium of the bladder and urethra. These changes and their functional consequences are briefly discussed in this overview.

Age-Related CNS Changes in Adults with Urinary Incontinence

Normal aging may affect neurons in the CNS at a cellular and synaptic level. Just as cognitive decline has been observed in older humans without associated neurodegenerative disease, the age-associated myelin or neuronal loss can lead to impaired inhibitory control of micturition. Control of micturition involves several regions of the brain coordinating afferent and efferent signaling of the storage and micturition reflexes [145]. Common changes in cortical pathways seen in older adults could involve the regions of the brain responsible for voiding control. Griffiths et al. [146] used functional magnetic resonance imaging (fMRI) in 10 continent women aged 30–79 years to study regional brain responses during bladder filling via urethral catheter. Activation of bilateral insula and dorsal anterior cingulate cortex decreased with age. The authors interpreted their results to suggest that with increasing age, weaker signals in the bladder control network as a whole and/or changes in medial prefrontal cortex function, which exerts inhibitory control of the pontine micturition center (PMC), or connecting pathways may be responsible for the development of urgency incontinence.

White matter changes were associated with urinary complaints in a cohort of nondisabled elderly people in the Leukoaraiosis And DISability (LADIS) Study [147]. White matter hyperintensities (WMH) seen on MRI in the right inferior frontal region correlated with incontinence, incontinence severity, and degree of bother in a cohort of 100 community-dwelling individuals [148]. In another study, Tadic et al. [149] demonstrated by fMRI that brain activity in 25 women with UI during bladder filling was positively correlated with global WMH in the PMC. Their findings provide some clues to the possible role of white matter damage in the genesis of urgency incontinence and to the cerebral mechanisms of bladder control in older women.

PNS Alterations Can Occur with Age-Related LUTS

Parasympathetic and sympathetic preganglionic neurons project to the major pelvic ganglion to make contact with postganglionic neurons innervating the bladder and urethra. Age-related changes in innervation leading to micturition disturbances have been extensively studies in animals and humans. In humans, Gilpin et al. [150] determined the effect of age on the autonomic innervation of the urinary bladder in a group of 54 patients with an age range of 20–79 years, all of whom had a normal urodynamic study. They reported a reduction in the number of nerves with progressing age, as did Hald and Horn [151]. In aged rats, voiding dysfunction was attributed to a loss of monoaminergic innervation of the lumbosacral spinal nuclei [152]. They found by quantitative image analysis significant age-associated declines in the innervation of most regions, including the intermediolateral cell nucleus, sacral parasympathetic nucleus, dorsal gray commissure, and in the ventral horn, including the dorsolateral nucleus, which in the rat is one of the component nuclei homologous to Onuf's nucleus in humans. Lesions in Onuf's nucleus are associated with voiding dysfunction characteristic of Shy-Drager syndrome. Mohammed and Santer [153] found that the total neuronal numbers of rat lumbosacral primary afferent neurons did not change with age (from 3 to 24 months of age). However, the effects of NO on the bladder and also its expression in dorsal root ganglion neurons were reduced in aged rats [139, 154]. Similarly, a reduction in vanilloid receptor type 1 in the lumbosacral dorsal root ganglia was found in older rats [155]. In anesthetized rats, Hotta et al. [156] showed that compared to young adult animals (2–3 months), aged rats (26–29 months) exhibited (1) bladders with nearly six times higher volumes; these volumes were accommodated at lower pressures; (2) reduction of bladder contractions induced by pelvic nerve stimulation; and (3) a decrease of the pelvic afferent nerve activity sensing bladder volume. They attributed their findings to (a) changes in the mechanical properties of the bladder, (b) changes in the contractile properties of the detrusor smooth muscle during efferent stimulation, and (c) changes in the ability of its afferent innervation to sense bladder volume. They also suggested that such changes could explain the increase in residual volume, the inability to postpone voiding, and the decrease in flow rate seen in elderly humans.

The conduction velocity of myelinated and unmyelinated fibers of the pelvic nerve in rats was found not to change with age. Only the number of unmyelinated fibers was significantly reduced in older rats, particularly those with a diameter smaller than 0.7 μm [157]. Further evidence for an age-dependent reduction in sensory functions was presented by Smith et al. [158], who suggested that their calculations approximating wall stress during filling indicated loss of bladder volume sensitivity with increasing age. The findings by Kenton et al. [159] support age-dependent reduction of sensory functions also in humans. They compared current perception thresholds (CPT) in the urethra and bladder of women with idiopathic overactive bladder to asymptomatic controls and demonstrated that the CPT was significantly higher in older women.

This suggests that sensory neuropathy in the lower urinary tract increases with age and may contribute to the increase in OAB/DO seen with aging.

Age-Related Bladder Remodeling: Structural Changes of the Bladder and Urethra

A morphometric study of human bladder specimens from two different age groups revealed that the area density of smooth muscle to connective tissue ratio decreased with age in both men and women [160], suggesting that aging is associated with a relative increase in detrusor fibrosis. This is not in agreement with some reported findings in rats, where morphometric analysis showed a significant age-dependent increase in the mean thickness of the muscularis layer, whereas the collagen density significantly decreased in the muscularis and in the lamina propria layers [161]. However, in another study, histological examination of the bladder of older Fisher rats revealed urothelial thinning, decreased muscle mass, and increased collagen content [162]. Thus, reports on the effects of aging on rat bladder morphology show conflicting results, suggesting that the aging process in animals may not reliably reflect what is occurring in humans.

A reduced number of caveolae (invaginations of the plasma membrane) in bladder smooth muscle cells have been observed in human [163] and rat specimens [164]. Since the caveolae provide a mechanism for compartmentalization and integration of signal transduction, they play an important role in normal smooth muscle function. However, their precise role in age-related detrusor dysfunction remains to be established.

Levy and Wight [165] observed a significant increase of collagen fibers in the lamina propria and around the neurovascular bundles of human bladders, and Ewalt et al. [166] noticed a replacement of elastin by collagen within the muscle fibers accompanied by increased collagen deposits at the basal membrane. These findings were suggested to explain the reduced elasticity and potentially the reduced bladder capacity of the aging detrusor. Strasser et al. [167] found that age was associated with apoptosis of striated muscle cells in a cadaver study of the rhabdosphincter of the urethra, which corresponds to an age-related decrease in maximal urethral pressure [168]. Thus, in humans, aging may be accompanied by structural LUT changes, including bladder fibrosis and decreased functional musculature in the bladder and urethra [169] (Fig. 2.8).

Biochemical and Receptor Alterations with Aging

The influence of age on muscarinic receptor density and sensitivity has been investigated in animal models with partly conflicting results. Age-related changes in muscarinic receptor function have been reported, but in vitro studies with bladder tissue from old vs. young rats have yielded contradictory results that partly may be strain specific. For example, in Fischer 344 rats, muscarinic receptor-mediated detrusor contraction was either increased [170], unchanged [171, 172], or decreased [162, 173]. In Wistar rats [161, 174], unchanged muscarinic receptor-mediated bladder contraction was reported. However, many studies in Sprague–Dawley rats have demonstrated decreased muscarinic receptor-mediated detrusor contractions [175–177]. In a study of estrogen on older rats, Watanabe et al. [178] found that M2 receptor mRNA expression, but not M3 receptors, was significantly upregulated in older animals. This finding was corroborated by an increased voiding frequency in these two groups elicited by muscarine. Whatever age-related changes in muscarinic receptor functions have been demonstrated in animal bladder, they do not seem to be predictive for what is occurring in humans. Particularly, they do not seem to be associated with a change in the response to antimuscarinics, for there is no evidence for reduced therapeutic benefits from such treatment in older adult patients [179, 180].

A study by Mansfield et al. [181], using radioligand-binding assay, showed that the total number of muscarinic receptors in the human male detrusor decreased with age. This study also found a decrease in mRNA expression of M3

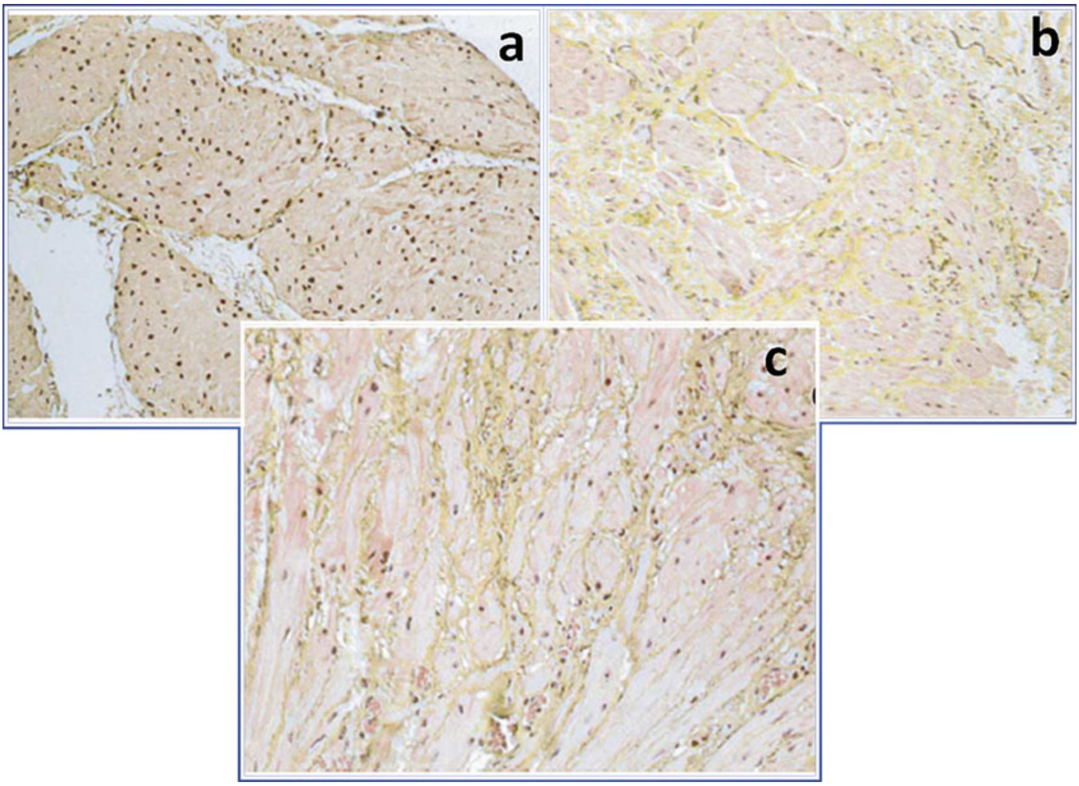


Fig. 2.8 Light microscopy picture from human detrusor muscle. This image shows a combined muscle cell, collagen (*yellow*), and elastin stain (original magnification × 150). (**a**) Normal detrusor, (**b**) Male with prostatic obstruction, (**c**) Elderly female without LUTS. *From*: *Nordling J*. *Exp Gerontol*. *2002 Aug–Sep*;*37*(8, 9):*991–9*

receptors with age in both male and female subjects, but no change in M2 receptors. Due to the lack of highly specific antibodies for the muscarinic receptor subtypes, it was not possible to decide if these changes in MRNA expression were accompanied by a change in protein expression. The functional consequences of the findings were not reported. In contrast to these findings, Wuest et al. [182] found that mRNA detected for M2, M3, P2X1, and P2X3 receptors did not change with age.

The mRNA expression of the purinergic P2X1 receptor was negatively correlated with age in samples of detrusor muscle from normal control male individuals. This negative association was not observed in samples from obstructed patients [183]. Yoshida et al. [184, 185] found a significant positive correlation between age and the purinergic component of human bladder preparation contraction and a significant negative correlation between age and the cholinergic component of human bladder preparation contraction [140]. The authors studied the neurotransmitter release from the detrusor during electrical field stimulation (EFS), using high-performance liquid chromatography. They found that acetylcholine release and age were significantly negatively correlated, while ATP release and age were positively correlated. In the guinea pig, aging decreased the neurogenic contraction of isolated detrusor induced by EFS, but did not alter the cholinergic component of the contraction [186]. Contractile properties or excitability of human detrusor muscle preparations from normal individuals did not vary with age, but declined in pathological conditions such as bladder outlet obstruction and idiopathic or neurogenic detrusor overactivity [187]. Wuest et al. [182] studied the putative age-dependence of concentration-response curves to the muscarinic agonist carbachol and the purinergic agonists ATP and α-β methylene-ATP in human detrusor muscle strips. They found, in accordance with the results of Yoshida et al. [184] that the sensitivity to α-β -methylene-ATP increased with age. However, patient age did not influence (1) EFS evoked contractions and the effects of several antimuscarinic drugs, (2) concentration-response curves for carbachol and their modulation by antimuscarinic agents, and (3) expression levels of receptor subtype mRNA. It was concluded that there was no evidence for age-related contractile deterioration in the detrusor. This is in contrast to findings in functional in vivo studies in humans (see below).

Functional Micturition Changes with Aging

The aging process of both genders is associated with significant changes in bladder function and clinical symptomatology. However, the pathophysiology behind the dysfunctions is sometimes difficult to establish, since it is often difficult to separate what can be attributed to "normal aging" from what is caused by comorbidities. LUTS are divided into storage (irritative), voiding (obstructive), and postmicturition components. Storage symptoms are urgency, frequency, nocturia, and urgency incontinence; voiding symptoms include a reduced force of stream, hesitancy, inability to empty the bladder, and straining and postmicturition symptoms include feeling of incomplete emptying and postmicturition dribble [188]. Unfortunately, none of these symptoms is disease specific or has a high correlation to a specific urodynamic pattern. Most of these symptoms have been suggested to be age dependent and attributed to various factors including reduced bladder capacity, changes in bladder sensation, and DO. Early uroflow studies demonstrated an age-dependent decrease in Q_{max} [189, 190], which was confirmed and shown to be similar in both sexes [168, 191], however, not demonstrable in symptomatic elderly men with nonobstructive voiding dysfunction [192].

Detrusor underactivity [193, 194], leading to emptying difficulties and symptoms sometimes overlapping with those of detrusor overactivity, may have many underlying causes. Some of the most frequently discussed are impaired detrusor contractility and decreased sensation [195]. Urodynamic assessment in older patients of both sexes without overt neurological disease showed higher residual volumes and lower detrusor shortening velocities, but no changes in isometric detrusor function [196]. In a series of patients, where the bladder capacity at first void was taken as measure of bladder sensation, this parameter showed a progressive increase with age, suggesting an age-dependent decrease in bladder sensation [197], a finding confirmed by several other investigators [159, 168]. In a clinical study of patients referred for LUTS or UI, Madersbacher et al. [191] found an increase in postvoid residual volume, along with a decrease of flow rates, voided volumes, and bladder capacity associated with increasing age. These findings were similar in both genders. Pfisterer et al. [168] assessed a group of 85 female volunteers aged between 20 and 90 years with a bladder diary, uroflowmetry, and detailed videourodynamics. Bladder capacity did not change with age, but was smaller in women with detrusor overactivity (DO) on urodynamics. Urine production and urine frequency did not differ significantly with age. Bladder sensation, detrusor contraction strength, maximal flow rate, and maximum urethral closure pressure were all negatively associated with age. It was concluded that there is a normal functional decline seen with aging in otherwise asymptomatic women. This study suggested a progressive decrease in detrusor contraction strength, which was in line with the findings of van Mastrigt [198], who demonstrated a statistically significant age-related decrease of the detrusor contractility parameter, W_{max}, in both sexes. Other investigators were unable to show any correlations between bladder contractility and age in symptomatic elderly men with nonobstructive bladder dysfunction [192] or between either maximum detrusor pressure or detrusor pressure at peak flow rate and age in LUTS patients of both sexes [191].

Normal age-related changes in the bladder and lower urinary tract should be clearly differentiated from pathological alterations seen with conditions such as OAB or LUTS. Detrusor underactivity and the related condition, "detrusor hyperactivity with impaired contractile function" (DHIC) [199] can also present with advancing age and should be diagnosed adequately in elderly individuals. The current available data from animal and human studies demonstrate that aging impacts the lower urinary tract function through ultrastructural and physiological alterations. The reported age-related changes in animals do not always correspond to what is found in humans and should be interpreted with caution. Overall, in humans, bladder sensation and contractility seem to decrease with advancing age as a possible consequence of neuronal loss and remodeling of the bladder and urethra.

Bladder Summary

Changes in bladder structure and function are common with advancing age. These can influence a wide variety of features in older patients including how they sense bladder fullness, whether they experience urinary urgency frequency, and the volume of urine they are able to hold. In addition, these changes can have significant effects with regard to urinary incontinence and bladder emptying efficiency. Identification of many of these changes has led to targets for therapy, particularly for OAB and urge urinary incontinence. Additional work will help to better define additional changes associated with bladder aging and may lead to new therapies in the future.

Conclusions

Studies in molecular and cellular biology, biochemistry, physiology, and biophysics have dramatically advanced our understanding of the genitourinary system across the human lifespan. Basic science and translational research hold the key to future advances in this field, including identification and development of new targets for clinical therapies. This chapter has focused on disease processes of the prostate and bladder, but similar advances have been made in other fields including kidney diseases, urolithiasis, sexual dysfunction, and urinary tract infection. Additional basic science concepts are addressed in other chapters as they relate to specific disorders of the aging genitourinary system. Future research will certainly help advance the science and subsequent clinical care for older adults.

References

1. Meigs JB. Risk factors for clinical benign prostatic hyperplasia in a community-based population of healthy aging men. J Clin Epidemiol. 2001;54:935–44.
2. Verhamme KM. Incidence and prevalence of LUTS suggestive of BPH in primary care - the triumph project. Eur Urol. 2002;42:323–8.
3. Neuhouser ML, Kristal AR, Penson DF. Steroid hormones and hormone-related genetic and lifestyle characteristics as risk factors for benign prostatic hyperplasia: review of epidemiologic literature. Urology. 2004;64(2):201–11.
4. Hannema SE, Hughes IA. Regulation of Wolffian duct development. Horm Res. 2007;67(3):142–51.
5. Evans GS. Cell proliferation studies in the rat prostate: II. The effects of castration and androgen-induced regeneration upon basal and secretory cell proliferation. Prostate. 1987;11:339–51.
6. Evans GS. Cell proliferation studies in rat prostate 1. The proliferative role of basal and secretory epithelial cells during normal growth. Prostate. 1987;10:163–78.
7. Colombel MC, Buttyan R. Hormonal control of apoptosis: the rat prostate gland as a model system. Methods Cell Biol. 1995;46:369–85.
8. Ho CK. Estrogen and androgen signaling in the pathogenesis of BPH. Nat Rev Urol. 2011;8:29–41.
9. Jacobsen SJ. Natural history of benign prostatic hyperplasia. Urology. 2001;58(6 Suppl 1):5–16.
10. Jakobsen H, Torp-Pedersen S, Juul N. Ultrasonic evaluation of age-related human prostatic growth and development of benign prostatic hyperplasia. Scand J Urol Nephrol Suppl. 1988;107:26–31.
11. Arenas M, Romo E, Royuela M, et al. Morphometric evaluation of the human prostate. Int J Androl. 2001;24:37–47.
12. Berges RR, Vukanovic J, Epstein JI, et al. Implication of cell kinetic changes during the progression of human prostatic cancer. Clin Cancer Res. 1995;1:473–80.
13. Colombel M, Vacherot F, Gil Diez S, et al. Zonal variation of apoptosis and proliferation in the normal prostate and in benign prostatic hyperplasia. Br J Urol. 1998;82:380–5.
14. Thompson TC, Southgate J, Kitchener G, Land H. Multistage carcinogenesis induced by ras and myc

oncogenes in a reconstituted organ. Cell. 1989;56:917–30.
15. Merz VW, Miller GJ, Krebs T, et al. Elevated transforming growth factor-beta 1 and beta 3 mRNA levels are associated with ras + myc-induced carcinomas in reconstituted mouse prostate: evidence for a paracrine role during progression. Mol Endocrinol. 1991;5:503–13.
16. Foster BA, Kaplan PJ, Greenberg NM. Peptide growth factors and prostate cancer: new models, new opportunities. Cancer Metastasis Rev. 1999;17:317–24.
17. Cunha GR, Hayward SW, Dahiya R, Foster BA. Smooth muscle-epithelial interactions in normal and neoplastic prostatic development. Acta Anat. 1996;155:63–72.
18. Hayward SW, Haughney PC, Rosen MA, et al. Interactions between adult human prostatic epithelium and rat urogenital sinus mesenchyme in a tissue recombination model. Differentiation. 1998;63:131–40.
19. Song Z, Wu X, Powell WC, et al. Fibroblast growth factor 8 isoform B overexpression in prostate epithelium: a new mouse model for prostatic intraepithelial neoplasia. Cancer Res. 2002;62:5096–105.
20. Feldman HA, Longcope C, Derby CA, Johannes CB, Araujo AB, Coviello AD, et al. Age trends in the level of serum testosterone and other hormones in middle-aged men: longitudinal results from the Massachusetts male aging study. J Clin Endocrinol Metab. 2002;87(2):589–98.
21. Harman SM, Metter EJ, Tobin JD, Pearson J, Blackman MR. Longitudinal effects of aging on serum total and free testosterone levels in healthy men. Baltimore longitudinal study of aging. J Clin Endocrinol Metab. 2001;86(2):724–31.
22. Suzuki K, Ito K, Ichinose Y, Kurokawa K, Suzuki T, Imai K, et al. Endocrine environment of benign prostatic hyperplasia: prostate size and volume are correlated with serum estrogen concentration. Scand J Urol Nephrol. 1995;29(1):65–8.
23. Sciarra F, Toscano V. Role of estrogens in human benign prostatic hyperplasia. Arch Androl. 2000;44(3):213–20.
24. Ellem SJ, Risbridger GP. The dual, opposing roles of estrogen in the prostate. Ann N Y Acad Sci. 2009; 1155:174–86.
25. Prins GS, Korach KS. The role of estrogens and estrogen receptors in normal prostate growth and disease. Steroids. 2008;73(3):233–44.
26. Bonkhoff H, Berges R. The evolving role of oestrogens and their receptors in the development and progression of prostate cancer. Eur Urol. 2009;55(3): 533–42.
27. Nicholson TM, Ricke WA. Androgens and estrogens in benign prostatic hyperplasia: past, present and future. Differentiation. 2011;82(4–5):184–99.
28. Cohen PG. Obesity in men: the hypogonadal-estrogen receptor relationship and its effect on glucose homeostasis. Med Hypotheses. 2008;70(2):358–60.
29. Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among US adults, 1999–2008. JAMA. 2010;303(3):235–41.
30. Story MT, Hopp KA, Meier DA, Begun FP, Lawson RK. Influence of transforming growth factor beta 1 and other growth factors on basic fibroblast growth factor level and proliferation of cultured human prostate-derived fibroblasts. Prostate. 1993;22(3):183–97.
31. Wang Z, Olumi AF. Diabetes, growth hormone-insulin-like growth factor pathways and association to benign prostatic hyperplasia. Differentiation. 2011;82(4–5):261–71.
32. Macoska JA. Chemokines and BPH/LUTS. Differentiation. 2011;82(4–5):253–60.
33. McLaren ID, Jerde TJ, Bushman W. Role of interleukins, IGF and stem cells in BPH. Differentiation. 2011;82(4–5):237–43.
34. Mori H, Maki M, Oishi K, Jaye M, Igarashi K, Yoshida O, et al. Increased expression of genes for basic fibroblast growth factor and transforming growth factor type beta 2 in human benign prostatic hyperplasia. Prostate. 1990;16(1):71–80.
35. Story MT, Hopp KA, Molter M, Meier DA. Characteristics of FGF-receptors expressed by stromal and epithelial cells cultured from normal and hyperplastic prostates. Growth Factors. 1994;10(4):269–80.
36. Sinowatz F, Schams D, Einspanier R, Arnold G, Pfeffer M, Temmim-Baker L, et al. Cellular localization of fibroblast growth factor 2 (FGF-2) in benign prostatic hyperplasia. Histol Histopathol. 2000; 15(2):475–81.
37. Mydlo JH, Kral JG, Macchia RJ. Differences in prostate and adipose tissue basic fibroblast growth factor: analysis of preliminary results. Urology. 1997;50(3):472–8.
38. Konno-Takahashi N, Takeuchi T, Nishimatsu H, Kamijo T, Tomita K, Schalken JA, et al. Engineered FGF-2 expression induces glandular epithelial hyperplasia in the murine prostatic dorsal lobe. Eur Urol. 2004;46(1):126–32.
39. Fiorelli G, De Bellis A, Longo A, Giannini S, Natali A, Costantini A, et al. Insulin-like growth factor-I receptors in human hyperplastic prostate tissue: characterization, tissue localization, and their modulation by chronic treatment with a gonadotropin-releasing hormone analog. J Clin Endocrinol Metab. 1991;72(4):740–6.
40. Dong G, Rajah R, Vu T, Hoffman AR, Rosenfeld RG, Roberts Jr CT, et al. Decreased expression of Wilms' tumor gene WT-1 and elevated expression of insulin growth factor-II (IGF-II) and type 1 IGF receptor genes in prostatic stromal cells from patients with benign prostatic hyperplasia. J Clin Endocrinol Metab. 1997;82(7):2198–203.
41. Jarrard DF, Bussemakers MJ, Bova GS, Isaacs WB. Regional loss of imprinting of the insulin-like growth factor II gene occurs in human prostate tissues. Clin Cancer Res. 1995;1(12):1471–8.
42. Konno-Takahashi N, Takeuchi T, Shimizu T, Nishimatsu H, Fukuhara H, Kamijo T, et al.

Engineered IGF-I expression induces glandular enlargement in the murine prostate. J Endocrinol. 2003;177(3):389–98.
43. Zhou D, Li S, Wang X, Cheng B, Ding X. Estrogen receptor alpha is essential for the proliferation of prostatic smooth muscle cells stimulated by 17beta-estradiol and insulin-like growth factor 1. Cell Biochem Funct. 2011;29(2):120–5.
44. Weber A, Wasiliew P, Kracht M. Interleukin-1 (IL-1) pathway. Sci Signal. 2010;3(105):cm1.
45. Pahl HL. Activators and target genes of Rel/NF-kappaB transcription factors. Oncogene. 1999; 18(49):6853–66.
46. Singh T, Newman AB. Inflammatory markers in population studies of aging. Ageing Res Rev. 2011;10(3):319–29.
47. Begley L, Monteleon C, Shah RB, Macdonald JW, Macoska JA. CXCL12 overexpression and secretion by aging fibroblasts enhance human prostate epithelial proliferation in vitro. Aging Cell. 2005;4(6):291–8.
48. Begley LA, Kasina S, MacDonald J, Macoska JA. The inflammatory microenvironment of the aging prostate facilitates cellular proliferation and hypertrophy. Cytokine. 2008;43(2):194–9.
49. McDowell KL, Begley LA, Mor-Vaknin N, Markovitz DM, Macoska JA. Leukocytic promotion of prostate cellular proliferation. Prostate. 2010;70(4):377–89.
50. Penna G, Fibbi B, Amuchastegui S, Cossetti C, Aquilano F, Laverny G, et al. Human benign prostatic hyperplasia stromal cells as inducers and targets of chronic immuno-mediated inflammation. J Immunol. 2009;182(7):4056–64.
51. Fujita K, Ewing CM, Getzenberg RH, Parsons JK, Isaacs WB, Pavlovich CP. Monocyte chemotactic protein-1 (MCP-1/CCL2) is associated with prostatic growth dysregulation and benign prostatic hyperplasia. Prostate. 2010;70(5):473–81.
52. Dimri GP. A biomarker that identifies senescent human cells in culture and in aging skin in vivo. Proc Natl Acad Sci U S A. 1995;92(20):9363–7.
53. Nishimura F, Terranova VP, Braithwaite M, Orman R, Ohyama H, Mineshiba J, et al. Comparison of in vitro proliferative capacity of human periodontal ligament cells in juvenile and aged donors. Oral Dis. 1997;3(3):162–6.
54. Hjelmeland LM, Cristofolo VJ, Funk W, Rakoczy E, Katz ML. Senescence of the retinal pigment epithelium. Mol Vis. 1999;5:33.
55. Kajstura J, Pertoldi B, Leri A, Beltrami CA, Deptala A, Darzynkiewicz Z, et al. Telomere shortening is an in vivo marker of myocyte replication and aging. Am J Pathol. 2000;156(3):813–9.
56. Chkhotua A, Shohat M, Tobar A, Magal N, Kaganovski E, Shapira Z, et al. Replicative senescence in organ transplantation-mechanisms and significance. Transpl Immunol. 2002;9(2–4):165–71.
57. Krishnamurthy J, Torrice C, Ramsey MR, et al. Ink4a/Arf expression is a biomarker of aging. J Clin Investig. 2004;114(9):1299–307.
58. Campisi J. Senescent cells, tumor suppression, and organismal aging: good citizens, bad neighbors. Cell. 2005;120(4):513–22.
59. Bavik C, Coleman I, Dean JP, et al. The gene expression program of prostate fibroblast senescence modulates neoplastic epithelial cell proliferation through paracrine mechanisms. Cancer Res. 2006;66(2):794–802.
60. Coppe JP, Patil CK, Rodier F, Sun Y, Munoz DP, Goldstein J, et al. Senescence-associated secretory phenotypes reveal cell-nonautonomous functions of oncogenic RAS and the p53 tumor suppressor. PLoS Biol. 2008;6(12):2853–68.
61. Bierhoff E, Vogel J, Benz M, Giefer T, Wernert N, Pfeifer U. Stromal nodules in benign prostatic hyperplasia. Eur Urol. 1996;29(3):345–54.
62. Begley LA, MacDonald JW, Day ML, Macoska JA. CXCL12 activates a robust transcriptional response in human prostate epithelial cells. J Biol Chem. 2007;282(37):26767–74.
63. Schauer IG, Ressler SJ, Rowley DR. Keratinocyte-derived chemokine induces prostate epithelial hyperplasia and reactive stroma in a novel transgenic mouse model. Prostate. 2009;69(4):373–84.
64. Kiefer F, Siekmann AF. The role of chemokines and their receptors in angiogenesis. Cell Mol Life Sci. 2011;68(17):2811–30.
65. Deering RE, Bigler SA, Brown M, Brawer MK. Microvascularity in benign prostatic hyperplasia. Prostate. 1995;26(3):111–5.
66. Shih SJ, Dall'Era MA, Westphal JR, Yang J, Sweep CG, Gandour-Edwards R, et al. Elements regulating angiogenesis and correlative microvessel density in benign hyperplastic and malignant prostate tissue. Prostate Cancer Prostatic Dis. 2003;6(2):131–7.
67. Pohlers D, Brenmoehl J, Löffler I, Müller CK, Leipner C, Schultze-Mosgau S, et al. TGF-β and fibrosis in different organs — molecular pathway imprints. Biochim Biophys Acta. 2009;1792(8):746–56.
68. Hinz B. Formation and function of the myofibroblast during tissue repair. J Investig Dermatol. 2007; 127(3):526–37.
69. Hinz B, Phan SH, Thannickal VJ, Galli A, Bochaton-Piallat M-L, Gabbiani G. The myofibroblast. Am J Pathol. 2007;170(6):1807–16.
70. Wynn TA. Cellular and molecular mechanisms of fibrosis. J Pathol. 2008;214(2):199–210.
71. Detlefsen S, Sipos B, Feyerabend B, Klöppel G. Pancreatic fibrosis associated with age and ductal papillary hyperplasia. Virchows Arch. 2005; 447(5):800–5.
72. Donath MY, Schumann DM, Faulenbach M, Ellingsgaard H, Perren A, Ehses JA. Islet inflammation in type 2 diabetes: from metabolic stress to therapy. Diabetes Care. 2008;31 Suppl 2:S161–4.
73. Scotton CJ, Chambers RC. Molecular targets in pulmonary fibrosis: the myofibroblast in focus. Chest. 2007;132(4):1311–21.
74. Gharaee-Kermani M. Recent advances in molecular targets and treatment of idiopathic pulmonary fibro-

sis: focus on TGFbeta signaling and the myofibroblast. Curr Med Chem. 2009;16(11):1400–17.
75. Frith J, Day CP, Henderson E, Burt AD, Newton JL. Non-alcoholic fatty liver disease in older people. Gerontology. 2009;55(6):607–13.
76. Novo E, Valfrè di Bonzo L, Cannito S, Colombatto S, Parola M. Hepatic myofibroblasts: a heterogeneous population of multifunctional cells in liver fibrogenesis. Int J Biochem Cell Biol. 2009;41(11): 2089–93.
77. Rieder F, Fiocchi C. Intestinal fibrosis in IBD—a dynamic, multifactorial process. Nat Rev Gastroenterol Hepatol. 2009;6(4):228–35.
78. Goldacre MJ. Demography of aging and the epidemiology of gastrointestinal disorders in the elderly. Best Pract Res Clin Gastroenterol. 2009;23(6): 793–804.
79. Barron DA, Strand DW, Ressler SJ, Dang TD, Hayward SW, Yang F, et al. TGF-beta1 induces an age-dependent inflammation of nerve ganglia and fibroplasia in the prostate gland stroma of a novel transgenic mouse. PLoS ONE. 2010;5(10):e13751.
80. Ma J, Gharaee-Kermani M, Kunju L, Hollingsworth J, Adler J, Arruda E, et al. Prostatic fibrosis is associated with lower urinary tract symptoms. J Urol. 2012;188(4):1375–81.
81. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. CA Cancer J Clin. 2010;60(5):277–300.
82. Kaufman JM. The decline of androgen levels in elderly men and its clinical and therapeutic implications. Endocr Rev. 2005;26(6):833–76.
83. Banerjee PP, Banerjee S, Brown TR. Increased androgen receptor expression correlates with development of age-dependent, lobe-specific spontaneous hyperplasia of the brown Norway rat prostate. Endocrinology. 2001;142(9):4066–75.
84. Pienta KJ, Bradley D. Mechanisms underlying the development of androgen-independent prostate cancer. Clin Cancer Res. 2006;12(6):1665–71.
85. Culig Z. Androgen receptor activation in prostatic tumor cell lines by Insulin-like growth factor-I, keratinocyte growth factor, and epidermal growth factor. Cancer Res. 1994;54(20):5474–8.
86. Craft N, Chhor C, Tran C, Belldegrun A, DeKernion J, Witte ON, et al. Evidence for clonal outgrowth of androgen-independent prostate cancer cells from androgen-dependent tumors through a two-step process. Cancer Res. 1999;59(19):5030–6.
87. Yeh S, Lin HK, Kang HY, Thin TH, Lin MF, Chang C. From HER2/Neu signal cascade to androgen receptor and its coactivators: a novel pathway by induction of androgen target genes through MAP kinase in prostate cancer cells. Proc Natl Acad Sci U S A. 1999;96(10):5458–63.
88. Torring N, Vinter-Jensen L, Sorensen FB, Flyvbjerg A, Nexo E. Systemic treatment with epidermal growth factor but not insulin-like growth factor I decreases the involution of the prostate in castrated rats. Urol Res. 2000;28(2):75–81.
89. Wen Y, Hu MC, Makino K, Spohn B, Bartholomeusz G, Yan DH, et al. HER-2/neu promotes androgen-independent survival and growth of prostate cancer cells through the Akt pathway. Cancer Res. 2000;60(24):6841–5.
90. Shi Y, Brands FH, Chatterjee S, Feng AC, Groshen S, Schewe J, et al. Her-2/neu expression in prostate cancer: high level of expression associated with exposure to hormone therapy and androgen independent disease. J Urol. 2001;166(4):1514–9.
91. Lee LF, Guan J, Qiu Y, Kung HJ. Neuropeptide-induced androgen independence in prostate cancer cells: roles of nonreceptor tyrosine kinases Etk/Bmx, Src, and focal adhesion kinase. Mol Cell Biol. 2001;21(24):8385–97.
92. Dai J, Shen R, Sumitomo M, Stahl R, Navarro D, Gershengorn MC, et al. Synergistic activation of the androgen receptor by bombesin and low-dose androgen. Clin Cancer Res. 2002;8(7):2399–405.
93. Debes JD, Comuzzi B, Schmidt LJ, Dehm SM, Culig Z, Tindall DJ. p300 regulates androgen receptor-independent expression of prostate-specific antigen in prostate cancer cells treated chronically with interleukin-6. Cancer Res. 2005;65(13): 5965–73.
94. Debes JD, Tindall DJ. The role of androgens and the androgen receptor in prostate cancer. Cancer Lett. 2002;187(1–2):1–7.
95. Hobisch A, Eder IE, Putz T, Horninger W, Bartsch G, Klocker H, et al. Interleukin-6 regulates prostate-specific protein expression in prostate carcinoma cells by activation of the androgen receptor. Cancer Res. 1998;58(20):4640–5.
96. Ueda T, Bruchovsky N, Sadar MD. Activation of the androgen receptor N-terminal domain by interleukin-6 via MAPK and STAT3 signal transduction pathways. J Biol Chem. 2002;277(9):7076–85.
97. Ueda T, Mawji NR, Bruchovsky N, Sadar MD. Ligand-independent activation of the androgen receptor by interleukin-6 and the role of steroid receptor coactivator-1 in prostate cancer cells. J Biol Chem. 2002;277(41):38087–94.
98. Culig Z. Interleukin-6 polymorphism: expression and pleiotropic regulation in human prostate cancer. J Urol. 2005;174(2):417.
99. Culig Z, Bartsch G, Hobisch A. Interleukin-6 regulates androgen receptor activity and prostate cancer cell growth. Mol Cell Endocrinol. 2002;197(1–2): 231–8.
100. Culig Z, Steiner H, Bartsch G, Hobisch A. Interleukin-6 regulation of prostate cancer cell growth. J Cell Biochem. 2005;95(3):497–505.
101. Lee SO, Chun JY, Nadiminty N, Lou W, Feng S, Gao AC. Interleukin-4 activates androgen receptor through CBP/p300. Prostate. 2009;69(2):126–32.
102. Lee SO, Chun JY, Nadiminty N, Lou W, Gao AC. Interleukin-6 undergoes transition from growth inhibitor associated with neuroendocrine differentiation to stimulator accompanied by androgen receptor

activation during LNCaP prostate cancer cell progression. Prostate. 2007;67(7):764–73.
103. Lee SO, Lou W, Hou M, de Miguel F, Gerber L, Gao AC. Interleukin-6 promotes androgen-independent growth in LNCaP human prostate cancer cells. Clin Cancer Res. 2003;9(1):370–6.
104. Lee SO, Lou W, Hou M, Onate SA, Gao AC. Interleukin-4 enhances prostate-specific antigen expression by activation of the androgen receptor and Akt pathway. Oncogene. 2003;22(39):7981–8.
105. Lee SO, Lou W, Johnson CS, Trump DL, Gao AC. Interleukin-6 protects LNCaP cells from apoptosis induced by androgen deprivation through the Stat3 pathway. Prostate. 2004;60(3):178–86.
106. Lee SO, Pinder E, Chun JY, Lou W, Sun M, Gao AC. Interleukin-4 stimulates androgen-independent growth in LNCaP human prostate cancer cells. Prostate. 2008;68(1):85–91.
107. Malinowska K, Neuwirt H, Cavarretta IT, Bektic J, Steiner H, Dietrich H, et al. Interleukin-6 stimulation of growth of prostate cancer in vitro and in vivo through activation of the androgen receptor. Endocr Relat Cancer. 2009;16(1):155–69.
108. Lee LF, Louie MC, Desai SJ, Yang J, Chen HW, Evans CP, et al. Interleukin-8 confers androgen-independent growth and migration of LNCaP: differential effects of tyrosine kinases Src and FAK. Oncogene. 2004;23(12):2197–205.
109. Araki S, Omori Y, Lyn D, Singh RK, Meinbach DM, Sandman Y, et al. Interleukin-8 is a molecular determinant of androgen independence and progression in prostate cancer. Cancer Res. 2007;67(14):6854–62.
110. MacManus CF, Pettigrew J, Seaton A, Wilson C, Maxwell PJ, Berlingeri S, et al. Interleukin-8 signaling promotes translational regulation of cyclin D in androgen-independent prostate cancer cells. Mol Cancer Res. 2007;5(7):737–48.
111. Seaton A, Scullin P, Maxwell PJ, Wilson C, Pettigrew J, Gallagher R, et al. Interleukin-8 signaling promotes androgen-independent proliferation of prostate cancer cells via induction of androgen receptor expression and activation. Carcinogenesis. 2008;29(6):1148–56.
112. Kasina S, Macoska JA. The CXCL12/CXCR4 axis promotes ligand-independent activation of the androgen receptor. Mol Cell Endocrinol. 2012; 351(2):249–63.
113. Begley LA, Kasina S, Mehra R, Adsule S, Admon AJ, Lonigro RJ, et al. CXCL5 promotes prostate cancer progression. Neoplasia. 2008;10(3):244–54.
114. Singh S, Singh UP, Grizzle WE, Lillard Jr JW. CXCL12-CXCR4 interactions modulate prostate cancer cell migration, metalloproteinase expression and invasion. Lab Invest. 2004;84(12):1666–76.
115. Sun Y-X, Schneider A, Jung Y, Wang J, Dai J, Wang J, et al. Skeletal localization and neutralization of the SDF-1(CXCL12)/CXCR4 axis blocks prostate cancer metastasis and growth in osseous sites in vivo. J Bone Miner Res. 2004;20(2):318–29.
116. Lehrer S, Diamond EJ, Mamkine B, Stone NN, Stock RG. Serum interleukin-8 is elevated in men with prostate cancer and bone metastases. Technol Cancer Res Treat. 2004;3(5):411.
117. Matsuda T, Junicho A, Yamamoto T, Kishi H, Korkmaz K, Saatcioglu F, et al. Cross-talk between signal transducer and activator of transcription 3 and androgen receptor signaling in prostate carcinoma cells. Biochem Biophys Res Commun. 2001;283(1):179–87.
118. Yang L, Wang L, Lin HK, Kan PY, Xie S, Tsai MY, et al. Interleukin-6 differentially regulates androgen receptor transactivation via PI3K-Akt, STAT3, and MAPK, three distinct signal pathways in prostate cancer cells. Biochem Biophys Res Commun. 2003;305(3):462–9.
119. Inoue K, Slaton JW, Eve BY, Kim SJ, Perrotte P, Balbay MD, et al. Interleukin 8 expression regulates tumorigenicity and metastases in androgen-independent prostate cancer. Clin Cancer Res. 2000;6(5):2104–19.
120. Lin DL, Whitney MC, Yao Z, Keller ET. Interleukin-6 induces androgen responsiveness in prostate cancer cells through up-regulation of androgen receptor expression. Clin Cancer Res. 2001; 7(6):1773–81.
121. Ghatak S, Ho SM. Age-related changes in the activities of antioxidant enzymes and lipid peroxidation status in ventral and dorsolateral prostate lobes of noble rats. Biochem Biophys Res Commun. 1996;222(2):362–7.
122. Bostwick DG, Alexander EE, Singh R, Shan A, Qian J, Santella RM, et al. Antioxidant enzyme expression and reactive oxygen species damage in prostatic intraepithelial neoplasia and cancer. Cancer. 2000;89(1):123–34.
123. Oberley TD, Zhong W, Szweda LI, Oberley LW. Localization of antioxidant enzymes and oxidative damage products in normal and malignant prostate epithelium. Prostate. 2000;44(2):144–55.
124. Malins DC, Johnson PM, Wheeler TM, Barker EA, Polissar NL, Vinson MA. Age-related radical-induced DNA damage is linked to prostate cancer. Cancer Res. 2001;61(16):6025–8.
125. Sies H. Glutathione and its role in cellular functions. Free Radic Biol Med. 1999;27(9–10):916–21.
126. Richie Jr JP. The role of glutathione in aging and cancer. Exp Gerontol. 1992;27(5–6):615–26.
127. Masse J. Selenium status in aging. Am J Clin Nutr. 1995;61(5):1172–3.
128. Ray AL, Semba RD, Walston J, Ferrucci L, Cappola AR, Ricks MO, et al. Low serum selenium and total carotenoids predict mortality among older women living in the community: the Women's Health and Aging Studies. J Nutr. 2006;136(1):172–6.
129. Simonoff M, Sergeant C, Garnier N, Moretto P, Llabador Y, Simonoff G, et al. Antioxidant status (selenium, vitamins A and E) and aging. EXS. 1992;62:368–97.

130. El-Bayoumy K. The protective role of selenium on genetic damage and on cancer. Mutat Res. 2001;475(1–2):123–39.
131. El-Bayoumy K, Sinha R. Molecular chemoprevention by selenium: a genomic approach. Mutat Res. 2005;591(1–2):224–36.
132. Clark LC, Combs Jr GF, Turnbull BW, Slate EH, Chalker DK, Chow J, et al. Effects of selenium supplementation for cancer prevention in patients with carcinoma of the skin. A randomized controlled trial. Nutritional prevention of cancer study group. JAMA. 1996;276(24):1957–63.
133. Facompre N, El-Bayoumy K. Potential stages for prostate cancer prevention with selenium: implications for cancer survivors. Cancer Res. 2009;69(7):2699–703.
134. Donkena KV, Young CY, Tindall DJ. Oxidative stress and DNA methylation in prostate cancer. Obstet Gynecol Int. 2010;2010:302051.
135. Vaughan CP, Johnson 2nd TM, Goode PS, Redden DT, Burgio KL, Markland AD. Vitamin D and lower urinary tract symptoms among US men: results from the 2005–2006 National Health and Nutrition Examination Survey. Urology. 2011;78(6):1292–7.
136. Lou YR, Qiao S, Talonpoika R, Syvala H, Tuohimaa P. The role of Vitamin D3 metabolism in prostate cancer. J Steroid Biochem Mol Biol. 2004;92(4):317–25.
137. Corder EH, Guess HA, Hulka BS, Friedman GD, Sadler M, Vollmer RT, et al. Vitamin D and prostate cancer: a prediagnostic study with stored sera. Cancer Epidemiol Biomarkers Prev. 1993;2(5):467–72.
138. Schwartz GG. Vitamin D, and intervention trials in prostate cancer: from theory to therapy. Ann Epidemiol. 2009;19(2):96–102.
139. Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, van Kerrebroeck P, Victor A, Wein A, Standardisation sub-committee of the International Continence Society. The standardisation of terminology of lower urinary tract function: report from the Standardisation sub-committee of the International Continence Society. Neurourol Urodyn. 2002;21(2):167–78.
140. Coyne KS, Sexton CC, Thompson CL, Milsom I, Irwin D, Kopp ZS, Chapple CR, Kaplan S, Tubaro A, Aiyer LP, Wein AJ. The prevalence of lower urinary tract symptoms (LUTS) in the USA, the UK and Sweden: results from the epidemiology of LUTS (EpiLUTS) study. BJU Int. 2009;104(3):352–60.
141. Stewart WF, Van Rooyen JB, Cundiff GW, Abrams P, Herzog AR, Corey R, Hunt TL, Wein AJ. Prevalence and burden of overactive bladder in the United States. World J Urol. 2003;20(6):327–36.
142. Coyne KS, Sexton CC, Vats V, Thompson C, Kopp ZS, Milsom I. National community prevalence of overactive bladder in the United States stratified by sex and age. Urology. 2011;77(5):1081–7.
143. Wehrberger C, Madersbacher S, Jungwirth S, Fischer P, Tragl KH. Lower urinary tract symptoms and urinary incontinence in a geriatric cohort - a population-based analysis. BJU Int. 2012;110(10):1516–21.
144. United Nations Department of Economic and Social Affairs Population Division. UN, 2002 World population ageing: 1950–2050. Available at: http://www.un.org/esa/ population/publications/worldageing19502050/. Accessed May 2012.
145. Fowler CJ, Griffiths D, de Groat WC. The neural control of micturition. Nat Rev Neurosci. 2008;9(6):453–66.
146. Griffiths DJ, Tadic SD, Schaefer W, Resnick NM. Cerebral control of the lower urinary tract: how age-related changes might predispose to urge incontinence. Neuroimage. 2009;47(3):981–6.
147. Poggesi A, Pracucci G, Chabriat H, Erkinjuntti T, Fazekas F, Verdelho A, Hennerici M, Langhorne P, O'Brien J, Scheltens P, Visser MC, Crisby M, Waldemar G, Wallin A, Inzitari D, Pantoni L, Leukoaraiosis And DISability Study Group. Urinary complaints in nondisabled elderly people with age-related white matter changes: the Leukoaraiosis And DISability (LADIS) Study. J Am Geriatr Soc. 2008;56(9):1638–43.
148. Kuchel GA, Moscufo N, Guttmann CR, Zeevi N, Wakefield D, Schmidt J, Dubeau CE, Wolfson L. Localization of brain white matter hyperintensities and urinary incontinence in community-dwelling older adults. J Gerontol A Biol Sci Med Sci. 2009;64(8):902–9.
149. Tadic SD, Griffiths D, Murrin A, Schaefer W, Aizenstein HJ, Resnick NM. Brain activity during bladder filling is related to white matter structural changes in older women with urinary incontinence. Neuroimage. 2010;51(4):1294–302.
150. Gilpin SA, Gilpin CJ, Dixon JS, Gosling JA, Kirby RS. The effect of age on the autonomic innervation of the urinary bladder. Br J Urol. 1986;58(4):378–81.
151. Hald T, Horn T. The human urinary bladder in aging. Br J Urol. 1998;82 Suppl 1:59–64.
152. Ranson RN, Dodds AL, Smith MJ, Santer RM, Watson AH. Age-associated changes in the monoaminergic innervation of rat lumbosacral spinal cord. Brain Res. 2003;972(1–2):149–58.
153. Mohammed HA, Santer RM. Total neuronal numbers of rat lumbosacral primary afferent neurons do not change with age. Neurosci Lett. 2001;304(3):149–52.
154. Mohammed H, Santer RM. Distribution and changes with age of nitric oxide synthase-immunoreactive nerves of the rat urinary bladder, ureter and in lumbosacral sensory neurons. Eur J Morphol. 2001;39(3):137–44.
155. Saleh HA. Vanilloid receptor type 1-immunoreactive nerves in the rat urinary bladder and primary afferent neurones: the effects of age. Folia Morphol (Warsz). 2006;65(3):213–20.
156. Hotta H, Morrison JF, Sato A, Uchida S. The effects of aging on the rat bladder and its innervation. Jpn J Physiol. 1995;45(5):823–36.

157. Nakayama H, Noda K, Hotta H, Ohsawa H, Hosoya Y. Effects of aging on numbers, sizes and conduction velocities of myelinated and unmyelinated fibers of the pelvic nerve in rats. J Auton Nerv Syst. 1998;69(2–3):148–55.
158. Smith PP, DeAngelis A, Kuchel GA. Detrusor expulsive strength is preserved, but responsiveness to bladder filling and urinary sensitivity is diminished in the aging mouse. Am J Physiol Regul Integr Comp Physiol. 2012;302(5):R577–86.
159. Kenton K, Lowenstein L, Simmons J, Brubaker L. Aging and overactive bladder may be associated with loss of urethral sensation in women. Neurourol Urodyn. 2007;26(7):981–4.
160. Lepor H, Sunaryadi I, Hartanto V, Shapiro E. Quantitative morphometry of the adult human bladder. J Urol. 1992;148(2 Pt 1):414–7.
161. Lluel P, Palea S, Barras M, Grandadam F, Heudes D, Bruneval P, Corman B, Martin DJ. Functional and morphological modifications of the urinary bladder in aging female rats. Am J Physiol Regul Integr Comp Physiol. 2000;278(4):R964–72.
162. Zhao W, Aboushwareb T, Turner C, Mathis C, Bennett C, Sonntag WE, Andersson KE, Christ G. Impaired bladder function in aging male rats. J Urol. 2010;184(1):378–85.
163. Elbadawi A, Yalla SV, Resnick NM. Structural basis of geriatric voiding dysfunction. II. Aging detrusor: normal versus impaired contractility. J Urol. 1993;150(5 Pt 2):1657–67.
164. Lowalekar SK, Cristofaro V, Radisavljevic ZM, Yalla SV, Sullivan MP. Loss of bladder smooth muscle caveolae in the aging bladder. Neurourol Urodyn. 2012;31(4):586–92.
165. Levy BJ, Wight TN. Structural changes in the aging submucosa: new morphologic criteria for the evaluation of the unstable human bladder. J Urol. 1990;144(4):1044–55.
166. Ewalt DH, Howard PS, Blyth B, Snyder 3rd HM, Duckett JW, Levin RM, Macarak EJ. Is lamina propria matrix responsible for normal bladder compliance? J Urol. 1992;148(2 Pt 2):544–9.
167. Strasser H, Tiefenthaler M, Steinlechner M, Eder I, Bartsch G, Konwalinka G. Age dependent apoptosis and loss of rhabdosphincter cells. J Urol. 2000;164(5):1781–5.
168. Pfisterer MH, Griffiths DJ, Schaefer W, Resnick NM. The effect of age on lower urinary tract function: a study in women. J Am Geriatr Soc. 2006; 54(3):405–12.
169. Nordling J. The aging bladder–a significant but underestimated role in the development of lower urinary tract symptoms. Exp Gerontol. 2002;37(8–9): 991–9.
170. Kolta MG, Wallace LJ, Gerald MC. Age-related changes in sensitivity of rat urinary bladder to autonomic agents. Mech Ageing Dev. 1984;27:183–8.
171. Ordway GA, Esbenshade TA, Kolta MG, Gerald MC, Wallace LJ. Effect of age on cholinergic muscarinic responsiveness and receptors in the rat urinary bladder. J Urol. 1986;136:492–6.
172. Chun AL, Wallace LJ, Gerald MC, Wein AJ, Levin RM. Effects of age on urinary bladder function in the male rat. J Urol. 1989;141:170–3.
173. Pagala MK, Tetsoti L, Nagpal D, Wise GJ. Aging effects on contractility of longitudinal and circular detrusor and trigone of rat bladder. J Urol. 2001; 166:721–7.
174. Schneider T, Hein P, Michel-Reher MB, Michel MC. Effects of ageing on muscarinic receptor subtypes and function in rat urinary bladder. Naunyn Schmiedebergs Arch Pharmacol. 2005;372:71–8.
175. Yu HI, Wein AJ, Levin RM. Contractile responses and calcium mobilization induced by muscarinic agonists in the rat urinary bladder: effects of age. Gen Pharmacol. 1997;28:623–8.
176. Hegde SS, Mandel DA, Wilford MR, Briaud S, Ford AP, Eglen RM. Evidence for purinergic neurotransmission in the urinary bladder of pithed rats. Eur J Pharmacol. 1998;349:75–82.
177. Lluel P, Deplanne V, Heudes D, Bruneval P, Palea S. Age-related changes in urethrovesical coordination in male rats: relationship with bladder instability? Am J Physiol Regul Integr Comp Physiol. 2003; 284:R1287–95.
178. Watanabe T, Matsumoto M, Toji S, Miyagawa I. Effects of estrogen on age-related changes in muscarinic responsiveness of the urinary bladder and lumbosacral dorsal root ganglion cells in female rats. Mol Cell Biochem. 2008;318(1–2):53–61.
179. Michel MC, Schneider T, Krege S, Goepel M. Does gender or age affect the efficacy and safety of tolterodine? J Urol. 2002;168(3):1027–31.
180. Andersson KE, Chapple CR, Cardozo L, Cruz F, Hashim H, Michel MC, Tannenbaum C, Wein AJ. Pharmacological treatment of overactive bladder: report from the International Consultation on Incontinence. Curr Opin Urol. 2009;19(4):380–94.
181. Mansfield KJ, Liu L, Mitchelson FJ, Moore KH, Millard RJ, Burcher E. Muscarinic receptor subtypes in human bladder detrusor and mucosa, studied by radioligand binding and quantitative competitive RT-PCR: changes in ageing. Br J Pharmacol. 2005; 144(8):1089–99.
182. Wuest M, Morgenstern K, Graf EM, Braeter M, Hakenberg OW, Wirth MP, Ravens U. Cholinergic and purinergic responses in isolated human detrusor in relation to age. J Urol. 2005;173(6):2182–9.
183. Chua WC, Liu L, Mansfield KJ, Vaux KJ, Moore KH, Millard RJ, Burcher E. Age-related changes of P2X[1] receptor mRNA in the bladder detrusor from men with and without bladder outlet obstruction. Exp Gerontol. 2007;42(7):686–92.
184. Yoshida M, Homma Y, Inadome A, Yono M, Seshita H, Miyamoto Y, Murakami S, Kawabe K, Ueda S. Age-related changes in cholinergic and purinergic neurotransmission in human isolated bladder smooth muscles. Exp Gerontol. 2001;36(1):99–109.

185. Yoshida M, Miyamae K, Iwashita H, Otani M, Inadome A. Management of detrusor dysfunction in the elderly: changes in acetylcholine and adenosine triphosphate release during aging. Urology. 2004;63(3 Suppl 1):17–23.
186. Gómez-Pinilla PJ, Pozo MJ, Camello PJ. Aging impairs neurogenic contraction in guinea pig urinary bladder: role of oxidative stress and melatonin. Am J Physiol Regul Integr Comp Physiol. 2007;293(2):R793–803.
187. Fry CH, Bayliss M, Young JS, Hussain M. Influence of age and bladder dysfunction on the contractile properties of isolated human detrusor smooth muscle. BJU Int. 2011;108(2 Pt 2):E91–6.
188. Andersson KE. Storage and voiding symptoms: pathophysiologic aspects. Urology. 2003;62(5 Suppl 2):3–10.
189. Jørgensen JB, Jensen KM, Mogensen P. Age-related variation in urinary flow variables and flow curve patterns in elderly males. Br J Urol. 1992;69(3): 265–71.
190. Jørgensen JB, Jensen KM, Mogensen P. Longitudinal observations on normal and abnormal voiding in men over the age of 50 years. Br J Urol. 1993; 72(4):413–20.
191. Madersbacher S, Pycha A, Schatzl G, Mian C, Klingler CH, Marberger M. The aging lower urinary tract: a comparative urodynamic study of men and women. Urology. 1998;51(2):206–12.
192. Ameda K, Sullivan MP, Bae RJ, Yalla SV. Urodynamic characterization of nonobstructive voiding dysfunction in symptomatic elderly men. J Urol. 1999;162(1):142–6.
193. Andersson KE. Detrusor underactivity/underactive bladder: new research initiatives needed. J Urol. 2010;184(5):1829–30.
194. van Koeveringe GA, Vahabi B, Andersson KE, Kirschner-Herrmans R, Oelke M. Detrusor underactivity: a plea for new approaches to a common bladder dysfunction. Neurourol Urodyn. 2011;30(5): 723–8.
195. Smith PP. Aging and the underactive detrusor: a failure of activity or activation? Neurourol Urodyn. 2010;29(3):408–12.
196. Malone-Lee J, Wahedna I. Characterisation of detrusor contractile function in relation to old age. Br J Urol. 1993;72(6):873–80.
197. Collas DM, Malone-Lee JG. Age-associated changes in detrusor sensory function in women with lower urinary tract symptoms. Int Urogynecol J Pelvic Floor Dysfunct. 1996;7(1):24–9.
198. Van Mastrigt R. Age dependency of urinary bladder contractility. Neurourol Urodyn. 1992;11:315–7.
199. Resnick NM, Yalla SV. Detrusor hyperactivity with impaired contractile function. An unrecognized but common cause of incontinence in elderly patients. JAMA. 1987;257(22):3076–81.

Comorbidity and Underlying Medical Disease

3

Camille P. Vaughan and Theodore M. Johnson II

Introduction

While many urologists see patients across a wide range of ages, the proportion of patients over the age of 65 will increase significantly in the coming years. Population-based estimates project that in the USA the number of adults over the age of 65 will double to 71.4 million, and the number of those over 85 will increase 126 %, to 9.6 million [4]. Most adults over the age of 65 have at least one chronic medical condition and more than half have at least two [5]. Older adults with multiple comorbid conditions are at greater risk for potentially avoidable hospitalization and adverse outcomes from medications than those with a single medical problem [5]. In addition to age-related changes affecting the lower urinary tract, many of the most prevalent chronic medical conditions such as cardiovascular disease, metabolic disease, and neurodegenerative disease (Table 3.1) are associated with lower urinary tract symptoms and other urologic conditions. Careful consideration of patient preferences and goals, comorbid medical conditions, polypharmacy, cognition, and functional status reduces the potential for adverse events related to surgical interventions and pharmacologic therapies [6]. In this chapter we will broadly review common diseases that affect older adults and the impact these conditions have on the management of urologic disease.

C.P. Vaughan, M.D., M.S. (✉)
Department of Veterans Affairs, Birmingham/Atlanta Geriatric Research Education and Clinical Center, Atlanta, GA, USA

Division of General Medicine and Geriatrics, Emory University School of Medicine, Atlanta, GA, USA

Atlanta VA Medical Center, 1670 Clairmont Road, Decatur, GA 30033, USA
e-mail: camille.vaughan@emory.edu

T.M. Johnson II, M.D., M.P.H.
Emory Division of General Medicine and Geriatrics, Department of Medicine, Atlanta VA Medical Center, 1670 Clairmont Road, Mailstop:11B, Decatur, GA 30033, USA
e-mail: ted.johnson@va.gov

Case

Introduction

Mr. B is a 72-year-old widower residing in an assisted living facility with a past medical history significant for Parkinson disease diagnosed 10 years ago, hypercholesterolemia, constipation, depression, and benign prostatic enlargement (BPE). He complains of urinary urgency, frequency, and nocturia three times at night. Urgency urinary incontinence occurs once a week if he waits too long between voids. His medications include the following: carbidopa/levodopa

(continued)

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_3,

(continued)

25/100 mg two tablets four times daily, pramipexole 1 mg three times daily, polyethylene glycol as needed, simvastatin 20 mg daily, and sertraline 100 mg daily. Physical examination is notable for global bradykinesia and stooped posture. He has decreased arm swing with walking. He performs a timed up and go in 15 s and uses his arms to push himself up from a chair. His Mini-Cog score is 4/5—he is able to remember 2/3 items on delayed recall and he correctly performs a clock-draw test. He has 1+ lower extremity edema to the calves bilaterally and 2+ dorsalis pedis pulses bilaterally. His blood pressure while seated is 128/68 mmHg. A prostate exam reveals a mildly enlarged gland estimated to be 30 g with no tenderness or nodules noted. Measurement of residual volume by bladder ultrasound immediately post-void is 30 mL.

Initial Management Strategy

Mr. B has Parkinson disease and evidence of prostate enlargement on examination. He has minimal urinary retention. Mr. B has evidence of a side effect of dopamine agonist therapy with lower extremity edema. Orthostatic hypotension and excessive daytime sleepiness are also potential side effects from dopaminergic therapy. Additional history and physical examination would help to determine the best course of treatment. First, inquire if Mr. B has had any previous falls because this can be predictive for future falls [1]. Obtaining information regarding daily intake of caffeinated beverages and alcohol is also important. On physical examination, checking a standing blood pressure is essential to assess for the presence of orthostatic hypotension, which becomes more common as Parkinson disease progresses.

Behavioral and lifestyle interventions should be considered as first-line therapy [2]. Based on Mr. B's cognitive screening test [3], he likely does not have significant cognitive impairment, which increases the chance that lifestyle changes and behavioral treatment approaches might be useful. Reducing or eliminating caffeine, pelvic floor muscle exercise-based urge suppression, and scheduled voiding have limited side effects and may be effective. If Mr. B does not have a previous history of frequent falls or orthostasis on examination, it would be reasonable to consider a selective alpha 1a-blocker. The assisted living facility can likely check his blood pressure following initiation of the new medication. Consulting with a neurologist with specialty training in movement disorders, a physical therapist, an occupational therapist, and/or a geriatrician could also benefit this patient. Developing a multidisciplinary team approach to care allows patients with complex comorbid disease to benefit from a range of specialists who can improve function and quality of life.

Cardiovascular Disease

Cardiovascular disease is the leading cause of mortality among US adults. Multiple cardiovascular conditions may coexist within an individual patient such as systolic and diastolic heart failure, cerebrovascular accidents, chronic kidney disease, and peripheral vascular disease. All of these conditions impact the incidence and progression of urologic disease. In the following section, we explore conditions associated with cardiovascular disease and how they impact providing high-quality urologic care to geriatric patients.

Table 3.1 Common comorbid conditions associated with urologic conditions and considerations for urologic treatment

Category	Common comorbid conditions among older adults	Associated urologic condition	Consideration for urologic treatment
Cardiovascular disease	Hypertension	Nocturia Erectile dysfunction	Consider risk of orthostatic hypotension if implementing alpha-blocker therapy or phosphodiesterase inhibitor Blood pressure target in most older adults is 150/80 [13]
	Vascular disease	Erectile dysfunction	Consider risk of hypotension if implementing phosphodiesterase inhibitor
	Lower extremity edema	Nocturia	Consider trial of daytime compression stockings prior to diuretic therapy
Metabolic disease	Obesity	BPH Urinary incontinence Nocturia (if obstructive sleep apnea (OSA) present)	Screen for sleep disorder if nocturia is bothersome Weight loss can improve incontinence
	Diabetes	Urinary frequency (uncontrolled DM) Urinary incontinence Urinary retention (long term) Erectile dysfunction	Glycemic control and weight loss may prevent or improve some symptoms
Neurologic disease	Stroke	Urinary incontinence (functional or urgency)	Assess functional status for Prompted or Scheduled voiding Consider anticholinergic burden of medications
	Parkinson disease	Urgency Nocturia Frequency Urgency incontinence Erectile dysfunction	Consider behavioral/lifestyle approaches Consider anticholinergic burden of medications Assess risk of hypotension prior to prescribing alpha-blocker or phosphodiesterase therapy May be TURP candidate depending on urodynamic assessment
	Multiple System Atrophy	Detrusor-sphincter-dyssynergia Urinary retention Erectile dysfunction	Assess fall risk prior to prescribing alpha-blocker therapy Clean intermittent catheterization (CIC) may be necessary Poor surgical (TURP) candidates
	Multiple Sclerosis	Urinary urgency Frequency Nocturia Urgency incontinence Detrusor-sphincter-dyssynergia Urinary retention Erectile dysfunction	Symptoms vary considerably in MS depending on location of lesions Consider anticholinergic burden of medications

Hypertension

Hypertension is the most common medical diagnosis among older adults [7] and is a major contributing factor in the development of renal disease and cardiovascular disease later in life. Hypertension likely impacts the development of lower urinary tract symptoms and erectile dysfunction through these mechanisms. Additionally, concurrent therapy for hypertension often impacts therapeutic decision-making for urologic conditions among geriatric patients.

Hypertension has been associated with having two or more episodes of nocturia in older men and women [8–11]. While the pathophysiologic mechanisms are not completely understood, conditions associated with hypertension such as obstructive sleep apnea (OSA) and congestive heart failure lead to atrial stretch and increased production of atrial natriuretic peptide (ANP). ANP release increases sodium excretion by the kidneys. ANP release often occurs at night, especially with sleep and recumbency, and it results in increased urine production overnight. The circadian control of arginine vasopressin may also be disrupted in older individuals, with lower than appropriate levels at night, resulting in production of a dilute urine, causing nocturnal polyuria, and therefore nocturia. Optimization of comorbid conditions associated with nocturia may also result in improvement [12].

Hypertension as a comorbid condition often impacts therapeutic decisions for urologic conditions. The Hypertension in the Very Elderly Trial (HYVET) suggests a blood pressure target of 150/80 mmHg is sufficient to reduce fatal and nonfatal stroke in addition to all-cause mortality among older adults [13]. However, previous studies have suggested increased risk of mortality among older adults with treated hypertension and systolic blood pressure measurement less than 139 mmHg [14]. Impaired autoregulation of cerebral blood flow in the presence of hypertension may predispose older adults to orthostasis [15]. Older adults often have a blunted baroreceptor reflex which may result in a reduction in heart rate in response to hypotension, predisposing older adults to presyncope and syncope [16]. Orthostatic hypotension and a blunted baroreceptor reflex are among the conditions which increase the risk of falls in older adults [17]. In men with BPE, first-line medical treatment often involves peripheral alpha 1-adrenergic antagonists (alpha-blockers). Nonselective peripheral alpha blockers may be useful as adjuvant antihypertensive therapy, but increase the risk for orthostatic hypotension and subjective feelings of dizziness and light-headedness in older adults. Selective peripheral alpha blockers, which are more selective for the prostatic alpha-1a receptor, have less potential for antihypertensive effects, although up to 1 in 12 patients may experience orthostatic hypotension [18]. In men with congestive heart failure, the use of alpha 1 adrenergic blockers for BPE without a beta blocker has been shown to increase the risk of hospital admission for heart failure exacerbation [19]. Thoughtful consideration of fall risk, measurement of orthostatic blood pressure, and assessment of comorbid conditions are essential to mitigate adverse events among older men initiating alpha-blocker therapy.

Vascular Disease

Vascular disease encompasses conditions involving the peripheral, cardiac, and central nervous system blood supply. The risk of vascular disease increases with age, tobacco use, and certain comorbid conditions such as hypertension, diabetes mellitus, hypercholesterolemia, and conditions associated with chronic inflammation such as systemic lupus erythematosus (SLE) or human immunodeficiency virus (HIV). Vascular disease not only increases the risk of erectile dysfunction in men but also impacts treatment options and may preclude the use of phosphodiesterase inhibitor therapy. Clinicians must be aware of these risks when making treatment decisions in this patient population.

Vascular disease also predisposes older patients to conditions which may result in lower extremity edema. Lower extremity edema influences the development of nocturia as interstitial dependent fluid is mobilized back into the circulation while in a recumbent position, which results in ANP release, and then a solute diuresis results in increased urine production overnight. Daytime compression stockings have been shown to be a useful component of effective nonpharmacologic treatment for lower extremity edema in many individuals who have sufficient arterial supply to the lower extremities [12]. Assessing an older adult's ability to successfully apply the compression stockings is important. Engaging a caregiver to assist may be essential to increase the likelihood of adherence to therapy.

Loop diuretics are often used to treat lower extremity edema and volume overload in conditions such as congestive heart failure, cirrhosis, and chronic kidney disease. For the patient with overactive bladder or urinary incontinence, the addition of a diuretic to the medication regimen can lead to worsened urinary symptoms which can further complicate social engagement [20]. Depending on the half-life of the diuretic, the timing of the dose can often be adjusted to coincide with times the patient anticipates being in a familiar setting [21]. This can help to facilitate easier access to toilet facilities.

Metabolic Disease

Obesity

The increase in prevalence of obesity among US adults is the most important factor in the potential for decreased lifespan among future generations [22]. Obesity influences the development of urologic disease indirectly through metabolic changes and directly through increased intra-abdominal pressure. Obesity increases the risk of the metabolic syndrome (impaired glucose tolerance, elevated triglycerides, hypertension, and low HDL cholesterol), which predisposes adults to cardiovascular disease and diabetes. Obesity is also a risk factor for OSA. Several studies have shown that the complaint of nocturia may be a harbinger for underlying OSA and treatment of OSA may reduce the frequency of nocturia [23, 24]. Cross-sectional studies suggest obesity may influence the development of benign prostatic hyperplasia, although the mechanism is not known and more research is needed [25]. Among women without diabetes mellitus, modest weight reduction with 10 % loss of body weight as well as bariatric surgery have been shown to improve urinary incontinence [26, 27].

Diabetes Mellitus

Diabetes mellitus (diabetes) places older adults at risk for additional multiple chronic conditions and increases the risk of postoperative infections and poor wound healing. The rise in prevalence of diabetes mirrors the increase in obesity among the US population; yet even in the absence of obesity or with statistical control for body-mass index, diabetes is associated with increased prevalence of urinary incontinence [28]. While both type 1 and type 2 diabetes have been shown to be associated with higher rates of urological disease, more often it is type 2 diabetes that is relevant in the older patient.

Diabetes likely impacts urological disease at multiple levels. Most obviously, very poorly controlled diabetes will result in glucosuria and polyuria, due to exceeding the glucose transportation threshold within the kidney, which will particularly exacerbate lower urinary tract symptoms. In several cross-sectional studies, intensity of diabetes management modality (insulin > medications > diet) is associated with higher rates of urological morbidity. Because more intense management strategies are used in those with more severe disease, some cross-sectional studies such as these may be confounded. Ideally, one would study the effect of more intensive management of diabetes on urological symptoms. Even though type 2 diabetes mellitus is most relevant to the care of older adults [29], the best information about the effect of intensive management and improved glucose control has been done with younger adults with type 1 diabetes mellitus. Because of the quality of evidence, it is considered here in this discussion, recognizing that this might not be perfectly extrapolated.

Complications of long-standing diabetes include microvascular damage and neurological injury to structures such as the kidneys, bladder, urethral sphincter, and corpus cavernosa of the penis. The most frequent urodynamic findings in the patient with diabetes are detrusor hyperreflexia or impaired detrusor contractility, with detrusor areflexia being less common [30]. Diabetes is associated with higher rates of infectious complications. Women with non-insulin-dependent diabetes mellitus are more likely to have asymptomatic bacteriuria and are also more likely to have acute urinary tract infection [31, 32]. Evidence points to the degree of glucose control being highly important. Having diabetes and having poorer control of diabetes as assessed by having higher hemoglobin A1c levels have been associated with higher rates of erectile dysfunction among men [33]. Interestingly, even having a "prediabetes state," as evidenced by impaired glucose tolerance, has been linked to higher prevalence of urinary incontinence for women [29]. Among African American and white women aged 70–79, urge urinary incontinence (but not stress urinary incontinence) was strongly related in a cross-sectional analysis to the diabetes therapy used (highest rates of urgency incontinence with insulin therapy, followed by medication, and then by diet) [34].

Newly available evidence from treatment trials strengthens the link between diabetes and urological conditions. While limited clinical trial data in women with type 1 diabetes do not suggest that intensive glycemic control decreases the long-term risk of incontinence in women with type 1 diabetes, research does suggest weight loss can decrease incontinence in women with prediabetes and in those with type 2 diabetes [35]. Women nearly 50 years of age on average with a body mass index of 35 kg/m^2 who had intensive lifestyle modification over a 3-year period had a 20 % decrease in stress urinary incontinence compared to controls [36].

Among men with mild to moderate nonproliferative retinopathy and microalbuminuria who had a 1–15-year history of diabetes, those who received intensive glucose management over a 10-year period had a lower prevalence of erectile dysfunction at the end of the trial [37]. The degree to which this was reduced might be better understood in a clinical context: a mean HbA1c of 8.8 % imparted a 1.5 to 2-fold greater odds of erectile dysfunction compared to a mean HbA1c of 8.0 % [38]. Early implementation of intensive therapy in young men with established type I diabetes mellitus and limited microvascular complications could reduce the burden of erectile dysfunction for these men as they age. The pathophysiology and possible mechanisms by which diabetes might promote urologic complications are unclear, thus it is unlikely that a single mechanism underlies both voiding and sexual dysfunction in diabetes [39].

Neurologic Disease

Because the autonomic and somatic nervous systems are intimately involved in normal bladder function, many neurologic diseases are associated with lower urinary tract symptoms. The most prevalent neurologic diseases in older adults are stroke and neurodegenerative diseases including Alzheimer's dementia, Parkinson disease, and Parkinson-plus syndromes. Adults with demyelinating conditions such as multiple sclerosis also often experience bothersome urinary symptoms. Lower urinary tract symptoms can further worsen the diminished quality of life that often accompanies these conditions and can increase burden for caregivers. Older adults with concomitant neurodegenerative disease may also be more susceptible to cognitive side effects related to common medications used to treat urinary symptoms or postoperative cognitive complications such as delirium.

Stroke

After a stroke, patients may experience lower urinary tract symptoms depending on the region of the brain affected. Strokes affecting the frontoparietal regions have been associated with decreased ability to sense bladder fullness as well as detrusor hyperactivity [40, 41]. Patients may describe UI that occurs without recognizing a need to void [41]. Scheduled voiding or prompted voiding with the support of a caregiver may be the most appropriate treatment strategy to avoid UI in these patients. Patients with multiple small vessel ischemic strokes may experience worsening urinary urgency, particularly if the basal ganglia are involved [40]. Additionally, MRI studies of the brain have shown increased white matter hyperintensities in areas related to bladder function, such as the anterior cingulate cortex, are correlated with the presence of urinary incontinence [42, 43]. White matter hyperintensities represent areas of white matter wasting and are more prevalent in adults with risk factors for vascular disease. In these patients lifestyle, behavioral and pharmacologic treatments aimed at reducing urgency may be more effective.

Urinary incontinence after a stroke may also be related to functional impairments and not necessarily direct effects on bladder function. However, urinary incontinence following a stroke is a marker for worse survival [44]. A multidisciplinary stroke rehabilitation team with nursing staff and therapists who focus on improving urinary incontinence can be an effective way to improve urinary symptoms in the setting of an acute stroke [45, 46].

Parkinson Disease

Most pharmacologic treatments in Parkinson disease (PD) target the motor symptoms of tremor, rigidity, and bradykinesia and have led to increased lifespan in PD patients compared to the pre-levodopa era [47]. As a result, the non-motor symptoms of PD including sexual dysfunction and lower urinary tract symptoms have more impact on quality of life than the motor symptoms as the disease progresses [48]. Urinary urgency, frequency, and nocturia are more common in adults with Parkinson disease than in age-matched controls [49, 50]. Levodopa and dopamine agonists can impact urinary symptoms. Some patients notice improvement in urinary symptoms with dopaminergic therapy, although in patients with the on/off syndrome, dopaminergic medication may worsen urinary urgency [51, 52]. Current treatment recommendations based on expert opinion suggest that antimuscarinic medications be prescribed for these symptoms [53]. Treatment of concomitant constipation is also important especially if antimuscarinic therapy is initiated, because the anticholinergic side effects of these drugs may contribute to the autonomic burdens of PD. Behavioral and lifestyle changes often recommended for urgency incontinence may also be of benefit, although more studies are needed [54]. Behavioral and lifestyle changes have less potential for side effects than antimuscarinic medications which can be problematic in this population. Because 75 % of PD patients will have evidence of cognitive impairment 10 years after diagnosis, it is important to consider the overall anticholinergic burden of prescribed medications [55, 56].

Because PD is a disease of aging, many men with Parkinson disease will have concomitant BPE. Treatment of lower urinary tract symptoms in men with PD and evidence of BPE may involve the use of alpha blockers. As PD progresses there is increased potential for autonomic dysfunction which often manifests in orthostatic hypotension. In addition, dopaminergic medications can cause hypotension. Previously, the risk of orthostatic hypotension was discussed in the context of choosing between nonselective and selective peripheral alpha blockers. In men with PD and BPE, it is important to carefully consider the risk of orthostatic hypotension prior to beginning an alpha blocker as falls are a major source of morbidity and mortality in this patient population [57].

Surgical intervention for BPE may be considered in men with PD. The increased risk of autonomic dysfunction as PD progresses increases the risk of urinary retention. Urodynamic evaluation to assess detrusor muscle function is essential prior to surgical intervention to relieve outlet obstruction. Recent evidence suggests surgical therapy for BPE in men with PD can lead to improved urinary outcomes when patients are carefully selected using preoperative urodynamic evaluation [58].

Multiple System Atrophy

Multiple System Atrophy (MSA) is a Parkinson-plus syndrome characterized by motor dysfunction similar to idiopathic PD but with significant autonomic dysfunction early in the course of disease. Orthostatic hypotension and urinary retention are common. Patients with MSA often also complain of urinary urgency, frequency, and nocturia. These patients are not as likely to respond well to antimuscarinic therapy because it may worsen urinary retention. In men with concomitant BPE, five-alpha reductase inhibitors may be the only useful pharmacologic therapy as these patients have significant risk of orthostatic hypotension even with selective alpha blockers. Patients with MSA are often not candidates for surgical intervention because of impaired detrusor function. Clean intermittent catheterization or an indwelling catheter may be necessary as the disease progresses [59].

Multiple Sclerosis

Urinary symptoms as a result of multiple sclerosis (MS) can occur during acute flares of the disease or can occur with accumulated burden of spinal cord involvement [43]. Patients with MS often experience irritative symptoms and demonstrate detrusor hyperactivity on urodynamic evaluation. Voiding symptoms can also occur secondary to detrusor sphincter dyssynergia (DSD). Urinary retention secondary to impaired detrusor contractility occurs in some cases. Because the etiology of urinary symptoms in the setting of MS is variable, and patients can have different pathophysiologic causes depending on the level of neurologic impairment, careful assessment based on symptom report and physical examination is essential. Common comorbid conditions in the setting of MS such as constipation and cognitive impairment also have implications for choice of therapy. A multidisciplinary approach to bladder management in patients with MS has been shown to improve quality of life and reduce disability compared to usual care with only a general practitioner or neurologist [60].

Summary

In this chapter we have reviewed the most common comorbid conditions associated with urological disease among older adults. Additionally, older adults frequently have more than one comorbid condition. Comorbidity in geriatric patients impacts the management of multiple urologic conditions with implications for perioperative care, behavioral and pharmacologic treatment options, and care coordination. Engagement of a multidisciplinary team of providers should be considered for many patients to maximize opportunities for improving quality of life and independence.

References

1. Tinetti ME, Kumar C. The patient who falls. JAMA. 2010;303(3):258–66.
2. Ginger VAT, Yang CC. The diagnosis and treatment of patients with neurologic dysfunction of the urinary bladder. In: Low PA, Benarroch EE, editors. Clinical autonomic diseases. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008.
3. Borson S, Scanlan J, Brush M, Vitaliano P, Dokmak A. The Mini-Cog: a cognitive 'vital signs' measure for dementia screening in multi-lingual elderly. Int J Geriatr Psychiatry. 2000;15(11):1021–7.
4. Department of Health and Human Services, Administration on Aging Projected Future Growth of the Older Population. http://www.aoa.gov/AoARoot/Aging_Statistics/future_growth/future_growth.aspx. Accessed 13 Apr 2012.
5. Wolff JL, Starfield B, Anderson G. Prevalence, expenditures, and complications of multiple chronic conditions in the elderly. Arch Intern Med. 2002;162(20):2269–76.
6. American Geriatrics Society Expert Panel on the Care of Older Adults with Multimorbidity. Guiding Principles for the Care of Older Adults with Multimorbidity: An Approach for Clinicians. J Am Geriatr Soc. 2012;60:E1–E25.
7. Hung W, Ross J, Boockvar K, Siu A. Recent trends in chronic disease, impairment and disability among older adults in the United States. BMC Geriatr. 2011;11(1):47.
8. Burgio KL, Johnson 2nd TM, Goode PS, et al. Prevalence and correlates of nocturia in community-dwelling older adults. J Am Geriatr Soc. 2010;58(5):861–6.
9. Johnson TM, Sattin RW, Parmelee P, Fultz NH, Ouslander JG. Evaluating potentially modifiable risk factors for prevalent and incident nocturia in older adults. J Am Geriatr Soc. 2005;53(6):1011–6.
10. McKeigue PM, Reynard JM. Relation of nocturnal polyuria of the elderly to essential hypertension. Lancet. 2000;355(9202):486–8.
11. Goldman N, Lin IF, Weinstein M, Lin Y-H. Evaluating the quality of self-reports of hypertension and diabetes. J Clin Epidemiol. 2003;56(2):148–54.
12. Vaughan CP, Endeshaw Y, Nagamia Z, Ouslander JG, Johnson TM. A multicomponent behavioural and drug intervention for nocturia in elderly men: rationale and pilot results. BJU Int. 2009;104(1):69–74.
13. Beckett NS, Peters R, Fletcher AE, et al. Treatment of hypertension in patients 80 years of age or older. N Engl J Med. 2008;358(18):1887–98.
14. Oates DJ, Berlowitz DR, Glickman ME, Silliman RA, Borzecki AM. Blood pressure and survival in the oldest old. J Am Geriatr Soc. 2007;55(3):383–8.
15. Mukai S, Gagnon M, Iloputaife I, Hamner JW, Lipsitz LA. Effect of systolic blood pressure and carotid stiffness on baroreflex gain in elderly subjects. J Gerontol Biol Sci Med Sci. 2003;58(7):M626–30.
16. James MA, Potter JF. Orthostatic blood pressure changes and arterial baroreflex sensitivity in elderly subjects. Age Ageing. 1999;28(6):522–30.
17. American Geriatrics Society, British Geriatrics Society. Clinical practice guidelines: prevention of falls in older persons. J Am Geriatr Soc. 2011;59:148–57.

18. Fine SR, Ginsberg P. Alpha-adrenergic receptor antagonists in older patients with benign prostatic hyperplasia: issues and potential complications. J Am Osteopath Assoc. 2008;108(7):333–7.
19. Dhaliwal AS, Habib G, Deswal A, et al. Impact of alpha 1-adrenergic antagonist use for benign prostatic hypertrophy on outcomes in patients with heart failure. Am J Cardiol. 2009;104(2):270–5.
20. Ekundayo OJ, Markland A, Lefante C, et al. Association of diuretic use and overactive bladder syndrome in older adults: a propensity score analysis. Arch Gerontol Geriatr. 2008;49(1):64–8.
21. Ouslander JG. Management of overactive bladder. N Engl J Med. 2004;350(8):786–99.
22. Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among US adults, 1999–2008. JAMA. 2010;303(3):235–41.
23. FitzGerald MP, Mulligan M, Parthasarathy S. Nocturic frequency is related to severity of obstructive sleep apnea, improves with continuous positive airways treatment. Am J Obstet Gynecol. 2006;194(5): 1399–403.
24. Hajduk I, Strollo PJ, Jasani R, Atwood CJ, Houck P, Sanders M. Prevalence and predictors of nocturia in obstructive sleep apnea-hypopnea syndrome - a retrospective study. Sleep. 2003;26(1):61–4.
25. Parsons JK, Sarma AV, McVary K, Wei JT. Obesity and benign prostatic hyperplasia: clinical connections, emerging etiological paradigms and future directions. J Urol. 2009;182(6 Suppl):S27–31.
26. Subak LL, Wing R, West DS, et al. Weight loss to treat urinary incontinence in overweight and obese women. N Engl J Med. 2009;360(5):481–90.
27. Burgio KL, Richter HE, Clements RH, Redden DT, Goode PS. Changes in urinary and fecal incontinence symptoms with weight loss surgery in morbidly obese women. Obstet Gynecol. 2007;110(5): 1034–40.
28. Lawrence JM, Lukacz ES, Liu I-LA, Nager CW, Luber KM. Pelvic floor disorders, diabetes, and obesity in women. Diabetes Care. 2007;30(10): 2536–3541.
29. Brown JS, Vittinghoff E, Lin F, Nyberg LM, Kusek JW, Kanaya AM. Prevalence and risk factors for urinary incontinence in women with type 2 diabetes and impaired fasting glucose. Diabetes Care. 2006;29(6):1307–12.
30. Kaplan SA, Te AE, Blaivas JG, McGuire EJ. Urodynamic findings in patients with diabetic cystopathy. J Urol. 1995;153(2):342–4.
31. Zhanel GG, Nicolle LE, Harding GKM, The Manitoba Diabetic Urinary Infection Study Group. Prevalence of asymptomatic bacteriuria and associated host factors in women with diabetes mellitus. Clin Infect Dis. 1995;21(2):316–22.
32. Boyko EJ, Fihn SD, Scholes D, Chen C-L, Normand EH, Yarbro P. Diabetes and the risk of acute urinary tract infection among postmenopausal women. Diabetes Care. 2002;25(10):1778–83.
33. Romeo JH, Seftel AD, Madhun ZT, Aron DC. Sexual function in men with diabetes type 2: association with glycemic control. J Urol. 2000;163(3):788–91.
34. Jackson RAM, Vittinghoff EP, Kanaya AMM, et al. Urinary incontinence in elderly women: findings from the Health, Aging, and Body Composition Study. Obstet Gynecol. 2004;104(2):301–7.
35. Phelan S, Kanaya AM, Subak LL, et al. Prevalence and risk factors for urinary incontinence in overweight and obese diabetic women: action for health in diabetes (Look Ahead) study. Diabetes Care. 2009;32(8):1391–7.
36. Brown JS, Wing R, Barrett-Connor E, et al. Lifestyle intervention is associated with lower prevalence of urinary incontinence. Diabetes Care. 2006;29(2): 385–90.
37. Klein R, Klein BEK, Moss SE. Ten-year incidence of self-reported erectile dysfunction in people with long-term type 1 diabetes. J Diabetes Complications. 2005;19(1):35–41.
38. Wessells H, Penson DF, Cleary P, et al. Effect of intensive glycemic therapy on erectile function in men with type 1 diabetes. J Urol. 2011;185(5): 1828–34.
39. Brown JS, Wessells H, Chancellor MB, et al. Urologic complications of diabetes. Diabetes Care. 2005;28(1):177–85.
40. Sakakibara R, Hattori T, Yasuda K, Yamanishi T. Micturitional disturbance after acute hemispheric stroke: analysis of the lesion site by CT and MRI. J Neurol Sci. 1996;137(1):47–56.
41. Pettersen R, Stien R, Wyller TB. Post-stroke urinary incontinence with impaired awareness of the need to void: clinical and urodynamic features. BJU Int. 2007;99(5):1073–7.
42. Kuchel GA, Moscufo N, Guttmann CR, et al. Localization of brain white matter hyperintensities and urinary incontinence in community-dwelling older adults. J Gerontol Biol Sci Med Sci. 2009;64A(8):902–9.
43. Fowler CJ, Dalton C, Panicker JN. Review of neurologic diseases for the urologist. Urol Clin North Am. 2010;37(4):517–26.
44. Patel M, Coshall C, Rudd AG, Wolfe CDA. Natural history and effects on 2-year outcomes of urinary incontinence after stroke. Stroke. 2001;32(1):122–7.
45. Thomas L, Cross S, Barrett J, et al. Treatment of urinary incontinence after stroke in adults. Cochrane Database Syst Rev. 2008;1(CD004462).
46. Wikander B, Ekelund P, Milsom I. An evaluation of multidisciplinary intervention governed by functional independence measure (FIM SM) in incontinent stroke patients. Scand J Rehabil Med. 1998;30(1): 15–21.
47. Joseph C, Chassan JB, Koch M-L. Levodopa in Parkinson disease: a long-term appraisal of mortality. Ann Neurol. 1978;3(2):116–8.
48. Gallagher DA, Lees AJ, Schrag A. What are the most important nonmotor symptoms in patients with

Parkinson's disease and are we missing them? Mov Disord. 2010;25:2493–500.
49. Winge K, Skau A-M, Stimpel H, Nielsen KK, Werdelin L. Prevalence of bladder dysfunction in Parkinsons disease. Neurourol Urodyn. 2006;25(2):116–22.
50. Campos-Sousa RN, Quagliato E, da Silva BB, de Carvalho RM, Jr Ribeiro SC, de Carvalho DFM. Urinary symptoms in Parkinson's disease: prevalence and associated factors. Arq Neuropsiquiatr. 2003;61(2B):359–63.
51. Brusa L, Petta F, Pisani A, et al. Acute vs chronic effects of l-dopa on bladder function in patients with mild Parkinson disease. Neurology. 2007;68(18):1455–9.
52. Uchiyama T, Sakakibara R, Hattori T, Yamanishi T. Short-term effect of a single levodopa dose on micturition disturbance in Parkinson's disease patients with the wearing-off phenomenon. Mov Disord. 2003; 18(5):573–8.
53. Zesiewicz TA, Sullivan KL, Arnulf I, et al. Practice parameter: treatment of nonmotor symptoms of Parkinson disease: report of the quality standards subcommittee of the American Academy of Neurology. Neurology. 2010;74(11):924–31.
54. Vaughan CP, Juncos JL, Burgio KL, Goode PS, Wolf RA, Johnson 2nd TM. Behavioral therapy to treat urinary incontinence in Parkinson disease. Neurology. 2011;76(19):1631–4.
55. Aarsland D, Kurz MW. The epidemiology of dementia associated with Parkinson disease. J Neurol Sci. 2010;289(1–2):18–22.
56. Ehrt U, Broich K, Larsen JP, Ballard C, Aarsland D. Use of drugs with anticholinergic effect and impact on cognition in Parkinson's disease: a cohort study. J Neurol Neurosurg Psychiatry. 2010;81(2):160–5.
57. Balash Y, Peretz C, Leibovich G, Herman T, Hausdorff JM, Giladi N. Falls in outpatients with Parkinson's disease: frequency, impact and identifying factors. J Neurol. 2005;252(11):1310–5.
58. Roth B, Studer UE, Fowler CJ, Kessler TM. Benign prostatic obstruction and Parkinson's disease—should transurethral resection of the prostate be avoided? J Urol. 2009;181(5):2209–13.
59. Winge K, Fowler CJ. Bladder dysfunction in Parkinsonism: mechanisms, prevalence, symptoms, and management. Mov Disord. 2006;21(6):737–45.
60. Khan F, Pallant JF, Pallant JI, Brand C, Kilpatrick TJ. A randomised controlled trial: outcomes of bladder rehabilitation in persons with multiple sclerosis. J Neurol Neurosurg Psychiatry. 2010;81(9):1033–8.

Frailty

4

Tomas Lindor Griebling

Frailty is a condition often conceptually associated with advancing age. However, it should not be considered an inevitable or necessarily a normal part of the aging process. Frailty is considered to be one of the geriatric syndromes, meaning that it is multifactorial, is linked to aging, and can have a variety of clinical outcomes and effects. In the most popular validated conceptual model, often referred to as the "frailty phenotype," frailty is characterized by several measureable clinical changes [1]. These include unintentional weight loss of ≥10 pounds in 1 year, low levels of physical activity, self-reported exhaustion, weakness as measured by diminished handgrip strength, and slow walking speed (Table 4.1). In this model, frailty was defined as the presence of three or more of these characteristics. Intermediate frailty was defined as having one or two of the variables. In other studies, intermediate frailty is sometimes referred to as "prefrailty." Older adults with none of the variables were considered nonfrail. The validation study for this model was performed in a community-based sample of 5,317 men and women over 65 years of age. These researchers identified an overall prevalence of frailty of 6.9 %. Subjects were followed longitudinally, and the incidence rate of new onset frailty after 4 years was 7.2 %.

It is clearly recognized that there is overlap between the concepts of frailty, comorbidity, and disability. However, these entities are not identical [2]. Comorbidity generally refers to underlying diseases or disorders which can be associated with specific health outcomes or issues. Examples of common comorbidities in older adults include diabetes mellitus, hypertension, Parkinson's disease, congestive heart failure, arthritis, and inflammatory bowel disease. Progression of these types of chronic conditions can lead to some of the component changes of the frailty phenotype. Thus, comorbidities can be viewed as potential etiological factors for frailty. Disability refers to the need for assistance to perform various activities. This is often considered within the framework of the activities of daily living (ADLs) such as bathing, dressing, and grooming or the instrumental activities of daily living (IADLs) such as preparing food, shopping, or managing finances. Disability is generally considered to be one of the potential outcomes of progressing frailty. A wide variety of factors can influence all of these conceptual areas including comorbidity, frailty, and disability (Fig. 4.1).

It is also important to note that although the overall prevalence of frailty is typically higher in older adults, frailty can develop at any age. Indeed, some young and middle-aged people develop frailty due to changes in functional status or accumulation of functional deficits. In this younger age group, frailty may also be linked to both comorbidity and disability as previously described.

T.L. Griebling, M.D., M.P.H., F.A.C.S., F.G.S.A., A.G.S.F. (✉)
Department of Urology and The Landon Center on Aging, University of Kansas School of Medicine, 5021 Sudler, Mailstop 3016, 3901, Rainbow Blvd., Kansas City, KS 66160, USA
e-mail: tgriebling@kumc.edu

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_4,

Table 4.1 Characteristics associated with the frailty phenotype

- Unintentional weight loss (≥10 pounds/year)
- Low levels of physical activity
- Self-reported exhaustion
- Weakness with diminished handgrip strength
- Slow walking speed

Adapted from Fried LP, Tangen CM, Walston J, et al: Frailty in older adults: evidence for a phenotype. J Gerontol A BiolSci Med Sci 2001, 56A: M146–M156

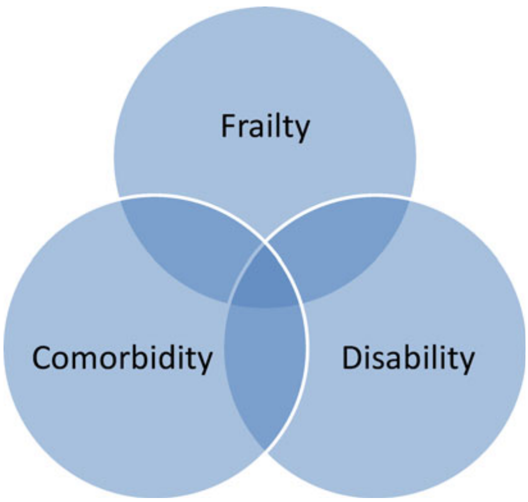


Fig. 4.1 This Venn diagram illustrates that frailty is conceptually related to both underlying comorbidities and disability. In this paradigm, comorbidity is usually seen as an etiological factor for frailty, and disability is seen as an outcome of both comorbidity and frailty. However, interactions between these domains are complex and can be influenced by multiple factors such as medications, surgery, external stressors, and caregiver issues

Other Models Regarding Development of Frailty

An alternative conceptual model and operational definition of frailty uses the concept of accumulated deficits as the main risk factor for the syndrome. In this framework, a numeric index can be used to quantify these characteristics. Multisystem deterioration is combined with loss of physiologic reserve capacity to cope with these changes. This can lead to a cycle of deterioration including several components such as decreased physical activity, worsening of chronic comorbid diseases, and malnutrition. In turn, these changes can lead to worsening frailty. Small insults to health may result in accumulated changes which lead to progressive frailty. This has been described as a "domino" effect [3]. It is possible that some treatments including medications or surgery could help to prevent or retard this accumulation of deficits process thereby slowing development of clinical frailty.

One recent study examined the utility of the Deficit Accumulation Index (DAI), an instrument which assesses 39 preoperative variables, in 102 patients ≥65 years of age undergoing abdominal surgery [4]. Development of postoperative complications was used as the outcome measure. The DAI was found to correlate well to the previously described phenotypic definition of the frailty syndrome. However, in this particular study, the DAI was not statistically predictive of postoperative outcomes. The Braden Scale [5], a validated instrument used to predict risk of developing pressure ulcers was also used in this analysis. The first Braden Scale score measured within 24 h after surgery was an independent predictor of complications within 30 days of surgery including length of hospital stay and need for nursing home placement at discharge (both, $p<0.005$). This indicates that a simple numerical summation of accumulated deficits may not capture the subtle factors associated in other types of frailty analysis.

Association of Frailty with Comorbidities and Biomarkers

Several studies have examined the relationships between frailty and distinct clinical parameters or measureable biomarkers. These studies have yielded some intriguing results. Atrial fibrillation (AF) is the most common cardiac arrhythmia in older adults. AF has previously been linked to cardiovascular complications including worsening congestive heart failure, stroke, and dementia. A study of 23,174 hospitalized patients with AF confirmed associations with worse clinical outcomes and worse metabolic profiles [6]. Therefore, it was felt that AF could be a potential marker for more global frailty.

Using a life-space analysis, Xue et al. demonstrated that those who were less mobile were significantly more likely to be classified as frail [7]. They also showed that compared to women who left their neighborhoods at least four times weekly, those who did not were 1.7 more times likely to become frail ($p < 0.005$). After adjusting for confounding variables, those who were homebound had a threefold increase in frailty-free mortality ($p < 0.01$). The presence of multiple androgen hormone deficiencies has also been linked to increased frailty in elderly women [8]. A cohort of 494 women who were 70–79 years of age were analyzed regarding deficiencies in free testosterone, dehydroepiandrosterone sulfate (DHEAS), and insulin-like growth factor-1 (IGF-1). Although deficiencies in a single hormone were not statistically associated with the frailty phenotype compared to subjects with no hormonal deficiencies, there was a trend identified in each case. However, those with either two or all three hormonal deficiencies had a much greater likelihood of frailty (OR 2.79, 95 % CI 1.06–7.32). Thus, multiple anabolic hormonal deficiencies may be linked to subsequent development of the frailty syndrome in elderly women. In a similar cross-sectional analysis of 250 women between 76 and 86 years of age (mean 79.6 ± 2.7), the prevalence of frailty was 6.8 % [9]. The combination of sarcopenia and either severe osteopenia or osteoporosis was strongly associated with frailty (OR 6.4, 95 % CI 1.1–36.8). These physiologic changes were either directly or indirectly linked to all of the characteristics of the frailty phenotype (Table 4.1) including weight loss, decreased physical activity, sense of exhaustion, diminished grip strength, and slower gait speed.

One of the most intriguing areas of current research has examined the associations between inflammation and frailty. Free radial formation and oxidative stress are associated with the development of cellular and tissue inflammation.

Two studies have linked frailty in older women with increases in rates of inflammatory diseases and levels of inflammatory biomarkers [10, 11]. Although these concepts have not yet been validated for incorporation into the operational definitions for the frailty phenotype, the results are intriguing and raise important questions for future research focused on the associations between inflammation and frailty.

Clinical Assessment of Frailty

Several studies have focused on preoperative assessment of frailty in an attempt to identify potentially modifiable risk factors for postoperative complications [12]. One study examined the comprehensive geriatric assessment (CGA) of 400 older adult who were at least 74 years of age or older undergoing cardiac surgery [13]. A combination of the five classic characteristics of the frailty phenotype (Table 4.1) and also performance status and biomarkers was used. Strong associations were identified between frailty and postoperative mortality risk. Another prospective study of 3,826 patients undergoing cardiac surgery at a single center identified an overall prevalence rate of frailty of 4.1 % [14]. Using impairment in ADLs, ambulation, or dementia as the operational definition of frailty, these authors showed that frailty was strongly associated with both mortality (OR 1.8, 95 % CI 1.1–3.0) and nursing home discharge (OR 6.3, 95 % CI 4.2–9.4). It would be interesting to see if the strength of the observed associations would change using a more traditional operational definition of frailty such as the frailty phenotype (Table 4.1) or the accumulated deficiencies model.

Early translational research has shown that frailty can be easily assessed in the outpatient clinical setting, although there is still debate about the best available measurement methodology [15]. Some authors have attempted to use a questionnaire for this purpose, but results have been mixed when compared to direct functional measurement methods [16]. Numerous assessment tools described elsewhere in this textbook are available to measure functional status components including mobility, gait, cognition, and level of independence with ADLs and IADLs.

Associations Between Frailty and Clinical Outcomes

In the original landmark study by Fried and colleagues, which was used to validate the most commonly used model of frailty, frequently called the "frailty phenotype," the syndrome was found to be an independent predictor of several negative clinical outcomes [1]. Based on longitudinal analysis of 5,317 older adults enrolled in a community-based cardiology health study, frailty was defined by presence of three or more of the characteristics previously described including weight loss, low physical activity levels, self-reported exhaustion, weak hand, and diminished gait speed (Table 4.1). Presence of frailty was predictive of death at 3 and 7 years (both, $p<0.05$). At 84 months of follow-up, mortality in the frail group was 43 %, compared to 23 % in the intermediately frail group and 12 % in the nonfrail group ($p<0.05$). In the bivariate, unadjusted analyses, frailty was also found to be an independent predictor of falls, hospitalization, worsening mobility, and developing ADL disability (all, $p<0.05$). Subjects identified with intermediate frailty, defined as having either one or two of the characteristics components, were found to have intermediate risks of these various clinical outcomes. Overall likelihood of frailty was noted to be higher in women and those in lower socioeconomic categories. The gender differences were in part intrinsic, because older women generally have lower muscle mass compared to men. This may predispose them to more vulnerability with continued aging. This operational definition of frailty, based on these five classic clinical characteristics, has been utilized in a wide array of other research studies. Some of the more recent research on this topic will be summarized in the context of applicability to geriatric urology.

Association of Frailty with General Medical Outcomes

Frailty has been examined as a risk factor for negative clinical outcomes, particularly in older adults. In an analysis from the Women's Health and Aging Study, this operational definition of the frailty phenotype was shown to be an independent predictor of death, institutionalization, and development of disabilities in ADLs and IADLs [17]. The syndrome has also been linked to subsequent development of ADL dependence in a longitudinal study of 749 elderly women [18]. Presence of multiple frailty risk factors was associated with a dose-dependent risk of developing ADL dependence over time. This helps to support overlap and similarities between the classic frailty phenotype and the alternative model of accumulated deficiencies.

In a longitudinal analysis of 754 community dwelling, nondisabled persons over 70 years of age, the five classic characteristics used to define the frailty phenotype (Table 4.1), and other variables were analyzed [19]. Subjects were followed for 6 years. Endpoints included chronic disability, need for long-term nursing home placement, and death. Slow gait speed, unintentional weight loss, and low physical activity levels were statistically predictive of these outcomes (all, $p<0.05$). Slow gait speed was found to be the strongest predictor of chronic disability (HR 2.97, 95 % CI 2.32–3.80) and nursing home placement (HR 3.86, 95 % CI 2.23–6.67). It was also the only identified predictor of injurious falls (HR 2.19, 95 % CI 1.33–3.60). Cognitive impairment was also identified as an important predictor variable in this analysis.

Associations Between Frailty and Surgical Outcomes

A number of studies have looked at postoperative complications in elderly surgical patients as a function of preoperative frailty status. However, to date, examination of these issues in geriatric urology patients has been quite limited [20]. A recent literature review regarding frailty in geriatric surgical patients noted that increasing numbers of older adults, including those with frailty, are undergoing surgical therapy [21]. This highlights the need for surgeons who treat older adults to acquire additional training regarding frailty and its potential risk on clinical outcomes. Exercise, medications, and nutritional support were all identified as variables that could potentially modify frailty in older adults.

Robinson and colleagues sought to examine the utility of several validated measures of frailty, disability, and comorbidity across multiple domains [22]. The cohort included 110 patients 65 years of age or older undergoing major surgery with postoperative intensive care unit (ICU) stays. Mean age was 74 ± 6 years. The primary endpoint of interest was mortality within 6 months after surgery. Sixteen of the 110 patients died in this time frame for a prevalence of 15 %. Preoperative functional dependence for ADLs was the strongest predictor of mortality (OR 13.9, 95 % CI 2.992–65.487). The presence of four or more markers for frailty had a strong sensitivity (81 %) and specificity (86 %) to predict mortality. The authors noted that this type of comprehensive preoperative analysis represents a shift in the usual evaluation methodology for surgeons. Additional research will help to refine use of this analytic paradigm, particularly in elderly patients undergoing either major or minor urologic surgical procedures.

The association between frailty and risk of need for postoperative discharge to nursing home care or other institutional settings has also been examined [23]. A cohort of 223 older adults with a mean age of 73 ± 6 years undergoing major surgery and subsequent intensive care unit (ICU) stays was analyzed. Fourteen frailty characteristics were assessed across six domains including comorbidity burden, functional status, nutrition, cognition, presence of other geriatric syndromes, and extrinsic frailty. Overall, 30 % required discharge institutionalization. Mobility limitations as measured by the up-and-go test and functional dependence for ADLs were identified as the strongest predictive variables. The results appeared to be dose dependent, with accumulation of frailty risk factors more strongly portending need for nursing home placement. A similar study of 594 patients 65 years of age or older undergoing elective surgery showed increased risks of discharge to either nursing homes or assisted living facilities with accumulation of frailty risk factors [24]. Preoperative frailty status was also predictive of increased length of hospital stay and other postoperative complications. Another study of 125 surgical patients aged 70 years or older yielded similar results for length of stay, discharge disposition, and complications [25]. These various studies provide strong evidence on the relationships between frailty and postoperative surgical issues in older adults.

Emergency surgery has long been associated with increased risks of general postoperative complications. A review of the National Surgical Quality Improvement Program (NSQIP) participant use files was conducted to explore issues of frailty in cases requiring emergency rather than elective surgery [26]. A total of 35,334 patients who were 60 years of age or older and underwent emergency general surgical procedures over a 4-year time interval were studied. Frailty was measured as a continuous variable using a modified frailty index. Logistic regression demonstrated that increasing frailty was strongly associated with mortality within 30 days following emergency surgical intervention. Postoperative wound complications and wound infections were also linked to frailty status.

Two recent studies have shown associations between preoperative frailty and subsequent development of postoperative delirium. A prospective study of 63 elderly patients undergoing noncardiac surgery compared a number of variables for development of postoperative delirium [27]. In this study, 16 subjects (25.4 %) developed delirium. There were no significant differences between the groups that did and did not have delirium with regard to age, gender, anesthesia risk category, type of surgery, or change in preoperative and postoperative pain scores. However, frailty score was predictive of delirium (OR 1.84, 95 % CI 1.07–3.1) as was preoperative depression (OR 1.42, 95 % CI 1.06–1.91). Another study of 142 consecutive patients undergoing vascular surgery examined relationships between frailty and delirium [28]. Mean age was 68 ± 11 years, with range from 21 to 87 years. Ten of the 142 subjects developed postoperative delirium for an overall incidence of 7 %. Multiple variables including frailty were associated with this complication, which highlights the multifactorial etiology of delirium. Interestingly, frailty was not associated with an increased length of hospital stay in this study, although this was likely due to a variety of other factors.

Frailty has also been examined as a risk factor for postoperative complications in a number of specific types of surgery, although there has been little research on this in urology. In a small study of 37 elderly women, mean age 73 years old, undergoing gynecologic surgery for treatment of cancer, 16 % were classified as frail, 27 % were intermediately frail, and 57 % were nonfrail [29]. Postoperative complications occurred in 63 % of those with frailty compared to only 24 % of the nonfrail patients ($p = 0.04$). Interestingly, body mass index (BMI) was significantly higher in the frail patients compared to the other two groups ($p = 0.02$). This supports the concept that frailty is not always associated with low BMI. It can occur in overweight and obese patients as well. A similar study examined postoperative complications within 30 days of elective laparoscopic cholecystectomy in a group of 57 patients over 65 years of age (mean 73 ± 8.8 years) [30]. The prevalence of frailty was high at 56.1 %. Postoperative complications occurred in 84.6 % in the frail group compared to 15.4 % of the fit group ($p = 0.023$). Prolonged postoperative hospital stay of more than 2 days was also significantly higher in the frail group ($p = 0.023$). Comprehensive geriatric assessment was felt to be useful in this regard to identify frail patients at increased risk of complications. Mortality and complications were also significantly higher in a cohort of 42 older adults with >10 % burn injuries [31]. Frailty was felt to be a reflection of decreased functional reserve capacity in this study, including the ability to tolerate multiple surgical debridement procedures.

Two studies have examined the risks and clinical outcomes of increased frailty in older adults undergoing colorectal surgical procedures. In a prospective, observational study of 60 geriatric patients, mean age was 75 ± 8 years, and all patients underwent elective colorectal surgical procedures [32]. Prevalence of frailty was 38 %, intermediate frailty 22 %, and 40 % were nonfrail. Risk of mortality could not be adequately assessed in this study as only one subject (2 %) died. However, frailty was associated with both increased rates of institutionalization after discharge ($p < 0.01$) and hospital readmission within 30 days ($p = 0.044$). A similar study at clinical centers in Japan and Singapore examined outcomes in 83 patients with a mean age of 81.5 years (range 75–93 years) [33]. Postoperative complications were significantly more frequent among the 27.7 % of the cohort with underlying frailty (OR 4.03, 95 % CI 1.43–11.64).

Although not a surgical cohort, one recent study has examined the relationship between androgen deprivation therapy (ADT) for prostate cancer in older men and the risk of developing frailty [34]. Using a case–control design, elderly men on ADT were more likely to be obese and demonstrate either frailty or intermediate frailty compared to controls. Falls occurred in 14.3 % of the ADT group and 2.8 % of the controls ($p = 0.02$). This indicates ADT is associated with both frailty and other geriatric syndromes. Future prospective studies will be needed to examine the risks of ADT and frailty progression in elderly men with a history of prostate cancer.

Methods to Optimize Outcomes in Frail Older Surgical Patients

Multiple methods have been examined in an attempt to optimize outcomes for frail older adults undergoing surgery. Comprehensive geriatric assessment (CGA) to improve identification of frailty and those at risk is considered to be an important assessment method.

A study by Harkin and colleagues examined the utility of a geriatric consult service specifically for older adults undergoing surgery [35]. A total of 256 frail elderly patients were enrolled. They underwent a combined total of 311 general surgical procedures including major abdominal or vascular procedures as well as some minor surgeries. Multiple common conditions routinely seen in geriatric patient populations were identified and addressed by the geriatric consult team. These included dementia, delirium, polypharmacy, multiple comorbidities, and diminished nutritional and functional status. A sizeable proportion of procedures were actually performed for what was termed “maintenance care.” This included treatment of pressure ulcers, provision of chronic intravenous access, and feeding or drainage tubes. These researchers found that the comprehensive geriatric assessment provided by the consult team was very useful in this surgical cohort.

Future Research on Frailty

Although the frailty phenotype and other models conceptualizing frailty are extremely useful and widely used in both clinical and translational research, these operational definitions are not yet universally accepted. A very recent report presented the results of a scientific process attempting to develop consensus on this topic [36]. Using a Delphi method, this panel of experts concluded that there was strong value in screening for frailty in older adults. In addition, several conceptual domains considered vital to the clinical and research definitions of frailty were identified. These included the six domains of gait speed, mobility, physical performance, nutritional status, mental health, and cognition. However, it was felt that additional research would be required to generate a fully operational definition of the syndrome of frailty. Similarly, no consensus was reached regarding laboratory biomarkers to use in the definition, or specific paths or procedures for measuring functional status in the six identified core domains.

Conclusions

Frailty is a complex clinical syndrome that occurs frequently in older adults. A variety of risk factors and measureable physiological changes have been identified. Multiple studies in both nonsurgical and surgical patients have linked frailty to negative clinical outcomes in older adults. Additional research will be needed to specifically examine these issues within the framework of geriatric urology. Methods to prevent frailty progression may also prove useful in geriatric patients. The role of interventions among young or middle-aged patients to decrease or prevent frailty remains relatively unexplored. In addition, more work is needed to establish a consensus on the best operational definitions for the condition. This will help to develop additional methods of both assessment and optimization to hopefully improve clinical outcomes for older adults.

References

1. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56A:M146–56.
2. Fried LP, Ferrucci L, Darer J, et al. Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. J Gerontol A Biol Sci Med Sci. 2004;59:255–63.
3. Heppenstall CP, Wilkinson TJ, Hanger HC, Keeling S. Frailty: dominos or deliberation? N Z Med J. 2009;122:42–53.
4. Cohen RR, Lagoo-Deenadayalan SA, Heflin MT, et al. Exploring predictors of complication in older surgical patients: a deficit accumulation index and the Braden Scale. J Am Geriatr Soc. 2012;60:1609–15.
5. Braden BJ, Bergstrom N. Predictive validity of the Braden Scale for pressure sore risk in a nursing home population. Res Nurs Health. 1994;17:459–70.
6. Fumagalli S, Tarantini F, Guarducci L, et al. Atrial fibrillation is a possible marker of frailty in hospitalized patients: results of the GIFA Study. Aging Clin Exp Res. 2010;22:129–33.
7. Xue QL, Fried LP, Glass TA, et al. Life-space constriction, development of frailty, and the competing risk of mortality: the Women's Health and Aging Study I. Am J Epidemiol. 2008;167:240–8.
8. Cappola AR, Xue QL, Fried LP. Multiple hormonal deficiencies in anabolic hormones are found in frail older women: the Women's Health and Aging Studies. J Gerontol A Biol Sci Med Sci. 2009;64A:243–8.
9. Frisoli Jr A, Chaves PH, Ingham SJM, Fried JP. Severe osteopenia and osteoporosis, sarcopenia, and frailty status in community-dwelling older women: results from the Women's Health and Aging Study (WHAS) I. Bone. 2011;48:952–7.
10. Chang SS, Weiss CO, Xue QL, Fried LP. Association between inflammatory-related disease burden and frailty: results from the Women's Health and Aging Studies (WHAS) I and II. Arch Gerontol Geriatr. 2012;54:9–15.
11. Chang SS, Weiss CO, Xue QL, Fried LP. Patterns of comorbid inflammatory diseases in frail older women: the Women's Health and Aging Studies I and II. J Gerontol A Biol Sci Med Sci. 2010;65A:407–13.
12. Bagnall NM, Faiz O, Darzi A, Athanasiou T. What is the utility of preoperative frailty assessment for risk stratification in cardiac surgery? Interact Cardiovasc Thorac Surg. 2013;17(2):398–402. doi:10.1093/icvts/ivt197.
13. Sündermann S, Dademasch A, Praetorius J, et al. Comprehensive assessment of frailty for elderly high-risk patients undergoing cardiac surgery. Eur J Cardiothorac Surg. 2011;39:33–7.
14. Lee DH, Buth KJ, Martin BJ, et al. Frail patients are at increased risk for mortality and prolonged institutional care after cardiac surgery. Circulation. 2010;121:973–8.

15. Kim H, Higgins PA, Canaday DH, et al. Frailty assessment in the geriatric outpatient clinic. Geriatr Gerontol Int. 2013. doi:10.1111/ggi.12057.
16. Matthews M, Lucas A, Boland R, et al. Use of a questionnaire to screen for frailty in the elderly: an exploratory study. Aging Clin Exp Res. 2004;16:34–40.
17. Bandeen-Roche K, Xue QL, Ferrucci L, et al. Phenotype of frailty: characterization in the Women's Health and Aging Studies. J Gerontol A Biol Sci Med Sci. 2006;61A:262–6.
18. Boyd CM, Xue QL, Simpson CF, et al. Frailty, hospitalization, and progression of disability in a cohort of disabled older women. Am J Med. 2005;118:1225–31.
19. Rothman MD, Leo-Summers L, Gill TM. Prognostic significance of potential frailty criteria. J Am Geriatr Soc. 2008;56:2211–6.
20. Brown NA, Zeniloman ME. The impact of frailty in the elderly on the outcome of surgery in the aged. Adv Surg. 2010;44:229–49.
21. Partridge JSL, Harari D, Dhesi JK. Frailty in the older surgical patient: a review. Age Ageing. 2012;41:142–7.
22. Robinson TN, Eiseman B, Wallace JI, et al. Redefining geriatric preoperative assessment using frailty, disability and co-morbidity. Ann Surg. 2009;250:449–55.
23. Robinson TN, Wallace JI, Wu DS, et al. Accumulated frailty characteristics predict postoperative discharge institutionalization in the geriatric patient. J Am Coll Surg. 2011;213:37–44.
24. Makary MA, Segev DL, Pronovost PJ, et al. Frailty as a predictor of surgical outcomes in older patients. J Am Coll Surg. 2010;210:901–8.
25. Dasgupta M, Rolfson DB, Stolee P, et al. Frailty is associated with postoperative complications in older adults with medical problems. Arch Gerontol Geriatr. 2009;48:78–83.
26. Farhat JS, Velanovich V, Falvo AJ, et al. Are the frail destined to fail? Frailty index as predictor of surgical morbidity and mortality in the elderly. J Trauma Acute Care Surg. 2012;72:1526–31.
27. Leung JM, Tsai TL, Sands LP. Preoperative frailty in older surgical patients is associated with early postoperative delirium. Anesth Analg. 2011;112:1199–201.
28. Pol RA, van Leeuwen BL, Wisser L, et al. Standardised frailty indicator as predictor for postoperative delirium after vascular surgery: a prospective cohort study. Eur J Vasc Endovasc Surg. 2011;42:824–30.
29. Courtney-Brooks M, Tellawi AR, Scalici J, et al. Frailty: an outcome predictor for elderly gynecologic oncology patients. Gynecol Oncol. 2012;126:20–4.
30. Lasithiotakis K, Petrakis J, Venianaki M, et al. Frailty predicts outcome of elective laparoscopic cholecystectomy in geriatric patients. Surg Endosc. 2013;27:1144–50.
31. Masud D, Norton S, Smailes S, et al. The use of a frailty scoring system for burns in the elderly. Burns. 2013;39:30–6.
32. Robinson TN, Wu DS, Stiegmann GV, Moss M. Frailty predicts increased hospital and six-month healthcare cost following colorectal surgery in older adults. Am J Surg. 2011;202:511–4.
33. Tan KY, Kawamura YJ, Tokomitsu A, Tang T. Assessment for frailty is useful for predicting morbidity in elderly patients undergoing colorectal cancer resection whose comorbidities are already optimized. Am J Surg. 2012;204:139–43.
34. Bylow K, Hemmerich J, Mohile SG, et al. Obese frailty, physical performance deficits, and falls in older men with biochemical recurrence of prostate cancer on androgen deprivation therapy: a case–control study. Urology. 2011;77:934–40.
35. Hardin RE, Jemtel TL, Senilman ME. Experience with dedicated geriatric surgical consult services: meeting the need for surgery in the frail elderly. Clin Interv Aging. 2009;4:73–80.
36. Rodríguez-Mañas L, Féart C, Mann G, et al. Searching for an operational definition of frailty: a Delphi method based consensus statement. The frailty operative definition-consensus conference project. J Gerontol A Biol Sci Med Sci. 2013;68:62–7.

Medication Use and Polypharmacy in Older Adults

5

Marty L. Eng and James T. Birch Jr.

Introduction

Polypharmacy is a common problem in the clinical management of the older adult. However, the issue of multiple medications is more complex than simply adding up the number of medications being used. In fact, combination therapy may be the standard of care for some chronic conditions commonly experienced by older adults. The key is to regularly assess medication regimens with a mind to identify, assess, resolve, and document potential medication-related problems. In this chapter, we will review the current extent of the polypharmacy problem, describe the risk factors for developing polypharmacy, highlight age-related changes in pharmacokinetics and pharmacodynamics, discuss common classes of drugs used for urological conditions and the influence of age, review some key tools to reduce polypharmacy, and assess outcomes of polypharmacy and other medication-related problems common in geriatrics.

M.L. Eng, PharmD, C.G.P., B.C.P.P., C.D.P., F.A.S.C.P. (✉)
Department of Pharmacy Practice, School of Pharmacy, Cedarville University, 251 N. Main St., Cedarville, OH 45314, USA
e-mail: martyeng@cedarville.edu

J.T. Birch Jr., M.D., M.S.P.H.
Department of Family Medicine, University of Kansas Hospital, 3901 Rainbow Blvd., MS-1005, Kansas City, KS 66160, USA
e-mail: jbirch@kumc.edu

Epidemiology of Polypharmacy

In the USA alone, the prevalence of polypharmacy among older adults ranges from 7.8 % to 69.8 % [1–7]. The prevalence in other countries such as the UK, Netherlands, Denmark, and Germany ranges from 19 % to 90 % [7–23]. The prevalence of polypharmacy seems to differ based on the setting including community dwelling older adults, long-term care or assisted living residents, or hospital inpatients. Irrespective of setting or country, polypharmacy seems to be consistently increasing.

In the USA, prevalence of polypharmacy seems to be increasing recently. In 1996, Lassila et al. reported a polypharmacy prevalence of 10 % in a rural US cohort [24]. In 1999, Fillit et al. reported a prevalence of 15 % polypharmacy in a cross-sectional survey of Medicare patients [25]. Kaufmann et al. reported high polypharmacy use of 44 % in men and 57 % in women over 65 years of age [26]. In the hospital setting, polypharmacy seems to increase during hospitalization but return to pre-admission rates on discharge. One study found about 70 % prevalence of polypharmacy in a hospital cohort of older adults [1]. In summary, polypharmacy is common. It seems to be more prevalent in hospitalized than community-dwelling older adults. Over time, polypharmacy has been increasing and polypharmacy in other countries appears to be comparable to that seen in the USA.

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_5,

Risk Factors for Polypharmacy

Among the studies reviewed, litanies of potential risk factors were reported. In general, risk factors may be categorized as demographic, health status, and access to health care [27]. They include older age, female gender, and higher number of chronic illnesses. Chronic conditions included heart failure, depression, hypertension, anemia, asthma, angina, diverticulosis, osteoarthritis, gout, and diabetes mellitus. In addition, Dwyer et al. found Medicaid use, need of assistance with less than five activities of daily living (ADLs), length of stay in long term care between 3 and 6 months, and smaller, not-for-profit facilities as potential risk factors for polypharmacy [3]. One commentary suggested that clinical guidelines may also be a contributing factor. Risk factors from studies conducted in other countries appear to be similar [8–18].

Difficulty arises in making sense of these data when one considers potential for confounding based on the complexity of the patient cohort. For example, heart failure was associated with polypharmacy. However, this is not surprising given the standard treatment regimen will contain more than three medications from the start. On the other hand, older adults are frequently started on short-term medications which are continued indefinitely, considered unnecessary upon subsequent review and should be stopped. These factors form the basis of the STOPP Criteria [28] that will be discussed in a later section and further reinforces the fact that the "number of medications" alone is not adequate to determine risk–benefit or to define polypharmacy. It should be kept in mind that the main study designs are survey and observational cohorts. Therefore, interpretation is subject to those inherent limitations. In other words, these data suggest associations and not cause and effect.

Defining Polypharmacy and Medication-Related Problems

There is no universally accepted definition of polypharmacy. This creates difficulty with discussion and comparative research on the topic. The simplest definition of polypharmacy is the concomitant use of two or more medications. Usually medication use is implied as chronic but acute use of medications may also lead to medication-related problems. However, as mentioned above, there may be times when multiple medications used concomitantly may be appropriate in the older adult. The word *polypharmacy* also has associated negative connotations.

Among the studies cited thus far, a common definition has been the use of five or more medications. Excessive polypharmacy is sometimes defined as the use of nine or more medications. While polypharmacy has been associated with adverse outcomes as discussed in the previous section, it should also be kept in mind that use of more than one medication may be appropriate for select patients according to standards of care. What is less clear is how well those guidelines fit the older adult population. Nevertheless, it is crucial to recognize that there are principles and tools to help reduce the adverse outcomes of inappropriate polypharmacy. This will be the focus of the following sections.

Another definition used less often, but perhaps more accurately, is "medication use without clinical indication." This highlights another dimension of the literature that addresses potentially inappropriate medication use in older adults. The limitations of the definitions of polypharmacy should be kept in mind when interpreting the literature and attempting to apply study results to patients. Viktil et al. studied a Norwegian cohort to determine if defining a cutoff for the number of medications would be useful in identifying medication-related problems. No difference was seen between users of five or more medications compared with less than five medications in ability to identify risk for medication-related problems [29]. Other factors may need to be considered when assessing drug regimens in older adults. They include changes with age in pharmacokinetics, pharmacodynamics, renal function, concomitant illness and chronic disease. Tobi et al. found that the definition of polypharmacy used in a study resulted in differences in prevalence when the definition changed [30]. This underscores the need for some consensus on the definition of polypharmacy. It also highlights the necessity for the definition to have an element of functionality. The variations in definition should be kept in mind when reviewing the polypharmacy literature.

Outcomes

The bulk of the literature supports an association of polypharmacy with negative outcomes. These outcomes include increases in malnutrition, adverse drug events, accidental falls, and use of potentially inappropriate medications [5, 6, 31, 32]. Again, this is similar to what has been published in other countries [16, 19–22]. Additionally, a study from Bosnia suggested an increase in cognitive decline [21], and a study from Finland suggested an increase in mortality [23].

While much has been done to describe the prevalence, risk factors, and outcomes of polypharmacy (Table 5.1), the literature is conflicted regarding the magnitude of benefit of interventions (Table 5.2) targeted at reducing polypharmacy. Interventions have ranged from individual application of criteria to system-based interventions using electronic medical records. It seems that the "best practice" approach is to be judicious when prescribing new medications and vigilant in monitoring and documenting the benefits and harms of currently administered medications in older adult patients by performing regular and consistent medication reconciliation.

Key Concepts

- Polypharmacy is the use of more than one medication concomitantly. Typically, studies define it as use of more than five medications.
- While polypharmacy has been associated with negative and positive outcomes, individualized risk–benefit must be considered.
- The appropriate use is more important to consider than number of medications alone. Is the drug working? Document the evidence. Is it still needed? Document the continued need or consider discontinuation.

Table 5.1 Prevalence, risk factors, and outcomes associated with polypharmacy in the USA

References	Setting	Polypharmacy estimate (PolyRX = ≥5 meds) (Excessive PolyRX ≥9 meds)	Risk factors for polypharmacy
Gallagher [1]	Hospital	69.8 % control 65.8 % intervention	N/A
Tamura [2]	Nursing home	46.2 % excessive polyRX	N/A
Dwyer [3]	Nursing home	60.3 % (use ≤8 meds) 39.7 % (use ≥9 meds)	Women, white, Medicaid, >3 comorbidities, assistance with <5 ADLs, LOS 3–6 months, smaller, not-for profit facilities
Loya [4]	Community US–Mexico border	38.5 %	Living on US side of the border

References	Setting	Polypharmacy estimate (≥5 meds)	Outcomes/consequences
Heuberger [5]	Community	51.1 %	Increased malnutrition
Bourgeois [6]	Community and emergency room (ED)	15.4 % overall 16 % community 12.4 % ED	Increased adverse drug events
Huang [33]	Community, diabetes	14.2 % overall (≥7 meds)	Increased incidence of falls
Lau [34]	Community	7.8 % (≥9 meds)	Increased potentially inappropriate meds (Beers Criteria)
Buck [32]	Community	46.4–57.6 % (≥6 meds)	Increased potentially inappropriate meds (Beers Criteria)

Beers Criteria [35]

Table 5.2 Published interventions used to reduce polypharmacy in the USA

References	PolyRX Prevalence	Intervention	Outcome
Hamilton [36]	N/A	STOPP criteria	PIM identified better than Beers Criteria in older hospitalized adults
Gallagher [1]	69.8 % control 65.8 % intervention	START/STOPP criteria	Improved med use in hospital
Tamura [2]	46.2 % excessive polypharmacy	Geriatrician fellows review	Decreased overall number of meds, scheduled meds, PRN, high risk, contraindicated, potential drug interactions in nursing home residents
Trygstad [37]	Not stated	Pharmacist prospective and retrospective reviews: Beers Criteria, prescription advantage list, clinical initiatives	Decreased drug cost per month per resident, lower risk hospitalization
Flood [38]	32 % (≥9 meds)	Interdisciplinary team on oncology acute care unit in hospital	Not assessed
Weber [39]	40 % (≥8 meds)	Electronic medical record intervention	Decreased number psych meds and falls
Garfinkel [40]		Geropalliative approach	Decreased mortality Decreased referral rate to acute care facilities

- In the absence of clinical trial evidence, the principles of pharmacokinetics and pharmacodynamics in aging should be applied. The most significant to urology is probably decreased renal function and increased sensitivity to anticholinergic effects.
- There are several tools that could be used such as the Beers Criteria [35], Medication Appropriateness Index [41], and the Anticholinergic Burden Scale [42] to reduce the negative outcomes associated with polypharmacy.

Pharmacokinetic and Pharmacodynamic Changes with Age

Pharmacokinetics (Table 5.3)

Absorption

Aging is difficult to study. Many studies of age-related changes have demonstrated differences from younger populations but the clinical importance is often less well known. With age, the skin loses elasticity and barrier function declines. Motility decreases in the gastrointestinal tract which clinically may cause a delay in onset of effect and a prolonged duration of effect of medications in general. Bioavailability via intestinal absorption, however, is preserved.

Distribution

With age, albumin may decline steadily. However alterations in albumin are usually important only for acute changes with the use of highly protein-bound drugs. Because aging is a chronic occurrence, most changes in albumin with age will not be clinically important because free drug will be eliminated over five half-lives. There is conflicting information regarding changes in alpha-acid glycoprotein. This may be less important than albumin changes as most drugs are bound to albumin. There is an increase in body fat to lean body mass largely due to declines in lean body mass. As a result, volume of distribution of fat-soluble drugs may be expected to be larger which would prolong the time to effect and time to elimination. Examples of fat-soluble medications include diazepam and propranolol. On the other hand, water-soluble drugs may exhibit effects consistent with smaller volumes of distribution including quicker onset and shorter activity. Examples of water soluble medications include digoxin, lithium, and aminoglycosides.

Table 5.3 Pharmacokinetic changes with aging

Pharmacokinetic parameter	Age-related change	Potential clinical effect	Examples
Absorption	Thinner epidermis	Higher risk of skin tears	
Absorption	Delayed gastric emptying	Delayed onset of effect	
Absorption	Decreased sphlanchnic blood flow	Delayed onset of effect	
Absorption	Decreased surface area	Delayed onset of effect	
Absorption	Slowed gastrointestinal motility	Delayed onset of effect	
Distribution	Increased body fat	Volume of distribution for fat soluble drugs increases delaying effects and elimination	Benzodiazepines
Distribution	Decreased muscle mass	Volume of distribution for water soluble drugs decreases shortening effects and time to elimination	Digoxin, lithium, aminoglycosides
Distribution	Decreased albumin	Effects only seen with acute changes in protein with highly protein bound (>90 %) drugs. Otherwise, not usually clinically evident	Warfarin, phenytoin
Distribution	Increased alpha acid glycoprotein	Reduced free concentration of drugs bound to this protein	Lidocaine, propranolol
Metabolism	Decreased liver blood flow	Low potential for clinically evident effect	
Metabolism	Decreased liver mass	Low potential for clinically evident effect	
Metabolism	Phase I reactions decreased	Longer half-life of phase I metabolized drugs	Benzodiazepines such as diazepam, clonazepam, flurazepam, alprazolam
Elimination	Decreased renal function	Accumulation of renally eliminated drugs	Any renally eliminated med: digoxin, gabapentin, antibiotics

Compiled and adapted from Klotz [43], Dharmarajan [44], Kaeslti [45]

Table 5.4 Pharmacodynamic changes with aging

– Loss of baroreceptor response (increasing risk for orthostatic hypotension)
– Decreased response to beta blockers
– Increased response to CNS agents (acetylcholine, dopamine, GABA)

Metabolism

There is variability in the literature regarding the influence of age on the metabolism of individual substances. Changes with age in cytochrome P450 (CYP 450) metabolism have been noted but information is inconsistent on a population level. Usually, CYP 450 activity may not be clinically evident. However, the presence of polypharmacy may either increase the induction or inhibition of metabolic enzymes and warrants vigilance both with medication administration prior to starting new therapies and periodically thereafter. One metabolic characteristic that has been consistently noted is reduced phase I metabolism. Phase I metabolism includes oxidation. These processes occur primarily in the liver. However, phase II metabolism is largely unchanged with age and typically occurs in the kidneys. A classic example of the importance of this change is with benzodiazepines. All of the benzodiazepines except lorazepam, oxazepam, and temazepam are phase I metabolized. Hence, most geriatric recommendations include these three medication options when benzodiazepine use cannot be avoided. Use of other benzodiazepines is likely subject to more variability in clinical response and predictability is less certain. However, with involvement of the phase I pathway, the expected clinical response is prolonged activity because of decreased metabolism.

Table 5.5 Two commonly used estimations for renal function [33]

Estimation	Calculation	Use	Limitations
Cockcroft–Gault [46]	$\frac{(140-age)*Ideal\,Body\,Weight}{SCr \times 72}$ $[\times 0.85\,if\ woman]$	Chronic estimation Age 18 years or older	Extreme overweight requires adjustment Low SCr (<0.7) assume 0.7 mg/dL in calculation May underestimate
Modified Dietary Renal Disease (MDRD) Estimation [47]	$186 \times \text{SCr} \times \text{age} \times (0.742\ \text{women}) \times (1.210\ \text{if African American})$	Chronic estimation Age 18 years or older	Has undergone many revisions. Most drug references use C-G and use of MDRD would result in mis-dosing patients

SCr = serum creatinine (mg/dL)

Table 5.6 Renal drugs guideline [48]

Must be renally adjusted	Avoid use CrCl <30 mL/min	No consensus on dosing
– Acyclovir	– Chlorpropamide	– Allopurinol
– Amantadine	– Colchicine	– Atenolol
– Ciprofloxacin	– Cotrimoxazole	– Cetirizine
– Gabapentin (for pain)	– Glyburide	– Cimetidine
– Memantine	– Meperidine	– Famciclovir
– Nitrofurantoin	– Propoxyphene	– Famotidine
– Probenecid	– Spironolactone	– Fexofenadine
– Ranitidine	– Triamterene	– Hydrochlorothiazide
– Rimantidine		– Metformin
– Valacyclovir		– Metocloproamide
		– Sotalol (for atrial fibrillation)
		– Topiramate (for epilepsy)

Elimination

Elimination may occur through the gastrointestinal tract or via urination after filtration by the kidneys. Changes in bowels with age may affect absorption, as previously stated. However, these changes have not been noted to alter elimination of medications or their metabolites. On the other hand, kidney function has been consistently noted to decline steadily with age. The estimated rate of decline is 10 mL/min/decade of life starting after age 40 years. This decline in function may be worsened by other common chronic diseases such as hypertension and diabetes. This makes estimation of renal function essential in avoiding possible adverse outcomes due to inappropriate dosing by failure to factor in estimated renal function. There are several ways to estimate renal function. Each method has its own limitations. An in-depth comparison of these tools is beyond the scope of this chapter. However, here are a few key pearls:

- Estimations are not equal to one another.
- Estimations do not replace clinical judgment.
- Estimations have limitations that should be considered when dosing medications.
- Product labeling has traditionally been based on the Cockcroft–Gault Estimation [46] of creatinine clearance.

Therefore, estimations by other methods do not correlate with the available product labeling. This is changing over time and the clinician should determine what estimation the product labeling was based upon before applying this information to a particular patient (Table 5.5).

A recent consensus panel of experts was convened to review commonly used medications in older adults that should be renally dosed based upon the patient's creatinine clearance using Cockcroft–Gault estimation [46]. They appear in Table 5.6. The first two columns contain medications that the panel recommended to be renally dosed. The additional columns contain medications that simply should be avoided when estimated renal function falls below 30 mL/min and there were a number of medications for which the panel could not come to a consensus.

Pharmacodynamics (Table 5.4)

Acetylcholine

Due to declines in the acetylcholine system with age, older adults consistently present with higher sensitivity to anticholinergic medications. Recently, attention has been turned to explore the concept of anticholinergic burden [42]. This concept will be discussed in more depth in a later section in this chapter. The basic idea is that many medications have some anticholinergic effect and that given together they may exert more pronounced side effects than normally expected.

Baroreceptors

Baroreceptor response declines with age. This predisposes older adults to orthostatic hypotension and falls. This is especially true in the presence of medications that may exert alpha-blocking activity or other antihypertensive mechanisms. In addition, in some clinical conditions such as Parkinson's disease, there might be even more sensitivity.

Dopamine

Dopamine receptors seem to be more sensitive to antagonism. This results in more Parkinson-like symptoms with the use of medications such as metoclopramide which may not have the same risk in younger adults. Another class of medications that older adults would be susceptible to are the antipsychotics. Guidelines in older adults typically warn against the use of conventional antipsychotics in favor of atypical antipsychotics. Even still, because of the risk of stroke and death in older adults, use of atypical antipsychotics should be reserved for the most severe of cases which do not respond to nonpharmacologic interventions. These medications should be used at the lowest effective dose for the shortest possible duration. Monitoring for effect and toxicity should be frequent and well documented.

Alpha Receptors

While newer alpha blockers used for benign prostatic hypertrophy are pharmacologically more specific and have less incidence of hypotension in clinical trials, it must be remembered that these studies were conducted in healthier, younger patients, typically in their upper 50s. Older adults are often taking more complex combinations of medications with antihypertensive potential and have multiple chronic diseases that may also add to an orthostatic outcome.

Assessing Polypharmacy

Drug Induced Causes

Acetylcholinesterase Inhibitors

In postmarketing studies, use of cholinesterase inhibitors for cognitive impairment in dementia patients has been associated with subsequent initiation of anticholinergic agents for urinary incontinence. Gill et al. reported a HR of 1.55 (1.39–1.72) for this association [49]. Later, a prospective cohort showed a prevalence of 10.6 % where oxybutynin or tolterodine was prescribed after being given an acetylcholinesterase inhibitor [49]. This subsequent anticholinergic use was associated with faster decline in activities of daily living when compared to those who did not start an anticholinergic agent. Cognitive function did not seem to be affected. Most recently, Boudreau reported 35 % of acetylcholinesterase inhibitor users receiving concomitant anticholinergic agents based on retrospective database information collected between 2000 and 2007 [50]. All of these data bring attention to an important clinical dilemma. Currently, it seems that the best approach would be to use the least number of medications to manage either cognitive impairment or urinary incontinence. However, this risk–benefit needs to be explored further and discussed openly and regularly with patient and/or caregivers before initiation of therapy.

Opioid Analgesics

While the pharmacology of opioid analgesics suggests the potential to cause urinary retention and thus overflow incontinence, there is a lack of randomized studies to elucidate the clinical importance of this problem outside of the postoperative setting. However, within the postoperative setting, irrespective of age, there remains an increased risk of developing urinary retention [51].

Anticholinergic Burden

There is growing interest in the concept of anticholinergic burden. An assessment instrument has been developed and is widely used to estimate the degree of burden associated with use of multiple medications that have anticholinergic properties [42]. One study suggested that 47 % of an older adult cohort received medications with possible anticholinergic activity [52]. This was associated with higher 2-year mortality OR 1.56 (95 % CI = 1.36–1.79) and underscores the need to carefully consider risk versus benefits of such agents with utilization for the shortest amount of time necessary. Also, in the presence of polypharmacy, concomitant use of other medications with lesser anticholinergic activity may not just be additive. Addition of a moderately anticholinergic medication in this case could lead to an exponential rise in the overall "burden." The concept of anticholinergic burden needs further investigation in the general older adult population. However, there are subgroups that have shown consistent vulnerability to anticholinergic cognitive decline. These include patients with dementia, Parkinson's disease, mild cognitive impairment, age-associated memory impairment, and schizophrenia [53]. In these populations in particular, it may be quite important to pay particular attention to anticholinergic burden.

Outcomes of Anticholinergic Use

Whether and to what degree anticholinergics used in the treatment of urinary incontinence contribute to cognitive decline is a controversial issue. In 2009, Campbell et al. performed a systematic review of the evidence regarding the associations of anticholinergic medications use with cognitive function [54]. Out of 27 studies, they found that all but two suggested an association between the anticholinergic activity of medications and either delirium, cognitive impairment, or incident dementia.

Another study by Carriere et al. was completed in a French cohort to evaluate the risk for cognitive decline and incident dementia [55]. Use of anticholinergic medications occurred in 7.5 % of the cohort with 1.3 % representing those used for urinary incontinence. In women, verbal fluency declined but not global cognitive functioning. In men, there was a decline in visual memory but not executive function. The risk of incident dementia over 4 years was demonstrated by a HR of 1.65 (1.00–2.73) with continuous use but was not increased when these medications were discontinued (HR 1.28; 95 % CI = 0.59–2.76). Limitations in these data include self-reported medication use and high dropout rate which limits the ability to generalize these results.

Campbell et al. studied community-dwelling African Americans over the age of 70 years with intact cognitive function at baseline who had high use of medications with potential anticholinergic activity over 6 years (53 %) and moderate prevalence of use of medications with definite anticholinergic effects (11 %) [56]. Use of definite anticholinergic medications in this study increased the risk for cognitive impairment with an OR 1.46 (95 % CI = 1.07–1.99; $p = 0.02$). However, the use of medications with possible anticholinergic effects did not reach clinical significance.

A subsequent study by Campbell et al. confirmed an incident delirium rate of 22 % but anticholinergic drug use was not increased despite 57 % use of at least one possible anticholinergic medication and 28 % use of at least one definite anticholinergic medication in an urban hospital cohort [57]. Possible reasons that a difference was not seen were mostly systematic and included low baseline risk, possible underreporting, adjustments for known risk factors for delirium, and medication use based on medication orders and not actual administration of medication [41].

Lastly, Fox et al. used the anticholinergic cognitive burden scale and the Mini Mental State Exam (MMSE) to determine whether use of medications with anticholinergic activity increases

Table 5.7 Levels of anticholinergic drug risks

Low	Moderate	High
Citalopram	Nortriptyline	Amitriptyline
Escitalopram	Paroxetine	Doxepin
Fluoxetine	Diphenhydramine	Clozapine
Mirtazapine	Chlorpromazine	Thioridazine
Quetiapine	Olanzapine	Atropine
Temazepam	Oxybutynin (ER)	Dicyclomine
Ranitidine	Tolteridine	Hyocyamine
Lithium	Desipramine	Tolterodine
	Meperidine	Diphenhydramine Oxybutynin Imipramine Meclizine Hydroxyzine Chlorpheniramine Brompheniramine Propantheline Darifenacin Clemastine Flavoxate Orphenadrine Trimipramine

Carnahan [42], Chew [59], Rudolph [52]

risk of cognitive impairment in community-dwelling older adults and hospitalized older adults over an interval of 2 years [58]. In 13,004 older adults, they found 47 % used a medication with anticholinergic activity. There was a 0.33 point decline in MMSE with the use of medications with definite anticholinergic activity and a 0.02 point decline with the use of medication with possible anticholinergic activity. Two-year mortality, however, was increased in both use of definite anticholinergic medications OR 1.68 (95 % CI = 1.30–2.16; $p < 0.01$) and use of possible anticholinergic medications OR 1.56 (95 % CI = 1.36–1.79; $p < 0.001$). Most patients (65 %) were normal at baseline. Only 10 % had moderate-severe cognitive impairment and 25 % had mild-moderate cognitive impairment at baseline.

In summary, while there is some conflicting evidence regarding the effects of anticholinergic medications in older adults, the majority of the literature suggests an overall negative effect of anticholinergic medication use in older adults. It is less clear how individual anticholinergic medications fit in this larger context. Strength of anticholinergic activity and measures of anticholinergic burden may help until these conflicts are resolved. Table 5.7 presents commonly used medications in older adults and estimated severity of anticholinergic influence. Care should be taken to avoid use of stronger anticholinergics in older adults when possible and the potential anticholinergic load should be kept in mind when considering the addition of anticholinergic medications with possibly weaker effects.

Case Study

A 75-year-old man presents to the outpatient urology clinic with complaints of urinary incontinence. He wakes up three times a night to urinate. He has had three falls without injury in the last 3 months. His past medical history consists of mild cognitive impairment, Parkinson's disease, benign prostatic hyperplasia, depression, osteoarthritis, hypertension, and congestive heart failure. He currently lives with his wife in their own home. He is independent in his activities of daily living and instrumental activities of daily living.

His current medications include:

- rivastigmine 3 mg PO BID
- levodopa/carbidopa 25/100 mg PO QID,
- ropinirole 1 mg PO TID,
- citalopram 10 mg PO daily,
- hydrocodone/acetaminophen 5 mg/325 mg PO Q6 hours PRN pain,
- lisinopril 10 mg PO daily,
- digoxin 0.250 mg PO daily,
- furosemide 20 mg PO daily,
- metoprolol 50 mg PO BID,
- acetaminophen/diphenhydramine 500 mg/25 mg 2 tablets PO HS for sleep.

(continued)

(continued)

Questions for Consideration

- What risk factors for polypharmacy are present in this patient's history?
- Which medications are potentially inappropriate based on the Beer's Criteria?
- Which medications posed the most risk for urologic problems?
- What pharmacokinetic and pharmacodynamic changes with age may alter response to medications that he is taking?
- What other potential medication-related problems may be present given the information presented in this case study?

The Prescribing Cascade

Geriatric patients, unfortunately, present to clinicians with a multitude of symptoms and functional impairments. Many clinicians act in haste to prescribe symptomatic relief and provide comfort for the patient with prescription medication rather than facilitating and initiating the use of nonmedicinal therapies for symptom management. In addition to creating another risk for polypharmacy, hasteful drug treatment of the multisymptomatic patient also unnecessarily exposes older adults to the sequelae of the "*prescribing cascade* [60]." This is a model of prescribing behavior wherein the physician misinterprets an adverse drug reaction as being a symptom of a new or unrelated medical problem which results in the inappropriate prescribing of a second drug [61]. The initiation of cholinesterase inhibitors for the treatment of dementia is very common in older adults and patients receiving a cholinesterase inhibitor are statistically more likely to be prescribed a variety of anticholinergic medications [62]. To complicate matters further, urinary incontinence is very common in frail older adults and is common occurrence in patients with advancing dementia and functional decline. Prescribing anticholinergic drugs for this urinary problem can aggravate or precipitate delirium, gait disturbances, falls, and exacerbate functional decline [49].

Urinary dysfunction is one of the most common problems in the geriatric population, especially among nursing home residents where the prevalence can be 50 % or more compared to 30 % in community-dwelling older adults [2]. Incontinence is the predominant finding and hallmark symptom involved in most of the lower urinary tract disorders [2, 3]. Additional voiding symptoms include burning, frequency, a sensation of incomplete emptying, and hesitancy or difficulty with initiating the flow of urine [3]. Overactive bladder (OAB) is also common and consists of the reported symptoms of urinary frequency and urgency. OAB can occur with or without incontinence and is of equal incidence in men and women with cancer, diabetes, congestive heart failure, or neurogenic disorders [2]. Contrary to popular belief, these problems are not a normal part of aging. The causes are frequently multifactorial and can be related to many overlapping medical conditions [3]. Unfortunately, many older adults do not receive the appropriate types of evaluation for these disorders and will invariably be prescribed anticholinergic medications empirically. The use of these drugs in this setting provides an example of a common and important prescribing cascade [61].

There are a plethora of other drugs and drug classes that can cause incontinence. Healthcare providers who prescribe medications should be mindful of the potential for deleterious effects to the older adult by lack of awareness of this phenomenon. Treatment options for voiding disorders will not be covered in this section but are included in the chapter on nonsurgical management of urinary incontinence (Chap. 11).

Urinary incontinence (UI) is defined as the involuntary loss of urine. There are four major categories of UI [62]:

- Stress incontinence
- Urge incontinence
- Overflow incontinence
- Functional incontinence

In addition, many older adults experience mixed urinary incontinence with more than one of these four categories occurring simultaneously.

The most common combination of mixed incontinence includes urge and stress incontinence.

Urologic referral is always appropriate for symptoms that are poorly managed or fail to respond to standard therapy. Underlying conditions such as delirium, urinary tract infection, or fecal impaction can lead to transient urinary incontinence [62, 63]. Potential pharmacologic causes of urinary incontinence should be considered by all urologists and other healthcare providers involved in the active evaluation of elderly patients who present with urinary dysfunction of all types.

Urinary Incontinence and Urinary Frequency

Stress Incontinence

The most common pharmacologic agents that can cause stress incontinence are the alpha-adrenergic antagonists including doxazosin, prazosin, tamsulosin, terazosin, and alfuzosin. Women are especially susceptible to UI when taking these alpha blockers [64]. The mechanism is primarily via the bladder sphincter relaxation that occurs with alpha blockade thus permitting leakage of urine [65]. In addition, data from the Women's Health Initiative Study revealed that systemic estrogen replacement can increase the risk of symptomatic stress UI in women [66].

Urge Incontinence

Diuretics

Diuretic medications cause urinary frequency by their basic pharmacodynamic nature. Any diuretic agent can precipitate or aggravate urge incontinence (UI). This is due to the high urine flow from the kidneys which results in frequent detrusor contractions.

In addition to UI, the OAB syndrome is known to be quite common in older adults and has negative impacts on quality of life [67]. Symptoms of OAB include urinary urgency, urinary frequency, nocturia, and/or urge incontinence singularly or in combination. Additionally, the use of diuretic therapy increases in older age for treatment of chronic conditions such as hypertension and heart failure [67]. Diuretics can aggravate or precipitate urinary frequency and in some patients might cause urinary urgency and UI. The use of loop diuretics seems to have a stronger association with OAB than non-loop diuretics [67].

The antineoplastic agents cyclophosphamide and iphosphamide are known to cause hemorrhagic and non-hemorrhagic cystitis due to the effects of the metabolite acrolein, with subsequent irritative urinary symptoms of urgency, frequency, and dysuria [64]. Simultaneous administration of MESNA (2-mercaptoethane sulfonate sodium) has been shown to reduce this risk by binding acrolein in urine and reducing the contact of this irritant with the bladder epithelium.

Caffeine

Caffeine has often been identified as a cause of urinary frequency and urge incontinence due to both its diuretic effect and direct irritant effects on bladder epithelium. It also acts by increasing the velocity of smooth muscle contraction and detrusor pressure thus increasing the probability of involuntary loss of urine [68, 69]. A prospective cohort study by Jura et al. suggests that the symptoms associated with caffeine more likely occur among patients with high consumption of caffeine (>300 mg/day; ≥4 cups of coffee or 10 cups/ cans of tea or soda) [68].

However, a study published in May 2012 by Townsend et al. concluded that there was no statistically significant progression of UI symptoms in women who increase or decrease their caffeine intake over 2 years. Limitations identified in the study, however, included the fact that the conclusions were based on self-reported symptoms by study participants which were not verified by a physician. Treatment for incontinence was also not assessed or considered during the data collection [69]. Seaman et al. reported conflicting data that caffeine did not appear to influence urge urinary incontinence [70]. Clearly, more research is needed to clarify the effect of caffeine on UI. Until more is known, reduction or elimination of caffeine intake will likely continue to be recommended by urologists to reduce the potential detrusor irritability, modify the known diuretic effect of caffeine, and thus improve urinary frequency.

Sedative Hypnotics and Alcohol

Sedative hypnotics and alcohol can contribute to urge incontinence by the common mechanism of central inhibition of micturition [65]. Alcohol additionally has a diuretic effect by the mechanism of reducing output of antidiuretic hormone in the brain.

Overflow Incontinence

Overdistention of the urinary bladder occurs either due to the decreased contractility of the detrusor muscle or a bladder outlet obstruction [62]. It can easily be diagnosed with the finding of high post-void residual volume. The large amount of urine stored in the bladder subsequently causes leakage or patients present with symptoms of hesitancy, decreased caliber of the urinary stream or post-void dribbling, and a sense of incomplete emptying [62]. BPH, diabetes, pelvic trauma, pelvic surgery, spinal cord injuries, and degenerative neurologic disorders are common causes of overflow incontinence (OI). However, the urologist should be acquainted with the medications or therapeutic classes that can cause or contribute to OI [65]. Antidepressant medications, particularly the tricyclics, as well as antipsychotics, sedative hypnotics, and antihistamines have varying degrees of anticholinergic properties [65]. They can be associated with OI by decreasing bladder contractions. Narcotic analgesics, alcohol, other central nervous system depressants, and calcium channel blockers can precipitate OI via the same physiologic mechanism.

The alpha-adrenergic agonists and beta-adrenergic blockers cause bladder sphincter contraction with subsequent obstruction to the outflow of urine [65].

Urinary Retention

Urinary retention (UR) is the acute or chronic impairment of the ability to empty the bladder [62, 71]. Acute retention is often sudden and painful [62]. The bladder is unable to empty even though it is full. Chronic retention is usually not painful and is associated with increased residual urine [62]. The causes for UR are multifactorial. Medications are a very common cause for UR. However, there are other predisposing factors such as BPH, UTI, neurogenic bladder dysfunction, bedrest or recumbency, constipation, and being in an unfamiliar environment, which alone or in combination do contribute to UR and increase susceptibility to its occurrence by medications.

Table 5.8 Medications that can contribute to urinary retention (UR) in older adults

Analgesics
• Opioids and opioid analogs
• Carbamazepine
Antiarrhythmics
• Dispyramide
• Procainamide
• Quinidine
• Flecainide
Antispasmodics
• Hyoscine butylbromide (scopolamine)
• Dantrolene
Antihypertensives
• Hydralazine
• Nifedipine
Antiparkinsonian
• Amantadine
• Benztropine
• Levodopa
• Bromocriptine
• Dopamine agonists
• Orphenadrine
• Procyclidine
Antipsychotics
• Haloperidol
• Chlorpromazine
• Fluphenazine
• Prochlorperazine
• Clozapine
• Risperidone
• Ziprasidone
Bronchodilators
• Ipratropium
• Oxitropium
• Tiotropium
• Theophylline
Hormonal agents
• Estrogen
• Progesterone
• Testosterone
• Gonadotropin-releasing hormone

(continued)

Table 5.8 (continued)

Muscle relaxants • Baclofen • Cyclobenzaprine • Diazepam
Mydriatic eyedrops • Atropine • Cyclopentolate
Sympathomimetics • Phenylephrine • Pseudoephedrine
Over-the-counter • NSAIDs • Cough and cold preparations
Others • Tricyclic antidepressants • Carbamazepine • Opioid analgesics • Anesthetic agents • Fluoxetine (when used in combination with other SSRIs and/or benzodiazepines) • Citalopram (when used in combination with aripiprazole) • Reboxetine
Recreational drugs • Ecstasy
Topical agents • Imiquimod 5 % cream (for genital warts) • Isotretinoin 1 mg/kg for 3 months (for severe acne)

Any medication with anticholinergic properties can precipitate UR. Nonsteroidal anti-inflammatory drugs may contribute via the inhibition of detrusor muscle contraction which is mediated by prostaglandins [62]. In the postoperative period for hip arthroplasty, the incidence of UR can be as high as 78 % [62]. In non-elderly patients, the incidence of UR in the postoperative period can vary between 6 and 50 % [71]. Postoperative pain, bladder instrumentation, anesthetic technique, the type of pharmacologic agent used for inducing anesthesia, medications given intraoperatively, and large volumes of intravenous fluids administered during the perioperative period can singularly or collectively contribute to the development of UR after surgery [51, 62, 71]. In one study, urinary retention seemed to occur in the highest frequency for patients receiving epidural analgesia [72]. The incidence of UR associated with outpatient surgery is likely procedure dependent with hernia or anal surgery being associated with the highest risk [51]. Narcotics can contribute to UR by two mechanisms. They reduce detrusor contractility and increase tone in the bladder neck and if constipation occurs, urinary retention can result.

Additional drug classes and names of medications that can precipitate UR include but are not limited to those listed in Table 5.8: [62, 64, 71].

Recommendations

How does the urologist approach the elderly patient who presents with voiding dysfunction? When considering voiding disorders in the older adult, it is very important to obtain a targeted basic history from the patient with bothersome symptoms or his/her caregiver. A detailed medication history including both prescription medications, over-the-counter medications, and any herbal medications or supplements is imperative. This step is extremely important because medication side effects are known to cause many different voiding problems. It is also one of the ACOVE-3 quality indicators for the screening and care of urinary incontinence in vulnerable elders (Tables 5.9 and 5.10) [62, 73, 74].

When prescribing medical therapy for voiding disorders, identifying goals of care is of primary importance. Attempting to measure the impact of urological symptoms on patient's quality of life can facilitate this process. Potential adverse reactions, drug–drug interactions, and drug–disease interactions should be reviewed and discussed. There are many electronic tools available that make these assessments quick and easy. Sometimes more frail elderly patients and their family members may choose not to take prescribed medications considering the risk of experiencing side effects of medications. Another important step is to use the Beers Criteria for prescribing medications in older adults. The list of medications that are deemed potentially inappropriate for use in older adults was updated in 2012 with collaboration of the American Geriatrics Society [35]. The Beers Criteria contains invaluable information on medication use in older adults. It should not replace professional

Table 5.9 Quality indicators for medication use in vulnerable elders

1.	Medication list: up to date, accessible, includes non-RX meds
2.	Periodic drug review: at least annually
3.	Clearly defined indication
4.	Patient education
5.	Documentation of response to all therapy
6.	If receiving warfarin: education on diet, drug interactions, risk–benefit
7.	Monitoring warfarin
8.	ACE inhibitor: monitor creatinine and potassium
9.	Diuretics: monitor electrolytes
10.	Avoid propoxyphene
11.	Avoid high dose benzodiazepine (> 1 month use)
12.	Avoid strong anticholingergics whenever possible
13.	Avoid barbiturates
14.	Avoid meperidine
15.	Avoid ketorolac for > 5days
16.	Avoid skeletal muscle relaxants
17.	Avoid ticlopidine
18.	NSAIDs document gastrointestinal bleeding risk
19.	Tolteridine better tolerated than oxybutynin

Adapted from data in [73]

judgment, nor should it be the sole basis of prescribing for an individual patient [76]. Taking that approach is at odds with the very principles of geriatric medicine which strongly suggests tailoring care to each patient's individual needs, circumstances, and wishes [76]. Quality of care and quality of life can be greatly enhanced in the older adult by the careful and judicious use of prescription and over-the-counter (OTC) medications.

When performing urodynamic studies, it is often prudent to discontinue any medications that could potentially cause voiding symptoms, voiding disorders, or impact other urodynamic parameters before the procedure. The patient needs to be awake to allow communication of the bladder sensations being experienced during the procedure [61]. In contrast, continuation of medications during the urodynamic testing period may be clinically indicated to determine if certain medications are working or improving voiding parameters. In acute retention, placement of a urethral catheter to decompress the bladder is paramount to decrease intraluminal pressure and pain [62]. Again, a thorough medication review should be initiated, with discontinuation of any offending drugs followed by reassessment of voiding ability before proceeding with more invasive treatment options.

Table 5.10 Quality indicators for hospitalization and surgery of vulnerable elders

1.	VTE prophylaxis if at risk
2.	Endocarditis prophylaxis if at risk
3.	Document max barrier precautions for central venous catheter
4.	Temporary central venous catheter (CVC): document need, infection risk
5.	Document need Q3 days for indwelling urinary catheter
6.	Evaluate delirium
7.	Increase mobility within 48 h
8.	If falls during hospitalization, perform evaluation for fall risk within 24 h
9.	Aspiration precautions
10.	Prevent ventilator-associated pneumonia (VAP)
11.	If CAP (community acquired pneumonia) present, start antibiotics within 4 h
12.	Give oxygen when O_2 sat <90 % on room air
13.	After IV to PO switch, document benefit/response
14.	Hemodynamic Sstability at discharge for pts with CAP
15.	Discharge and needs assessment
16.	Preoperative care and capacity to give consent
17.	Preoperative goals
18.	Preoperative pulmonary assessment
19.	Preoperative cardiovascular assessment
20.	Preoperative diabetes assessment
21.	Preoperative delirium assessment

Adapted from data in [75]

Conclusion

Voiding disorders are common in older adults. Medications can contribute to different voiding problems and can also be used to correct them. The urologist should be mindful of all drug-induced causes of urinary symptoms of urgency, frequency, incontinence, and retention. Efforts to avoid complicating the diagnosis and care of urinary problems in older adults can usually be accomplished by approaching any "new" symptom in an older adult *first* as a possible side effect or adverse drug effect of a currently prescribed medication [60]. This will help to reduce the risk of contributing to a prescribing cascade and additional polypharmacy.

The following things should be considered prior to prescribing any new medication [60]:

- Obtain a careful history of symptoms so that the best or most appropriate intervention can be identified.
- Re-evaluate the absolute need for what is suspected to be the medication causing the new symptom.
- Reduce the dosage of the offending medication to the lowest dose possible to treat the condition for which it is indicated.
- Identify and prescribe alternative medications that might be safer for use in older adults.
- Consider nondrug treatments including behavioral modification for management of the patient's symptoms before starting any new medications.
- Use the Beers Criteria [35] as a "guideline" for prescribing in older adults
- Identify potential side effects, drug–drug interactions, and drug–disease interactions; share this information with the patient.
- The use of another drug to treat adverse drug events should be the choice of last resort.

Not all voiding symptoms in older adults can be completely eliminated, but improvements in quality of care, quality of life, and self-esteem for the patient are goals that are often attainable with judicious and careful use of medications.

References

1. Gallagher PF, O'Connor MN, O'Mahony D. Prevention of potentially inappropriate prescribing for elderly patients: a randomized controlled trial using STOPP/START criteria. Clin Pharmacol Ther. 2011;89:845–54.
2. Tamura BK, Bell CL, Lubimir K, Iwasaki WN, Ziegler LA, Masaki KH. Physician intervention for medication reduction in a nursing home: the polypharmacy outcomes project. J Am Med Dir Assoc. 2011;12:326–30.
3. Dwyer LL, Han B, Woodwell DA, Rechtsteiner EA. Polypharmacy in nursing home residents in the United States: results of the 2004 National Nursing Home Survey. Am J Geriatr Pharmacother. 2010;8:63–72.
4. Loya AM, Gonzalez-Stuart A, Rivera JO. Prevalence of polypharmacy, polyherbacy, nutritional supplement use and potential product interactions among older adults living on the United States-Mexico border: a descriptive, questionnaire-based study. Drugs Aging. 2009;26:423–36.
5. Heuberger RA, Caudell K. Polypharmacy and nutritional status in older adults: a cross-sectional study. Drugs Aging. 2011;28:315–23.
6. Bourgeois FT, Shannon MW, Valim C, Mandl KD. Adverse drug events in the outpatient setting: an 11-year national analysis. Pharmacoepidemiol Drug Saf. 2010;19:901–10.
7. Aparasu RR, Mort JR, Brandt H. Polypharmacy trends in office visits by the elderly in the United States, 1990 and 2000. Res Social Adm Pharm. 2005;1:446–59.
8. Nobili A, Licata G, Salerno F, et al. Polypharmacy, length of hospital stay, and in-hospital mortality among elderly patients in internal medicine wards. The REPOSI study. Eur J Clin Pharmacol. 2011;67:507–19.
9. Nobili A, Franchi C, Pasina L, et al. Drug utilization and polypharmacy in an Italian elderly population: the EPIFARM-elderly project. Pharmacoepidemiol Drug Saf. 2011;20:488–96.
10. Slabaugh SL, Maio V, Templin M, Abouzaid S. Prevalence and risk of polypharmacy among the elderly in an outpatient setting: a retrospective cohort study in the Emilia-Romagna region. Italy Drugs Aging. 2010;27:1019–28.
11. Harugeri A, Joseph J, Parthasarathi G, Ramesh M, Guido S. Prescribing patterns and predictors of high-level polypharmacy in the elderly population: a prospective surveillance study from two teaching hospitals in India. Am J Geriatr Pharmacother. 2010;8:271–80.
12. Gokce Kutsal Y, Barak A, Atalay A, et al. Polypharmacy in the elderly: a multicenter study. J Am Med Dir Assoc. 2009;10:486–90.
13. Wawruch M, Zikavska M, Wsolova L, et al. Polypharmacy in elderly hospitalised patients in Slovakia. Pharm World Sci. 2008;30:235–42.
14. Schuler J, Duckelmann C, Beindl W, Prinz E, Michalski T, Pichler M. Polypharmacy and inappropriate prescribing in elderly internal-medicine patients in Austria. Wien Klin Wochenschr. 2008;120:733–41.
15. Rozenfeld S, Fonseca MJ, Acurcio FA. Drug utilization and polypharmacy among the elderly: a survey in Rio de Janeiro City, Brazil Rev Panam Salud Publica. 2008;23:34–43.
16. Haider SI, Johnell K, Thorslund M, Fastbom J. Analysis of the association between polypharmacy and socioeconomic position among elderly aged > or =77 years in Sweden. Clin Ther. 2008;30:419–27.
17. Corsonello A, Pedone C, Corica F, Incalzi RA. Polypharmacy in elderly patients at discharge from the acute care hospital. Ther Clin Risk Manag. 2007;3:197–203.

18. Linjakumpu T, Hartikainen S, Klaukka T, Veijola J, Kivela SL, Isoaho R. Use of medications and polypharmacy are increasing among the elderly. J Clin Epidemiol. 2002;55:809–17.
19. Jyrkka J, Enlund H, Lavikainen P, Sulkava R, Hartikainen S. Association of polypharmacy with nutritional status, functional ability and cognitive capacity over a three-year period in an elderly population. Pharmacoepidemiol Drug Saf. 2011;20:514–22.
20. Banerjee A, Mbamalu D, Ebrahimi S, Khan AA, Chan TF. The prevalence of polypharmacy in elderly attenders to an emergency department - a problem with a need for an effective solution. Int J Emerg Med. 2011;4:22.
21. Alic A, Pranjic N, Ramic E. Polypharmacy and decreased cognitive abilities in elderly patients. Med Arh. 2011;65:102–5.
22. Jyrkka J, Enlund H, Korhonen MJ, Sulkava R, Hartikainen S. Patterns of drug use and factors associated with polypharmacy and excessive polypharmacy in elderly persons: results of the Kuopio 75+ study: a cross-sectional analysis. Drugs Aging. 2009;26:493–503.
23. Jyrkka J, Enlund H, Korhonen MJ, Sulkava R, Hartikainen S. Polypharmacy status as an indicator of mortality in an elderly population. Drugs Aging. 2009;26:1039–48.
24. Lassila HC, Stoehr GP, Ganguli M, et al. Use of prescription medications in an elderly rural population: the MoVIES project. Ann Pharmacother. 1996;30:589–95.
25. Fillit HM, Futterman R, Orland BI, et al. Polypharmacy management in Medicare managed care: changes in prescribing by primary care physicians resulting from a program promoting medication reviews. Am J Manag Care. 1999;5:587–94.
26. Kaufman DW, Kelly JP, Rosenberg L, Anderson TE, Mitchell AA. Recent patterns of medication use in the ambulatory adult population of the United States: the Slone survey. JAMA. 2002;287:337–44.
27. Hajjar ER, Cafiero AC, Hanlon JT. Polypharmacy in elderly patients. Am J Geriatr Pharmacother. 2007;5:345–51.
28. Gallagher P, Ryan C, Byrne S, Kennedy J, O'Mahony D. STOPP (Screening Tool of Older Persons' Prescriptions) and START (Screening Tool to Alert Doctors to Right Treatment): Consensus validation. Int J Clin Pharmacol Ther. 2008;46(2):72–83.
29. Viktil KK, Blix HS, Moger TA, Reikvam A. Polypharmacy as commonly defined is an indicator of limited value in the assessment of drug-related problems. Br J Clin Pharmacol. 2007;63:187–95.
30. Tobi H, Faber A, van den Berg PB, et al. Studying co-medication patterns: The impact of definitions. Pharmacoepidemiol Drug Saf. 2007;16(4):405–11.
31. Lau DT, Mercaldo ND, Harris AT, Trittschuh E, Shega J, Weintraub S. Polypharmacy and potentially inappropriate medication use among community-dwelling elders with dementia. Alzheimer Dis Assoc Disord. 2010;24:56–63.
32. Buck MD, Atreja A, Brunker CP, et al. Potentially inappropriate medication prescribing in outpatient practices: prevalence and patient characteristics based on electronic health records. Am J Geriatr Pharmacother. 2009;7:84–92.
33. Huang ES, Karter AJ, Danielson KK, Warton EM, Ahmed AT. The association between the number of prescription medications and incident falls in a multi-ethnic population of adult type-2 diabetes patients: The Diabetes and Aging Study. J Gen Intern Med. 2009;25(2):141–6.
34. Lau DT, Mercaldo ND, Shega JW, Rademaker A, Weintraub S. Functional decline associated with polypharmacy and potentially inappropriate medications in community-dwelling older adults with dementia. Am J Alzheimers Dis Other Demen. 2011;26(8):606–15.
35. American Geriatric Society 2012 Beers Criteria Update Expert Panel. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2012;60:616–31.
36. Hamilton H, Gallagher P, Ryan C, Byrne S, O'Mahony D. Potentially inappropriate medications defined by STOPP criteria and the risk of adverse drug events in older hospitalized patients. Arch Intern Med. 2011;171(11):1013–19.
37. Trygstad TK, Christensen DB, Wegner SE, Sullivan R, Garmise JM. Analysis of the North Carolina long-term polypharmacy initiative: a multiple-cohort approach using propensity-score matching for both evaluation and targeting. Clin Ther. 2009;31(9):2018–37.
38. Flood KL, Carroll MB, Le CV, Brown CJ. Polypharmacy in hospitalized older adult cancer patients: experience from a prospective, observational study of an oncology acute care for elderly unit. Am J Geriatr Pharacother. 2009;7(3):151–8.
39. Weber V, White A, McIlvired R. An electronic medical record-based intervention to reduce polypharmacy and falls in an ambulatory rural elderly population. J Gen Intern Med. 2008;23(4):399–404.
40. Garfinkel D, Zur-Gil S, Ben-Israel J. The war against polypharmacy: a new cost-effective geriatric palliative approach for improving drug therapy in disabled elderly people. Isr Med Assoc J. 2007;9(6):430–4.
41. Samsa GP, Hanlon JT, Schmader K, et al. A summated score for the Medication Appropriateness Index: Development and assessment of clinimetric properties including content validity. J Clin Epidemiol. 1994;47(8):891–6.
42. Carnahan RM, Lund BC, Perry PJ, Pollock BG, Culp KR. The Anticholinergic Drug Scale as a measure of drug-related anticholinergic burden: associations with serum anticholinergic activity. J Clin Pharmacol. 2006;46:1481–6.
43. Klotz U. Pharmacokinetics and drug metabolism in the elderly. Drug Metab Rev. 2009;41(2):67–76.
44. Dharmarajan TS, Ugalino JA. Understanding the pharmacology of aging. Hosp Physician. 2000;1(1):1–12.

45. Kaeslti LZ, Wasilewski-Rasca AF, Bonnabry P, Vogt-Ferrier N. Use of transdermal drug formulations in the elderly. Drugs Aging. 2008;35(4):269–80.
46. Cockcroft DW, Gault MH. Prediction of creatinine clearance form serum creatinine. Nephron. 1976;16:31–41.
47. Levey AS, Coresh J, Greene T, et al. Using standardized serum creatinine values in the Modification of Diet in Renal Disease Study Equation for estimating glomerular filtration rate. Ann Intern Med. 2006;145(4):247–54.
48. Hanlon JT, Aspinall SL, Semla TP, et al. Consensus guidelines for oral dosing of primarily renally cleared medications in older adults. J Am Geriatr Soc. 2009;57(2):335–40.
49. Gill SS, Mamdani M, Naglie G, et al. A prescribing cascade involving cholinesterase inhibitors and anticholinergic drugs. Arch Intern Med. 2005;165(7):808–13.
50. Boudreau DM, Yu O, Gray SL, Raebel MA, Johnson J, Larson EB. Concomitant use of cholinesterase inhibitors and anticholinergics: Prevalence and outcomes. J Am Geriatr Soc. 2011;59:2069–76.
51. Darrah DM, Griebling TL, Silverstein JH. Postoperative urinary retention. Anesthesiol Clin. 2009;27:465–84.
52. Rudolph JL, Salow MJ, Angelini MC, McGlinchey RE. The anticholinergic risk scale and anticholinergic adverse effects in older persons. Arch Intern Med. 2008;168:508–13.
53. Wagg A, Verdejo C, Molander U. Review of cognitive impairment with antimuscarinic agents in elderly patients with overactive bladder. Int J Clin Pract. 2010;64:1279–86.
54. Campbell N, Boustani M, Limbil T, et al. The cognitive impact of anticholinergics: a clinical review. Clin Interv Aging. 2009;4:225–33.
55. Carriere I, Fourrier-Reglat A, Dartigues JF, et al. Drugs with anticholinergic properties, cognitive decline, and dementia in an elderly general population: the 3-city study. Arch Intern Med. 2009;169:1317–24.
56. Campbell NL, Boustani MA, Lane KA, et al. Use of anticholinergics and the risk of cognitive impairment in an African American population. Neurology. 2010;75:152–9.
57. Campbell N, Perkins A, Hui S, Khan B, Boustani M. Association between prescribing of anticholinergic medications and incident delirium: a cohort study. J Am Geriatr Soc. 2011;59(Suppl 2):S277–81.
58. Fox C, Livingston G, Maidment ID, et al. The impact of anticholinergic burden in Alzheimer's dementia-the LASER-AD study. Age Ageing. 2011;40:730–5.
59. Chew ML, Mulsant BH, Pollock BG, et al. Anticholinergic activity of 107 medications commonly used by older adults. J Am Geriatr Soc. 2008;56:1333–41.
60. Rochon PA, Gurwitz JH. Optimising drug treatment for elderly people: the prescribing cascade. BMJ. 1997;315(7115):1096–9.
61. Shah D, Badlani G. Treatment of overactive bladder and incontinence in the elderly. Rev Urol. 2002;4(Suppl 4):S38–43.
62. Srulevich M, Chopra A. Voiding disorders in long-term are. Ann Long Term Care Clin Care Aging. 2008;16(12 Supplement):39–43.
63. Resnick NM, Yalla SV. Management of urinary incontinence in the elderly. N Engl J Med. 1985;313(13):800–5.
64. Drake MJ, Nixon PM, Crew JP. Drug-induced bladder and urinary disorders. Incidence, prevention and management. Drug Saf. 1998;19(1):45–55.
65. Weiss BD. Diagnostic evaluation of urinary incontinence in geriatric patients. Am Fam Physician. 1998;57(11):2675–84, 88, 90.
66. Hendrix SL, Cochrane BB, Nygaard IE, et al. Effects of estrogen with and without progestin in urinary incontinence. JAMA. 2005;293(8):935–48.
67. Ekundayo OJ, Markland A, Lefante C, et al. Association of diuretic use and overactive bladder syndrome in older adults: a propensity score analysis. Arch Gerontol Geriatr. 2009;49(1):64–8.
68. Jura YH, Townsend MK, Curhan GC, Resnick NM, Grodstein F. Caffeine intake, and the risk of stress, urgency and mixed urinary incontinence. J Urol. 2011;185(5):1775–80.
69. Townsend MK, Resnick NM, Grodstein F. Caffeine intake and risk of urinary incontinence progression among women. Obstet Gynecol. 2012;119(5):950–7.
70. Seaman AM. Caffeine not tied to worsening urinary incontinence. 2012. http://www.nlm.nih.gov/medlineplus/news/fullstory_124610.html. Accessed 27 Apr 2012.
71. Verhamme KM, Sturkenboom MC, Stricker BH, Bosch R. Drug-induced urinary retention: incidence, management and prevention. Drug Saf. 2008;31(5):373–88.
72. Dolin SJ, Cashman JN. Tolerability of acute postoperative pain management: nausea, vomiting, sedation, pruritus, and urinary retention. Evidence from published data. Br J Anaesth. 2005;95(5):584–91.
73. Shrank WH, Polinski JM, Avorn J. Quality indicators for medication use in vulnerable elders. J Am Geriatr Soc. 2007;55:S373–82.
74. Wenger NS, Roth CP, Shekelle P. Introduction to the assessing care of vulnerable elders-3 quality indicator measurement set. J Am Geriatr Soc. 2007;55(Suppl 2):S247–252.
75. Arora VM, McGory ML, Fung CH. Quality indicators for hospitalization and surgery in vulnerable elders. J Am Geriatr Soc. 2007;55:S347–58.
76. Resnick B, Pacala JT. 2012 Beers Criteria. J Am Geriatr Soc. 2012;60(4):612–3.

6 Dementia, Delirium, and Depression

Heather S. Anderson

Introduction

Cognitive changes are common in older adults and may be acute or chronic. The three main diagnoses associated with alterations in cognitive status include dementia, delirium, and depression. All of these conditions can influence care of the geriatric urologic patient. This chapter will explore each of these conditions in detail, with emphasis on the etiology, clinical evaluation, and treatment.

Dementia

Prevalence and Impact

Whenever an older adult experiences memory loss, there is always a concern that this represents dementia. For an individual to be diagnosed with dementia, they need to have experienced a decline in cognition to such a degree that it interferes with everyday function (i.e., they are having difficulty managing finances, they have had to stop driving or working, or they have otherwise had to limit their daily activities due to cognitive symptoms). There are multiple causes of dementia, but there are also reversible forms of memory loss including depression, delirium, medication effect, some vitamin deficiencies, thyroid disease, and excess alcohol use. Normal age-related changes also occur, so it is important to have a strong understanding of characteristic features of the different forms of dementia. A systematic approach to the evaluation and treatment of dementia is also important.

Evaluation

All individuals being evaluated for dementia should undergo at least a brief cognitive assessment such as the Mini-Mental State Examination (MMSE) [1] or the Mini-Cog [2]. If questions remain about the etiology or severity of the cognitive dysfunction, the patient could be referred to a memory disorder clinic or for neuropsychological testing. A full neurologic examination should also be performed to evaluate for characteristic examination findings of some dementia syndromes. Note should particularly be made of any focal neurologic deficit, extraocular movement abnormality, movement disorder, increased muscle tone, Parkinsonian exam findings such as cogwheel rigidity or bradykinesia, postural instability, or gait abnormality. A series of tests should also be performed to rule out reversible causes of memory loss (Table 6.1). These tests include a non-contrast CT or MRI of the brain, thyroid function, vitamin B12 level, syphilis testing, and screening for depression. An evaluation of the patient's medication list for possible drug interactions is also important. Loved ones sometimes

H.S. Anderson, M.D. (✉)
Department of Neurology, University of Kansas Medical Center, 3901 Rainbow Blvd., Mail Stop 6002, Kansas City, KS 66160, USA
e-mail: handerson3@kumc.edu

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_6,

Table 6.1 Reversible causes of memory loss

• Hypothyroidism
• Neurosyphilis
• Vitamin B12 deficiency
• Medication adverse events or side effects

ask that neuroimaging be repeated every few years to assess how the imaging has changed. The primary reason for initial imaging is to evaluate possible cerebrovascular disease, subdural hematoma, tumor, or any other vascular or structural etiology of cognitive decline. Unless the clinical history is suggestive of stroke or if there has been a head injury or any other indication for neuroimaging, cognitive function is generally monitored clinically rather than radiographically.

Normal Age-Related Cognitive Changes

Elderly patients and their loved ones often attribute cognitive changes to age, so it is important to understand the normal cognitive changes which occur with age. Mild global cerebral atrophy begins occurring at the age of 40 [3] with 0.32 % loss of whole-brain volume per year [4]. Typical cognitive symptoms attributed to age are the "tip of the tongue" syndrome where the retrieval of memories slows down. The accuracy of the recall or quality of the cognitive performance and decision making is the same as it always has been; the speed of the cognitive performance is just slower.

Mild Cognitive Impairment

Mild cognitive impairment (MCI) is diagnosed if a patient develops cognitive symptoms which are very mild, are not just age-related, and are not significant enough to interfere with daily activities and thus do not meet criteria for dementia. There are multiple causes of MCI including vascular changes, depression, and medications; however, a significant proportion of individuals with MCI go on to develop Alzheimer's disease and other forms of dementia. A thorough search for reversible causes of memory loss as previously described is warranted. There are currently no FDA-approved treatments available for MCI. In one randomized, double-blind, placebo-controlled trial of vitamin E and donepezil in MCI [5], the rate of progression to Alzheimer's disease in those individuals receiving donepezil was reduced during the first 12 months of the study. However, at 3 years there was no difference in the rate of progression to Alzheimer's disease compared to placebo. In carriers of one or more apolipoprotein E-e4 (APOE-e4) alleles who were treated with donepezil, however, a lower rate of progression to Alzheimer's disease was evident throughout the 3-year follow-up.

Alzheimer's Disease

The most common cause of dementia, accounting for 60–80 % of cases [6], is Alzheimer's disease. Most patients with Alzheimer's disease develop symptoms at age 65 or older, and the classic presentation is the gradual onset and gradual progression of cognitive decline. To meet the *Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV)* [7] criteria for Alzheimer's disease, the individual must experience a decline in memory function as well as at least one of the following symptoms:

1. Impaired ability to generate coherent speech or understand spoken or written language
2. Impaired ability to recognize or identify objects, assuming intact sensory function
3. Impaired ability to execute motor activities, assuming intact motor abilities, sensory function and comprehension of the required task
4. Impaired ability to think abstractly, make sound judgments, and plan and carry out complex tasks

The early symptoms of Alzheimer's disease include memory loss and executive dysfunction. Examples of memory impairment include forgetfulness of common events or items including conversations, appointments, medicines, or names, repetition of questions and statements, and misplacement of items. Examples of executive dysfunction include difficulty managing household finances, changes in driving habits and safety, and difficulty with meal preparation and operation of appliances. Apathy and depression are also early symptoms of Alzheimer's disease. Impairment of long-term memory, behavior changes, and difficulty speaking, swallowing, and walking are later symptoms.

The greatest risk factor for developing Alzheimer's disease is age. One in eight individuals aged 65 and older (13 %) and approximately 50 % of individuals aged 85 and older have Alzheimer's disease [8]. Some genetic causes of Alzheimer's disease do exist; however, true familial forms of the condition probably account for less than 1 % of cases. These mutations include genes for the amyloid precursor protein (chromosome 21), presenilin 1 protein (chromosome 14), and presenilin 2 (chromosome 1). There is a growing body of evidence to suggest that there is a possible maternal transmission of risk for Alzheimer's disease. One popular theory of the cause of Alzheimer's disease involves the amyloid cascade hypothesis [9] which states that accumulation of amyloid plaques causes Alzheimer's disease. A competing hypothesis theorizes that the plaques and tangles are clinical outcomes, but the actual cause is mitochondrial dysfunction [10, 11]. Mitochondrial DNA is inherited from the mother, which, along with the increasing evidence of a possible maternal transmission of risk for Alzheimer's disease, helps support the mitochondrial hypothesis. Another risk factor for developing Alzheimer's disease includes the APOE-e4 allele, however, inheriting one or two copies of the gene does not guarantee that one will develop Alzheimer's disease. The inheritance of the gene just increases the risk. Mid-life metabolic risk factors including cardiovascular disease, obesity, hypertension, and smoking [12], as well as head trauma, traumatic brain injury, and MCI are also risk factors. There is a growing body of evidence that lifestyle factors such as physical activity and fitness levels have an impact on brain health. In patients with Alzheimer's disease, individuals with higher levels of cardiorespiratory fitness develop less brain atrophy compared to less physically fit individuals [13].

Unfortunately no treatments are available to reverse the memory loss and degenerative changes associated with Alzheimer's disease. There are four medications approved by the U.S. Food and Drug Administration (FDA) to temporarily slow worsening of symptoms for about 6–12 months. Multiple other potential disease-modifying medications are currently being investigated for the treatment of Alzheimer's disease. The available medications include acetylcholinesterase inhibitors [donepezil (Aricept), rivastigmine (Exelon), or galantamine (Razadyne)] and an NMDA receptor antagonist [memantine (Namenda)]. Rivastigmine and galantamine are FDA approved for mild to moderate Alzheimer's disease (the rivastigmine patch is also approved for severe Alzheimer's disease), and donepezil is FDA approved for mild, moderate, and severe Alzheimer's disease. Memantine is FDA approved for moderate and severe Alzheimer's disease. Side effects of memantine are relatively uncommon; however, there is a small risk of dizziness (7 %), headache (6 %), and constipation (5 %). Most patients tolerate memantine fairly well. In contrast, acetylcholinesterase inhibitors have more potential side effects. The medications are generally well tolerated, however, potential side effects include upset stomach, diarrhea, vivid dreams, and urinary incontinence or increased urinary frequency. It is critical to specifically ask about these side effects after initiation of the medication to hopefully avoid the addition of other medications to treat these side effects. This can help to prevent development of the "prescribing cascade" where additional medications are added to treat symptoms caused by side effects of medication. If a patient cannot tolerate one of the acetylcholinesterase inhibitors, potential options are to try a lower dose or slower titration of the medication or a trial of another medication in the class.

Vascular Dementia

If there is a sudden onset of cognitive dysfunction, one of the primary considerations should be a vascular etiology such as a stroke. A step-wise progression is also highly suggestive of multi-infarct dementia. Neuroimaging in multi-infarct demen-

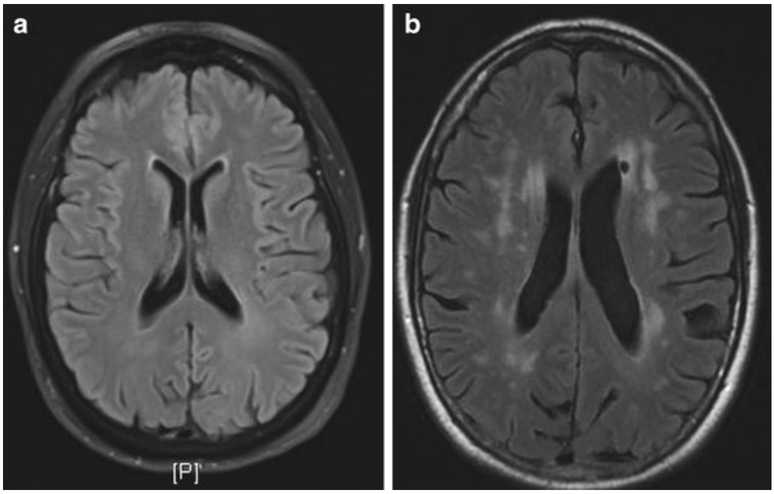


Fig. 6.1 (**a**) Sixty-year-old woman with fibromyalgia, chronic fatigue, and anxiety and no dementia. Note the very mild age-related atrophy and absence of significant white matter disease. (**b**) Forty-six year-old man with hepatitis C, history of leukemia, end-stage liver disease status post-liver transplant, sleep apnea, and hypertension. Note the white matter hyperintensities

tia reveals focal infarcts, and the neurological examination reveals focal deficits. Evaluation of individuals with multi-infarct dementia should include evaluation of vascular risk factors including diabetes, hypertension, hyperlipidemia, tobacco use, atrial fibrillation, and other cardio-embolic sources, as well as neuroimaging.

In addition to multiple infarcts, small vessel damage can also cause vascular dementia. In contrast to the abrupt onset and step-wise progression of multi-infarct dementia, cognitive dysfunction associated with small-vessel damage presents as a slow and insidious decline. This gradually progressive decline can easily be confused with Alzheimer's disease. Small-vessel vascular dementia results from loss of smooth muscle cells and hyalinization, narrowing, and thickening of the small blood vessels in the subcortical and periventricular white matter region of the brain [14]. These small-vessel changes result in chronic hypoperfusion and degeneration of white matter [14] leading to focal or confluent hyperintensities on T2-weighted magnetic resonance imaging. Increased intensity of white matter has been linked to increased prevalence of urinary incontinence in some MRI-based studies (Fig. 6.1) [15].

Treatment of vascular dementia should certainly focus on addressing vascular risk factors and addition of an antiplatelet agent such as aspirin, aspirin/dipyridamol (Aggrenox), or clopidogrel (Plavix), however, cholinesterase inhibitors may provide some cognitive enhancing effects in vascular dementia [16].

Mixed Dementia

Pure forms of dementia syndromes, including Alzheimer's disease, are actually less common than mixed vascular dementia with Alzheimer's disease [17, 18]. A thorough clinical history should be performed to evaluate possible step-wise or gradual progression as well as vascular risk factors. A neurological examination and neuroimaging should be performed, and treatment with an acetylcholinesterase inhibitor and aggressive management of vascular risk factors should be implemented.

Dementia with Lewy Bodies and Parkinson's Disease Dementia

When obtaining the clinical history about a patient's cognitive dysfunction, it is important to ask about other associated symptoms including visual hallucinations, tremor, gait disturbance, fluctuations in cognitive function, sleep disturbances such as REM behavior disorder, and dysautonomia. Presence of such clinical symptoms should raise the possibility of a Parkinsonian condition. If the cognitive symptoms and/or dementia begin more than a year after development of the full motor symptoms of Parkinson's disease, then this represents Parkinson's disease dementia (PDD). However, if the cognitive and/or psychiatric symptoms including delusions and hallucinations begin within a year of onset of the motor symptoms, or if they are present from the beginning, then this represents dementia with Lewy bodies (DLB) [19]. Key characteristics of DLB include fluctuating cognition (especially attention and awareness/alertness), visual hallucinations, and symptoms of Parkinson's disease. Characteristics which are highly suggestive of DLB include REM behavior disorder, sensitivity to neuroleptics (which make the motor symptoms worse), and reduced dopaminergic activity in the basal ganglia on SPECT or PET scans [20].

Parkinson's disease is a common neurodegenerative condition in older adults, affecting 1.8 % of people over the age of 65 [21]. Risk factors for the development of PDD include hallucinations early in the disease course, akinetic-rigid type Parkinson's disease, old age, comorbid depression, and nicotine abuse [21]. Both PDD and DLB result in cognitive as well as functional decline of motor symptoms, and there is decreased quality of life and increased psychological burden for caregivers of DLB and PDD compared to Alzheimer's disease [22].

Patients with PDD and DLB have deficits in cholinergic function, so therapies with acetylcholinesterase inhibitors can be used to treat the cognitive symptoms of these conditions. Acetylcholinesterase inhibitors have also been shown to reduce neuropsychiatric symptoms. Only rivastigmine (Exelon) is FDA approved for the treatment of PDD, and currently no acetylcholinesterase inhibitors are approved for the treatment of DLB. Since both DLB and PDD share the pathological hallmark of Lewy bodies, and they share many of the same clinical features, DLB and PDD are thought to likely represent different ends of a clinical spectrum [23]. Therefore, rivastigmine is frequently used in the treatment of DLB. Memantine has also been shown to produce significant cognitive benefit compared to placebo in a randomized, controlled trial in subjects with either DLB or PDD [24].

Treatment of the delusions, hallucinations, and agitation in DLB and PDD can be challenging since neuroleptic medications should be avoided, if at all possible, to prevent worsening of motor symptoms. A careful medication history should be taken, and if the psychiatric symptoms began after initiation or dosage change of a medication, the medication change should be reversed. Treatable factors of confusion and memory loss should also be evaluated (Table 6.1). Reduction of polypharmacy and reduction of medications for Parkinson's disease should be attempted. If psychotic symptoms persist, then initiation of rivastigmine should be considered. If psychotic symptoms remain a problem, depression and/or anxiety could be contributing to the agitation, so use of an antidepressant should be considered, with initiation of atypical antipsychotics such as quetiapine (Seroquel) and clozapine (Clozaril) if necessary. Use of the lowest effective dose should be the goal.

Frontotemporal Dementia

When obtaining the clinical history about a patient's cognitive dysfunction, it is also important to ask about behavioral or personality changes in addition to receptive or expressive aphasia. Early behavioral and/or language deficits in a patient with an identified change in cognitive function should raise the possibility of frontotemporal dementia (FTD). Patients with FTD characteristically have relative sparing of memory, especially early in the disease course. This neurodegenerative process is often referred to as Pick disease; however, the more accurate terminology is FTD for the clinical symptomatology. The diagnosis of Pick disease cannot be made until Pick bodies are found at autopsy. FTD often occurs in persons under the age of 65, and in persons aged 45–64 years of age, the prevalence is 15 per 100,000 [25–27].

In the evaluation of FTD, cognitive testing can be challenging, especially in patients with prominent aphasia. Therefore, the utility of evaluation of memory with cognitive tests such as the MMSE [1] is limited. Memory function is relatively spared in FTD, compared to Alzheimer's disease where memory loss is a prominent early feature. The history and input from loved ones is critical in detecting the behavioral, personality, and language disturbances. A referral for a neuropsychological evaluation may be necessary. Neuroimaging using CT or MRI structural brain-imaging techniques is important in the evaluation of FTD and reveals frontal and temporal atrophy [28].

The three most common variants of FTD include the behavioral variant, semantic dementia, and progressive non-fluent aphasia. Prominent personality changes and socially inappropriate behavior are the key features of behavioral variant FTD [29, 30]. Apathy, lack of initiation, diminished interest, and inactivity are the most common initial symptoms associated with behavioral variant FTD [30, 31]. In semantic dementia, patients have fluent, effortless speech which lacks meaning or depth. They tend to use broad terms rather than specific words and have difficulty comprehending words in conversations. Patients with semantic dementia tend to not recognize familiar faces or objects. Personality and behavioral changes may occur in semantic dementia, just like in behavioral variant FTD. In progressive non-fluent/agrammatic aphasia, word-finding difficulty is prominent with difficulty pronouncing words, and speech is effortful, non-fluent, and hesitant. Limited speech output and phonemic paraphasia are common in progressive non-fluent aphasia. Patients may have impaired comprehension and repetition as well as difficulty in reading. They may develop Parkinsonian symptoms as seen in primary progressive aphasia (PSP) or corticobasal degeneration (CBD). Another aphasia syndrome, logopenic variant PSP, is characterized by prominent word-finding difficulties, pausing often to think of a word. They do not lose the meaning of words; however, they later have problems understanding and holding on to lengthy conversations. Alzheimer's disease is the most common cause of logopenic PSP.

FTD is a progressive neurodegenerative condition for which there is no cure. Pharmacologic treatment options are available for symptom management, and selective serotonin reuptake inhibitors are commonly used for management of the behavioral symptoms. For more aggressive, disruptive behavior, low doses of atypical antipsychotics may be used. Patients with FTD have normal cholinergic function, so acetylcholinesterase inhibitors would not be expected to be of benefit. Also, there have been reports of worsening agitation on donepezil in patients with FTD [32].

Creutzfeldt–Jakob Disease

A rare and fatal form of dementia is Creutzfeldt–Jakob Disease (CJD), the most common human prion disease. The most common form of CJD is the sporadic form (85 % of cases), but there are also familial (10–15 %), iatrogenic (1 %), and variant forms [33]. In the sporadic form of CJD, there is no gender predilection, and the average age of onset is 60 years [34, 35]. The characteristic clinical features of CJD include the development of myoclonus, particularly startle-myoclonus, and rapidly progressive cognitive decline. The median time to death from onset of symptoms is 5 months, and by 1 year, 90 % of patients with sporadic CJD have died [34, 36].

Patients can present with fatigue, sleep disorders, and loss of appetite; behavioral or cognitive changes; or focal deficits such as vision loss, ataxia, weakness, or difficulty in speaking [37]. Over the course of a few months, patients can become lost in their own home and have significant changes in memory and judgment.

Some tests are available for the evaluation of a patient with suspected CJD; however, none of them are 100 % sensitive or specific. Characteristic patterns on EEG consist of synchronized biphasic or triphasic sharp-wave complexes. Finding 14-3-3 protein in CSF is supportive of a diagnosis of CJD. The 14-3-3 protein is a normal protein which is released in any condition resulting in rapid neuronal loss such as stroke or encephalitis, so its presence in the CSF is not specific to CJD.

MRI brain patterns, however, have been highly correlated with a diagnosis of CJD where DWI > FLAIR hyperintensities in the cingulate, striatum, and neocortical gyrus are highly suggestive of CJD. Having subcortical and cortical ribboning, hypointensities are supportive of a diagnosis of CJD [38]. A definitive diagnosis can only be made at autopsy where neuronal loss and spongiform pathology are identified in the brain and spinal cord.

The mode of transmission of sporadic CJD is unknown because exposure to patients with the disease, even intimate exposure and occupational exposures (e.g., surgeons, pathologists, butchers, ranchers, cooks), does not increase the risk of contracting the disease. Ingestion of food, including ingestion of brains, does not seem to explain the transmission. Sporadic CJD can, however, be transmitted by medical procedures. Unfortunately no effective treatments exist for curing, slowing, or halting the disease progression of CJD.

Normal Pressure Hydrocephalus

The classic triad of being "wet, wobbly, and wacky" is highly suggestive of normal pressure hydrocephalus (NPH) [39, 40]. This symptom triad of urinary incontinence, gait ataxia, and dementia, coupled with ventriculomegaly on brain imaging, should certainly raise concern for NPH. "Normal pressure" is actually a misnomer since there are probably intermittent transient elevations in intracranial pressure with the pressure returning to normal transiently after ventricular dilatation. The cause of the hydrocephalus may be diminished CSF reabsorption at the arachnoid granulations. Risk factors for the development of NPH include previous history of subarachnoid or intracranial hemorrhage, head injury, meningitis or encephalitis, brain tumor, or craniotomy. The prevalence of NPH has been found to be 0.02 % in a Norwegian study [41], 1.4–2.9 % in Japanese studies [42, 43], and perhaps as high as 14 % in residents of extended care facilities [44].

The earliest feature of NPH is typically the gait disturbance which is characterized as broad based and shuffling with an apraxic, "magnetic" quality like the feet are stuck to the floor. NPH patients often have marked difficulty taking the first step (start hesitation) or difficulty with turning. Pyramidal tract findings may also be present on neurologic examination. The urinary symptoms of NPH can consist of urinary frequency, urgency, or incontinence. The cognitive symptoms of NPH typically consist of prominent memory loss. Neuropsychological testing typically shows frontal and subcortical deficits such as forgetfulness, decreased attention, and bradyphrenia (slowness of thought).

Enlarged ventricles can be as a result of obstructive hydrocephalus, communicating hydrocephalus, or hydrocephalus ex vacuo. In diagnosing NPH (communicating hydrocephalus), review of the neuroimaging reveals ventricular enlargement which is out of proportion to sulcal atrophy. Brain MRI in NPH also reveals transependymal flow, flow void within the cerebral aqueduct and third ventricle (the "jet sign"), temporal horn enlargement, and rounding of the frontal horns. Hydrocephalus ex vacuo, on the other hand, typically has sulcal atrophy and significant white matter disease. Prominent medial temporal cortical atrophy would argue for a diagnosis of hydrocephalus ex vacuo.

The treatment for NPH consists of ventriculoperitoneal shunt placement, and a lumbar puncture is important for diagnostic and prognostic purposes. A high-volume lumbar puncture with removal of 30–50 mL of cerebrospinal fluid (CSF) combined with a gait assessment before and immediately after the procedure helps to determine if the patient is a shunt candidate. Prior to the lumbar puncture, have the patient walk a set distance, time the walk, count the steps, and describe the gait in detail. A formal physical therapy gait assessment can be helpful for documenting any change in gait. Immediately following the lumbar puncture, repeat the gait assessment. If the patient is a shunt candidate, there should be improvement in the gait. Repeat gait assessment approximately 3 h after the lumbar puncture usually reveals mild worsening of the gait compared to immediately after the lumbar puncture. Repeat gait assessment the next morning usually reveals a return of gait to baseline. If there is improvement in the gait following a high-volume lumbar puncture, consult Neurosurgery for consideration of shunt placement [45].

Unfortunately urinary incontinence, gait disturbance and are not specific to NPH and can be seen in neurodegenerative conditions or even just in advanced age. Also, making the determination between hydrocephalus and hydrocephalus ex vacuo on imaging can be challenging at times. Shunt placement is not without risk and has been associated with bleeding and infectious complications, shunt malfunction, worsening dementia, and subdural hematomas. Also, in one study, even if gait improvement occurred with shunt placement, only one-third of patients continued to experience gait improvement at 3 years [46] and even fewer experienced long-term benefits in memory or urinary incontinence.

Supportive Treatment for All Causes of Dementia

As is the case in all causes of dementia, support and education are critical to the care of patients, caregivers, and families. Providing education on the disease process and expectations is helpful for both patients and their caregivers. Early in the disease course, patients may have insight into their cognitive difficulties. It is important to recognize that neuropsychiatric features of dementia are sometimes part of the disease and are not deliberate behaviors. Participation in support groups and being made aware of available community resources including daycare programs, respite care, assisted living, and companionship services are often invaluable. Home safety assessments and providing assistance with activities of daily living can help patients safely stay in their homes longer. Driving evaluations are critical for patients even if they have only mild cognitive deficits, particularly if there have been previous citations or crashes or if driving safety concerns have been raised by loved ones [47]. Guidance and assistance are also important in addressing financial and legal issues such as conservatorship or durable power of attorney. Assessing and addressing the psychological health and well-being of loved ones, particularly the caregivers, are critical.

Delirium

Delirium is an acute confusional state which develops rapidly, usually over hours to days, and is characterized by reduced level of consciousness and difficulty focusing, shifting, or maintaining attention. Delirium is a very common condition in older adults. Although it can certainly occur in the outpatient setting, it is the most common complication seen in hospitalized older adults [48]. Delirium occurs in 11–42 % of hospitalized patients, although these rates are likely underestimates [49]. Up to half of older patients develop delirium postoperatively; especially after hip fracture repair and vascular surgery [48]. Preventing, recognizing, and treating delirium is critical in the care of older adults. Compared to hospitalized older patients without delirium, the occurrence of delirium increased the length of hospitalization by an average of 8 days, increased discharge mortality by twofold, and increased time in institutional care. Physical and cognitive recovery were also worse at 6–12 months [50].

Patients with dementia are at increased risk of developing delirium; however, the acute confusion of delirium is a separate disease process from dementia. Other risk factors for delirium include other central nervous system disease, advanced age or frailty, preexisting functional impairment in activities of daily living, sensory deprivation (especially loss of hearing and vision), metabolic derangements, infections (especially urinary tract infections or pneumonia but also some other infections), multiple medical comorbidities, recent surgery, trauma, or hospitalization, alcohol or opiate use or withdrawal, polypharmacy, pain, and history of prior episodes of delirium. Identifying a patient's delirium risk factors prior to surgery, upon admission to a hospital, or during other transitions of care, helps to determine their level of risk for developing delirium and helps initiate a targeted prevention and treatment plan. The patient's underlying level of

Table 6.2 Mnemonic for reversible causes of delirium [76]

Drugs	Any new additions, increased doses, or interactions
	Consider over-the-counter drugs and alcohol
	Consider especially high-risk drugs (anticholingerics, tricyclic antidepressants, some opioids, alcohol)
Electrolyte disturbances	Especially dehydration, sodium imbalance
	Thyroid abnormalities
Lack of drugs	Withdrawals from chronically used sedatives, including alcohol and sleeping pills
	Poorly controlled pain (lack of analgesia)
Infection	Especially urinary and respiratory tract infections
Reduced sensory input	Poor vision, poor hearing
Intracranial	Infection, hemorrhage, stroke, tumor
	Rare: consider only if new focal neurologic findings, suggestive history, or work-up otherwise negative
Urinary, fecal	Urinary retention: "cystocerebral syndrome"
	Fecal impaction
	Foley catheter
Myocardial, pulmonary	Myocardial infarction, arrhythmia, exacerbation of heart failure, exacerbation of chronic obstructive pulmonary disease, hypoxia

functioning needs to be considered as well in determining the delirium risk. A frail older adult would be more likely to develop delirium with relatively minor inciting factors such as mild dehydration or a single dose of an anticholinergic medication such as diphenhydramine. A more robust older adult would likely require more significant inciting factors such as a prolonged or complicated hospitalization, severe illness, or multiple psychotropic medications to induce delirium. A helpful mnemonic and list of reversible causes of delirium can be found in Table 6.2.

It is important to review the medication list, including non-prescription medications, for any that can be safely stopped. When evaluating medication changes, we often consider whether there has been an addition to or deletion from a medication list, however, we often don't think about changes in timing of medications. If a medication had been given in the morning and is now being given in the evening due to new prescription instructions or perhaps a different person administering the medication, then the medication might be affecting sleep. For example, donepezil can cause vivid dreams, particularly when administered at night. Other factors to consider in the evaluation of delirium is whether there have been changes in sleep habits or sleep environment such as a change in bedtime, roommate, or sleep habits of the bed partner. Lastly, transitions from home to a new facility can be disruptive and can contribute to confusion.

In the evaluation and treatment of delirium in the hospital, the algorithm proposed by Inouye 2006 [51] is helpful. Determining the patient's baseline cognitive function is critical in determining when and if there has been an acute change in cognitive status. If possible, it is important to obtain history about baseline cognitive function from loved ones as well as from the patient. Screening cognitive assessments such as the MMSE [1] or the Mini-Cog [2] can also be used if appropriate and possible to administer.

To diagnose delirium, several assessment tools are available; however, the Confusion Assessment Method (CAM) [52] is simple and easy to use and interpret. For a diagnosis of delirium, the CAM requires presence of acute onset with fluctuating course and inattention and either disorganized thinking or an altered level of alertness. Cognitive function should be monitored in patients with delirium or those identified at risk for the development of delirium. Any acute change warrants an assessment of the precipitating causes, management of the acute symptoms, and minimization of the risk of complications. It is important to remember that delirium is often hyperactive; however, hypoactive delirium can certainly occur in older adults as well. Therefore, evaluation of the patient who is less communicative and more lethargic is equally as important as for the agitated patient. Reversible causes of delirium (Table 6.2) as well as other conditions such as depression, mania, and acute psychosis need to be ruled out in the evaluation of acute confusion.

Treatment of delirium consists of identifying and treating underlying medical conditions, reviewing medication lists, and limiting or eliminating medications if possible, especially psychoactive medications or opiates. Provision of supportive care includes maintaining adequate hydration and nutrition, maintaining a quiet safe environment with familiar people and objects, communicating clearly, providing aids to orientation, and avoiding restraints including urinary catheters and intravenous lines. Making sure patients have their hearing aids and glasses if they use them is important for communication and orientation. If necessary, low doses of a neuroleptic or a benzodiazepine with a short half-life can be used for distressing or disruptive behavior. Educating caregivers about delirium risk factors and early changes in mental status as well as scheduling close follow-up helps to prevent recurrence of delirium. Caregivers should also be made aware that very elderly patients and those with preexisting cognitive symptoms are especially susceptible to prolonged confusion associated with an episode of delirium. After the metabolic derangement or infection is treated and laboratory results normalize, the confusion can persist for several days or more. Patients with dementia generally improve after an episode of delirium; however, loved ones need to be aware that the patient may not ever quite return to their pre-delirium cognitive baseline.

Depression

Epidemiology of Depression

Major depressive disorder is defined by the *Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV)* as one or more major depressive episodes, each of which lasts at least 2 weeks [7]. There are three different depressive disorders: dysthymic disorder, major depressive disorder, and depressive disorder not otherwise specified (NOS). Depressive symptoms and clinical depression are common in the geriatric population, with 5–15 % of community-dwelling older adults suffering from depression [53]. In long-term care facilities, 10 % of residents have major depressive disorder and 29 % have depressive symptoms [54]. The prevalence of depression may also rise after the age of 75–80 [55]. Assessing signs and symptoms of depression in this population can be more complicated than in younger individuals [56] because cognitive symptoms can make a detailed history more challenging to elicit. There can also be reluctance to admit symptoms of depression, and the patient or others may be in denial. Also, coexisting medical conditions can mimic or mask depressive symptoms. Older patients may not express as many feelings of guilt but may be more somatically preoccupied. Patients and loved ones can also assume that depressive symptoms are a normal response to loss of function. A depressed mood in the geriatric population is often complicated by personal changes in health and impaired health of or loss of a spouse or partner. Other issues include financial insecurity, changes in physical functioning and loss of mobility including loss of balance, loss of independence including the inability to drive, and moving from their home. These situational factors are not causes of depression; however, they can certainly make depressive symptoms worse. Depression should be differentiated from grief by the presence of depressive symptoms more than 2 months after the loss. Conditions associated with a high incidence of depression in older adults include stroke, dementia, myocardial infarction, coronary artery bypass grafting, and terminal illnesses [56]. Other risk factors for depression include female gender, having one or more chronic medical conditions, and family history. A positive family history is the strongest risk factor for major depression (HR = 2.01; 95 % CI = 1.51, 2.68) [57]. Depression in the geriatric population is associated with increased psychological suffering, mortality, suicide, functional disability, cognitive symptoms, and healthcare utilization and costs and reduced well-being and quality of life. Depression in older adults is actually associated with a higher risk of death from suicide than for any other age group [56].

Presentation

Depression is a frustrating and sometimes debilitating condition, especially in older adults. Denial of symptoms is common, even when the individual is identified by loved ones as being depressed, and there are several potential reasons for this denial. First, there is a cultural perception that those who are depressed are weak in spirit and lack the motivation to improve. Therefore, to admit that they are depressed may be perceived as a character flaw. Second, the negativity and depressed mood may have been present for so long that the individual may not realize what it feels like to be happy. They may interpret their feels as being normal and not realize that there is a whole other spectrum of emotions and reactions which they do not normally experience. Some individuals state that they are not being negative, they are just being "realistic" and don't realize that the negative outlook really flavors their perception of reality. Sometimes the symptoms of depression are recognized more by family members than by the individual themselves.

Depression often occurs along with dementia [58] and is often an early sign of cognitive decline [59, 60]. Depression can itself cause cognitive symptoms, often referred to as pseudodementia. Cognitive characteristics of pseudodementia include difficulty concentrating and giving up easily on tasks and cognitive tests.

Sometimes individuals can have depression with psychotic features including paranoia and delusions which complicates management, especially if they have superimposed dementia. Occasionally they also have anxiety, and recognizing the presence of both is critical in management of symptoms. Depression, but also anxiety, can affect sleep. An evaluation for depression should be considered if there is early-morning awakening. Likewise, anxiety should be considered if initial insomnia is present. Underlying sleep disorders such as sleep apnea or restless legs syndrome should be considered in the evaluation of fragmented sleep because an underlying sleep disorder can exacerbate or mimic depressive symptoms.

The morbidity associated with depression can be great, and care should be taken to address the risk of suicidal ideation and attempt. Adults age 75 and older have the highest rates of suicide of all age groups in most industrialized countries [61], with white men age 85 years and older having the highest rates of suicide [62]. Factors associated with an increased risk of suicide include family conflict, serious physical illness, loneliness, and both major and minor depression in the 75+ year old age group [61], and suicide risk was greater in the younger elderly group with economic problems compared to the older elderly group.

Multiple studies have shown associations between depression in older adults and a variety of urologic conditions and symptoms [63–65]. Patients with urinary incontinence often suffer from depression [66], although causality is often difficult to determine. Urinary incontinence can lead to decreased physical activity and avoidance of events outside of the home. This can lead to increased rates of social isolation, which is associated with increased rates of depression [67]. However, there are also some studies that suggest biochemical changes associated with depression in older adults may predispose affected patients to problems with urinary incontinence [68]. Similar links to depression have been identified in patients with advanced genitourinary cancers [69]. Surgeries such as radical cystectomy and urinary diversion can have important influence on changes in body perception [70]. In some patients this can lead to problems with depression. Similarly, sexual dysfunction has been linked to depression in both men and women, and the causality is likely bidirectional [71]. Older adults with underlying sexual difficulties may be more likely to develop problems with depression. However underlying comorbidities including depression may lead to erectile dysfunction or other sexual problems.

Evaluation

Because clinical depression and depressive symptoms are so common in the geriatric population, routine screening is important. It is helpful for clinicians to perform a baseline mood assessment at the initial visit and to periodically reassess mood as needed. The most popular scale for depression screening in older adults is the Geriatric Depression Scale (GDS_{15}) [72]. Scores on the GDS_{15} range from 0 to 15, and scores of 6–9 are suggestive of depression while scores of 10–15 are almost always depression.

In the evaluation of depression, it is important to rule out potentially reversible causes of a mood disorder. Certain metabolic conditions such as hypothyroidism and vitamin B12 deficiency can cause mood disturbances, so it is important that these parameters be checked. Medications such as beta-blockers, benzodiazepines, calcium-channel blockers, opioids, statins, and others can potentially contribute to depressive symptoms, so a medication check is critical in the evaluation of a depressed patient.

The mnemonic SIGECAPS helps identify key symptoms to assess that can raise suspicion for depression:

Sleep disorder (either increased or decreased sleep)
Interest deficit (anhedonia)
Guilt (worthlessness, hopelessness, regret)
Energy deficit
Concentration deficit
Appetite disorder (either decreased or increased)
Psychomotor retardation or agitation
Suicidality

Treatment

Multiple classes of antidepressants are available for general management of depression; however, special consideration should be taken in the treatment of depression in the elderly population. Tricyclic antidepressants such as amitryptyline, imipramine, nortryptyline, or desipramine should be avoided in the geriatric population due to anticholinergic effects. Selective serotonin reuptake inhibitors (SSRIs) such as escitalopram (Lexapro) or citalopram (Celexa) are generally very well tolerated and can improve the mood of depressed patients. Other antidepressants such as trazodone and mirtazapine can be considered, especially if the patient presents with insomnia as well as depression. In the occasional situation where depressive symptoms are resistant to medical management or side effects interfere with therapy, another therapeutic option is the use of electroconvulsive shock treatment (ECT). ECT in depressed elderly patients may have a higher immediate response rate than in younger individuals [73]. ECT may be particularly useful in patients with acute suicidality.

Primary care physicians, geriatricians, neurologists, and others can all treat depression. However, if the depression is refractory to treatment or if there is risk of harm to the patient or others, then a psychiatric consultation is warranted and might require emergent hospitalization in a geriatric psychiatric facility if one is available.

Use of antidepressants has been shown to be effective in management of depression in elderly patients, and depressed nursing home residents treated with antidepressants experience a modest response [74]. Studies have also shown that the combination of antidepressant therapy and psychological interventions are more effective than either alone [75]. Skepticism of clinical psychology and reluctance to initiate an antidepressant medication can be barriers to the treatment of depression in older adults.

Conclusion

Dementia, delirium, and depression are all common conditions frequently seen in older adults. These conditions may occur in conjunction with a variety of urologic disorders and in some cases may influence the urologic symptoms. Dementia and depression can occur in association with urinary incontinence, sexual disorders, and other urologic conditions. Delirium is a common postoperative complication that can negatively influence both morbidity and mortality. Careful evaluation and treatment of these conditions can help to reduce associated problems and improve overall function and quality of life for older adults undergoing urologic care.

References

1. Folstein MF, Folstein SE, McHugh PR. Mini-mental state: a practical method for grading the cognitive state of patients for the clinicians. J Psychiatr Res. 1975;12:189–98.
2. Borson S, Scanlan J, Brush M, Vitaliano P, Dokmak A. The Mini-Cog: a cognitive 'vital signs' measure for

dementia screening in multi-lingual elderly. Int J Geriatr Psychiatry. 2000;15:1021–7.
3. Takao H, Hayashi N, Ohtomo K. A longitudinal study of brain volume changes in normal aging. Eur J Radiol. 2011;81(10):2801–4.
4. Scahill RI, Frost C, Jenkins R, Whitwell JL, Rossor MN, Fox NC. A longitudinal study of brain volume changes in normal aging using serial registered magnetic resonance imaging. Arch Neurol. 2003; 60:989–94.
5. Petersen RC, Thomas RG, Grundman M, et al. Vitamin E and donepezil for the treatment of mild cognitive impairment. N Engl J Med. 2005;352: 2379–88.
6. Thies W, Bleiler L. 2011 Alzheimer's disease facts and figures. Alzheimers Dement. 2011;7:208–44.
7. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. Washington, DC: American Psychiatric Association; 1994.
8. Hebert LE, Scherr PA, Bienias JL, Bennett DA, Evans DA. Alzheimer disease in the US population: prevalence estimates using the 2000 census. Arch Neurol. 2003;60:1119–22.
9. Hardy JA, Higgins GA. Alzheimer's disease: the amyloid cascade hypothesis. Science. 1992;256:184–5.
10. Swerdlow RH. Brain aging, Alzheimer's disease, and mitochondria. Biochim Biophys Acta. 1812;2011: 1630–9.
11. Swerdlow RH, Burns JM, Khan SM. The Alzheimer's disease mitochondrial cascade hypothesis: Progress and perspectives. Biochim Biophys Acta. 2013.
12. Whitmer RA, Sidney S, Selby J, Johnston SC, Yaffe K. Midlife cardiovascular risk factors and risk of dementia in late life. Neurology. 2005;64:277–81.
13. Burns JM, Cronk BB, Anderson HS, et al. Cardiorespiratory fitness and brain atrophy in early Alzheimer disease. Neurology. 2008;71:210–6.
14. Pantoni L. Cerebral small vessel disease: from pathogenesis and clinical characteristics to therapeutic challenges. Lancet Neurol. 2010;9:689–701.
15. Kuchel GA, Moscufo N, Guttmann CR, et al. Localization of brain white matter hyperintensities and urinary incontinence in community-dwelling older adults. J Gerontol A Biol Sci Med Sci. 2009;64:902–9.
16. Black SE. Vascular cognitive impairment: epidemiology, subtypes, diagnosis and management. J R Coll Physicians Edinb. 2011;41:49–56.
17. Schneider JA, Arvanitakis Z, Bang W, Bennett DA. Mixed brain pathologies account for most dementia cases in community-dwelling older persons. Neurology. 2007;69:2197–204.
18. Lim A, Tsuang D, Kukull W, et al. Clinico-neuropathological correlation of Alzheimer's disease in a community-based case series. J Am Geriatr Soc. 1999;47:564–9.
19. Mollenhauer B, Forstl H, Deuschl G, Storch A, Oertel W, Trenkwalder C. Lewy body and Parkinsonian dementia: common, but often misdiagnosed conditions. Dtsch Arztebl Int. 2010;107:684–91.
20. McKeith IG, Dickson DW, Lowe J, et al. Diagnosis and management of dementia with Lewy bodies. Third report of the DLB consortium. 2005. pp. 1863–1872.
21. Emre M. Dementia associated with Parkinson's disease. Lancet Neurol. 2003;2:229–37.
22. Bostrom F, Jonsson L, Minthon L, Londos E. Patients with Lewy body dementia use more resources than those with Alzheimer's disease. Int J Geriatr Psychiatry. 2007;22:713–9.
23. Lippa CF, Duda JE, Grossman M, et al. DLB and PDD boundary issues: diagnosis, treatment, molecular pathology, and biomarkers. Neurology. 2007;68:812–9.
24. Aarsland D, Ballard C, Walker Z, et al. Memantine in patients with Parkinson's disease dementia or dementia with Lewy bodies: a double-blind, placebo-controlled, multicentre trial. Lancet Neurol. 2009;8: 613–8.
25. Pasquier F, Delacourte A. Non-Alzheimer degenerative dementias. Curr Opin Neurol. 1998;11:417–27.
26. The Lund and Manchester Groups. Clinical and neuropathological criteria for frontotemporal dementia. J Neurol Neurosurg Psychiatry. 1994;57:416–8.
27. Ratnavalli E, Brayne C, Dawson K, Hodges JR. The prevalence of frontotemporal dementia. Neurology. 2002;58:1615–21.
28. Wittenberg D, Possin KL, Rascovsky K, Rankin KP, Miller BL, Kramer JH. The early neuropsychological and behavioral characteristics of frontotemporal dementia. Neuropsychol Rev. 2008;18: 91–102.
29. Neary D, Snowden JS, Gustafson L, et al. Frontotemporal lobar degeneration: a consensus on clinical diagnostic criteria. Neurology. 1998;51: 1546–54.
30. Mendez MF, Lauterbach EC, Sampson SM. An evidence-based review of the psychopathology of frontotemporal dementia: a report of the ANPA Committee on Research. J Neuropsychiatry Clin Neurosci. 2008;20:130–49.
31. Cardarelli R, Kertesz A, Knebl JA. Frontotemporal dementia: a review for primary care physicians. Am Fam Physician. 2010;82:1372–7.
32. Mendez MF, Shapira JS, McMurtray A, Licht E. Preliminary findings: behavioral worsening on donepezil in patients with frontotemporal dementia. Am J Geriatr Psychiatry. 2007;15:84–7.
33. Johnson RT. Prion diseases. Lancet Neurol. 2005;4:635–42.
34. Brown P, Gibbs Jr CJ, Rodgers-Johnson P, et al. Human spongiform encephalopathy: the National Institutes of Health series of 300 cases of experimentally transmitted disease. Ann Neurol. 1994;35:513–29.
35. Will RG, Matthews WB. A retrospective study of Creutzfeldt-Jakob disease in England and Wales 1970–79. I: Clinical features. J Neurol Neurosurg Psychiatry. 1984;47:134–40.
36. Johnson RT, Gibbs Jr CJ. Creutzfeldt-Jakob disease and related transmissible spongiform encephalopathies. N Engl J Med. 1998;339:1994–2004.

37. Bernoulli CC, Masters CL, Gajdusek DC, Gibbs Jr CJ, Harris JO. Early clinical features of Creutzfeldt-Jakob disease (subacute spongiform encephalopathy). In: Prusiner SB, Hadlow WJ, editors. Slow transmissible diseases of the nervous system. New York, NY: Academic; 1979. p. 229–41.
38. Vitali P, Maccagnano E, Caverzasi E, et al. Diffusion-weighted MRI hyperintensity patterns differentiate CJD from other rapid dementias. Neurology. 2011;76:1711–9.
39. Adams RD, Fisher CM, Hakim S, Ojemann RG, Sweet WH. Symptomatic occult hydrocephalus with "normal" cerebrospinal-fluid pressure. A treatable syndrome. N Engl J Med. 1965;273:117–26.
40. Petersen RC, Mokri B, Laws Jr ER. Surgical treatment of idiopathic hydrocephalus in elderly patients. Neurology. 1985;35:307–11.
41. Brean A, Eide PK. Prevalence of probable idiopathic normal pressure hydrocephalus in a Norwegian population. Acta Neurol Scand. 2008;118:48–53.
42. Tanaka N, Yamaguchi S, Ishikawa H, Ishii H, Meguro K. Prevalence of possible idiopathic normal-pressure hydrocephalus in Japan: the Osaki-Tajiri project. Neuroepidemiology. 2009;32:171–5.
43. Hiraoka K, Meguro K, Mori E. Prevalence of idiopathic normal-pressure hydrocephalus in the elderly population of a Japanese rural community. Neurol Med Chir (Tokyo). 2008;48:197–9. discussion 199-200.
44. Marmarou A, Young HF, Aygok GA. Estimated incidence of normal pressure hydrocephalus and shunt outcome in patients residing in assisted-living and extended-care facilities. Neurosurg Focus. 2007; 22:E1.
45. Akiguchi I, Ishii M, Watanabe Y, et al. Shunt-responsive Parkinsonism and reversible white matter lesions in patients with idiopathic NPH. J Neurol. 2008;255:1392–9.
46. Klassen BT, Ahlskog JE. Normal pressure hydrocephalus: how often does the diagnosis hold water? Neurology. 2011;77:1119–25.
47. Iverson DJ, Gronseth GS, Reger MA, Classen S, Dubinsky RM, Rizzo M. Practice parameter update: evaluation and management of driving risk in dementia: report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2010;74:1316–24.
48. Young J, Inouye SK. Delirium in older people. BMJ. 2007;334:842–6.
49. Siddiqi N, House AO, Holmes JD. Occurrence and outcome of delirium in medical in-patients: a systematic literature review. Age Ageing. 2006;35: 350–64.
50. McCusker J, Cole M, Dendukuri N, Han L, Belzile E. The course of delirium in older medical inpatients: a prospective study. J Gen Intern Med. 2003;18: 696–704.
51. Inouye SK. Delirium in older persons. N Engl J Med. 2006;354:1157–65.
52. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegal AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. Ann Intern Med. 1990;113:941–8.
53. Blazer DG. Depression in late life: review and commentary. J Gerontol A Biol Sci Med Sci. 2003;58: 249–65.
54. Seitz D, Purandare N, Conn D. Prevalence of psychiatric disorders among older adults in long-term care homes: a systematic review. Int Psychogeriatr. 2010;22:1025–39.
55. Palsson S, Skoog I. The epidemiology of affective disorders in the elderly: a review. Int Clin Psychopharmacol. 1997;12 Suppl 7:S3–13.
56. Martin LM, Fleming KC, Evans JM. Recognition and management of anxiety and depression in elderly patients. Mayo Clin Proc. 1995;70:999–1006.
57. Wang J, Williams J, Lavorato D, Schmitz N, Dewa C, Patten SB. The incidence of major depression in Canada: the National Population Health Survey. J Affect Disord. 2010;123:158–63.
58. Amieva H, Le Goff M, Millet X, et al. Prodromal Alzheimer's disease: successive emergence of the clinical symptoms. Ann Neurol. 2008;64:492–8.
59. Ng TP, Niti M, Zaw MH, Kua EH. Depressive symptoms and incident cognitive impairment in cognitively well-functioning older men and women. J Am Geriatr Soc. 2009;57:1058–63.
60. Lopez OL, Jagust WJ, Dulberg C, et al. Risk factors for mild cognitive impairment in the cardiovascular health study cognition study: part 2. Arch Neurol. 2003;60:1394–9.
61. Waern M, Rubenowitz E, Wilhelmson K. Predictors of suicide in the old elderly. Gerontology. 2003;49: 328–34.
62. National Center for Injury Prevention and Control. United States suicide injury deaths and rates per 100,000. 1999–2002. http://www.cdc.gov/ncipc/wisqars/. Accessed 14 May 2008.
63. Milsom I, Kaplan SA, Coyne KS, Sexton CC, Kopp ZS. Effect of bothersome overactive bladder symptoms on health-related quality of life, anxiety, depression, and treatment seeking in the United States: results from EpiLUTS. Urology. 2012;80:90–6.
64. Pintarelli VL, Perchon LF, Lorenzetti F, Toniolo Neto J, Dambros M. Elderly men's quality of life and lower urinary tract symptoms: an intricate relationship. Int Braz J Urol. 2011;37:758–65.
65. Johnson TV, Abbasi A, Ehrlich SS, Kleris RS, Raison CL, Master VA. Nocturia associated with depressive symptoms. Urology. 2011;77:183–6.
66. Coyne KS, Kvasz M, Ireland AM, Milsom I, Kopp ZS, Chapple CR. Urinary incontinence and its relationship to mental health and health-related quality of life in men and women in Sweden, the United Kingdom, and the United States. Eur Urol. 2012;61: 88–95.
67. Losada A, Marquez-Gonzalez M, Garcia-Ortiz L, Gomez-Marcos MA, Fernandez-Fernandez V, Rodriguez-Sanchez E. Loneliness and mental health in a representative sample of community-dwelling Spanish older adults. J Psychol. 2012;146:277–92.

68. Zorn BH, Montgomery H, Pieper K, Gray M, Steers WD. Urinary incontinence and depression. J Urol. 1999;162:82–4.
69. Segrin C, Badger TA, Figueredo AJ. Stage of disease progression moderates the association between social support and depression in prostate cancer survivors. J Psychosoc Oncol. 2011;29:552–60.
70. Hedgepeth RC, Gilbert SM, He C, Lee CT, Wood Jr DP. Body image and bladder cancer specific quality of life in patients with ileal conduit and neobladder urinary diversions. Urology. 2010;76:671–5.
71. Atlantis E, Sullivan T. Bidirectional association between depression and sexual dysfunction: a systematic review and meta-analysis. J Sex Med. 2012;9:1497–507.
72. Sheikh J, Yesavage J. Geriatric depression scale (GDS): recent evidence and development of a shorter version. In: Clinical gerontology: a guide to assessment and intervention. New York, NY: The Hawthorne Press; 1986. p. 165–73.
73. Tew Jr JD, Mulsant BH, Haskett RF, et al. Acute efficacy of ECT in the treatment of major depression in the old-old. Am J Psychiatry. 1999;156:1865–70.
74. Boyce RD, Hanlon JT, Karp JF, Kloke J, Saleh A, Handler SM. A review of the effectiveness of antidepressant medications for depressed nursing home residents. J Am Med Dir Assoc. 2011;13(4): 326–31.
75. Cuijpers P, Dekker J, Hollon SD, Andersson G. Adding psychotherapy to pharmacotherapy in the treatment of depressive disorders in adults: a meta-analysis. J Clin Psychiatry. 2009;70:1219–29.
76. GRS. Geriatrics review syllabus: a core curriculum in geriatric medicine. 6th ed. New York, NY: The American Geriatrics Society; 2006.

7 Mobility, Gait, Balance, and Falls

Christine Hsieh, Stephanie Fleegle, and Christine A. Arenson

Introduction

All physicians and healthcare providers need to be aware of issues of mobility and the risk of falls when caring for older adults. Gait and balance disorders are common causes of injury, disability, and diminished quality of life for older adults. Gait impairment has been reported in 15–20 % of adults over the age of 65 and increases to 40–50 % after 85 years of age [1]. Up to 30 % of those 65 years and older report difficulty walking three city blocks or climbing one flight of stairs, and about 20 % require an assistive device to ambulate [2]. Self-reported "mobility difficulties" including difficulty with walking a quarter mile or walking up ten steps, increased among all age groups over an 8-year period [3]. Over two million older Americans fall annually, and falls are the leading cause of death from injury among adults over 65 years of age. It is imperative to consider gait and balance concerns when making treatment recommendations and also to remain vigilant for increasing falls risk and mobility impairment that may follow from treatments including medications, bed rest, and urinary catheters.

Normal Changes with Aging

There are no generally accepted standards that define normal gait patterns associated with aging [4]. Changes in gait may be related to adaptations following alterations in aging sensory and motor systems in order to improve and maintain stability [5]. Commonly seen changes include a bent posture, 10–20 % reduction in gait velocity and stride length compared to younger individuals, increased time in double support phase with both feet on the ground, trunk and limb rigidity, widened base, and en bloc turning. Despite these frequently observed changes, slowed gait is not necessarily a normal part of the aging process [6]. In fact, in one population-based longitudinal study of older adults, up to 20 % maintained normal gait patterns into very old age [7]. As with many changes commonly associated with aging, it is difficult to differentiate changes related to decreased physical activity and the burden of chronic conditions all too common with aging, as opposed to inevitable changes of the aging process per se.

C. Hsieh, M.D. (✉)
Department of Family Medicine, Thomas Jefferson University Medical School, 833 Chestnut Street, Philadelphia, PA 19107, USA
e-mail: Christine.Hsieh@jefferson.edu

S. Fleegle, M.D.
Department of Family Medicine, Thomas Jefferson University Medical School, 111 S 11th Street #6230, Philadelphia, PA 19107, USA

C.A. Arenson, M.D.
Department of Family Medicine, Thomas Jefferson University Medical School, 1015 Walnut Street, Suite 401, Philadelphia, PA 19107, USA
e-mail: christine.arenson@jefferson.edu

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_7,

Common Causes of Impaired Gait and Balance

Difficulties with gait and balance in older adults are often multifactorial. Many medical conditions can contribute to gait dysfunction, including conditions that affect strength and balance and cause pain, dyspnea, decreased sensory perception, fatigue, deformity, and decreased ability to accommodate potentially hazardous surroundings. Osteoarthritis and orthostatic hypotension are among the most common problems identified along with gait disorders [8]. Certain medications may be associated with gait and balance impairment. Some medications used in the treatment of urologic conditions in older adults, for example, the alpha-blockers for benign prostate hyperplasia in men, can cause orthostatic hypotension. One study found that joint pain was the most commonly reported symptom (32 %) contributing to gait dysfunction, followed by stroke (1 %), visual impairment (1 %), and back or neck pain (0.5 %) [9]. Acute medical illness and recent surgery or hospitalization may predispose to deconditioning and contribute to gait dysfunction [5]. Table 7.1 lists commonly found medical conditions associated with gait and balance disorders [4, 10].

Table 7.1 Medical conditions associated with gait and balance disorders

Cervical spondylosis
Cerebellar disorders
Chronic lower extremity edema
CNS tumor
Congestive heart failure
Delirium
Dementia
Depression
Diabetic neuropathy
Hepatic encephalopathy
Lumbar stenosis
Myelopathy
Normal-pressure hydrocephalus
Orthostatic hypotension
Osteoarthritis (hips and knees)
Overt hypo- or hyperthyroidism
Parkinson's disease
Peripheral arterial disease
Peripheral neuropathy
Postorthopedic surgery
Stroke (hemiparesis/hemiplegia)
Subdural hematoma
Uremia
Visual impairment
Vitamin B12 deficiency
Vestibular disorders (vertigo)

Alexander NB. Gait disorders in older adults. J Am Geriatr Soc. 1996;44(4):434–51
Alexander NB, Goldberg A. Gait disorders: search for multiple causes. Cleve Clin J Med. 2005;72(7):586–600

Oftentimes, a certain gait pattern may be observed in an older patient who presents with gait or balance concerns. Table 7.2 describes specific pathologic gait patterns [6]. A patient may report feeling "off balance" or weak. Changes in gait may be noticed by caregivers who can help give a history and may report that the patient "appears drunk," often associated with cerebellar ataxia, or appears to have episodes of their feet being frozen to the ground, a common parkinsonian symptom [6]. Parkinson's disease (PD) and Parkinsonism are important causes of gait and balance impairment. Classically the gait associated with PD is described as "shuffling," with a shortened stride length and low step height. In addition to gait impairment, characteristics such as bradykinesia, muscle rigidity, resting tremor, and postural instability may be subtle at first but gradually worsens. Patients with PD have flexion of the neck, elbows, waist, and knees and have reduced arm swing. Festination refers to the patient's tendency to take short accelerating steps leading into forward propulsion when the center of gravity is moved forward, as if the legs need to catch up with the rest of the body. Episodes of freezing as well as "en bloc" turning, where the patient's upper and lower body move as a unit without normal arm and hip rotation, may also be seen [11].

Frontal gait disorder, or "gait apraxia," refers to a patient who not only has intact motor and peripheral sensory function but also has central lesions that impair the ability to have coordinated movements and normal ambulation. Patients with frontal gait disorder have a magnetic type of gait with start and turn hesitation and possible freezing episodes. Normal-pressure hydrocephalus (NPH) demonstrates frontal gait patterns,

Table 7.2 Specific gait patterns

Type of gait	Description	Associated signs	Causes
Sensory ataxia	Unsteady, worse when visual input withdrawn, worse at night. Patients complain of distal paresthesias	Romberg sign present, impaired position and vibratory sense, distal sensory loss, no vertigo	Sensory neuropathy, neuronopathy, dorsal column dysfunction
Cerebellar ataxia	Wide based, staggering, arms abducted, truncal tremor, "drunken"	Dysmetria, dysarthria, dysdiadochokinesia, postural instability, positive Romberg, nystagmus	Cerebellar degeneration, lesion, ischemia, drug or alcohol intoxication, thiamine, B12 deficiency, multiple sclerosis
Vestibular ataxia (vertiginous)	Unsteady gait, falling to one side, postural imbalance, weaving	Vertigo, nausea, or nystagmus, positive Romberg; normal sensation, reflexes, strength	Acute: labrynthitis Chronic: Meniere's disease
Cautious (senile)	Wide based, careful, slow, like walking on ice, arms and legs abducted, en bloc turns	Associated with anxiety, fear of falling, or open spaces	Post-fall syndrome, NPH, peripheral neuropathy, visual impairment, deconditioning
Steppage gait	Resulting from foot drop, excessive flexion of hips and knees when walking, short strides, slapping quality, tripping	Atrophy of distal leg muscles, loss of ankle jerk, distal sensory loss, foot drop,	Motor neuropathy, frontal disease
Magnetic or apractic gait	Difficulty initiating step (start hesitation), turn hesitation, freezing, feet stuck to floor	Grasp reflexes, dementia, incontinence	Normal-pressure hydrocephalus, multi-infarct state, frontal disease
Parkinsonian	Short stepped, shuffling, with hips, knees, and spine flexed forward. Center of gravity in front of patient leading to propulsion and festination, en bloc turns	Bradykinesia, muscular rigidity, postural instability, rest tremor, reduced arm swing	Parkinsonism: Basal ganglia lesion, Parkinson's disease, PSP, drug induced
Antalgic gait	Limping, avoid bearing full weight, limited range of motion, slow and short steps	Pain in leg, worse with leg, hip, thigh movement, and weight-bearing	Degenerative joint disease, injury, trauma, connective tissue disease
Waddling gait	Wide based, swaying, toe-walk, lumbar lordosis, symmetric	Proximal muscle weakness of lower extremities, hip dislocation, use arms to get up from chair	Myopathy, myositis, muscular dystrophy
Spastic hemiparetic	Extension and circumduction of weak and spastic limb, flexed arm, slow and stiff gait	Weakness on same side, hyperreflexia, extensor plantar response, flexed arm	ACA stroke, structural lesion, corticospinal disease, vitamin B12 deficiency, sacral plexus radiculopathy
Spastic paraparetic	Stiffness, extension, adduction, and/or scissoring both legs	Bilateral leg weakness, hyperreflexia, spasticity, extensor plantar response	Thoracic spinal cord, foramen magnum, or parasagittal lesion
Dystonic	Abnormal posture of foot or leg, distorted gait, foot dragging, hyperflexion of hips	Worse with the action of walking, may improve when walking backwards, myoclonus	
Choreic	Irregular, dance like, slow, and wide based; spontaneous knee flexion and leg rising	Athetotic and choreic movements of upper extremities	Huntington's disease
Psychogenic	Bizarre and nonphysiologic gait, rare fall or injury, lurching	Give-way weakness, Hoover's sign, conversion signs, normal DTRs	Conversion disorder, malingering

Zawora M, Liang TW, Jarra H. Neurological problems in the elderly. In: Arenson C, Busby-Whitehead J, Brummel-Smith K, O'Brien JG, Palmer MH, Reichel W, editors. Reichel's care of the elderly, clinical aspects of aging, vol. Chapter 14. 6th ed. New York, NY: Cambridge University Press; 2009. p. 143

commonly beginning with a gait that is wide based and unsteady and features reduced foot-floor “magnetic” clearance [12]. It is frequently under-recognized, but if diagnosed early, the condition may be reversible with proper treatment such as placement of a ventriculoperitoneal shunt [12]. The classic triad of gait impairment, urinary incontinence, and dementia is not always present, particularly early in the disease process. Therefore, it is important that the practitioner consider this diagnosis for a patient who has an isolated gait impairment with the above characteristics.

Consequences of Gait and Balance Problems

The most common cause of injury in geriatric patients is falling preceded by gait impairment [13]. Besides contributing to the risk of falling, abnormal gaits in general are associated with greater risk of institutionalization and death. A study of community-dwelling adults between ages 70 and 99 demonstrated a correlation between the severity of gait abnormality and likelihood of institutionalization or death, where those with moderate to severe impairment carried a greater risk [1].

Clinical Assessment

The assessment of gait and balance is closely related to assessing the patient’s risk of falling and fall history. Current guidelines recommend that older persons be screened for falls [14], and those who report a fall should be evaluated for gait and balance difficulties. For those who are found to have gait abnormalities or balance problems or report a history of a fall, a comprehensive assessment should be performed [13–15]. Referral to a geriatrician or rehabilitation physician may be necessary for a potentially overwhelming task of addressing the underlying cause or causes and initiating appropriate preventive measures [16].

After obtaining a thorough history with the patient and caregiver if present, observation of the gait upon entrance in the room may be the first opportunity to assess a patient’s overall gait pattern. Features to be noted include stance, base, initiation, velocity, stride length, cadence, fluidity of movements, and deviation. Table 7.3 summarizes some typical physical examination findings which may help to elucidate the underlying diagnosis and aid in further workup [6].

Table 7.3 Physical examination findings

Maneuver/condition	Finding	Implication
Sitting	Unable to sit upright	Profound imbalance and/or weakness
	Titubation (tremor of the trunk and head)	Cerebellar disease
	Leaning to one side	Hemiparesis or basal ganglia disorder
Rising from chair	Unable to rise without using arms to push-off	Proximal muscle weakness (myopathy), arthritis, or basal ganglia disorder
Standing	Wide-based stance	Cerebellar disease, dorsal column dysfunction
	Stiff neck and head, avoiding motion	Vestibular disease, pain
	Unstable with sternal nudge	Back problems or neurologic problems
Walking on toes and heels		Peripheral neuropathy
Gait	Freezing or start hesitation	Parkinsonism
	Reduced arm swing	Parkinsonism
	Involuntary movements	Huntington’s disease, basal ganglia disease
Turning	Widened base, extra steps rather than pivoting on one foot	Cerebellar disease, hemiparesis, reduced proprioception
	En bloc turns	Parkinsonism, cautious gait, frontal lobe gait
Romberg sign	Sway/instability with eyes closed	Impaired proprioception

Zawora M, Liang TW, Jarra H. Neurological problems in the elderly. In: Arenson C, Busby-Whitehead J, Brummel-Smith K, O’Brien JG, Palmer MH, Reichel W, editors. Reichel’s care of the elderly, clinical aspects of aging, vol. Chapter 14. 6th ed. New York, NY: Cambridge University Press; 2009. p. 142

The Timed Up and Go (TUG) test is an efficient and reliable way to assess a patient's gait. Patients are asked to rise from a seated position, walk 3 m at their normal pace, turn around, walk back to their seat, and sit down. Patients may use their normal assistive devices such as a walker or cane. A score of less than 10 s is considered normal. A time of more than 14 s is considered abnormal and puts the patient at increased risk of falling. The TUG has been shown to have 87 % sensitivity and 87 % specificity for predicting falls in older persons [17–19].

The functional reach test is another reliable and quick way of evaluating balance and postural stability. The patient stands with one hand outstretched in front of his or her body and is asked to reach as far forward as possible without moving his or her feet. The inability to reach beyond 7 in. has been identified as a predictor of falling in older persons [20, 21].

Other means of assessing gait and stability include the Berg Balance Scale and the Tinetti Performance-Oriented Mobility Assessment (POMA). However, each of these tests takes between 10 and 20 min to perform and thus may not be practical in most outpatient settings [5, 22].

Falls

In older adults, the major consequence of gait and balance impairment is falls. Falls often lead to serious morbidity and mortality in the older population. In the United States, falls occur in approximately one-third of community-dwelling adults over the age of 65, and the rate of falling rises to 50 % in adults over the age of 80 [23]. Older adults experience significantly more morbidity and mortality from a fall compared with younger people.

The leading cause of unintentional injury in people over the age of 65 is an unintentional fall [24]. Approximately 2.2 million older adults were treated in emergency departments for nonfatal injuries from falls in 2009, resulting in more than 581,000 hospitalizations [24]. In 2008, unintentional fall was the number one cause of injury deaths in the over 65-year-old age group resulting in more than 19,700 deaths [24]. In a retrospective study of nearly 5,000 patients 65 years and older who presented to a level 1 trauma emergency room for injuries related to falls or motor vehicle collisions, the mortality rates were higher for patients who fell (25.3 %) than for patients involved in motor vehicle collision (7.8 %) [25]. There have been an increasing number of deaths from falls among older adults in the past decade [26]. The rates of fall-related deaths differ by gender, race, and ethnicity. Men are more likely than women to die from a fall [24]. Older Caucasian adults are 2.5 times more likely to die from a fall compared to older African-American adults [24]. Older non-Hispanics are more likely to die from a fall than Hispanics [24].

Women have higher rates of fall-related injuries than men [24]. Serious injury also increases with age. The rates of serious fall-related injuries for adults 85 years and older were four times that of adults 65–74 years of age [24]. In a study of over 1,500 patients, similar falls resulted in serious injury 30 % of the time in adults over the age of 65 versus 4 % in patients less than 65 years old [27]. Falls are the most common cause of traumatic brain injuries and hip fractures [24, 28]. Hip fractures are a leading cause of hospitalization for older adults, and complications of hip fractures contribute to a large proportion of death due to falls [29, 30]. The total cost for treating fall-related injuries for older adults in the United States exceeded 19 billion in 2000. These costs included hospital and nursing home care, professional services, rehabilitation, community-based services, medical equipment, and prescription medications [31].

Fall injuries not only lead to significant morbidity and mortality, but they are also associated with decreased mobility, functional decline, and greater risk for nursing home placement [27, 32, 33]. A 3-year prospective study of 1,100 community-dwelling older adults found that those who experienced a fall had a decline in activities of daily living (ADLs). Activity restriction was reported in 24 % of older adults who had fallen compared with 15 % of non-fallers. Twelve percent of the older adults in this study had long-term admissions to a nursing home after a fall [34].

Forty percent of all nursing home admissions are a direct or indirect result of falling and gait instability [35]. Once in the nursing home, the risk of falls is nearly three times that of community-dwelling older adults [36]. Falling, even without serious injury, can have a significant psychological impact on older adults. Fear of falling is more likely to develop in adults who have previously fallen [37]. The prevalence of older adults living in the community who experience fear of falling ranges from 26 to 55 % [38]. Fear of falling can lead to increased dependence, reduction in mobility, and decreased performance of ADLs [39]. A study of 673 community-dwelling older adults found that 60 % of older adults who have fallen report moderate activity restriction, and 15 % reported severe activity restrictions due to fear of falling [40]. Fear of falling is associated with loss of confidence in the ability to ambulate safely and self-imposed activity restrictions leading to increasing dependence and functional decline, social isolation, feelings of helplessness, depression, and decreased quality of life [41].

Table 7.4 Medical conditions and risk factors associated with falls in older adults living in the community

History of falls
Age >80 years female
Low body mass index
Gait and balance impairment
Use of assistive device
Decreased muscle strength
Dizziness
Functional limitations, impaired activities of daily living (ADL)
Pain
Orthostatic hypotension
Visual impairment
Depression
Urinary incontinence
Dementia and/or other cognitive impairments
Arthritis
Diabetes
Vitamin D deficiency
Stroke, cerebrovascular accident
Parkinson's disease
Peripheral neuropathy
Medications (greater than 4 or any psychoactive medication use)
Environmental home hazards
Recent hospital discharge (within 1 month)

Tinetti ME, Kumar C. The patient who falls "It's Always a Trade-off". JAMA. 2010;303(3):258–66.
Thurman DJ, Stevens JA, Rao JK, Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter: assessing patients in a neurology practice for risk of falls (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2008; 70(6): 473–9.
Mahoney J, Sager M, Dunham NC, Johnson J. Risk of falls after hospital discharge. J Am Geriatr Soc.1994; 42:269–74.

Risk Factors

Many of the factors that increase the risk of falling are known. Falls can be prevented by identifying these factors and attempting to modify the risk for falls. Older adults who have fallen are at risk for recurrent falls [42]. A relatively small number of falls result from an external event that would cause most people to fall or from a single readily identifiable cause such as syncope. However, the majority of falls result from multiple interacting factors, marking falls as a classic geriatric syndrome. Numerous risk factors have been associated with falls among community-living older adults [43–45] (Table 7.4). A systematic review identified the strongest risk factors for falling including previous falls, decreased muscle strength, gait and balance impairment, and the use of specific medications [43]. Some risk factors are non-modifiable such as age and gender. Increasing age predisposes to falls in part due to the physiologic changes that occur with aging such as decrease in gait speed and step length and loss of muscle strength. However, many risk factors are potentially modifiable, such as urinary incontinence and gait impairment. Conditions that are certain to increase risk of falls are stroke, dementia, disorders of gait and balance, and the need for assistive devices to ambulate [44]. Parkinson's disease, peripheral neuropathy, lower extremity weakness, and substantial vision loss are all associated with increased risk of falls [44].

Certain medications have been associated with falls such as psychotropic medications and antihypertensives. Table 7.5 lists classes of medi-

Table 7.5 Classes of medications that increase risk of falls

Antihypertensives
Sedatives and hypnotics
Antipsychotics and neuroleptics
Antidepressants
Benzodiazepines (long and short acting)
Anticonvulsants
Cardiac drugs: digoxin, Type IA antiarrhythmics
Diuretics
Nonsteroidal anti-inflammatory drugs
Alpha-blockers

Leipzig RM, Cumming RG, Tinett ME. Drugs and falls in older people: a systematic review and meta-analysis. I. Psychottropic drugs. J Am Geriatr Soc. 1999;47:30–9.
Leipzig RM, Cumming RG, Tinetti ME. Drugs and falls in older people: a systematic review and meta-analysis. II. Cardiac and analgesic drugs. J Am Geriatr Soc. 1999;47:40–50
Woolcott JC, Richardson KJ, Weins MO, et al. Meta-analysis of the impact of 9 medication classes on falls in elderly persons. Arch Intern Med. 2009;169(21): 1952–60.
Ensrud KE, Blackwell TL, Mangione CM, et al. Central nervous system-active medications and risk for falls in older women. J Am Geriatr Soc. 2002; 50:1629.

cations that have been associated with increased risk for falls [46–49]. In one prospective study of 2,241 women, those using long- and short-acting benzodiazepines, antidepressants such as tricyclics and selective serotonin receptor inhibitors (SSRI), and anticonvulsants were at increased risk for experiencing falls [49]. However, narcotic medications were not associated with increased risk of falls in this study nor in a recent meta-analysis of medications that increase falls in older adults [48, 49]. Adding new medications or changes in dosing of medications may increase the risk of falls in older adults. Polypharmacy or the use of four or more prescription medications is strongly correlated with an increase risk of falling [43, 47].

Urologic medications such as alpha-adrenergic antagonists, also called alpha-blockers, are used for treatment of benign prostatic hyperplasia. These medications are also commonly used to treat hypertension by relaxing the muscles in the walls of blood vessels. However, adverse effects could occur such as dizziness and orthostatic hypotension which could increase risk for falls. Antimuscarinic (anticholinergic) medications are often used to treat overactive bladder with symptoms of urgency, frequency, and nocturia. Older antimuscarinic drugs are not selective for receptors in the bladder and may have more adverse effects such as dry mouth and blurry vision. Poor vision may contribute to falls in older adults. However, newer medications are more selective for the bladder and may have less adverse effects [50].

Environmental hazards in the home can contribute to the increased risk of falls. Specific home hazards that can cause falls are poor lighting, unsafe stairways, irregular or slippery floor surfaces, loose rugs, lack of hand rails or grab bars, and general clutter. Studies show that the risk of falling increases as the number of risk factors increases [23]. In the frail older adult, the risk of falls is also high during the month after hospital discharge [45]. This may be related to various effects of hospitalization such as generalized weakness related to bed rest and deconditioning as well as changes in medications.

Screening

Patients may not seek care or report a fall unless they are injured, so falls are often undetected. Almost 60 % of those with a history of a fall in the previous year will have a subsequent fall [51]. The American Geriatrics Society (AGS) and British Geriatrics Society (BGS) 2010 guidelines for prevention of falls in older adults recommend that all community-dwelling adults older than 65 years of age be asked yearly about falls, including frequency of falls and whether they have difficulty with gait or balance [14]. Those who screen positive for falls, or who are identified as being at risk for falling, should be assessed for known risk factors. A patient with a single fall in the last year should be evaluated for gait and balance with an in-office screen such as TUG or Functional Reach Test [52]. TUG is probably the most efficient in busy practice settings. Patients found to have abnormal gait and balance, who seek medical attention for a fall, or have a history of recurrent falls should undergo a multifactorial assessment for falls [14]. This can help identify factors that put an older adult at risk for falls and recommend appropriate interventions to modify these risks.

Assessment

A multifactorial risk assessment should begin with a detailed history of the fall or falls, including the circumstances such as location, position, and injury sustained in the fall. Details including what the patient was doing at the time of the fall and whether they had any prodromal symptoms or loss of consciousness are important in determining causation. Any witnesses to the fall should be questioned as to the circumstances of the fall. Assessment for fall risk factors listed in Table 7.4 should be completed. A thorough medical history must be obtained, including acute and chronic medical problems, focusing on any neurologic disease, cardiac disease, arthritis, and urinary incontinence. A medication review should be performed to identify medications that increase risk of falls as well as any new medications or recent medication dosage changes. Over-the-counter medications which may have anticholinergic or sedative effects can increase the risk of falls and should also be reviewed.

The physical examination should focus on factors that increase the risk for falls including a cognitive evaluation and vision and hearing assessments. Postural blood pressure measurements should be obtained to evaluate for orthostasis, and a cardiovascular examination should assess for any irregular heart rhythm or rate. Neurologic examination should include assessment for focal deficits, and performance of the Romberg test to assess postural stability, reflexes, sensation, proprioception, tremor, coordination, and cerebellar and vestibular function. Musculoskeletal examination should include detection of any gross deformities, muscle strength, and tone. A gait and balance examination should also be performed. Examination of the feet and appropriate footwear for comfort, support, and stability is also important to decrease risk of falls.

The patient's ability to perform ADLs and instrumental activities of daily living (IADLs) should be assessed for functional ability to do these activities safely. Depression is associated with increased risk for falls, so a depression screen is an important component of the complete assessment.

There are no standard tests or studies to assess for the cause of falls. Thus, laboratory testing and diagnostic studies should be guided by the history and physical examination and based on specific medical conditions, symptoms, and physical findings. For example, if a patient has symptoms of syncope or chest discomfort, cardiac evaluation such as Holter monitoring may be warranted. If the patient is on diuretics, assessment of electrolytes is indicated. A radiologic study may be appropriate to evaluate for injury after a fall such as a fracture or head trauma. A nuclear bone density (DEXA) scan may be ordered if there is concern for osteoporosis which increases a patient's risk for fracture after a fall.

Management and Prevention

Clinical studies of interventions to prevent falls have included single as well as multifactorial interventions. Single interventions include cardiac pacing, vision improvement, home safety modifications, medication reduction, vitamin D supplementation, referral to physical therapy, or exercise [43, 53].

Common cardiovascular conditions that are associated with falls due to syncope or hypotension include carotid sinus hypersensitivity, vasovagal syndrome, and cardiac arrhythmias [14]. One published trial of cardiac pacing for patients with carotid hypersensitivity who had fallen showed a significant reduction of falls [54].

Many older adults develop cataracts, macular degeneration, glaucoma, and other ocular changes that can cause visual impairment. However, studies regarding vision correction to improve risk of falls have not been universally effective. One study that included a comprehensive vision assessment which resulted in new eyeglasses actually found an increased risk of falling in the intervention group [55]. This may be because older adults need time to adjust to new vision prescriptions. Studies on cataract surgery to improve vision and reduce falls have had mixed results. One trial including expedited cataract surgery showing reduction of falls [56] but a trial evaluating second cataract surgery showed no benefit [57].

A Cochrane Database review of studies that included formal assessment of the home environment and modifications to improve home safety did not clearly demonstrate reduction of falls when provided as a single intervention in older adults who did not have identified fall risks. However, older adults who had a previous fall or were at high risk for falls did show benefit from a targeted home safety modification [53].

Older adults frequently have multiple medical problems that may require treatment with multiple medications. Anticoagulants, antidepressants, and antihypertensives are classes of medications that are often prescribed to older adults, but all increase the risk of falls. The clinician should always give careful consideration to the potential benefit of the medication versus the possible increased risk of falls. Reducing the number of medications has been associated with decreased risk of falls [58]. Medications with adverse side effects of confusion, impaired alertness, and dizziness have been identified as a significant risk factor for falls. Withdrawal of psychoactive medications reduced the rate of falls by 66 % in one randomized controlled trial [59].

Low levels of serum 25-OH-vitamin D are associated with impaired muscle strength and possibly neuromuscular function [14]. A meta-analysis of five trials showed that vitamin D reduced risk of falls by 22 % compared with patients receiving calcium or placebo [60]. However, the Cochrane Database review analyzed 13 trials, comprising a total of 23,112 participants, and found no significant benefit from vitamin D supplementation [53]. A subgroup analysis found a significant reduction in falls in patients with low vitamin D levels [53]. A recent United States Preventive Services Task Force (USPSTF) study reviewed nine trials of vitamin D supplementation and found a 17 % reduction in risk for falls [61]. These researchers also found that vitamin D supplementation was most beneficial in patients who were vitamin D deficient [61]. The USPSTF recommends vitamin D supplementation to prevent falls in community-dwelling adults 65 years of age or older who are at increased risk for falls [61].

Exercise is the best studied single intervention to prevent falls. The Cochrane Database review of a large number of randomized controlled trials on multicomponent exercise, including strength, balance, flexibility, or endurance training showed a reduction in both the rate of falls and risk of falling [53]. Tai Chi has also been shown to be effective in these regards [53]. However, Tai Chi was not beneficial in fall reduction in frail older adults [62]. Although Tai Chi may be the best studied single-component exercise modality, other types of exercise classes that included just gait, balance, or functional training have been shown to reduce rate of falls [53]. The USPSTF recently reviewed 18 studies of exercise or physical therapy in community-dwelling older adults and similarly found a statistically significant reduction in risk for falling [61]. The benefit of exercise and physical therapy was greater in high-risk populations [61]. The USPSTF recommends exercise or physical therapy to prevent falls in community-dwelling adults 65 years or older who are at increased risk for falls [61].

Many studies utilize a multifactorial approach to prevent falls in older adults. The most effective trials include identifying individualized risk factors and targeting interventions to address and modify these issues, such as targeted physical therapy or exercise, medication changes, and home safety evaluation. The 2009 Cochrane Database review found that multifactorial evaluation and intervention reduced the rate of falls in older adults living in the community [53]. Multifactorial intervention in cognitively impaired older adults was found to be beneficial in one study [63] but not effective in another study [64]. Recent studies of multifactorial interventions to reduce falls risk in older adults have shown limited benefit [65, 66]. The USPSTF reviewed the results of six studies of multifactorial clinical assessment with comprehensive

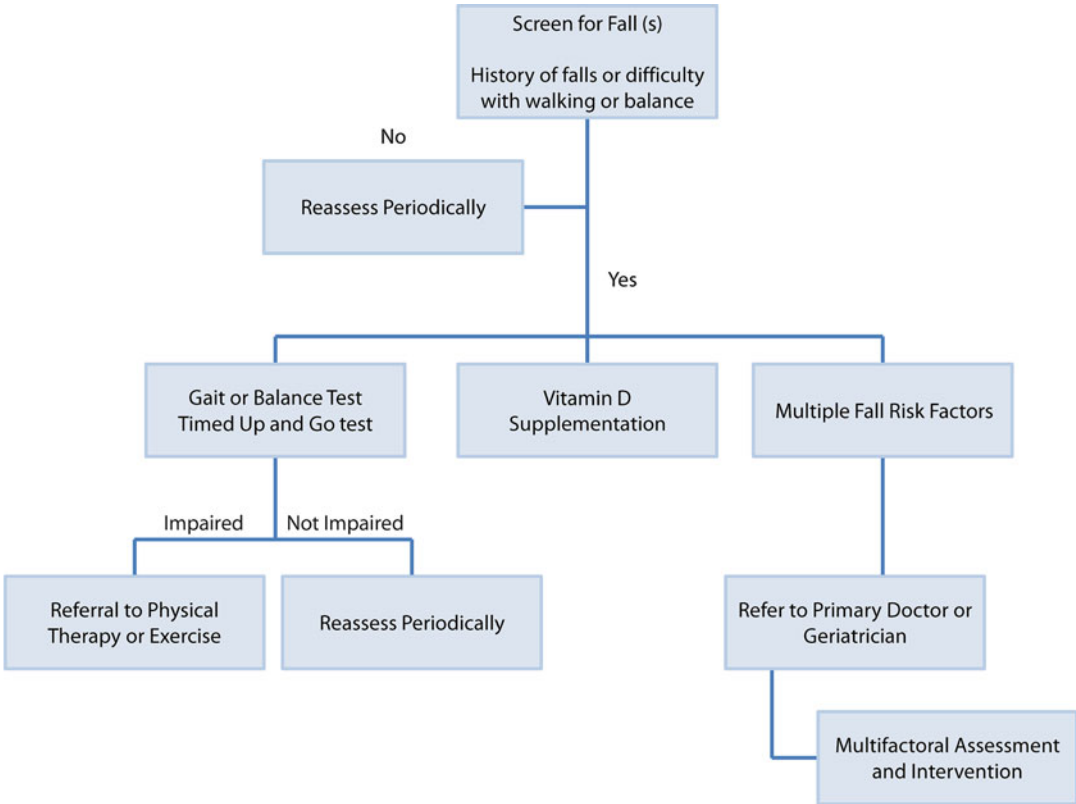


Fig. 7.1 Clinical algorithm for prevention of falls in older persons living in the community

management and found no significant reduction in falls risk [61]. However, they acknowledge that differences in the combinations of the interventions in each study make interpretation of the evidence challenging [61]. The USPSTF recommends multifactorial risk assessment with comprehensive management of identified risks to prevent falls only in appropriate high-risk individuals as the likelihood of benefit is small [61].

A clinical algorithm for prevention of falls in older persons living in the community is presented in Fig. 7.1 based on the recommendations of the USPSTF and the American Geriatrics Society and British Geriatrics Society [14, 61]. Older adults should be screened periodically, or at least yearly, for falls and those who have had falls or impaired gait or mobility based on history and a brief office assessment such TUG should be referred for exercise or physical therapy and should be prescribed adequate vitamin D supplementation. In older adults with multiple risk factors for falls, a referral to a geriatrician or primary care physician may be necessary to perform a comprehensive falls risk assessment and ensure appropriate multifactorial interventions are implemented.

Urologic Conditions Associated with Falls and Fractures

Specific urologic conditions that have been associated with mobility and increased risk of falls include functional incontinence, urinary incontinence, and nocturia. Functional incontinence may occur in older adults who have difficulty with gait or mobility. These patients may have difficulty physically walking or transferring on or off the commode independently. Faster gait speed in community-dwelling older women has been shown in one study to be associated with decreased incontinence [67]. Studies have shown that urge incontinence is associated with increased risk of falling in community-dwelling older women [68, 69]. Urinary incontinence has also been shown to be a risk factor for recurrent falls among elderly in the long-term care settings [70]. Ambulatory older adults reporting two or more episodes of nocturia during the night have significantly greater risk of falling [71]. Thus, urge incontinence and nocturia are important risk factors for falls in the older person, and early diagnosis and treatment may decrease the risk of falls. Counseling to prevent falls in patients with nocturia may include: Get up slowly and sit on edge of bed for few minutes before standing, keep path to bathroom free of loose rugs and clutter, wear nonskid slippers, put up grab bars next to the toilet, and install night light or turn on lights on the way to bathroom [72].

Androgen deprivation therapy is a common treatment for prostate cancer. It has not been directly associated with falls; however, androgen deprivation therapy decreases bone mineral density and leads to progressive osteoporosis and increases the risk of bone fractures [73, 74]. Thus, prevention and treatment of osteoporosis in men on androgen deprivation therapy is important to reduce the likelihood of fracture in the event of a fall.

Summary

All patients over 65 years of age should be asked yearly about falls or difficulty with mobility. Caregivers for patients with cognitive impairment should also be questioned about falls. Patients who screen positive for falls or difficulty with gait and mobility should be assessed for risk factors for falls. Urologic providers should assess for falls and maintain a high index of suspicion for gait and balance problems that may lead to decreased mobility and falls. High-risk individuals should be referred for comprehensive assessment by a physiatrist or geriatrician. It is also critical to be aware of the potential for new medications, including many for incontinence or benign prostatic hyperplasia to have anticholinergic or orthostatic side effects that could contribute to or worsen an older patient's risk of falls.

Medical conditions such as urinary incontinence and nocturia should be addressed. If there is difficulty with gait or mobility, patients should be referred to a physical therapist for gait and balance training, muscle strengthening, and assessment of need for assistive device such as a cane or walker. Patients should have a review for medications that could predispose to falls, such as anticholinergic medications. These should be changed or removed if possible depending on the risk and benefit of the specific medication. A review of home safety should be done, and an in-home safety assessment should be performed. This can help to identify home fall hazards and recommend modifications such as installation of grab bars, removal of loose rugs, improvements in lighting, and installation of handrails for stairs to help prevent falls. Patients should be advised to take vitamin D at least 800 mcg daily. If a patient has renal disease or osteoporosis, a 25-OH-vitamin D level should be measured to assess for vitamin D deficiency. Patients at risk for osteoporosis such as those patients on androgen deprivation therapy should have a bone density screening with a DEXA scan. In addition, they should be advised to take calcium supplementation and be considered for a medication to improve bone density such as bisphosphonates to prevent fractures.

References

1. Verghese J, LeValley A, Hall CB, Katz MJ, Ambrose AF, Lipton RB. Epidemiology of gait disorders in community-residing older adults. J Am Geriatr Soc. 2006;54(2):255–61.
2. Centers for Disease Control and Prevention. Prevalence and most common causes of disability among adults—United States. MMWR Morb Mortal Wkly Rep. 2005;58(16):421–6.
3. Crimmins EM, Beltran-Sanchez H. Mortality and morbidity trends: is there compression of morbidity? J Gerontol B. 2011;66(1):75–86.
4. Alexander NB. Gait disorders in older adults. J Am Geriatr Soc. 1996;44(4):434–51.
5. Salzman B. Gait and balance disorder in older adults. Am Fam Physician. 2010;82(1):61–8.

6. Zawora M, Liang TW, Jarra H. Neurological problems in the elderly. In: Arenson C, Busby-Whitehead J, Brummel-Smith K, O'Brien JG, Palmer MH, Reichel W, editors. Reichel's care of the elderly, clinical aspects of aging. Chapter 14. 6th ed. New York, NY: Cambridge University Press; 2009. p. 140–70.
7. Bloem BR, Gussekloo J, Lagaay AM, Remarque EJ, Haan J, Westendorp RG. Idiopathic senile gait disorders are signs of subclinical disease. J Am Geriatr Soc. 2000;48(9):1098–101.
8. Hough JC. Gait disorders in the elderly. Am Fam Physician. 1987;35(6):191–6.
9. Bloem BR, Haan J, Lagaay AM, van Beek W, Wintzen AR, Roos RA. Investigation of gait in elderly subjects over 88 years of age. J Geriatr Psychiatry Neurol. 1992;5(2):78–84.
10. Alexander NB, Goldberg A. Gait disorders: search for multiple causes. Cleve Clin J Med. 2005;72(7):586–600.
11. Axer H, Axer M, Sauer H, Witte OW, Hagemann G. Falls and gait disorders in geriatric neurology. Clin Neurol Neurosurg. 2010;112(4):265–74.
12. Krauss JK, Faist M, Schubert M, et al. Evaluation of gait in normal-pressure hydrocephalus before and after shunting. In: Ruzicka E, Hallett M, Jankovic J, editors. Gait disorders. Philadelphia, PA: Lippincott Williams & Wilkins; 2001. p. 301–9.
13. Chang JT, Ganz DA. Quality indicators for falls and mobility problems in vulnerable elders. J Am Geriatr Soc. 2007;55 suppl 2:S327–34.
14. American Geriatrics Society, British Geriatrics Society. Clinical practice guidelines: prevention of falls in older persons. J Am Geriatr Soc. 2011;59:148–57.
15. American Geriatrics Society, British Geriatrics Society, and American Academy of Orthopaedic Surgeons Panel on Falls Prevention Guideline for the prevention of falls in older persons. J Am Geriatr Soc. 2001;49(5):664–72.
16. Robinson KM, Siebens H. Rehabilitation. In: O'Donnell PD, editor. Geriatric urology. Chapter 40. 1st ed. Boston, MA: Little Brown and Company; 1994. p. 479–91.
17. Podsiadlo D, Richardson S. The timed "Up and Go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc. 1991;39(2):142–8.
18. Shumway-Cook A, Brauer S, Woollacott M. Predicting the probability for falls in community-dwelling older adults using the timed up and go test. Phys Ther. 2000;80(9):896–903.
19. Perell KL, Nelson A, Goldman RL, Luther SL, Prieto-Lewis N, Rubenstein LZ. Fall risk assessment measures: an analytic review. J Gerontol A Biol Sci Med Sci. 2001;56(12):M761–6.
20. Lin MR, Hwang HF, Hu MH, Wu HD, Wang YW, Huang FC. Psychometric comparisons of the timed up and go, one-leg stand, functional reach, and Tinetti balance measures in community-dwelling older people. J Am Geriatr Soc. 2004;52(8):1343–8.
21. Duncan PW, Studenski S, Chandler J, Prescott B. Functional reach: predictive validity in a sample of elderly male veterans. J Gerontol. 1992;47(3):M93–8.
22. Tinetti ME. Performance-oriented assessment of mobility problems in elderly patients. J Am Geriatr Soc. 1986;34:119–26.
23. Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. N Engl J Med. 1988;319:1701–7.
24. Centers for Disease Control and Prevention, National Center for Injury Prevention and Control. Web–based Injury Statistics Query and Reporting System (WISQARS) [online]. Accessed 3 Jun 2012.
25. Sampalis JS, Nathanson R, Villencourt J, et al. Assessment of mortality of older trauma patients sustaining injuries from falls or motor vehicle collisions treated in level 1 trauma centers. Ann Surg. 2009;249(3):488–9.
26. Centers for Disease Control and Prevention (CDC). Fatalities and injuries from falls among older adults – United States, 1993–2003 and 2001–2005. MMWR Morb Mortal Wkly Rep. 2006;55(45):1221–4.
27. Sterling DA, O'Connor JA, Bonadies J. Geriatric falls: injury severity is high and disproportionate to mechanism. J Trauma. 2001;50(1):116–9.
28. Jager TE, Weiss HB, Coben JH, Pepe PE. Traumatic brain injuries evaluated in U.S. emergency departments, 1992–1994. Acad Emerg Med. 2000;7(2):134–40.
29. National Hospital Discharge Survey (NHDS), National Center for Health Statistics. Available at: http://www.cdc.gov/nchs/hdi.htm. Assessed 14 Sept 2011.
30. Deprey SM. Descriptive analysis of fatal falls of older adults in a Midwestern county in the year 2005. J Geriatr Phys Ther. 2009;32(2):23–8.
31. Stevens JA, Corso PS, Finkelstein EA, Miller TR. The costs of fatal and nonfatal falls among older adults. Inj Prev. 2006;12:290–5.
32. Alexander BH, Rivara FP, Wolf ME. The cost and frequency of hospitalization for fall-related injuries in older adults. Am J Public Health. 1992;82(7):1020–3.
33. Donald IP, Bulpitt CJ. The prognosis of falls in elderly people living at home. Age Ageing. 1999;28:121–5.
34. Tinetti ME, Williams CS. The effect of falls and fall injuries on functioning in community-dwelling older persons. J Gerontol A Biol Sci Med Sci. 1998; 53(2):M112–9.
35. Tinetti ME, Williams CS. Falls, injuries due to falls, and the risk of admission to a nursing home. N Engl J Med. 1997;337(18):1279–84.
36. Rubenstein LZ, Josephson KR, Robbins AS. Falls in the nursing home. Ann Intern Med. 1994;121(6): 442–51.
37. Tinetti ME, Mendes de Leon CF, Doucette JT, Baker DI. Fear of falling and falls-related efficacy in relationship to functioning among community-living elders. J Gerontol. 1994;49:M140.
38. Lach HW. Incidence and risk factors for developing fear of falling in older adults. Public Health Nurs. 2005;22(1):45–52.
39. Li F, Fisher KJ, Hammer P, McAuley E, Wilson NL. Fear of falling in elderly persons, association with

falls, functional ability, and quality of life. J Gerontol B Psychol Sci Soc Sci. 2003;58:P283–90.
40. Deshpande N, Metter EJ, Lauretani F, et al. Activity restriction induced by fear of falling and objective and subjective measures of physical function: a prospective cohort study. J Am Geriatr Soc. 2008;56:615.
41. Tinetti ME. Prevention of falls and fall injuries in elderly persons: a research agenda. Prev Med. 1994;23:756–62.
42. Me T, Speechley M, Ginter SF. Risk factors for falls among elderly person living in the community. N Engl J Med. 1988;319:1701–7.
43. Tinetti ME, Kumar C. The patient who falls "It's Always a Trade-off". JAMA. 2010;303(3):258–66.
44. Thurman DJ, Stevens JA, Rao JK, Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter: assessing patients in a neurology practice for risk of falls (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2008; 70(6): 473–9. http://www.neurology.org/cgi/content/full/70/6/743. Assessed 14 Apr 2012.
45. Mahoney J, Sager M, Dunham NC, Johnson J. Risk of falls after hospital discharge. J Am Geriatr Soc. 1994;42:269–74.
46. Leipzig RM, Cumming RG, Tinett ME. Drugs and falls in older people: a systematic review and meta-analysis. I. Psychotropic drugs. J Am Geriatr Soc. 1999;47:30–9.
47. Leipzig RM, Cumming RG, Tinetti ME. Drugs and falls in older people: a systematic review and meta-analysis. II. Cardiac and analgesic drugs. J Am Geriatr Soc. 1999;47:40–50.
48. Woolcott JC, Richardson KJ, Weins MO, et al. Meta-analysis of the impact of 9 medication classes on falls in elderly persons. Arch Intern Med. 2009;169(21):1952–60.
49. Ensrud KE, Blackwell TL, Mangione CM, et al. Central nervous system-active medications and risk for falls in older women. J Am Geriatr Soc. 2002;50:1629.
50. Andersson KE. Overactive Bladder-New Antimuscarinics for Treatment. Business Briefing: North American Pharmacotherapy 2004-Issue 2. 111–6.
51. Nevitt MC, Cummings SR, Hudes ES. Risk factors for injurious falls: a prospective study. J Gerontol. 1991;46:M164.
52. Scott V, Votova K, Scanlan A, Close J. Multifactorial and functional mobility assessment tools for fall risk among older adults in community, home-support, long term and acute care settings. Age Ageing. 2007;36:130–9.
53. Gillespie LD, Robertson MC, Gillespie WJ, et al. Interventions for preventing falls in older people living in the community. Cochrane Database Syst Rev. 2009;2, CD007146.
54. Kenny RA, Seifer CM. SAFE PACE 2 syncope and falls in the elderly pacing and carotid sinus evaluation: a randomized controlled trial of cardiac pacing in older adults with falls and carotid hypersensitivity. Am J Geriatr Cardiol. 1999;8(2):87–7.
55. Cumming RG, Ivers R, Clemson L, et al. Improving vision to prevent falls in frail older people. A randomized trial. J Am Geriatr Soc. 2007;55:175–81.
56. Harwood RH, Foss AJ, Osborn F, Gregson RM, Zaman A, Masud T. Falls and health status in elderly women following first eye cataract surgery: a randomized controlled trial. Br J Ophthalmol. 2005;89(1):53–9.
57. Foss AJ, Harwood RH, Osborn F, Gregson RM, Zaman A, Masud T. Falls and health status in elderly women following second cataract surgery: a randomized controlled trial. Age Ageing. 2006;35(1):66–71.
58. Tinetti ME, McAvay G, Claus E. Does multiple risk factor reduction explain the reduction in fall rate in the Yale FICSIT Trial? Frailty and Injuries Cooperative Studies of Intervention Techniques. Am J Epidemiol. 1996;144(4):389–99.
59. Campbell AJ, Robertson MC, Gardner MM, Norton RN, Buchner DM. Psychotropic medication withdrawal and a home-based exercise program to prevent falls: a randomized, controlled trial. J Am Geriatr Soc. 1999;47(7):850–3.
60. Bichoff-Ferrari HA, Dawson-Hughes B, Willett WE, et al. Effect of vitamin D on falls: a meta-analysis. JAMA. 2004;291:1999–2006.
61. Moyer VA. Prevention of falls in community-dwelling older adults: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2012;157(3):1–8.
62. Wolf SL, Sattin RW, Kutner M, et al. Intense Tai Chi exercise training and fall occurrences in older transitionally frail adults: a randomized controlled trial. J Am Geriatr Soc. 2003;51(12):1693–701.
63. Mahoney JE, Shea TA, Przybelski R, et al. Kenosha County falls prevention study: a randomized controlled trial of an intermediate-intensity, community-based multifactorial falls intervention. J Am Geriatr Soc. 2007;55(4):489–98.
64. Shaw FE, Bond J, Richardson DA, et al. Multifactorial intervention after a fall in older people with cognitive impairment and dementia presenting to the accident and emergency department: randomized controlled trial. BMJ. 2003;326(7380):73–3.
65. Perula LA, Varas-Fabra F, Rodriguez V, et al. Effectiveness of a multifactorial intervention program to reduce falls incidence among community-living older adults: a randomized controlled trial. Arch Phys Med Rehabil. 2012;93(10):1677–84.
66. De Vries OJ, Peeters GM, Elders PJ, et al. Multifactorial intervention to reduce falls in older people at high risk of recurrent falls: a randomized controlled trial. Arch Intern Med. 2010;170(13):1110–7.
67. Brown JS, Seeley DG, Fong J, Black DM, Ensrud KE, Grady D. Urinary incontinence in older women: who

is at risk? Study of Osteoporotic Fractures Research Group. Obstet Gynecol. 1996;87(5 Pt 1):715–21.
68. Brown JS, Vittinghoff E, Wyman JF, Stone KL, Nevitt MC, Ensrud KE, et al. Urinary incontinence: does it increase risk for falls and fractures? Study of Osteoporotic Fractures Researc h Group. J Am Geriatr Soc. 2000;48(7):721–5.
69. Moon SJ, Kim YT, Lee TY, Moon H, Kim MJ, Kim SA, et al. The influence of overactive bladder on falling: a study of females aged 40 and older in the community. Int Neurourol J. 2011;15(1):41–7.
70. Hasegawa J, Kuzuya M, Iguchi A. Urinary incontinence and behavioral symptoms are independent risk factors for recurrent and injurious falls, respectively, among residents in long-term care facilities. Arch Gerontol Geriatr. 2010;50(1):77–81.
71. Stewart RB, Moore MT, May FE, Marks RG, Hale WE. Nocturia: a risk factor for falls in the elderly. J Am Geriatr Soc. 1992;40(12):1217–20.
72. A Home Fall Prevention Checklist for Older Adults. Centers for Disease Control and Prevention. Available at: http://www.cdc.gov/HomeandRecreationalSafety/pubs/English/booklet_Eng_desktop-a.pdf. Assessed 21 Sept 2012.
73. Daniell HW, Dunn SR, Ferguson DW, Lomas G, Niazi Z, Stratte PT. Progressive osteoporosis during androgen deprivation therapy for prostate cancer. J Urol. 2000;163:181–6.
74. Townsend MR, Sanders WH, Northway RO, Graham Jr SD. Bone fractures associated with luteinizing hormone-releasing agonists used in the treatment of prostate carcinoma. Cancer. 1997;79:545–50.

8 Pressure Ulcers

Ronni Chernoff and Christine Bradway

Pressure ulcers, also called decubitus ulcers or bedsores, have been described for centuries [1]. They are often associated with pain, infection, and poor clinical outcomes. The development of pressure ulcers has been reported in hospitalized patients [2–5], nursing home and institutionalized residents [6–9], and home care patients [10–12]. Pressure ulcers constitute a serious problem in all care settings, add a significant cost burden to the medical system, and contribute to patient suffering. It has been reported that pressure ulcers affect approximately 2.5 million patients annually [13]. This represents a significant increase in the number of hospitalizations that included pressure ulcers and their complications as a diagnosis.

Pressure ulcers vary widely in site, size, and depth, but it is generally recognized that the presence of any pressure ulcer increases hospital length of stay, cost of care, and negative patient outcomes. Approximately 60,000 patients die annually with complications associated with the presence of a pressure ulcer [14]. The annual cost of care for pressure ulcers in the USA is estimated at between $9.1 billion to $11.6 billion with individuals' costs ranging from $20,900 to $151,500 in addition to the costs associated with the primary diagnosis and hospitalization. A hospital length of stay increases between 12 and 14 days when a pressure ulcer and associated complications develop [14].

Pathophysiology

Pressure ulcers have been defined as localized areas of tissue necrosis that occur when soft tissue is compressed between a bony prominence and a hard surface for prolonged periods of time [15, 16]. It is important to note that the primary injury occurs in the capillary bed where prolonged compression will lead to the impedance of circulation and, ultimately, tissue necrosis. Associated factors in tissue damage are shearing forces, infection, and blunted sensation in cutaneous tissue [1]. There is often a volume of damaged tissue before there are surface signs; by the time a surface erythema is reported, there may be significant tissue damage lying beneath the surface.

Basically pressure ulcers are the end result of inadequate blood circulation to deep tissues due to a multitude of preventable and non-preventable factors. It is also noteworthy that not all skin ulcers are pressure ulcers and may be misclassified as such [17].

R. Chernoff, Ph.D., R.D., L.D., C.S.G., F.A.D.A. (✉)
Geriatric Research Education and Clinical Center, Central Arkansas Veterans Healthcare System, 4300 W 7th Street 182/LR, Little Rock, AR 72205, USA
e-mail: ChernoffRonni@UAMS.EDU

C. Bradway, Ph.D., R.N.
Department of Biobehavioral Health Sciences, University of Pennsylvania School of Nursing, Fagin Hall, Room 312, Philadelphia, PA 19104, USA
e-mail: cwb@nursing.upenn.edu

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_8,

Risk Factors

Risk factors for the development of pressure ulcers have been described across the continuum of care and include numerous specific patient populations, such as those undergoing surgical procedures. In general, commonly cited patient-related factors that place older adults at increased risk for developing pressure ulcers include reduced mobility or immobility, poor nutritional status, urinary and fecal incontinence, impaired cognition, compromised vascular supply, and a decreased ability to sense pain [9, 18–20].

Skin color has also been identified as a potential risk factor as identification of changes in skin color and marking associated with pressure damage may be more difficult to assess in patients with more pigmented skin colors [18].

In the hospital setting, statistically significant care-related hospital-acquired pressure ulcer risk factors identified in older adults (age 65 or greater) undergoing surgery for hip fracture included surgical delay (defined as 24 h or longer between hospital admission and surgery), but did not include the amount of transport time to the hospital, duration of surgery, length of stay in the emergency department, or use of general anesthesia [2]. In a comprehensive review of the literature focused on hospitalized surgical patients, numerous risk factors were identified and categorized as intrinsic (those inherent among patients undergoing surgery), extrinsic (defined as those that increase the effect of other risk factors), and operating room (OR) specific [21] (Table 8.1).

Table 8.1 Selected pressure ulcer risk factors for surgical patients

Intrinsic risk factors	Extrinsic risk factors[a]	Operating room-specific risk factors
Age	Heat	Type of OR mattress
Comorbid health conditions	Shearing	OR time
Nutritional status: low pre-op serum albumin	Friction	Length of time hypotensive
Small body size	Moisture	Extracorporeal circulation

[a]Significant in combination with other risk factors
Source: Armstrong and Bortz [23]

Risk factors for nursing home residents may be similar or different than those identified in hospitalized individuals. In an innovative study [8] of the nursing home work environment, nursing facility attributes including staff cohesion, team-based care, and use of consistent staff assignments were examined in terms of pressure ulcer and incontinence risk. Although consistency of assignment showed no association, poor staff cohesion was significantly associated with an increased risk of pressure ulcer development. Self-developed and managed teams, rather than teams assigned by management staff resulted in a lower risk of pressure ulcer development compared to facilities where self-developed teams were not present. Additional facility-related factors described as less-likely to lead to the development of pressure ulcers in long-term care residents include receiving more than 2 h each day of care from certified nursing assistants, more than 15 min of care per day from registered nurses, and a low turnover rate (less than 25 %) among licensed practical nurses (LPNs) [22]. Patient-related risk factors for nursing home residents include having a history of a previous pressure ulcer and nutritional factors such as difficulty eating and significant weight loss. Treatment-related factors also include the use of an indwelling urinary catheter [22].

Instruments for Assessing Pressure Ulcer Risk

A critical component of preventing pressure ulcer development is assessment to identify the factors that put patients at highest risk. While physicians and nurses report positive attitudes regarding the importance of pressure ulcer assessment and prevention, this does not necessarily assure that prevention strategies are implemented [23, 24]. A number of instruments for predicting and documenting pressure ulcer risk have been developed and tested. Controversy exists as to the usefulness of assessment scales for research purposes versus clinical practice [25], if reliability and validity have been adequately examined [25, 26] and how clinicians and researchers should go about choosing the most appropriate scale for a specific care setting [27, 28]. Despite these issues, implementation of prevention strategies is an essential component of "best practice" and because most, if not all, older adults are at increased risk, risk assessment scales are commonly used in both research and clinical practice.

Because multiple factors influence risk, some scales have recently been reexamined. Updated instruments have been developed as a result of more current information regarding risk factors. For example, the Douglas scale is based on the Norton Scale which was one of the earliest scales [25, 27]. Other scales have been identified as more appropriate for critically ill patients including the Cubbin and Jackson scale [27]. Other scales have been developed with a focus on care settings as well as cultural factors which influence use. Because of this, some scales including the Waterlow Pressure Sore Risk Scale and the Norton Scale are more frequently used in Europe [26, 29], and the Braden Scale is more frequently used in the USA [30, 31].

The Braden Scale is currently the most widely tested and used scale [31, 32]. It was developed in the USA, initially validated and found to be reliable for use with hospitalized patients on medical-surgical units and also in long-term care settings including rehabilitation and skilled-nursing units in nursing homes [31]. It includes six subscales, each ranked numerically with the highest scores indicating "no problem" and the lowest scores indicating a significant problem. The six domains assessed by the Braden Scale include sensory perception, moisture, activity, mobility, nutrition, and friction/shear. The Braden Scale, as well as additional information for its use can be found at: http://www.consultgerirn.org/uploads/File/trythis/try_this_5.pdf.

Since its initial development and testing, additional factors contributing to risk of pressure ulcer development have been identified in some populations. Surgical patients, for example, have been studied and found to be at increased risk due to a number of factors not included in the Braden Scale such as length and type of the surgical procedure, additional factors specific to the operating room (OR) such as the type of sedation, positioning devices, hemodynamics, type of OR mattress, and comorbidities including diabetes, cardiovascular, and respiratory diseases [21, 32–34]. Therefore, for surgical patients, experts have recently recommended that in addition to the Braden Scale, a new pressure risk assessment instrument specifically focused on the special needs of this population be developed and tested [33]. Similarly, in the nursing home setting, Vap and Dunaye [30] studied the effectiveness of using the Braden scale in combination with federally mandated Minimum Data Set (MDS) documentation in preventing pressure ulcers. Both the Braden Scale and MDS appropriately identified pressure ulcer risk factors. However, the MDS only needs to be completed within 14 days of admission to a care facility. Therefore, the MDS may not be completed as soon after admission as the Braden Scale alone. Because of this, the authors suggested that nursing staff should consider using the Braden Scale alone immediately on admission to the nursing home to facilitate early identification of high-risk residents, followed by completion of the MDS within the 14-day required time frame.

The most common sites for pressure ulcers to develop are those where there are bony prominences such as the sacrum, pelvis or hip, or heels. The vast majority of ulcers (95 %) develop on the lower body area, the most common being in the pelvic area and lower leg [15].

Pressure Ulcer Classification

The National Pressure Ulcer Advisory Panel (NPUAP) devised a classification system to promote consistency in staging ulcers across facilities and among practitioners (Fig. 8.1) [15, 16]. Most commonly, a stage I ulcer is characterized by nonblanchable erythema of intact skin. Stage II ulcers have a partial thickness skin loss that may resemble a blister, abrasion, or shallow crater; this stage is consistent across different classification scales [15, 16]. Also consistent across scales is the characterization of stage III ulcers as full-thickness skin loss which may extend down

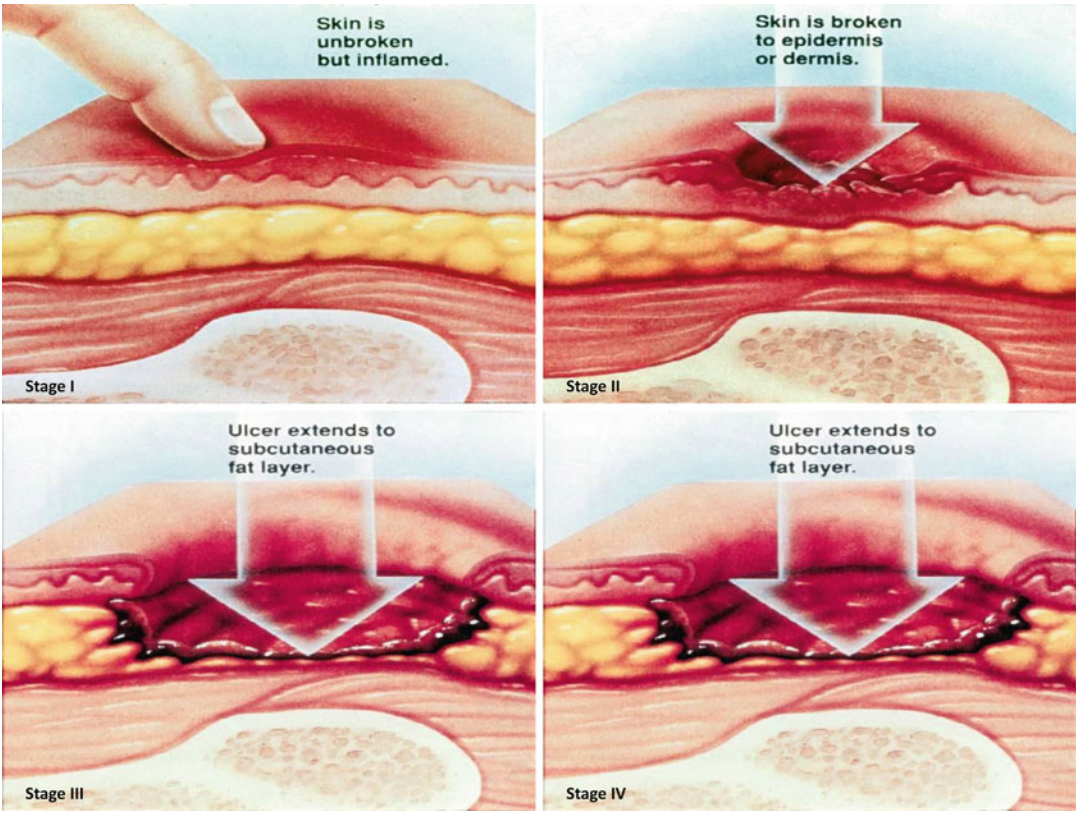


Fig. 8.1 Pressure ulcer staging

to, but not through, the underlying fascia. Stage IV pressure ulcers may have involvement of muscle, bone, and supporting tissue structures such as tendons may be exposed [16]. Other classification scales distinguish further stages by drainage, sinus tracts, and undermining tissue [15]. Despite the classification stratification, many pressure ulcers are difficult to stage due to the presence of an eschar. This may require surgical debridement to appropriately stage a pressure ulcer.

Despite the need for consistent and reliable staging of pressure ulcers, there seems to be limited reliability in the bedside staging of pressure ulcers regardless of the care site (hospital, long term care facility, and home care) [13]. The ability to distinguish between pressure ulcers and other types of ulcers such as venous stasis ulcers, surgical wounds, diabetic ulcers, and ulcers covered with an eschar appeared to be among the barriers to staging accuracy [13].

Prevention

The most important clinical factor in the development of pressure ulcers is immobility [18]. Immobility can be caused by central nervous system impairment including stroke, vegetative state, or end-stage dementia. Early identification of risk factors will contribute to the implementation of prevention strategies to minimize those risks. It has been reported that the four most important extrinsic factors that contribute to pressure ulcer development are pressure, shearing, friction, and moisture (Table 8.2). To the extent that these factors can be managed, this may be the most reasonable approach to prevention.

Surgical patients may have a higher level of risk for tissue damage associated with pressure due to their prolonged immobilization and pressure on skin and muscle associated with lying

Table 8.2 Factors that may contribute to pressure ulcer development

Inadequate blood supply	Diabetes
Wound infection	Obesity
Systemic infection	Repetitive and prolonged injury
Duration of surgery	Shearing forces
Suture material	Friction
Age	Moisture
Malnutrition	Pressure
Cancer and its treatments (radiation and chemotherapy)	Immobilization

anesthetized on a hard OR bed. Anesthesia can lead to altered tissue perfusion and decreased blood pressure, thereby contributing to tissue damage [19]. Patients who are positioned for lengthy surgical procedures (longer than 2.5 h) may be at increased risk for pressure ulcer development. Although it is difficult, if not impossible, to reposition a patient during surgery, use of pressure-relieving surfaces may help to reduce the risk [19, 20].

Early on, identification of the bed as a factor in the development of ulcers led to a proliferation of specialty beds, slings, water beds, and other devices to alleviate pressure on the sacrum. Other preventive strategies were considered, including prevention of infection, supplemental nutrition, surgical debridement, alleviating a moist environment, and minimizing shearing and friction [1]. Reducing pressure may be achieved by using pressure-relieving surfaces such as seat cushions, heel protectors, and mattresses [18].

The most commonly used pressure-relieving devices are mattresses or mattress overlays filled with water, gel, foam, or air. There are alternating pressure mattresses, low-air-loss beds, and air-fluidized mattresses, all of which contribute to reducing surface pressure in the immobile patient. Pressure redistribution mattresses have been shown to significantly reduce the incidence of pressure ulcers in long-term care patients [9, 21]. In the OR, air or gel pad overlays have been shown to reduce the postoperative development of pressure ulcers in patients undergoing lengthy surgical procedures [20]. This can be particularly useful in patients undergoing urologic surgical procedures which may involve prolonged placement in the dorsal lithotomy position which increases pressure on the back and sacrum.

Shear is defined as an applied force that can cause an opposite sliding motion in the tissues of the organism; for example, shear is created when skin or on underlying tissue structure is pulled in the opposite direction than the supporting bone [22, 23]. Shearing forces contribute to the development of pressure ulcers by creating vascular occlusion. For example, when a patient slides down in a chair or bed, small vessels are stretched to the point of occlusion [15]. Friction, in contrast, is when one surface is in contact with a second surface. For example, when a patient is dragged across the bed sheets, there is friction between the sheets and skin surface leading to tissue irritation and damage [15, 21].

Moisture is a common risk factor for the development of pressure ulcers. Moisture can be associated with perspiration, urinary incontinence, or fecal incontinence [15]. Skin will macerate if left in a moist environment, making it soft and susceptible to breakdown and infection [22].

Poor nutrition is often cited as a risk factor for the development of pressure ulcers, but despite a strong correlation between nutritional status and pressure ulcer development, there have been no studies that indicate that poor nutrition is a *cause* for pressure ulcers [18]. Poor nutrition, however, will impede healing and deserves a great deal of attention when interventions are considered.

Patient and caregiver resources and education to promote collaboration and involvement in all aspects of care is an essential component to prevention strategies suggested by healthcare professionals. The Association for the Advancement of Wound Care (AAWC) Public Awareness Task Force recently developed and made publicly available an evidence-based educational brochure ("Take the Pressure Off") that can be downloaded and used as a teaching tool in all settings (http://www.aawconline.org/patientcaregiver-resources/).

Pressure Ulcer Prevention Programs

Multicomponent pressure ulcer prevention programs have been described and are often implemented in clinical settings across the continuum of care. In acute care hospital settings, multicomponent strategies may include pressure ulcer-specific changes in nursing care such as addition of risk assessment and adoption of clinical guidelines developed by government or professional organizations combined with educational and/or quality improvement (QI) goals and measures [34]. For example, Kelleher et al. [4] developed and tested a multifaceted pressure ulcer prevention program in the 17-bed surgical intensive care unit (SICU) of an acute care hospital. Designed as a QI project, the study goals were to decrease hospital-acquired pressure ulcer (HAPU) prevalence and increase the use of pressure ulcer prevention interventions tailored to patients' individual needs. SICU staff instituted weekly peer-to-peer bedside nursing rounds directed by unit-based "skin care champions" to discuss essential elements of each patient's status. This included their use of the Braden Scale for Pressure Sore Risk score [35] findings from the hospital-developed evidence-based tool to guide nursing care of patients needing attention to skin care and other strategies being used for pressure ulcer prevention or treatment. Despite the high risk of pressure ulcer development in critically ill patients, overall program outcomes included a consistent downward trend in pressure ulcer prevalence. Although there were two calendar quarters where pressure ulcer prevalence rates spiked during times of extremely high patient acuity, there were three quarters with prevalence rates of zero. In addition, program results included an increased frequency of nursing staff using preventive interventions during the 3-year period when outcomes were tracked.

In another publication, Delmore et al. [5] describe successful strategies and challenges associated with implementation of a nurse-led, multicomponent, tertiary medical center facility-wide pressure ulcer prevention program. First, components of their current program were reviewed to identify areas for improvement. Next an 8-spoke prevention wheel was developed and implemented in selected areas of the hospital system including perioperative care. With the patient at the center of the prevention wheel, the 8-spokes included assessment; a specific skin care regimen; measures to prevent extrinsic risk factors; attention to nutrition and hydration; use of appropriate support surfaces; patient and family education; clinician education; and protocols and procedures to guide staff in preventive care. Despite challenges such as identification and development of appropriate and accurate data collection strategies and initial staff resistance, overall program outcomes included a reduction in HAPU prevalence from 7.3 % to 1.3 % over a 3-year period.

Pressure ulcers can be caused by medical devices including cervical collars, respiratory equipment, orthotics, and tubing. An example of a state-wide program aimed at preventing pressure ulcers specifically caused by medical devices included examination of mandatory adverse health event reports, root cause analysis, and use of an interprofessional team to develop best practices aimed at reducing device-related pressure ulcers in Minnesota hospitals [36]. Components of this program included development of an expanded model for HAPU reporting and data collection. This was facilitated by a state-wide group of wound, ostomy, continence (WOC) nurses, as well as development of tools and resources to strengthen existing individual Minnesota hospital protocols for prevention and treatment of pressure ulcers. First, detailed incidence and prevalence data and de-identified root cause analyses which identified patient, provider, and system-wide contributing factors were reported and examined. Then, in response to these findings, the Minnesota Pressure Ulcer Advisory Group, an interprofessional group of WOC nurses, respiratory therapists, trauma nurses, and others developed and distributed enhanced guidelines. The SAFE SKIN initiative for pressure ulcer prevention related to cervical collars and other respiratory medical devices is available online at: http://www.minhospitals.org/index/tools-app; http://www.stage.mnhospitals.org/index/tools-app/tool.353.

Descriptions of multicomponent pressure ulcer prevention programs implemented in nursing homes and in a home care setting have also been described. Based on the understanding that successful programs address multiple factors, including the care environment, patient and staff-related factors, and system-wide characteristics [37], many programs described in the literature focus on direct care as well as institutional or program-associated factors. For example, The National Nursing Home Improvement Collaborative [38] implemented a comprehensive QI program across 39 states and in 52 nursing homes to reduce pressure ulcer incidence and inform future research initiatives. Components of the program included organization of an expert panel that selected QI strategies from existing research, clinical practice, and expert opinion; educational sessions targeted at hands-on training in pressure ulcer assessment, treatment, and prevention; and implementation of "best practice" guidelines for care of long- and short-stay nursing home residents. Positive outcomes of the project included improved measurement of pressure ulcer QI metrics, identification of future research priorities, and a reduction in the incidence of nosocomial Stage III and IV pressure ulcers.

In Hong Kong, Kwong et al. [7] developed a pressure ulcer prevention program for a government-subsidized nursing home. Although this program included training, particularly in the form of assessment for licensed nursing staff, a significant focus of the program involved the non-licensed care providers (NLCPs). The training course included 2 h of lecture aimed at the NLCPs and 4 h of skills training aimed at both licensed nurses and NLCPs. Additional components of the program included collaboration and referral to non-nursing specialists such as physical therapists, dietitians, and occupational therapists, and implementation of an evidence-based prevention protocol. During the 12 weeks program implementation, both knowledge and skills of the nursing staff increased, and pressure ulcer prevalence and incidence rates both declined. Nursing staff expressed their perceptions of the benefits and challenges to program implementation which are being used to guide future research and program development.

Finally, an example of a home healthcare agency prevention program focused on obtaining pressure-relief seating surfaces for homebound elders [39] also included risk assessment using the Braden scale, collection of QI data based on Centers for Medicare and Medicaid (CMS) regulations, and patient and caregiver education. Individuals targeted in this program included those who were at significant risk of pressure ulcer development due to immobility and other comorbidities. However, they did not qualify for a Medicare reimbursed pressure-relief support surface because they were not currently wheelchair bound. By obtaining a small amount of grant funds to purchase seating surfaces for these patients, as well as implementing other components previously described, the incidence of pressure ulcers on the trunk and upper buttocks decreased. Agency nursing staff also expressed increased satisfaction and feelings of empowerment to improve patient care.

Healing

There has been speculation that adequate nutrition through early intervention will contribute to the prevention of pressure ulcers [40]. However, it seems unlikely because adequate nutrition does not mitigate the primary risks of pressure, shearing, friction, and moisture. Obese individuals, although not necessarily well-nourished, also develop pressure ulcers. Although there is lack of correlation between nutrition and pressure ulcer development, it is quite clear that nutrition is a major factor in wound healing [41].

Wound healing is fostered by the adequate availability of nutritional substrate needed to make new tissue. Key nutrients include protein, non-protein calories, vitamins, and minerals. There is evidence that inadequate intake of these key nutrients contributes to delayed wound healing, increased skin breakdown, and wound infection [42]. There is also evidence that many people do not consume, or have available, sufficient nutrients in their meals. This include both food and nutritional supplements such as oral liquid and enteral or parenteral feedings [42, 43].

Protein

Protein is always a nutrient of concern in wound care and for older adults. The Recommended

Dietary Allowance for protein is 0.8 g protein/kg body weight/day for adults regardless of age [44]. In older adults, this recommendation has been demonstrated to be too low to maintain nitrogen balance, support immune status, or heal wounds. When protein intake is linked to caloric intake, the recommended protein intake, based on ideal body weight, ranges from 1.4 to 2.0 g protein/kg body weight/day. Expert recommendations range from 1.2 to 2.0 g/kg body weight/day. However, these recommendations apply to otherwise healthy elderly adults and do not account for added demands of wound healing, trauma, surgery, or infection. This suggests that protein needs are higher than normal and, potentially, higher than these recommendations [44, 45]. Additionally, wound tensile strength is dependent on the quality and quantity of protein substrate available [42]. The quality of protein is defined by comparing the amino acid profile of a specific protein such as beef, chicken, fish, or soy, to the amino acid profile of egg, considered to be the reference standard [46].

In recent years, the addition of single amino acids to intact protein sources in order to enhance wound healing has been studied [47]. The amino acids most widely studied for their role in wound healing are arginine and glutamine. Arginine has a role in maintaining positive nitrogen balance and T-lymphocyte stimulation, among other functions, and therefore it has been hypothesized that it is a significant factor in promoting wound healing. Although arginine supplementation has shown increased collagen synthesis, the results of studies examining arginine supplementation on pressure ulcer healing have had variable results [47].

When pressure ulcer patients were provided supplementary arginine along with vitamin C and zinc, the rate of pressure ulcer healing was significantly improved when compared to a control group that did not receive the nutritional supplements [47]. In a multi-country (Czech Republic, Belgium, The Netherlands, and Curaçao) randomized controlled trial in non-malnourished pressure ulcer patients, an oral nutritional supplement containing protein enriched with arginine and micronutrients including zinc and antioxidant vitamins was offered [48]. This study demonstrated that a supplement accelerated the rate of healing in patients who had no signs of malnutrition.

Glutamine serves as a major respiratory fuel, and it is also an energy source for lymphocytes. Perhaps, more importantly, glutamine is necessary for stimulating the inflammatory immune response that occurs early in the wound healing process [47]. Despite the promise of glutamine as an agent in wound healing, it has yet to be shown to affect clinical outcomes. Glutamine supplementation has been shown to improve gut permeability and improve protein synthesis, thereby contributing to briefer hospitalizations due to reduced complications [47].

It is most important that there are adequate calories from non-protein sources available in order to protect the protein from being used for energy. Carbohydrates and fats should be the primary source of energy, allowing protein to be available for new tissue synthesis.

Micronutrients, Vitamins and Minerals

Other nutritional considerations in pressure ulcer healing are micronutrients including vitamins and minerals. The most common supplements are vitamin C and zinc. Vitamin C is essential in wound healing due to its role in collagen formation. Vitamin C, also known as ascorbic acid, is a necessary component in the hydroxylation of proline to hydroxyproline and lysine to hydroxylysine, both of which are needed to stabilize collagen [49]. Vitamin C supplements can be provided at levels from 500 to 1,000 mg/day. Providing higher levels of supplementation may not yield better results because tissue saturation occurs at much lower levels and the excess vitamin C will be excreted in urine.

Zinc is also frequently added to a wound care regimen. Zinc plays an important role in immune function and in DNA synthesis. The recommended level of supplementation is 220 mg/day, but it is difficult to find randomized clinical trials that provide evidence as to whether or not zinc really plays a pivotal role in the wound healing process. Most of the reports in the literature are case control or anecdotal [50].

Other micronutrients that have been considered for supplementation are vitamins A, D, and E. Vitamin A is an essential nutrient in the cell differentiation of epithelial tissue, therefore, it is required for the generation of new tissue needed for wound healing [51–53]. Vitamin D is important for maintaining healthy skin. A recent report examined vitamin D and its role in pressure ulcer healing through a case control study [54]. In this case–control study, vitamin D or vitamin D deficiency did not prove to be a risk factor for pressure ulcer development or healing. Another mineral that has been thought to enhance healing is copper. Copper is considered a trace mineral, needed in very small amounts. The role of copper in wound healing has only been postulated, and additional research will be needed to clarify this relationship [55].

Hydration

Dehydration is also a major issue in wound healing and adequate nutrition. Inadequate fluid intake can be a risk for pressure ulcer development as well as for tissue healing [56]. Determining adequate fluid volumes for rehydration is challenging because there are limited research reports on fluid requirements. Consensus leads to a minimal requirement of 1,500 mL/day and more if insensible losses including sweating, exudates, urinary incontinence, or other causes for unusual fluid losses exist [57]. A nutritional prescription that includes adequate levels of protein, energy substrate, vitamins, minerals, and fluid is necessary for proper wound healing [57, 58].

Summary

In summary, pressure ulcers are common in all healthcare settings and are associated with negative health outcomes as well as significant individual and system-wide financial consequences. Older adults, particularly those with urologic conditions such as urinary and fecal incontinence, are at high risk of developing pressure ulcers. These patients should be the target of thoughtful and systematic risk assessment, prevention, and treatment strategies, including minimizing the causative risk factors described in this chapter, and maximizing the environment for healing and prevention. Multicomponent programs of care that include the patient and lay caregivers working collaboratively with an interprofessional team are essential to achieving positive outcomes.

References

1. Parish LC, Witkowski JA, Crissey JT, editors. The decubitus ulcer in clinical practice. Berlin: Springer; 1997.
2. Baumgarten M, Rich SE, Shardell MD, et al. Care-related risk factors for hospital-acquired pressure ulcers in elderly adults with hip fracture. J Am Geriatr Soc. 2012;60:277–83.
3. Theisen S, Drabik A, Stock S. Pressure ulcers in older hospitalized patients and its impact on length of stay: a retrospective observational study. J Clin Nurs. 2011;20:1–8.
4. Kelleher AD, Moorer A, Makic MBF. Peer-to-peer nursing rounds and hospital-acquired pressure ulcer prevalence in a surgical intensive care unit. J Wound Ostomy Continence Nurs. 2012;39:152–7.
5. Delmore B, Leibovits S, Baldock P, et al. Pressure ulcer prevention program: a journey. J Wound Ostomy Continence Nurs. 2011;38:505–13.
6. de Souza DMST, de Gouveia Santos VLC. Incidence of pressure ulcers in the institutionalized elderly. J Wound Ostomy Continence Nurs. 2010;37:272–7.
7. Kwong EW-Y, Lau AT-Y, Lee RL-P, et al. A pressure ulcer prevention programme specially designed for nursing homes: does it work? J Clin Nurs. 2011;20: 2777–27868.
8. Temkin-Greener H, Cai S, Zheng NT, et al. Nursing home work environment and the risk of pressure ulcers and incontinence. Health Serv Res. 2012;47: 1179–200.
9. Pham B, Stern A, Chen W, et al. Preventing pressure ulcers in long-term care: a cost-effectiveness analysis. Arch Intern Med. 2011;171:1839–47.
10. Farren M, Martelly-Kebreau Y. OASIS-C importance of accurate pressure ulcer assessment and management in home healthcare: part II. Home Healthc Nurse. 2011;29:599–608.
11. Bergquist-Beringer S, Gajewski BJ. Outcome and assessment information set data that predict pressure ulcer development in older adult home health patients. Adv Skin Wound Care. 2011;24:404–14.
12. Bergquist-Beringer S, Daley CM. Adapting pressure ulcer prevention for use in home health care. J Wound Ostomy Continence Nurs. 2011;38:145–54.
13. Bruce TA, Shever LL, Tschannen D, et al. Reliability of pressure ulcer staging: a review of the literature and 1 institution's strategy. Crit Care Nurs Q. 2012;35:85–101.

14. National Pressure Ulcer Advisory Panel and European Pressure Ulcer Advisory Panel. Prevention and treatment of pressure ulcers: clinical practice guideline. Washington, DC: National Pressure Ulcer Advisory Panel; 2009.
15. Kanj LF, Wilking SVB, Phillips TJ. Pressure ulcers. J Am Acad Dermatol. 1998;38:517–38.
16. The National Pressure Ulcer Advisory Panel. Pressure ulcers prevalence, cost, risk assessment: consensus development conference statement. Decubitus. 1989;2:24–8.
17. Parish LC, Sibbald RG. 25 years of pressure ulcers and advances in skin and wound care. Adv Skin Wound Care. 2012;25:57–8.
18. Guy H. Pressure ulcer risk assessment. Nurs Times. 2012;108(4):16–20.
19. Baumgarten M, Margolis DJ, Locailio AR, et al. Pressure ulcers among elderly patients early in the hospital stay. J Gerontol A Biol Sci Med Sci. 2006;61:749–54.
20. Allman RM, Goode PS, Patrick MM, et al. Pressure ulcer risk factors among hospitalized patients with activity limitation. JAMA. 1995;273:865–70.
21. Primiano M, Friend M, McClure C, et al. Pressure ulcer prevalence and risk factors during prolonged surgical procedures. AORN J. 2011;94:555–66.
22. Walton-Geer PS. Prevention of pressure ulcers in the surgical patient. AORN J. 2009;89:538–48.
23. Armstrong D, Bortz P. An integrative review of pressure relief in surgical patients. AORN J. 2001;73:645–74.
24. Factora R. Year in review: National Pressure Ulcer Long-Term Care Study. J Am Med Dir Assoc. 2004;5:356–7.
25. Suen W, Parker VA, Harney L, et al. Internal medicine interns' and residents' pressure ulcer prevention and assessment abilities: results of an exploratory study. Ostomy Wound Manage. 2012;58:28–35.
26. Moore Z, Price P. Nurses' attitudes, behaviors and perceived barriers towards pressure ulcer prevention. J Clin Nurs. 2004;13:942–51.
27. Anthony D, Papanikolaou P, Parboteeah S, et al. Do risk assessment scales for pressure ulcers work? J Tissue Viability. 2010;19:132–6.
28. Kottner J, Dassen T, Tannen A. Inter- and intrarater reliability of the Waterlow pressure sore risk scale: a systematic review. Int J Nurs Stud. 2009;46:369–79.
29. Seongsook J, Inhsook J, Younghee L. Validity of pressure ulcer risk assessment scales: Cubbin and Jackson, Braden, and Douglas scale. Int J Nurs Stud. 2004;41:199–204.
30. Norton D. Research and the problem of pressure sores. Nurs Mirror Midwives J. 1975;140:65–7.
31. Vap PW, Dunaye T. Pressure ulcer risk assessment in long-term care. J Gerontol Nurs. 2000;26:37–45.
32. Pancorbo-Hidalgo PL, Garcia-Fernandez FP, Lopez-Medina IM, Alvarez-Nieto C. Risk assessment scales for pressure ulcer prevention: a systematic review. J Adv Nurs. 2006;54:94–110.
33. Bergstrom N, Braden BJ, Laguzza A, et al. The Braden scale for predicting pressure sore risk. Nurs Res. 1987;36:205–10.
34. He W, Liu P, Chen H-L. The Braden scale cannot be used alone for assessing pressure ulcer risk in surgical patients: a meta-analysis. Ostomy Wound Mange. 2012;58:34–40.
35. Soban LM, Hempel S, Munjas BA, et al. Preventing pressure ulcers in hospitals: a systematic review of nurse-focused quality improvement interventions. Jt Comm J Qual Patient Saf. 2011;37:245–52.
36. Braden B, Bergstrom N. A conceptual schema for the study of the etiology of pressure sores. Rehabil Nurs. 1987;12:8–16.
37. Apold J, Rydrych MA. Preventing device-related pressure ulcers. Using data to guide statewide change. J Nurs Care Qual. 2012;27:28–34.
38. Frantz RA, Gardner S, Specht JK, et al. Integration of pressure ulcer treatment protocol into practice: clinical outcomes and care environment attributes. Outcomes Manag Nurs Pract. 2001;5:112–20.
39. Lynn J, West J, Hausman S, et al. Collaborative clinical quality improvement for pressure ulcers in nursing homes. J Am Geriatr Soc. 2007;55:1663–9.
40. Hill-Brown S. Reduction of pressure ulcer incidence in the home healthcare setting. Home Healthcare Nurse. 2011;29:575–9.
41. Jaul E. Assessment and management of pressure ulcers in the elderly: current strategies. Drugs Aging. 2010;27:311–25.
42. Arnold M, Barbul A. Nutrition and wound healing. Plast Reconstr Surg. 2006;117(suppl):42S–58.
43. Liang L, Thomas J, Miller M, et al. Nutritional issues in older adults with wounds in a clinical setting. J Multidiscip Healthcare. 2008;1:63–71.
44. Wojcik A, Atkins M, Mager DR. Dietary intake in clients with chronic wounds. Can J Diet Pract Res. 2011;72:77–82.
45. Wolfe RR, Miller SL, Miller KB. Optimal protein intake in the elderly. Clin Nutr. 2008;27:675–84.
46. Pompeo M. Misconceptions about protein requirements for wound healing: results of a prospective study. Ostomy Wound Manage. 2007;53:30–8.
47. Matthews DE. Proteins and amino acids. In: Shils ME, Shike M, Ross AC, et al., editors. Modern nutrition in health and disease. 10th ed. Philadelphia, PA: Lippincott, Williams & Wilkins; 2006. p. 23–61. Chapter 2.
48. Desneves KJ, Todorovic BE, Cassar A, et al. Treatment with supplementary arginine, vitamin C and zinc in patients with pressure ulcers: a randomized controlled trial. Clin Nutr. 2005;24:979–87.
49. van Anholt RD, Sobotka L, Meijer EP, et al. Specific nutritional support accelerates pressure ulcer healing and reduces wound care intensity in non-malnourished patients. Nutrition. 2010;26:867–72.
50. Collins N. Adding vitamin C to the wound management mix. Adv Skin Wound Care. 2004;17:109–12.

51. Gray M. Does oral zinc supplementation promote healing of chronic wounds? J Wound Ostomy Continence Nurs. 2003;30:295–9.
52. Langemo D, Anderson J, Hanson D, et al. Nutritional considerations in wound care. Adv Skin Wound Care. 2006;19:297–303.
53. Gray M. Does oral supplementation with vitamins A or E promote healing of chronic wounds? J Wound Ostomy Continence Nurs. 2003;30:290–4.
54. Kalava UR, Cha SS, Takahashi PY. Association between vitamin D and pressure ulcers in older ambulatory adults: results of a matched case-control study. Clin Interv Aging. 2011;6:213–9.
55. Borkow G, Gabbay J, Zatcoff RC. Could chronic wounds not heal due to too low local copper levels? Med Hypotheses. 2008;70:610–3.
56. Stephenson FJ. Simple wound care facilitates full healing in post-earthquake Haiti. J Wound Care. 2011;20:5–10.
57. Popkin BM, D'Anci KE, Rosenberg IH. Water, hydration and health. Nutr Rev. 2010;68:439–58.

Elder Mistreatment

9

Sarah Teymoorian and Daniel L. Swagerty

Introduction

Elder mistreatment is a widespread problem whose recognition falls within the scope of nearly all physicians treating patients. Urologists, more than ever, are commonly long-term providers of care to their older adult patients over several years, developing meaningful therapeutic relationships. The patient's urologist may be in an excellent position to recognize the presence of abuse and neglect. However, studies have demonstrated that it is a problem under-recognized by most physicians. As mandated reporters in most states, physicians are crucial in recognizing the signs and symptoms of mistreatment and intervening early to prevent further harm to the patient.

Elder mistreatment is not a new problem, but it has only come to the attention of the medical and legal communities over the past 40 years, and few empirical studies are available on this topic. Although the term "elder abuse and neglect" is commonly used, "elder mistreatment" is often preferred as a more encompassing term. Specific subtypes of elder mistreatment that are discussed in the literature include physical abuse, sexual abuse, emotional abuse, financial exploitation, neglect, and self-neglect.

S. Teymoorian, M.D.
Department of Family Medicine,
Premier Physicians Medical Group, 300 Pasteur Dr,
Stanford, CA 94305, USA

D.L. Swagerty, M.D., M.P.H., A.G.S.F. (✉)
Department of Family Medicine and Landon Center
on Aging, University of Kansas Medical Center,
3901 Rainbow, Kansas City, KS 66103, USA
e-mail: dswagert@kumc.edu

Definition

There are many definitions of elder mistreatment used in the literature. In 2003, the National Research Council (NRC) defined elder mistreatment as "intentional actions that cause harm (whether or not harm was intended) or create a serious risk of harm to an older adult by a caregiver or other person who stands in a trust relationship to the elder, or failure by a caregiver to satisfy the elder's basic needs or to protect the elder from harm" [1]. Alternatively, the American Medical Association Diagnostic and Treatment guidelines define elder mistreatment as "acts of commission or omission that result in harm or threatened harm to the health or welfare of an older adult" [2].

If the mistreatment occurs in the home, it is referred to as domestic violence. If it occurs in institutional settings (hospitals, board and care homes, and assisted living and nursing facilities), it is known as institutional elder mistreatment.

Prevalence

It is difficult to collect accurate data on the extent of elder mistreatment. The true prevalence is hard to establish owing to the differences in definitions,

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_9,

classification, underreporting, and research methodology. There is general consensus that a large number of adults are affected. Elder mistreatment is estimated to occur in 5–10 % of the elderly population, suggesting that as many as 2.5 million older adults may be victims of mistreatment each year [3].

The Pillemer and Finkelhor Mistreatment Prevalence Study provided an initial estimate of elder mistreatment [4]. This survey of older adults in the Boston metropolitan area found a prevalence rate of 32 incidents per 1,000 older persons. However, financial exploitation and self-neglect were excluded from the study.

The 1996 National Elder Abuse Incidence Study showed that in domestic settings over 449,924 elderly, age 60 and over, experienced abuse, neglect, or self-neglect [5]. This was the first major investigation of mistreatment of the elderly in the USA. However, these results were not obtained directly from older adults; rather the study assessed Adult Protective Services records and sentinel (i.e., community professionals) reports. Thus, these results were thought to be an underestimate of true prevalence.

More recent data, published in 2010, found that 1-year prevalence was 4.6 % for emotional abuse, 1.6 % for physical abuse, 0.6 % for sexual abuse, 5.1 % for potential neglect, and 5.2 % for financial abuse by a family member. One in ten respondents reported emotional, physical, or sexual mistreatment or potential neglect in the past year. The most consistent correlates of mistreatment across abuse types were low social support and previous traumatic event exposure [6].

Types of Elder Mistreatment

Elder mistreatment may take many forms. The types of elder mistreatment are often classified as physical abuse and neglect, psychological abuse, financial exploitation, and violation of rights. Table 9.1 lists the various forms of elder mistreatment.

Table 9.1 Types of elder mistreatment

Type of mistreatment	Definition
Physical abuse	An act that may result in pain, injury, impairment, or illness (e.g., punching, kicking, or shoving)
Physical neglect	Failure of a caregiver (or the older adult) to provide goods or services that are necessary for optimal function or to avoid harm
Psychological abuse	Conduct that causes mental anguish in an older adult (e.g., verbal harassment or degradation)
Sexual abuse	Nonconsensual sexual contact of any kind, including physical or verbal sexual contact
Financial exploitation	Misappropriation of an older adult's assets for the benefit of another person
Violation of rights	Deprivation of any inalienable right (personal liberty, personal property, assembly, speech, privacy, voting) (e.g., taking personal items from an older adult)

Physical Abuse

Often the most graphic form of elder mistreatment, physical abuse is fortunately the least common form of elder mistreatment. The American Geriatrics Society Position Statement defines physical abuse as acts causing pain or injury. Specifically, it can be described as the purposeful infliction of physical trauma or pain or the willful deprivation by a caregiver of items necessary to avoid physical harm. Examples of physical abuse include hitting, punching, striking with objects, slapping, grabbing, biting, or otherwise causing bodily injury and threatening the person with or using a weapon [7].

Sexual Abuse

The National Center on Elder Abuse defines sexual abuse as "nonconsensual sexual contact of any kind" [8]. This can include unwanted sexual advances, fondling, forced viewing of pornography, sexualized kissing, oral–genital contact, digital penetration, and rape. Another definition is when an elder is "forced, tricked, coerced or manipulated into unwanted sexual contact . . . also includes sexual contact with elders who are unable to grant informed consent" [9].

Sexual abuse is the least recognized and reported form of mistreatment of older adults and represents less than 1 % of mistreatment reported in the USA. Due to the nature of their practice, urologists may be in one of the best positions to recognize sexual abuse. The typical sexual abuse victim is female (although males can indeed be victims), cognitively impaired, and physically frail. The abusers are commonly male (although females can be abusers) and may be caregivers, relatives, or residents in a long-term care facility. Older adults living in long-term care facilities may be at increased risk for sexual abuse because of their physical dependence on others for care [10–15].

Many older adults with cognitive impairment will be unable to report the abuse; thus, urologists should be aware of possible physical and behavioral indicators of sexual abuse. In a study involving 125 cases of elder sexual abuse, half of the victims had vaginal trauma and one-third had bruising to the labia. One half of the victims had injuries such as bruising or lacerations to non-genital body parts [16]. Anal injuries can also occur in male or female sexual abuse victims and should be a regular part of the sexual abuse exam. Other physical signs that may alert a physician to sexual abuse include a sexually transmitted infection, bleeding or bloodstained clothing or sheets, pain, or difficulty sitting [15].

Behavioral or emotional changes may also be a red flag for sexual abuse, especially in older adults with cognitive impairment. These changes may include fear of a particular individual, fear of bathing or dressing changes, or fear of being touched. The victim may show signs of anger, withdrawal, depression, or changes in sleep. These are certainly not specific findings in older adults, but in the appropriate context may prompt the physician to consider the possibility of sexual abuse [15, 17, 18]. Studies have shown that older adults with dementia are abused more often than those without dementia by people who are known to them such as a family member, caregiver, or another nursing home resident [19].

Most research on the sexual abuse of older adults has found few cases involving men as victims. The first national study of the sexual abuse of older adults in nursing homes revealed that the majority of alleged and confirmed male victims were white men with physical and cognitive limitations. The type of sexual abuse most frequently substantiated was fondling, but other forms included inappropriate sexual interest in the victim's body, exposure of private body parts to harass or humiliate, and showing the victim pornography. The sexual offenders in this study were more often men than women and were a mix of facility staff members and fellow residents [13].

One of the greatest challenges in the sexual abuse of older adults is how to respond to reports and resolve cases effectively. Sexual abuse often occurs in private and involves the violation of deep social taboos. For adult protective services (APS) caseworkers, these cases pose particular challenges because of the charged emotional content but also because they are difficult to prove. Many victims are unable or unwilling to testify, and it is difficult to obtain civil court orders to protect victims. Criminal prosecution of perpetrators rarely occurs [13].

Psychological or Emotional Abuse

Psychological or emotional abuse can be defined as the infliction of anguish, pain, or distress through verbal or nonverbal acts including verbal aggression, infantilization, intimidation, withholding affection, humiliation, harsh orders, isolation, purposeful confinement, denying food or privileges, or other forms of harassment [7]. Psychological abuse is often more difficult to detect and confirm than other forms of physical abuse. The behaviors of the older adult and the caregiver are important clues to detect psychological or emotional abuse. Caregiver behavior such as style of communication including impatience, irritability, and demeaning statements may indicate a type of verbal abuse. Also more subtle signs such as not providing social or emotional stimulation or restricting or preventing normal activities can result in social isolation of an older adult. Important behavioral clues from the older adult include nonspecific findings such as ambivalence, high levels of anxiety, fearfulness, or anger towards the caregiver. Other concerning behaviors include requests for sedating medications, lack of adherence to treatment plans, or frequently cancelled appointments [20].

Neglect

The most common form of mistreatment, neglect, can be defined as the failure to provide services necessary to maintain physical and mental health. The vulnerable older adult does not receive needed assistance with obtaining food, clothing, shelter, personal hygiene, medical care, as well as protection from health and safety hazards. It can include the intentional or unintentional withholding of these goods and services which results in the older adult's failure to thrive, such as malnutrition and dehydration [7, 21–23]. Neglect can be divided into active neglect, passive neglect, and self-neglect. Active neglect is when caregivers deliberately withhold care or services from an older adult and passive neglect is when caregivers do not deliberately withhold necessities but may be unaware of what is needed [24, 25].

Self-Neglect

Self-neglect has been defined by the National Center on Elder Abuse as "…the behavior of an elderly person that threatens his/her own health and safety. Self-neglect generally manifests itself in an older person as a refusal or failure to provide himself/herself with adequate food, water, clothing, shelter, personal hygiene, medication (when indicated), and safety precautions [8]." Self-neglect is the most common form of mistreatment that physicians will encounter in practice and accounts for the highest case load of Adult Protective Services workers. Unlike other forms of elder mistreatment, self-neglect is often not a purposeful act and may result from a lack of physical or mental capacity of the victim [21].

Financial Exploitation

The definition of financial exploitation varies among states and is also referred to as material exploitation, material abuse, financial abuse, or fiduciary abuse. Financial exploitation is misrepresentation of an older adult's assets for the benefit of another person. Examples would include taking, hiding, or misappropriating money or property for personal use or gain in violation of the older adult's wishes or trust. It may also include the improper use of conservatorship, guardianship or power of attorney, fraud, embezzlement, or undue influence [7]. Financial exploitation occurs in all socioeconomic, racial, and ethnic groups. Perpetrators can include, but are not limited to, family members, caregivers, friends, acquaintances, neighbors, landlords, contractors, professional fiduciaries, or scam artists [26].

Violation of Rights

Deprivation of any inalienable rights constitutes a violation of rights. This may include preventing the older adult from exercising their right to personal liberty, personal property, assembly, speech, privacy, or vote [23].

Under-Detection and Improper Reporting

A number of different factors seem to contribute to the under-detection and reporting of elder mistreatment [27]. The psychosocial aspects of elder mistreatment cause underreporting and render accurate prevalence estimates difficult. Often, victims may feel embarrassed, intimidated, or overwhelmed, and denial is a common coping strategy in victims, perpetrators, and healthcare providers [21]. A major obstacle is a lack of awareness on the part of physicians and other healthcare providers. Table 9.2 lists many of the reasons for the underreporting of elder mistreatment. The victim or person reporting the abuse

Table 9.2 Reasons for poor identification and underreporting of elder mistreatment by physicians

• Lack of training in identifying mistreatment
• Ageism
• Disbelief
• Isolation of victims
• Subtle presentation
• Reluctance to confront offenders
• Reluctance to report suspected abuse
• Unsure about reporting procedures
• Fear of jeopardizing relationships with hospitals or nursing facilities

Table 9.3 Predisposing factors for elder mistreatment

Patient risk factors
• Older age
• Lack of access to resources
• Low income
• Social isolation
• Minority status
• Low-level education
• Substance abuse
Caregiver risk factors
• Substance abuse
• Psychological disorder and/or character pathology
• Previous history of family violence
• Caregiver burnout and/or frustration
• Cognitive impairment

may be fearful of the consequences of reporting. Additionally, healthcare professionals might minimize complaints or symptoms because of disbelief, fear of accusing the perpetrator, ignorance of symptomatology, or reluctance to deal with the issue. Another issue in underreporting of elder mistreatment is ageism, which is the minimization of an older person's problems with lack of concern for their rights and needs.

In particular, physicians are seldom personally involved in detecting and reporting mistreatment. In general, health providers are often reluctant to address violence. Because physicians are usually the only person besides the immediate family and any caregiver who is involved in the care of the older adult, they may be in the best position to identify, report, and respond to suspected mistreatment. The physician is also likely to be the only person able to order the testing, hospital admission, or additional support services sometimes needed to address suspected cases.

Predisposing Factors for Mistreatment

There is no specific profile of victim or perpetrator of elder mistreatment. Elder mistreatment occurs among men and women of all racial, ethnic, and socioeconomic groups. The etiology of elder abuse and the characteristics of those involved are multifactorial [28, 29]. Understanding the common risk factors and characteristics of victims and perpetrators aids in addressing and intervening in elder mistreatment. Although there is no solid unifying theory for elder mistreatment, it is thought that there are four primary contributing factors [28]: (1) physical dependence, (2) caregiver stress, (3) family violence, and (4) pathologic abuse. Table 9.3 lists the commonly accepted risk factors for elder mistreatment.

Specific patient risk factors include female sex, age greater than 80 years, social isolation, functional decline, and cognitive impairment [30]. Additional risk factors for abuse may include history of family conflict or dysfunction. Disabilities that increase dependence on the caregiver, such as cognitive impairment and dementia, depression, substance abuse, and behavioral difficulties, increase the risk of elder mistreatment [28, 30, 31].

Characteristics of the caregiver are also very important risk factors for mistreatment. Specific risk factors include a single caregiver and an imbalance between the needs of the patient and the ability of the caregiver to meet those needs. Psychopathology of the caregiver, such as alcoholism, drug addiction, or severe psychological problems, is also a risk factor. Dependency of the caregiver on the older adult for emotional or financial support can also increase the risk of mistreatment [5, 32].

Consequences of Elder Mistreatment

Elder mistreatment has grave health and socioeconomic implications. The specific health consequences include greater morbidity and mortality [29]. A study of 2,812 older adults found that elder mistreatment was associated with a higher risk of nursing home placement and all-cause mortality [29, 33]. In another study of 9,318 older adults, elder mistreatment was associated with a higher mortality rate, particularly for cardiovascular mortality as well as increased emergency service use [34–36]. Mistreated older adults often have more physical and psychiatric disorders. Somatic complaints such as chronic pain and traumatic injuries are experienced more frequently in victims of mistreatment. A prospective study of community dwelling older adults reported a threefold increased risk of death for those with a reported history of elder mistreatment [29]. Socioeconomic consequences include increased hospitalizations, emergency department visits, and physician visits [33].

Title XX of the Social Security Act, passed in 1974, mandates states to develop and maintain protective service agencies for older adults. In 2004 the USA spent nearly $500 million on Adult Protective Services (APS) agencies. The scope and practices of APS agencies vary according to individual state laws, how those laws are interpreted, and the funding and interests in different jurisdictions. Regardless of state location, APS aims to provide coordinated care that includes social and health systems. APS agencies presume older adults have decision-making capacity and accept their choices until that adult is deemed to lack capacity by a healthcare professional. The underlying philosophy of APS is to protect an individual's right to self-determination, maintain a family unit whenever possible, and provide recommendations for the least restrictive living environment [37].

Prevention

Prevention of elder mistreatment is difficult and depends as much on the social support network as on the medical network. Preventing elder mistreatment involves identifying high-risk patients and caregivers and attempting to address the underlying issues. Screening patients and caregivers can be helpful. The mnemonic SAVED (*S*tress/social isolation, *A*lcohol/other drug abuse, *V*iolence (previous history), *E*motional (psychiatric disease), *D*ependency (dynamics in family)) is one way to screen for indicators of high-risk situations and possible abuse [38]. Helping patients obtain county or state assistance can also help reduce some high-risk situations.

Assessment of the Patient

History

As with most medical encounters, the key to detecting elder mistreatments begins with the patient's history. Table 9.4 lists essential features of history taking in the assessment of elder mistreatment. A basic understanding of the patient's medical problems and past diagnoses, especially depression, mental illness, or history of dementia or cognitive dysfunction, is important to note. Elements of their social history including ability to manage their own activities of daily living, need for caregiver assistance, and drug or alcohol abuse should be asked. Finally, inquiring about a history of previous violence or neglect is key component in this assessment.

The mistreated older adult often presents with somatic complaints [29]. Some indicators of abuse include a history of a delay in seeking medical care, conflicting or implausible accounts of the event, or a history of similar or suspicious episodes [28].

Table 9.4 Essential features of the history in the assessment of elder mistreatment

- Medical problems/diagnoses
- Detailed descriptions of the home environment (adequacy of food, shelter, supplies, etc.)
- Accurate descriptions of events related to injury or trauma (instances of rough handling, confinement, verbal or emotional abuse)
- History of previous violence
- Description of previous injuries and events surrounding them
- Description of berating, threats, or emotional abuse
- Improper care of medical problems, untreated injuries, poor hygiene, prolonged period before presenting for medical attention
- Depression or other mental illness
- Extent of confusion or dementia
- Drug or alcohol abuse
- Quality/nature of relationships with caregivers

Caregiver Assessment

Part of history taking in elder mistreatment includes the assessment of caregiver(s). Patients should be asked specifically if they have a caregiver and who this individual is (family, friend, paid caregiver). If the caregiver is present at the medical appointment, the clinician should observe relationship dynamics including signs of verbal abuse, threats, or fearfulness displayed by the patient in the presence of the caregiver [29].

Conducting the Interview

When abuse or neglect is suspected, it is best to interview the patient without the caregiver(s) present. However, an accurate history may be difficult to obtain if the older adult has impairments in cognition, vision, and/or hearing. Table 9.5 lists some communication tips for obtaining the best possible history from an older adult. The interview should be conducted in the most conducive environment in which the older adult can understand the context and content of the conversation as well as feel safe being open and honest.

The interview should begin with general questions concerning the conditions in the personal home or nursing facility. The interviewer should attempt to obtain an accurate understanding of the patient's daily life, including needs and assistance for personal care, meals, medication, shopping, and social support. The nature and quality of the relationship with caregiver(s) must be assessed, including how well the older adult's needs are being met, how safe the patient feels, and whether the patient desires a change in their caregiver(s) or living situation. The older adult's mental status should be assessed for indications of cognitive impairment, depression, and alcohol or substance abuse. The patient's financial situation may also need to be discussed, including whether financial dependency is present for either the older adult or caregiver on the other. If there is any concern that the older adult is being abused or neglected, the caregiver should also be interviewed. Care must be taken to be as objective as possible in any interview with the older adult and caregiver, including not over-interpreting comments or making suggestions. The interviewer should try to identify specific causes of stress, such as finances or dementia-related difficult behaviors. There are many caregiver burden scales available, including the widely accepted Zarit Burden Interview, which can help to quantify the amount of stress and burden [39].

If elder mistreatment is suspected, physicians should become much more specific in their questions. Table 9.5 provides a set of direct questions for such interviewing of the older adult patient. The patient and the suspected perpetrator should be interviewed separately and then together. In initially interviewing the suspected perpetrator, care should be taken to avoid confrontation. An accurate history can often be best obtained from the caregiver if their caregiver stresses and burdens are understood and acknowledged. Specific causes of stress, such as finances and dementia-related difficult behaviors, should be sought by the interviewer. The interviewer should seek to understand and empathize with the degree of stress and caregiver burden.

Table 9.5 Communication tips for interviewing older adults concerning elder mistreatment

General communication strategies
– Position yourself in front of the patient
– Speak slowly and clearly
– Favor monosyllabic words
– Use a low tone of voice
– Use a well-lit room to facilitate lip reading
– Use literature with large print
– A portable microphone with a headset should be available for patients with severe hearing impairment
Specific questions concerning mistreatment
– Do you have frequent disagreements with your caregiver (son, daughter, spouse, paid provider, etc.)?
– What happens when you disagree?
– Are you yelled at?
– Has anyone ever scolded or threatened you?
– Are you afraid of anyone at home?
– Have you ever gone without food or medicine?
– Have you ever had your glasses or hearing aid taken from you?
– Has anyone at home ever hurt you, like slapping, punching, or kicking you?
– Has anyone ever touched you without your permission?
– Has anyone ever made you do things that you did not want to do?
– Has anyone ever taken your things away without asking?
– Are you made to stay in your room?

Table 9.6 Basic features of the physical examination in assessing elder mistreatment

Area examined	Possible signs of mistreatment
Head	Traumatic alopecia or other evidence of direct physical violence; poor dental hygiene
Skin	Hematomas, welts, bite marks, pressure ulcers
Musculoskeletal	Fractures or signs of previous fractures
Neurologic	Cognitive impairment that is a risk factor for mistreatment and influences management decisions regarding capacity
Genitorectal	Poor hygiene, inguinal rash, impaction of feces
General	Weight loss, dehydration, poor hygiene, unkempt appearance

Physical Examination

Once the clinician has completed the history taking, a complete physical should be done. Basic features of the physical examination in assessing elder mistreatment are outlined in Table 9.6. Given the sensitive and often invasive nature of these examinations, all efforts should be taken to promote patient privacy and dignity. Important specific features include keeping the patient comfortable and warm during the examination, asking for permission prior to touching the patient, and explaining each step in the examination as you are doing it. Having a chaperone in the room with you is important for medical–legal reasons, and this individual should be distinct from the patient's caregiver.

Physical Abuse Findings

Physical abuse may include assault, battery, or force likely to produce injury. Other forms of physical abuse include sexual assault, prolonged or continual deprivation of food and water, and use of punitive or inappropriate physical or chemical restraint. The physical exam should identify signs of physical abuse including suspicious patterns of injury such as lesions in skinfolds (under the breast, axilla, popliteal fossa, groin) and inner thigh, circumferential lesions, linear lesions, and multiple fractures. Other signs of physical abuse may include pressure ulcers, burns, lacerations or abrasions, and hemorrhage [22, 28, 40].

Injury Assessment

As part of the assessment of the patient's injuries, the clinician should also make note of whether the history is consistent with the exam and whether there is evidence of old injuries such as healing fractures on X-rays [41]. A delay in seeking care for old or new injuries is concerning and is an important clinical examination finding.

Bruises

Accidental bruises often occur in predictable locations but are unusual on the neck, ear, genitalia, buttocks, or soles of the feet. Although bruises cannot be dated based on color, multiple bruises in various stages of healing are concerning for repeated trauma [42, 43]. Other bruises that should raise suspicion include bruises that retain the shape of an object or bruises with central clearing which may occur if underlying tissue has been struck with a solid object. Circumferential bruises around the arms, wrists, or legs may occur if the victim has been grabbed or held down by force. Unexplained genital lesions should be considered as possible markers of sexual abuse, including genital bruising.

Burns

Specific burn injuries that may be found on exam include cigar or cigarette burns, patterned burns from ropes, irons or stove burners, or immersion burns. Burns from immersion in hot water often have a sock and glove distribution or may include the buttock or genitalia. The soles of the feet, palms, or buttock may be less severely involved if they were held against the relatively cooler floor of a bathtub or sink.

Fractures

Fracture injuries are often found in more acute care settings and can result from falls or direct force. Skull and facial fractures, fractures in multiple locations, or fractures in multiple stages of healing should arouse suspicion for elder mistreatment. Other types of fractures that may be indicative of physical abuse based on the history include spinal vertebral fractures and occult fractures.

Neglect

Clinicians with long-standing patient–clinician relationships may notice changes in behavior which are concerning for self-neglect. Specifically, a new pattern of missing appointments or a new inability to take medications may prompt concerns. Self-neglect should also be considered when an older adult appears disheveled or displays evidence of poor hygiene. Malnutrition, dehydration, and muscle atrophy may be due to underlying medical conditions or due to neglect.

Financial Abuse

The evaluation for financial abuse should include an assessment of mental status and capacity. There are many validated cognitive screening tools that could be used to evaluate mental status and capacity. Assessing vulnerability for abuse such as depression, anxiety, or recent bereavement is critical. A referral for neuropsychiatric testing may be indicated if the patient has subtle findings or equivocal results on cognitive screening tests.

Possible financial abuse can be identified by an observant clinician. Examples include a patient who is no longer able to afford basic items, an elder who appears at appointments with a new friend, or a caregiver who appears intrusive or overly protective. If there is suspicion of financial abuse, the clinician should directly ask "Is anyone taking or using your money without your permission?" [44, 45].

Documentation

When documenting the interview and exam findings, it is important to take a forensic approach in providing a thorough, detailed written description. A forensic approach implies that the clinician is mindful of the legal implications of the findings of the interview and exam. Medical documents such as clinical notes, laboratory tests, radiographic imaging, and photographs will become legal documents.

Documentation should be legible (if handwritten) and concise, without alterations. Pertinent positive and negative findings as well as objectively reported facts are imperative. When possible, the patient's own words should be quoted, for example, "My daughter hit me with a broom handle." Specific dates, names, and times are necessary in this type of documentation. Interactions that the clinician observes between the patient and caregiver should also be described.

Forensic documentation of locations, patterns, and types of injuries may be done with detailed descriptions, sketches of body diagrams, and/or photographs. The size, color, shape, and location of injuries and bruises should be noted. For pressure ulcers, the size, depth, stage, and presence and color of exudates should be described. Forensic or medical photographs should be taken before medical treatment is given or invasive examination is performed (e.g., before a wound is cleaned or laceration is sutured). It is recommended that photographs be taken from several angles, whole body and close up with coin or ruler to illustrate the size of an injury. All photographs should be marked with date and time. If a crime is suspected, ask law enforcement to have their crime scene investigation unit take the photographs. If forensic photography is not an option, a medical photographer should be asked to take pictures [45, 46].

Elder Mistreatment Report

Forty-four US states, as well as the District of Columbia, Guam, Puerto Rico, and the Virgin Islands, have mandatory reporting laws that require healthcare professionals to report a reasonable suspicion of abuse. Table 9.7 describes important points in reporting elder mistreatment. Clinicians should determine the specific reporting requirements in their state [47, 48]. Reporters are immune from civil liability if they act in good faith and without malice. Conversely, healthcare providers can be found negligent if they fail to report suspected abuse.

The report should include a concise statement regarding the history and injury. A concluding statement should summarize the likelihood of abuse, for example, definite, accident, or indeterminate. Some state APS agencies will provide the clinician with a form to complete.

Management

After a report is filed to APS, the physician should notify the patient, caregiver, or facility involved in the report. These are key stakeholders in the resolution of mistreatment. There may be unusual circumstances in which the physician is concerned that disclosing the report to the patient and caregiver may escalate violence. An explanation from the physician of the need to make a report to help the patient's well-being can help the APS worker have a more successful visit [45].

If the patient lacks decisional capacity, they may require a competency determination in court. If the older adult is not competent to make decisions, a guardian may need to be appointed by the state. Unlike child abuse cases, if the older adult does have decisional capacity, he or she may refuse intervention after the APS investigation is complete [46].

Summary

Elder mistreatment, an important type of domestic or institutional violence, requires better recognition and intervention by physicians. Physicians detect elder mistreatment only through awareness, healthy suspicion, and screening. Table 9.8 lists the key points for recognition of elder mistreatment by physicians. A detailed, well-documented medical history and comprehensive physical examination are needed to identify and document when injury and neglect occur in older adult patients. Suspected cases must be reported and resources obtained for both the older adults and their caregivers when mistreatment is identified. Mistreatment can be prevented by creating and maintaining a healthy living environment for the older adult. Patient and caregiver education is also invaluable for preventing abuse and neglect.

Table 9.7 Reporting elder mistreatment

- All healthcare providers and administrators are mandated by law to report suspected elder mistreatment
- Laws differ from state to state
- You are immune from civil liability if you act in good faith and without malice
- If you fail to report, you risk fines, jail, or loss of license
- Report to state or county division of Adult Protective Services or child and family services
- Area agency on aging is usually a great resource
- National Domestic Violence Hotline: (800) 799-SAFE
- Older Women's League: (800) 825–3695

Table 9.8 Key points about elder mistreatment

- Prevalent—at least 5 % of all US older adult
- Physical abuse least common and physical neglect most common
- Poorly identified and reported by physicians
- Patient risk factors—cognitive and physical impairment, isolation, substance abuse, low income and education
- Caregiver risk factors—substance abuse, psychological/character pathology, caregiver burnout, cognitive impairment

References

1. Bonnie R. Elder Mistreatment: abuse, neglect and exploitation in an aging America. Washington, DC: National Academies Press; 2003.
2. Aravanis SC, Adelman RD, Breckman R, Fulmer TT, Holder E, Lachs M, et al. Diagnostic and treatment guidelines on elder abuse and neglect. Arch Fam Med. 1993;2(4):371–88.
3. Pavlik VN, Hyman DJ, Festa NA, et al. Quantifying the problem of abuse and neglect in adults: analysis of a statewide database. J Am Geriatr Soc. 2011;49(1):45–8.
4. Lachs MS, Pillemer K. Abuse and neglect of elderly persons. N Engl J Med. 1995;332(7):437–43.
5. National Center on Elder Abuse. National elder abuse incidence study. Washington, DC: American Public Human Services Association; 1998.
6. Acierno R, Hernandez MA, Amstadter AB, et al. Prevalence and correlates of emotional, physical, sexual and financial abuse and potential neglect in the United States: the national elder mistreatment study. Am J Public Health. 2010;100(2):292–7.
7. Paveza GJ. Elder mistreatment: an overview. In: Mezey MD, editor. The encyclopedia of elder care. New York, NY: Springer; 2001. p. 231–2.
8. National Center on Elder Abuse. Major types of elder abuse. US Administration on Aging Website [Updated 2007]. http://www.ncea.aoa.gov/ncearoot/main_site/faq/basics/types_of_abuse.aspx. Accessed 11 Nov 2011.
9. Speaking the unspeakable: an interview about sexual assault with Holly Ramsey-Klawsnik. Nexus 1998;4. Available at: http://www.preventelderabuse.org/nexus/hrklawsnik.html
10. Holt MG. Elder sexual abuse in Britain: preliminary findings. J Elder Abuse Negl. 1993;5:63–71.
11. Ramsey-Klawsnik H. Elder sexual abuse: preliminary findings. J Elder Abuse Negl. 1991;3:73–90.
12. Sobsey D, Doe T. Patterns of sexual abuse and assault. Sex Disabil. 1991;9:243–59.
13. Chihowski KC, Hughes S. Clinical issues in responding to alleged elder sexual abuse. J Elder Abuse Negl. 2008;20(4):377–400.
14. Teaster PB, Ramsey-Klawsnik H, Mendiondo MS, Abner E, Cecil K, Tooms M. From behind the shadows: a profile of sexual abuse of older men residing in nursing homes. J Elder Abuse Negl. 2007;19(1–2):29–45.
15. Schneider DC, Li X. Sexual abuse of vulnerable adults: the medical director's response. J Am Med Dir Assoc. 2006;7(7):442–5.
16. Burgess AW, Hanrahan NP, Baker T. Forensic markers in elder female sexual abuse cases. Clin Geriatr Med. 2005;21(2):399–412.
17. Dyer CB, Connolly MT, McFreely P. The clinical and medical forensics of elder abuse and neglect. In: Bonnie R, editor. Elder mistreatment: abuse, neglect and exploitation in an aging America. Washington, DC: National Academies Press; 2003.
18. Teitelman J, Copolillo A. Sexual abuse among persons with Alzheimer's disease: guidelines for recognition and intervention. Alzheimers Care Q. 2002;3:252–7.
19. Burgess AW, Phillips SL. Sexual abuse and dementia in older people. J Am Geriatr Soc. 2006;54(7):1154–5.
20. Pacala JT, Sullivan GM, editors. Geriatrics review syllabus: a core curriculum in geriatric medicine. 7th ed. New York, NY: American Geriatrics Society; 2010.
21. Reyes-Ortiz CA. Neglect and self-neglect of the elderly in long-term care. Ann Longterm Care. 2001;9:21–4.
22. Paris BE, Meier DE, Goldstein T, et al. Elder abuse and neglect: how to recognize warning signs and intervene. Geriatrics. 1995;50(4):47–51.
23. Swagerty DL, Takahasi P, Evans J. Elder mistreatment. Am Fam Physician. 1999;59(10):2804–8.
24. Kleinschmidt KC. Elder abuse: a review. Ann Emerg Med. 1997;30(4):463–72.
25. Fulmer T, Paveza GJ. Neglect in the elderly patient. Nurs Clin North Am. 1998;33:457–66.
26. Bernzta SI. Financial abuse. In: Mezey MD, editor. The encyclopedia of elder care. New York, NY: Springer; 2001. p. 21–4.
27. Rosenblatt DE. Elder abuse: what can physicians do? Arch Fam Med. 1996;5(2):88–90.
28. Lachs MS, Fulmer T. Recognizing elder abuse and neglect. Clin Geriatr Med. 1993;9(3):665–81.
29. Lachs MS, Williams CS, O'Brien S, Pillemer KA, Charlson MS. The mortality of elder mistreatment. JAMA. 1998;280(5):428–32.
30. Lachs BL, Fulmer T, et al. A prospective community based pilot study of risk factors for the investigation of elder mistreatment. J Am Geriatr Soc. 1994;42(2):169–73.
31. Hwalk MA, Neale AV, Goodrich CS, et al. The association of elder abuse and substance abuse in the Illinois Elder Abuse System. Gerontologist. 1996;36(5):694–700.
32. Lachs MS, Williams C, O'Brien S, et al. Older adults: an 11-year longitudinal study of adult protective service use. Arch Intern Med. 1996;156(4):449–52.
33. Lachs MS, Williams CS, O'Brien S, Pillemer KA. Adult protective service use and nursing home placement. Gerontologist. 2002;42(6):734–9.
34. Dong XQ, Simon MA, Beck TT, et al. Elder abuse and mortality: the role of psychological and social wellbeing. Gerontology. 2011;57(6):549–58.
35. Dong X, Simon M, de Leon CM, et al. Elder self-neglect and abuse and mortality risk in a community-dwelling population. JAMA. 2009;302(5):517–26.
36. Dong X, Simon MA, Evans DA. Prospective study of the elder self-neglect and emergency department use in a community population. Am J Emerg Med. 2012;30(4):553–61.
37. Otto JM. The role of adult protective services in addressing abuse. Generations. 2000;24(2):33–38.

http://www.apsnetwork.org/About/history.htm. Accessed 6 May 2012.
38. Kosberg JI. Preventing elder abuse: identification of high risk factors prior to placement decisions. Gerontologist. 1988;28(1):43–50.
39. Zarit SH, Orr NK, Zarik JM. The hidden victims of Alzheimer's disease: families under stress. New York, NY: University Press; 1985.
40. Dyer CD. Elder abuse and maltreatment: a report of the Blue Ribbon Panel in Family Violence. Austin: Texas Medical Association; 1999.
41. Canadian Task Force on the Periodic Health Examination. Periodic health examination, 1994 update: 4. Secondary prevention of elder abuse and mistreatment. CMAJ. 1994;151(10):1413–20.
42. Knight B, editor. Simpson's Forensic medicine. 11th ed. New York, NY: Oxford University Press; 1997.
43. Crane J. Injury interpretation. In: Stark MM, editor. Forensic science; a physician's guide to clinical forensic medicine. Totowa, NJ: Humana; 2000.
44. Widera E, Steenpass V, Marson D, Sudore R. Finances in the older patient with cognitive impairment: "he didn't want me to take over.". JAMA. 2011;305(7):698–706.
45. Mosqueda L, Dong X. Elder abuse and self-neglect: "I don't care anything about going to the doctor, to be honest.". JAMA. 2011;306(5):532–40.
46. Swagerty D. Elder mistreatment: identification and assessment. Clin Fam Pract. 2003;5(1):195–211.
47. The Eldercare Locator. Available at: http://eldercare.gov/Eldercare.NET/Public/mobile_index.aspx. Accessed 24 May 2011.
48. National Center on Elder Abuse. NCEA web site. Available at: http://www.elderabusecenter.org. Accessed 11 Nov 2011.

10 Urinary Incontinence: Evaluation and Diagnosis

Ananias C. Diokno, Michelle J. Lajiness, and Tomas Lindor Griebling

Introduction

Urinary incontinence is one of the most common urologic conditions diagnosed in older adults. It is imperative that clinical practitioners have a working knowledge of the different types of urinary incontinence and the factors that can cause this for older patients. This approach is critical in order to correctly diagnose urinary incontinence and to help make therapeutic decisions. It is indeed the starting point of management for all patients with urinary incontinence regardless of the clinical setting, including the outpatient clinic, acute care hospital, rehabilitation unit, or long-term care facility. This chapter presents an overview of the various types of urinary incontinence and methods for clinical evaluation and diagnosis.

A.C. Diokno, M.D., F.A.C.S. (✉) • M.J. Lajiness, M.S., F.N.P-B.C.
Beaumont Medical Office Building, 3535 W Thirteen Road, Suite 407, Royal Oak, MI 48073, USA
e-mail: adiokno@beaumont.edu; mlajiness@beaumont.edu

T.L. Griebling, M.D., M.P.H., F.A.C.S., F.G.S.A., A.G.S.F.
Department of Urology and The Landon Center on Aging, University of Kansas School of Medicine, 5021 Sudler, Mailstop 3016, 3901, Rainbow Blvd., Kansas City, KS 66160, USA
e-mail: tgriebling@kumc.edu

Types of Urinary Incontinence

The International Continence Society defines urinary incontinence (UI) as the involuntary loss of urine [1]. They define overactive bladder (OAB) as urinary urgency, with or without urinary incontinence, usually with urinary frequency and nocturia, in the absence of pathologic or metabolic factors that would explain these symptoms. There are two main categories of urinary incontinence including transient incontinence and persistent or chronic incontinence.

Transient Urinary Incontinence

Transient urinary incontinence is usually acute in nature and is typically reversible. The most common clinical presentation is new or sudden onset of UI in a patient who has previously been continent. Cases of transient UI are caused by temporary factors which are usually treatable. The mnemonic DIAPPERS (Table 10.1) has been described and used by clinicians to prompt the search for underlying factors that can lead to transient UI [2]. It is estimated that 30–50 % of incontinence in the elderly population is transient [4]. There are a wide variety of predisposing factors, many of which are prevalent in older adults that can cause transient UI.

Delirium is a common syndrome that occurs in older adults. It is characterized by changes in

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_10,

Table 10.1 Transient causes of urinary incontinence [2]

D—delirium, dementia, or both
I—infection
A—atrophic urethritis or vaginitis
P—pharmaceuticals or polypharmacy
P—psychological factors, especially depression
E—excessive urine output
R—restricted mobility
S—stool impaction

Table 10.2 Medications that cause transient urinary incontinence [5, 6]

Medication	Effect on urinary system
Alpha-adrenergic receptor antagonists	Smooth muscle relaxation of the bladder neck and urethra causing stress UI (mainly in women)
Tricyclic antidepressants Alpha-adrenergic agonists	Anticholinergic effect and alpha-adrenergic receptor agonist effect causing post-void dribbling, straining, and hesitancy in urine flow and even urinary retention
Psychotropics	May decrease afferent input resulting in decrease in bladder contractility. Can accumulate in elderly patients causing confusion resulting in functional incontinence
Cholinesterase inhibitors	Increase bladder contractility and may cause incontinence
Narcotic analgesics, opioids	Decrease bladder contractility, decrease afferent input. Depress the central nervous system causing sedation, confusion, and immobility, leading to urinary retention and overflow or functional UI
Calcium channel blockers	Impair bladder contractility, causing urinary retention and overflow UI
Diuretics	Overwhelm the bladder with rapidly produced urine for up to 6 h after ingestion. Increased urine output leads to UI
Methylxanthines	Increase urine output causing polyuria and bladder irritation
ACE inhibitors	Can cause coughing which could increase stress UI

mental status with inattention and a fluctuating course. In addition, patients with delirium often have alterations in level of consciousness and can experience hallucinations. Delirium may be hyperactive or hypoactive. UI is caused by lack of attention to bladder sensations and alterations in consciousness.

Urinary tract infections in older adults can cause urgency resulting in UI. This is due to the irritation of the bladder epithelium caused by the acute infection. Simply treating the infection will often clear the UI. Antibiotic therapy may be started empirically and should be adjusted if necessary based on culture and susceptibility results.

In women, atrophic urethritis or vaginitis can also cause transient UI. After menopause, the concentration of estrogen in the genitourinary tissues decreases, and this can lead to inflammation. This in turn leads to irritation of the lower urinary tract and may cause urgency and urge urinary incontinence. Treatment with topical vaginal estrogen replacement can help to reduce symptoms. This is usually administered two or three times weekly. This therapy is contraindicated in women with a personal history of breast or uterine cancer.

Polypharmacy is common in older adults. Many medications commonly used to treat comorbid conditions in elderly patients can actually cause UI. This can be due to a variety of factors including increased urine production, bladder overactivity, or urinary retention. For example, patients may experience nocturia and urinary leakage during their sleep if they begin to take a diuretic medication in the evening. Adjusting the timing or selection of medication can frequently help to improve or resolve the UI. Working with a patient's primary care provider to change medications can be very effective. A list of medications known to potentially cause or exacerbate UI is shown in Table 10.2.

Psychological factors including depression can cause transient UI. Older adults with new onset of UI should be screened for depression. A variety of validated assessment instruments are available for this purpose. Referral to a mental health provider may be necessary. Appropriate treatment of the mental health issues can often help to resolve the UI.

Excessive urine production can be a result of metabolic conditions such as congestive heart failure (CHF), pulmonary edema, diabetes insipidus, polydipsia, or hyperglycemia secondary to diabetes mellitus. Patients with significant peripheral edema often get increased urine production at night when they lie down, and the excess fluid in the lower extremities is recirculated. Obstructive sleep apnea can cause alterations in production of atrial natriuretic peptide and vasopressin which can lead to increased urine production at night. This can cause new onset nocturia and enuresis. Treatment of these metabolic conditions can help to alleviate the UI.

Limited or restricted mobility can aggravate or precipitate UI. Often older adults become incontinent simply because they have difficulty making it to the bathroom. If the restricted mobility is due to an acute condition such as a hip fracture, the incontinence will often spontaneously resolve as the patient becomes more mobile. Temporary use of a bedside commode or handheld urinal can be useful in some cases to provide increased independence during the mobility recovery process.

Stool impaction and chronic constipation are common causes of transient UI in older adults. Patients with these conditions often have either urinary retention with overflow incontinence or urinary urgency and urge incontinence. Bowel disimpaction followed by implementation of a bowel regimen can help to reverse the UI. Options for bowel regimens should be tailored to the patient's needs and can include stool softeners, fiber supplements, and non-cathartic laxatives.

Urinary retention should always be assessed in a patient that develops sudden UI due to overflow incontinence. Clinical manifestations include constant dribbling and frequent small-volume voids. Treatable causes of UI due to urinary retention include pelvic organ prolapse, benign prostatic hyperplasia, and urethral stricture disease.

Chronic Urinary Incontinence

Chronic incontinence continues over time and is unrelated to factors such as illness and medication usage [3]. When chronic incontinence develops in older adults, it is often associated with persistent long-term abnormalities of the structure or function of the lower urinary tract. UI in otherwise functional elderly patients can usually be attributed to bladder overactivity, bladder underactivity, urethral obstruction, or urethral incompetence [4]. Chronic UI can be further classified as stress, urge, mixed, overflow, functional, and continuous urinary incontinence.

Stress Urinary Incontinence

Stress urinary incontinence is the involuntary loss of urine associated with effort or physical exertion. Common provoking activities include coughing, laughing, sneezing, or standing up from a chair. All of these physical activities increase intra-abdominal pressure. Stress urinary incontinence occurs when the total bladder pressure exceeds the urethral closure pressure, often due to either urethral hypermobility or intrinsic sphincter deficiency [8]. In older men stress UI can be a result of prostate surgery including either radical prostatectomy for prostate cancer or transurethral resection or ablative procedure of the prostate to treat benign prostatic hyperplasia. However, stress UI is more common in older women. Women suffer stress UI as a result of an incompetent urethral sphincter caused by surgery, vaginal delivery, or muscle weakness or because of urethral hypermobility.

Urge Urinary Incontinence

Urge UI is characterized by the involuntary loss of urine associated with an abrupt and strong desire to void as a result of detrusor muscle overactivity or increased sensation in the overactive bladder [8]. Urge incontinence occurs when the detrusor muscle involuntarily contracts during bladder filling, forcing urine through the urethra. According to the Medical, Epidemiologic, and Social Aspects of Aging (MESA) questionnaire, urge UI and mixed UI were the most common forms of UI in elderly women [9]. Urge UI is the most common type of UI encountered in patients in long-term care facilities. A common cause of urge UI is neurological disease or injury (multiple sclerosis, spinal cord injury, cerebrovascular accident, Parkinson's disease), and these certainly complicate treatment of the UI.

Mixed Urinary Incontinence

Mixed urinary incontinence occurs when a patient has more than one of the other types of UI simultaneously. The most common combination is mixed urge and stress UI. The MESA study determined that a large proportion of elderly women have a significant degree of mixed UI, often making it difficult to treat the patient. In many cases, treating the stress UI can aggravate the urge UI, or treating the stress UI will not alleviate the urge UI. The MESA questionnaire shown in Fig. 10.1 can help to determine the predominant feature of the UI and help with treatment strategies [10].

Overflow Urinary Incontinence

Overflow UI occurs when there is incomplete emptying of the bladder during the voiding effort. Bladder outlet obstruction and underactive bladder contractility are the two most common causes of overflow UI [7]. Obstruction is rare in women

MESA URINARY INCONTINENCE QUESTIONNAIRE (UIQ)

NAME:______________________________________ DATE:______________
LAST, FIRST MI

Please check (√) the appropriate box.

1. Over the past 12 months, have you had urine loss beyond your control?
   _____ Yes_____ No

2. How long ago did your urine loss start? _____ years _____ months _____days

3. When does the urine loss usually occur?

   _____ Day time only

   _____ Night time only

   _____ Both day time and night time

4. Do you use anything for protection against leaked urine?

   _____ Yes (Go to the next question) _____ No

5. On average, how many of each of these do you use for protection? (Please write the number used and check each day or week)

	Number Used	
Sanitary napkins	_______	____each day or ____each week
Pads like those placed on furniture (ex. Blue pads)	_______	____each day or ____each week
Adult wetness control garments (ex. Attends, Depends)	_______	____each day or ____each week
Toilet paper or facial tissues	_______	____each day or ____each week
Something else (please list)	_______	____each day or ____each week
________________________________	_______	____each day or ____each week
________________________________	_______	____each day or ____each week

6. While awake, when you are having urine loss problems, how much urine would you say you lose without control EACH TIME?

   _____ A few drops to less than ½ teaspoon
   _____ ½ teaspoon to less than 2 tablespoons
   _____ 2 tablespoons to ½ cup
   _____ ½ cup or more

7. When you lose urine, does it usually:

   _____ Just create some moisture
   _____ Wet your underwear
   _____ Trickle down you thigh
   _____ Wet the floor

8. Generally, how many times do you usually urinate from the time you wake up to the time before you go to bed? _____ times.

9. Generally, how many times do you usually urinate after you have gone to sleep at night? _____ times

Fig. 10.1 MESA urinary incontinence questionnaire (UIQ)

Urge Incontinence Questions

1. Some people receive very little warning and suddenly find that they are losing, or about to lose urine beyond their control. How often does this happen to your?
_____Often (3) _____Sometimes (2) _____Rarely (1) _____Never (0)

2. If you can't find a toilet or find a toilet that is occupied and you have an urge to urinate, how often do you end up losing urine and wetting yourself?
_____Often (3) _____Sometimes (2) _____Rarely (1) _____Never (0)

3. Do you lose urine when you suddenly have the feeling that your bladder is full?
_____Often (3) _____Sometimes (2) _____Rarely (1) _____Never (0)

4. Does washing your hands cause you to lose urine?
_____Often (3) _____Sometimes (2) _____Rarely (1) _____Never (0)

5. Does cold weather cause you to lose urine?
_____Often (3) _____Sometimes (2) _____Rarely (1) _____Never (0)

6. Does drinking cold beverages cause you to lose urine?
_____Often (3) _____Sometimes (2) _____Rarely (1) _____Never (0) TOTAL SCORE=____/18

URGE SYMPTOMS INDEX LOOK-UP TABLE				
1/18 = 6%	5/18 = 28%	9/18 = 50%	13/18 = 72%	17/18=94%
2/18 = 11%	6/18 = 33%	10/18 = 56%	14/18 = 78%	18/18 = 100%
3/18 = 17%	7/18 = 39%	11/18 = 61%	15/18 = 83%	
4/18 = 22%	8/18 = 44%	12/18 = 67%	16/18 = 89%	

Stress Incontinence Questions

1. Does coughing gently cause you to lose urine?
_____Often (3) _____Sometimes (2) _____Rarely (1) _____Never (0)

2. Does coughing hard cause you to lose urine?
_____Often (3) _____Sometimes (2) _____Rarely (1) _____Never (0)

3. Does sneezing cause you to lose urine?
_____Often (3) _____Sometimes(2) _____Rarely (1) _____Never (0)

4. Does lifting things cause you to lose urine?
_____Often (3) _____Sometimes (2) _____Rarely (1) _____Never (0)

5. Does bending over cause you to lose urine?
_____Often (3) _____Sometimes (2) _____Rarely (1) _____Never (0)

6. Does laughing cause you to lose urine?
_____Often (3) _____Sometimes (2) _____Rarely (1) _____Never (0)

7. Does walking briskly cause you to lose urine?
_____Often (3) _____Sometimes (2) _____Rarely (1) _____Never (0)

8. Does straining, if you are constipated, cause you to lose urine?
_____Often (3) _____Sometimes (2) _____Rarely (1) _____Never (0)

9. Does getting up from a sitting to a standing position cause you to lose urine?
_____Often (3) _____Sometimes (2) _____Rarely (1) _____Never (0) TOTAL SCORE=____/27

STRESS SYMPTOMS INDEX LOOK-UP TABLE						
1/27 = 4%	5/27 = 19%	9/27 = 33%	13/27 = 48%	17/27 = 63%	21/27 = 78%	25/27 = 93%
2/27 = 7%	6/27 = 22%	10/27 = 37%	14/27 = 52%	18/27 = 67%	22/27 – 81%	26/27 = 96%
3/27 = 11%	7/27 = 26%	11/27 = 41%	15/27 = 56%	19/27 = 70%	23/27 = 85%	27/27 = 100%
4/27 = 15%	8/27 = 30%	12/27 = 44%	16/27 = 59%	20/27 = 74%	24/27 = 89%	

Fig. 10.1 (continued)

and if they are found to have overflow incontinence, it is usually related to detrusor underactivity. In contrast, outlet obstruction is a relatively common cause of overflow UI in men. Treatment of the obstruction usually leads to resolution of the urinary retention that caused the overflow incontinence. This may require the use of either medications or surgery. Patients with poor detrusor contractility often require either intermittent or indwelling urinary catheterization to adequately drain the bladder.

Functional Urinary Incontinence

Functional UI is caused by a person's inability or unwillingness to use toilet facilities. This is most commonly related to either mobility limitations or cognitive impairments. The cognitive changes can include both delirium and dementia and are frequently associated with loss of mental awareness of the sensation of bladder filling. Patients may also lose ability to recognize the toilet or lose understanding of the process needed to adjust clothing in order to void. Some patients simply develop a personal unwillingness to go to the toilet. In most cases, the definition of functional UI implies an intact urinary system; however, this is not always present in elderly patients. Frail older adults who require assistance with toileting are at an increased risk for functional UI [11] .

Continuous Urinary Incontinence

Some older adults complain of continuous wetness. Caregivers must be alert to this complaint because it can signify underlying urologic pathology. If one excludes constant overflow UI due to an overdistended bladder, and especially if the bladder is not distended, this raises suspicion for other anatomic abnormalities. Women with vesicovaginal or ureterovaginal fistula most commonly present with a complaint of constant urinary leakage. This may be confirmed during vaginal examination with the aid of a vaginal speculum. In some cases with tiny fistula, it can be difficult to distinguish from other vaginal discharge. Imaging studies and cystoscopy may be required to confirm diagnosis. Practitioners should be particularly concerned for fistula in patients who have a history of prior pelvic surgery, radiation therapy, or other vaginal procedures [7].

Epidemiology of Urinary Incontinence in Older Adults

It is a well-known fact that urinary incontinence is highly prevalent in older adults and that the prevalence increases with age. There is a significant difference between the UI rates of elderly people living in the community and those residing in nursing homes as well as those admitted to the hospital. The exact prevalence rate varies according to many factors including the population studied, the definition of UI used in the survey, and how the survey is conducted [11].

For community-dwelling elders who are older than 60 years old, the prevalence of UI ranges from 15 to 35 %. The rate is twice that for women than men. As many as one fourth to one third of those with UI describe their UI to be occurring daily or weekly [5, 6].

Surveys in nursing homes reported the prevalence of UI in nursing homes at 50 % [12]. A decade later, a study of the prevalence of UI 2 weeks after admission to nursing homes revealed an incontinence rate of 39 % [13]. A random survey of hospitalized elderly patients identified 11 % as having persistent UI at admission and 23 % at discharge [14]. Reports on the incidence rates of UI are skimpy. The most robust study was reported by Herzog et al. providing a 1-year incidence rate for older men of 10 % and 20 % for older women [9]. A New Zealand survey of community-based population reported that about 10 % of originally continent adults develop urinary incontinence over a 3-year period [15]. In nursing homes, the annual incidence of UI is reported to be 27 % [16].

Clinical Assessment

The evaluation for UI must be comprehensive, starting by eliciting the history and performing a focused physical examination. Urinalysis is an essential component of the evaluation. The majority of UI can be treated based on the history, physical examination, and urinalysis. Further testing should be based on the findings from this basic evaluation. Additional tests that could be considered include measurement of post-void residual urine, urodynamic testing, cystoscopy, and imaging of the urinary tract.

History

The clinical history should start with a detailed inventory of the symptoms of UI and any associated factors. Identify the characteristics of UI such as stress, urge, mixed, overflow, dribbling, or constant incontinence, and try to determine the most bothersome symptom. Use of the MESA questionnaire can be helpful in differentiating between urge and stress UI (Fig 13.1). The severity of the specific types of UI can be assessed using the subscale for urge UI (six items) and stress UI (nine items). The test/retest reliability on “any incontinence” is high with an agreement coefficient of $r=0.89$. The agreement between self-report on MESA and clinician assessment (validity) is high at 87 % for women [9] (Fig. 10.1).

It is important to determine the duration of UI. This can help to differentiate between transient and chronic UI. In addition, the frequency of UI and the amount of leakage should be determined. Some patients experience UI on a daily basis, while others only experience this at certain times. The amount of urine loss can range from drops of urine to massive leakage. Timing of leakage is important information that can help to identify the type of UI and possibly the underlying etiology.

Many older patients use absorbent pads or products to help control their urine leakage. Specific questions should be asked to determine the type of products and how often they are changed. Different products have different levels of absorbency, and this can help the clinician quantitate the frequency of incontinence and amount of urine loss.

Precipitants of UI should also be identified. These can include things like coughing, laughing, sneezing, standing, or lifting which cause stress UI. Patients with urge UI often describe UI episodes caused by hearing running water, going out into cold weather, or arriving home after being away for a period of time. Patients should specifically be questioned about any new medications, recent surgeries, radiation therapy, or other medical treatments that could lead to new UI symptoms. A list of medications commonly associated with UI is shown in Table 10.2.

Associated voiding symptoms should be characterized. These can include increased frequency of urination, nocturia, nocturnal enuresis, hematuria, or dysuria. Gross or persistent microhematuria should prompt consideration of additional evaluation with urinary tract imaging and cystourethroscopy. Dysuria should lead to consideration of underlying urinary tract infection (UTI) or other anatomic abnormality. The character of the urinary stream should also be determined. This can include changes such as interrupted stream, dribbling or splaying of the urine stream, or post-void dribbling. Other changes in the urinary stream can include alterations in urine color or odor. Cloudy and foul-smelling urine are frequent complaints among older adults with voiding problems and can signify UTI or proteinuria. Urinalysis and urine culture can be helpful in these cases.

A thorough past medical history is important to identify comorbid conditions that can influence UI. Common conditions in older adults that can lead to UI include diabetes mellitus, congestive heart failure, pulmonary edema, and various neurological disorders. The most common neurological problems associated with UI include a history of stroke, Parkinson disease, multiple sclerosis, or the dementing illnesses such as Alzheimer disease or vascular dementia. It is important to determine how well these underlying comorbidities have been managed. Sometimes improving the treatment for these conditions can lead to improvements in UI symptoms.

Other related medical history that could influence UI should also be obtained. This includes information about fluid intake over 24 h. In addition to total volume, the timing of fluid intake is important. Increased fluid consumption in the late afternoon or evening can lead to problems with increased nocturnal urine production and nocturia. The type of fluids consumed should also be determined. Caffeine can lead to bladder irritation which can cause urinary urgency and urge UI. Similarly, alcohol acts as both a bladder irritant and diuretic and can worsen UI symptoms.

Patients must be specifically questioned about bowel function. As previously described, chronic constipation and stool impaction can cause problems with UI. The frequency and consistency of bowel movements should be discussed. Patients will usually not offer this information without prompting or questioning from the healthcare provider. Similarly, patients should be asked if UI is causing any problems with sexual function. Many older adults with UI will decrease or avoid sexual activity because of a fear they will leak during intercourse. Again, patients will often not volunteer this information unless specifically asked.

Patients should be asked about any treatments they have already tried for their UI symptoms. This can help the practitioner determine what new treatments might be useful. It can also help to identify the type of UI a person is experiencing. Patients may have tried things that are known to be ineffective, and education about continence promotion can be useful for both patients and their caregivers. Obtaining prior medical records can be important, particularly in patients who have undergone prior surgery for UI.

Information about the living environment should also be obtained. This can include details about the location and number of toilets and the availability of any safety equipment such as raised toilet seats or grab bars in the bathroom. Some older adults may have difficulty reaching the toilet if it is on a different level of the house and requires the use of stairs to get to the bathroom. Patients should also be asked if they have used any alternate toileting options such as a bedside commode or handheld urinal. The general living condition of the home or residential environment should also be determined. Patients may be at increased risk for falls and associated injuries if they have environmental hazards on the way to the toilet. Adequate lighting is important to help prevent falls at night in patients with nocturia.

Patients and caregivers should also be asked about how urinary incontinence has impacted their abilities to perform certain activities or participate in social settings. Many older adults will stop going out of their home because of problems or fears of UI. This can lead to depression, social isolation, and decreased overall and health-specific quality of life [18, 19]. Use of a specific screening tool to check for depression should be considered such as the Geriatric Depression Scale (GDS). The GDS is a short, validated screening tool for depression in older adults [17].

Physical Examination

Physical examination is best completed using a systematic approach. This includes assessment of a variety of specific factors. General observation includes assessment of the appearance of the patient, their mobility, and their mental status. Is the patient well groomed? Is there a urine odor or visible leakage of urine on the patient's clothing? Are they using an absorbent pad or other urine containment product? Mobility status can be assessed as the patient enters the clinic or examination room. Are they able to walk independently, or do they require the use of a walker or cane, wheelchair, or other assistive device? Patients with significant frailty may be poorly mobile, and some may require the use of a stretcher or other equipment.

Assessment of cognitive status is important. Is the patient oriented and conversant? Do they display any signs of delirium or dementia? Are they able to provide their own history, or is most of this information obtained from the caregiver? A variety of validated instruments are available which can be used to measure cognitive function and screen for possible underlying problems. Patients with cognitive impairment are at higher risk of UI, particularly functional UI.

Other general examination findings may help to identify underlying comorbidity which could be associated with UI. Patients who are short of breath could have congestive heart failure or pulmonary edema. Neurological disorders such as multiple sclerosis and Parkinson disease usually have characteristic physical examination changes. These can help to identify the severity of the underlying condition which could be important targets for treatment.

Abdominal examination should include identification of any distension or tenderness. Organomegaly can be identified by palpation of an enlarged liver or spleen. In patients with significant urinary retention, the distended bladder might be palpable or percussible in the lower abdomen. Ultrasound bladder scanning can be useful to confirm the diagnosis if the bladder is identified by palpation or percussion on the general abdominal examination.

Perineal and rectal examination should include checking for perineal sensation. The nerves that control the bladder also provide sensory innervation to the skin of the perineum, and this can help the clinician determine if these neural pathways are intact. Rectal examination includes assessment of sphincter tone, including at rest and with active contraction. In addition, the presence of any fecal material in the rectal vault should be assessed. Stool guaiac can be checked to look for blood in the stool. Any anal or rectal mass should also be noted and may require additional evaluation.

In men, the prostate gland should be assessed in terms of contour, symmetry, and smoothness. Any localized hardness or nodules should be noted, and this may prompt additional evaluation for a possible prostate tumor or cancer. Estimation of prostate size can be done in several different ways. These include measuring the dimensions of the gland or estimating the volume. Some practitioners use volume estimates in terms of the amount of tissue that would be removed in a surgical resection for benign prostatic hyperplasia. Others use a gradation of small, medium, or large. Measuring or estimating the size of the prostate on digital rectal examination is a very inexact science. Although the examiner may comment and note the size, this will be mainly for his or her future reference for comparison of changes in the examination. Prostate size is not always correlated to the severity of a given patient's symptoms and at most only modest correlation exists [20].

The male genital examination should comment on whether the patient is circumcised or uncircumcised. If the foreskin is present, the clinician should determine if it can be retracted easily or there is evidence of phimosis (tight foreskin). The skin, glans, and shaft of the penis should be carefully inspected for masses or palpable plaque that could be suggestive of Peyronie's disease. The testes and scrotum should also be inspected for any abnormalities including masses. Examination for inguinal hernia should also be performed.

The female genital examination should assess the appearance of the vulva for any signs of skin excoriation or mass lesion. Women with chronic UI can develop skin irritation or breakdown, and this needs to be carefully evaluated. Urine drainage from the introitus should be noted and may suggest a fistula. The size of the vaginal introitus should be noted. Vaginal stenosis is not uncommon in older women. The urethral meatus should be examined for evidence of caruncle or urethral prolapse.

Pelvic examination includes both a speculum and bimanual examination. This is crucial for evaluation of women with complaints of urinary incontinence. Occasionally women can be reluctant to undergo pelvic examination for fear of leaking on the examiner. They should be reassured that the examiner is aware and prepared to handle the situation and the examination is important to help with the diagnosis and treatment of their condition. Patients should be examined with some urine in the bladder in order to do a provocative stress test and identify urine leakage from the urethra. If the patient voids immediately prior to the examination, this will limit interpretation of this portion of the pelvic examination. Inspection of the vaginal mucosa may reveal atrophic changes due to lack of estrogen including loss of rugation or evidence of inflammation.

Assessment of the pelvic floor muscle strength is recommended prior to the insertion of the speculum. The Brink digital assessment of pelvic floor muscle strength is performed by inserting two gloved lubricated fingers 6–8 cm into the vagina on a midsagittal plane [21]. Upon a count of three, the woman is asked to contract her pelvic floor muscles for as hard and as long as she is able. Pressure is scored from 0 (no perceptible pressure) to 6 (strong compression, causing the fingers to override). Displacement is scored from 0 (no lifting of fingers) to 5 (vigorous drawing in of fingers). This test has high inter-rater reliability in longitudinal studies, with an average 95 % agreement for pressure and 98 % for displacement [21].

The speculum examination must be standardized, and the POP-Q method is highly recommended as objective and reproducible [22]. Figure 10.2 shows detailed information on the measurements used for the POP-Q scoring system. This will not only assess the presence of a cystocele, rectocele, enterocele, or uterine prolapse but is also used to stage the degree of prolapse as well. Bimanual examination should report the presence or absence of the uterus and the status of the cervix including any palpable masses. The ovaries are usually not palpable or only barely palpable in older women. Incidental discovery of a silent ovarian mass in a patient

ENTER POPQ VALUES HERE:

(Aa) Anterior wall 3 cm from external urethral meatus _______ cm (-3 to +3)

(Ba) Most dependent part of anterior wall _______ cm (-3 to +TVL)

(C) Cervix or vaginal cuff _______ cm (±TVL)

(D) Posterior fornix (if no prior hysterectomy) _______ cm (±TVL)

(Ap) Posterior wall 3 cm from hymen _______ cm (-3 to +3)

(Bp) Most dependent part of posterior wall _______ cm (-3 to +TVL)

(GH) Genital hiatus _______ cm

(PB) Perineal body _______ cm

(TVL) Total vaginal length _______ cm

STAGING PELVIC ORGAN PROLAPSE USING THE POPQ MEASUREMENT

STAGE 0	STAGE I	STATE II	STAGE III	STAGE IV
__Aa = -3 cm	__Aa = -2 cm	__Aa =-1 to +1	__Aa = +2 to +3	__Ba = +3 or more
__Ba = -3 cm	__Ba = -2 cm	__Ba =-1 to +1	__Ba = +2 but <(+TVL-2)	__Bp = +3 or more
__Ap = -3 cm	__Ap = -2 cm	__Ap =-1 to +1	__Ap = +2 or +3	__C = + total TVL
__Bp = -3 cm	__Bp = -2 cm	__Bp =-1 to +1	__Bp = +2 but <(+TVL-2)	__ + TVL -1 or -2
__C =-(≤TVL-2)	__C = -2 to –(TVL-3)	__C = -1 to +1	__C = +2 but <(+TVL-2)	__D= + total TVL
__D =-(≤TVL-2)	__D = -2 to –(TVL-3)	__D = -1 to +1	__D = +2 but <(+TVL-2)	__ + TVL-1 or -2

NOTE: Stage is assigned to the most severe prolapsing organ
Measuring is rounded to the nearest centimeter
TVL means the total measured vaginal length

Fig. 10.2 POP-Q scoring system for pelvic organ prolapse

presenting with UI should be referred immediately to a gynecologist for additional evaluation. Notation should be made of any other abnormal adnexal masses palpated during the examination.

Direct observation for urine loss is helpful, especially if the clinician can document urine leakage from the urethra. The most common method is the provocative stress test. This is often performed with the patient in the dorsal lithotomy position. She is asked to cough vigorously, and any leakage of urine from the urethra at the time of cough is noted. Repeated cough may be necessary to elicit the urine leak, and patients need to cough with enough force during the examination. The test can also be performed by asking the patient to perform a Valsalva maneuver. Any urine leakage during this is also considered a positive stress test.

Another method for detecting urine leakage is to have the patient stand with a relatively full bladder. The patient is asked to place her feet about shoulder width apart and stand over a paper towel placed under her on the floor. She is then asked to cough a maximum of three times, and any leakage is noted and quantified [23]. Another method that is more involved includes the 24-h pad test [24, 25]. The patient uses pads and changes them on a regular basis. The pads are subsequently weighed to determine patterns and volume of urine loss experienced during each day and night. This test has a high 2-day reproducibility with correlation coefficients of $r=0.66$–0.82. Older women with both stress and urge UI have demonstrated capacity to conduct the test at home and provide reliable data. Pad tests may be negative for some women, particularly if they have mild UI. In these cases, provocative cough tests should be performed.

Rectovaginal examination should be performed as the final component of a complete pelvic examination. A single finger is placed in the vagina and another in the rectum. The septum between the organs is checked for any evidence of mass or lesion. A rectocele can also be identified on this part of the examination by asking the patient to perform a Valsalva maneuver.

Additional Office Tests

Post-Void Residual Volume Measurement

Measurement of post-void residual (PVR) urine volume can be done either by use of a special ultrasound machine or using bladder catheterization. The patient should be asked to void immediately prior to measurement of the PVR. An attempt should be made to observe the urinary stream if there is any question of obstructive voiding symptoms. Although a PVR of zero is ideal, this is seldom observed in clinical practice. There is no absolute PVR volume that is considered abnormal, and this must be correlated to the specific clinical situation. For example, if the patient has overflow-type incontinence secondary to acute urinary retention, the PVR may remain somewhat elevated even after several days of bladder decompression with an indwelling catheter. These patients should be monitored closely to make sure the PVR is decreasing with additional time. Most clinicians would consider a PVR of 100 mL or less acceptable in most elderly patients.

Urinalysis

A complete urinalysis includes both a chemical dipstick analysis of the urine and a microscopic analysis of the urine sediment. The dipstick is a cost-effective method of screening for significant comorbid conditions that could be contributing to the UI. For example, the presence of glucose in the urine could indicate underlying diabetes mellitus. Proteinuria could indicate the patient has some degree of renal impairment, glomerulonephritis, or other renal disease. High specific gravity suggests good concentrating capacity of the kidneys, although it could also signify dehydration. Low specific gravity could indicate overhydration with polyuria or a lack of the ability of the kidneys to concentrate urine adequately. The presence of blood, leukocytes, and nitrites may indicate hematuria or bacteriuria which could require additional evaluation. Urine cultures and antibiotic susceptibilities should be obtained if UTI is suspected. Urine microscopy is helpful to confirm these findings. Urine sediment can also reveal casts or other changes that could indicate underlying renal disease.

Urodynamic Testing, Cystoscopy, and Imaging Studies

Additional testing may be considered immediately after the history and physical examination are complete or could be delayed pending results of initial attempts at clinical management. These tests include various forms of urodynamic evaluation, cystoscopy, and imaging of the genitourinary tract.

Cystometry is appropriate for detecting detrusor contractility, compliance, and bladder capacity. The test can be helpful to identify either overactive or underactive detrusor muscle contractility. The AUA/SUFU Adult Urodynamics Guidelines state "Clinicians may perform multichannel filling cystometry when it is important to determine if altered compliance, detrusor overactivity or other urodynamic abnormalities are present (or not) in patients with urgency incontinence in whom invasive, potentially morbid or irreversible treatments are considered" [26]. The AUA/SUFU Guideline for the Diagnosis and Treatment of Overactive Bladder states "Urodynamics, cystoscopy and diagnostic renal and bladder ultrasound should not be used in the initial work-up of the uncomplicated patient" [27]. A recent review of the literature determined that "while urodynamic studies may change clinical decision making, there was not enough evidence to suggest whether this would result in better clinical outcomes" [28]. A study that considered only females 80 and over determined that "in octogenarian females, there is a poor correlation between storage symptoms and urodynamic diagnosis. Thus, urodynamics guides patient management and may avoid empirical prescribing associated with adverse effects in this clinically vulnerable population" [29]. This study however had a very small sample size and was a retrospective review. It cannot be determined if the knowledge would have changed clinical outcomes.

Uroflowmetry is a test that measures urine flow rates. A simple method to determine this is to use a stopwatch and measure the time it takes for the patient to empty the urine from the beginning to the end of the stream. An electronic uroflowmetry machine uses a device that records the speed of the urine stream over time. This can determine if the flow is continuous or interrupted and if the rate is fast or slow. The computer calculates the average and maximum flow rates in mL/s.

Multichannel urodynamics with pressure-flow testing can be useful to differentiate between bladder outlet obstruction and poor detrusor contractility with incomplete bladder emptying and overflow UI. Simultaneous pressure measurements of the bladder pressure (using a urethral catheter) and abdominal pressure (using a rectal catheter) are performed during both bladder filling and voiding. Sometimes this is combined with fluoroscopy and the use of contrast material to fill the bladder. This provides simultaneous measurement of pressures and anatomic information from the video fluoroscopy. This can be particularly useful in patients with a history of neurological disease or in those who have had prior surgery or tried therapies without success. Vesicoureteral reflux can be identified on video urodynamics in some cases.

Cystoscopy may be considered based on the presenting symptoms associated with UI. This is particularly helpful in patients who have tried other therapies for UI, but have not experienced improvement. It is also used in the evaluation of hematuria or to identify urethral strictures or other forms of bladder outlet obstruction. The AUA has recently published a guideline on the evaluation and follow-up of asymptomatic microhematuria in adults. The AUA recommendation includes definition of microhematuria and ruling out benign causes of microhematuria. Once a person has met the criteria and benign causes have been ruled out, then a urologic evaluation should be considered. The urologic evaluation recommends that all adults aged 35 years and older receive a cystoscopy and radiologic study (CT urography) to evaluate microhematuria [30].

Imaging of the urinary tract may be obtained in selected cases. These include patients with hematuria or those with unexplained recurrent urinary tract infections. A variety of imaging modalities are available. Renal ultrasound is particularly useful for identifying hydronephrosis, stones, or renal masses. Ultrasound alone is not adequate for complete evaluation for hematuria, and computed tomography (CT) of the abdomen and pelvis both with and without intravenous contrast is preferred if the patient's renal function allows. Intravenous pyelography (IVP) has been used in the past but has now been generally replaced with CT imaging techniques. Another alternative would be cystoscopy with retrograde pyelography, particularly if upper tract cytology specimens are needed or if the patient has any degree of underlying renal impairment that prevents administration of IV contrast material. Nuclear renal scanning can be used to identify functional ureteral obstruction. Magnetic resonance imaging (MRI) can be useful to evaluate pelvic organ prolapse in women.

Conclusion

Healthcare providers must recognize that UI is a common problem faced by a significant portion of the geriatric community. Unfortunately, many patients and providers incorrectly accept it as a normal part of the aging process without realizing that many contributory factors are pathologic and potentially reversible. It is the responsibility of healthcare providers to change this pervasive attitude among older adults. Ongoing research continues to add to our knowledge base of the underlying mechanisms of UI. Healthcare providers must work to identify the specific type or types of UI an older adult is experiencing in order to reach a correct diagnosis. In addition, the provider must sift through the multitude of potential pathologies before formulating a management strategy. However, with proper understanding of the multifactorial nature of UI and better methods for evaluation, the condition can be accurately diagnosed in most patients. Based on this information, providers can implement a variety of treatment strategies which are outlined in subsequent chapters of this book. Successful diagnosis and treatment of UI can certainly improve the quality of life for older adults, enabling them to live more meaningful lives.

References

1. Haylen BT, Ridder D, Freeman RM, Swift SE, Berghmans JL, Monga A, Petri E, Rizk DE, Sand PK, Schaer GN. An International Urogynecological Association, International Continence Society joint report on the terminology for female pelvic floor dysfunction. Neurourol Urodyn. 2009;29:4–20.
2. Resnick NM, Yalla SV. Geriatric incontinence and voiding dysfunction. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA, editors. Campbell's urology. 9th ed. Philadelphia, PA: Elsevier Saunders; 2007. p. 2305–12.
3. Newman D, Wein A. Managing and treating urinary incontinence. Baltimore, MD: Health Professionals Press; 2009. p. 85–122.
4. Diokno AC, Toh KL. Urinary incontinence in the elderly. In: Bourcier AP, McGuire EJ, Abrams P, editors. Pelvic floor disorders. Philadelphia, PA: Elsevier Saunders; 2004. p. 57–72.
5. Burgio KL, Matthews KA, Engel BT. Prevalence, incidence and correlates of urinary incontinence in healthy, middle-aged women. J Urol. 1991;146: 1255–9.
6. Diokno AC, Brock BM, Brown MB, Herzog AR. Prevalence of Urinary Incontinence and other urologic symptoms in the non- institutionalized elderly. J Urol. 1986;136:1022–5.
7. Ham RJ, Sloane PD. Primary care geriatrics: a case base approach. St Louis, MO: Mosby Yearbook; 1992. p. 385–403.
8. Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, et al. For the standardization subcommittee of the International Continence Society (2002) the standardization of terminology of lower urinary tract function: report from the Standardization Sub-Committee of the International Continence Society. Neurourol Urodyn. 2002;21:167–78.
9. Herzog AR, Diokno AC, Brown MB, et al. Two-year incidence, remission, and change patterns of urinary incontinence in noninstitutionalized older adults. J Gerontol. 1990;45(2):M67–74.
10. Diokno AC, Catipay JR, Steinert BW. Office assessment of patient outcome of pharmacologic therapy for urge incontinence. Int Urogynecol J Pelvic Floor Dysfunct. 2002;13(5):334–8.
11. Diokno AC, Brock BM, Herzog AR, Bromberg J. Medical correlates of urinary incontinence in the elderly. Urology. 1990;36:129–38.
12. National Center for Health Statistics. The National Nursing Home Survey: 1977 summary for the United States by Van Nostrand JF, et al. (DHEW Publication No. 79–1794). Vital and health statistics. Series 13, No. 43. Washington DC: Health Resources Services Administration, US Government Printing Office; 1979.
13. Palmer MH, German PS, Ouslander JG. Risk factors for urinary incontinence one year after nursing home admission. Res Nurs Health. 1991;14:405–12.
14. Palmer MH, McCormick KA, Langford A, Langlois J, Alvaran M. Continence outcomes: documentation on medical records in the nursing home environment. J Nurs Care Qual. 1992;6(3):36–43.
15. Campbell AJ, Reinken J, McCosh L. Incontinence in the elderly: prevalence and prognosis. Age Ageing. 1985;14:65.
16. Ouslander J, Kane R, Abrass I. Urinary incontinence in elderly nursing home patients. JAMA. 1982;248: 1194–8.
17. Sheikh JI, Yesavage JA. Geriatric Depression Scale (GDS): recent evidence and development of a shorter version. Clin Gerontol. 1986;5(1/2):165–73.
18. Fultz NH, Jenkins KR, Ostbye O, Taylor DH, Kabeto MU, Langa KM. The Impact of own and spouse's urinary incontinence on depressive symptoms. Soc Sci Med. 2005;60:2537–48.
19. Sung VW, West DS, Hernandez AI, Wheeler TI, Myers DI, Subak LI. Association between urinary incontinence and depressive symptoms in overweight and obese women. Am J Obstet Gynecol. 2009; 200(5):557 e1–7 e5.
20. Girman CJ, Jacobsen SJ, Guess HA, Oesterling JE, Chute CG, Panser LA, Lieber MM. Natural history of prostatism: relationship among symptoms, prostate volume and peak urinary flow rate. J Urol. 1995;153(5):1510–5.
21. Brink CA, Wells TJ, Sampselle CM, et al. A digital test for pelvic muscle strength in women with urinary incontinence. Nurs Res. 1994;43(6):352–6.
22. Diokno AC, Bourodulin G. A new vaginal speculum for pelvic organ prolapse quantification (POPQ). Int Urogynecol J Pelvic Floor Dysfunct. 2005;16(5): 384–8.
23. Miller JM, Ashton-Miller JA, Delancey JO. Quantification of cough- related urine loss using the paper towel test. Obstet Gynecol. 1998;91(5 pt 1): 705–9.
24. Lose G, Jorgensen L, Thunedborg P. 24 hour home pad weighing test versus 1 hour ward test in the assessment of mild stress incontinence. Acta Obstet Gynecol Scand. 1989;68(3):211–5.
25. Victor A, Larsson G, Asbrin AS. A simple patient-administered test for objective quantitation of the symptom of urinary incontinence. Scand J Urol Nephrol. 1987;21(4):277–9.
26. Winters JC, Dmochowski RR, Goldman HB, Herndon CDA, Kobashi KC, Kraus SR, Lemack GE, Nitti VW, Rovner ES, Wein AJ, American Urological Association (AUA) Guideline. Adult urodynamics: AUA/SUFU guideline. 2012. Linthicum, MD, American Urological Association. http://www.auanet.org/education/guidelines/adult-urodynamics.cfm.
27. Gormley EA, Lightner DJ, Burgio KL, Chai TC, Clemens JQ, Culkin DJ, Das AK, Foster Jr HE, Scarpero HM, Tessler CD, Vasavada SP, American Urological Association (AUA) Guideline. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline. J Urol. 2012;188 (6 Suppl):2455–63.

28. Glazener CMA, Lapitan MCM. Urodynamic studies for management of urinary incontinence in children and adults (review). Cochrane Database Syst Rev. 2012;1:CD003195.
29. Bromage SJ, Dorkin TJ, Chan L, Tse V. Urodynamics in the octogenarian female: is it worthwhile? Int Urogynecol J. 2010;21:1117–21.
30. Davis R, Jones JS, Barocas DA, Castle EP, Lang EK, Leveillee RJ, Messing EM, Miller SD, Peterson AC, Turk TMT, Weitzel W, American Urology Association (AUA) Guideline. Diagnosis, evaluation and follow-up of asymptomatic microhematuria (AMH) in adults: AUA guideline. J Urol. 2012;188(6 Suppl): 2473–81.

Urinary Incontinence: Nonsurgical Treatments

11

Diane K. Newman, Kathryn L. Burgio, Alayne D. Markland, and Patricia S. Goode

Introduction

Lower urinary tract symptoms (LUTS) including urinary incontinence (UI) can often be successfully treated with nonsurgical options, including behavioral treatments and drug therapies. Combining these interventions has also been shown to improve outcomes. Behavioral interventions are considered first-line treatment options for adults and include toileting programs with scheduled, timed, or prompted voiding and habit or bladder training; caffeine and fluid management; pelvic floor muscle training; stress and urge reduction strategies; nocturia reduction strategies; constipation management; and functional and environmental changes [1]. Drug therapy for LUTS includes alpha-blocker agents and 5-alpha-reductase inhibitors for men. Medications for overactive bladder (OAB) include antimuscarinic and beta-adrenergic medications for men and women and topical vaginal estrogens for women. This chapter will review the nonsurgical treatments of behavioral interventions and drug therapy in older adults with UI and related LUTS. Devices include intraurethral inserts, intravaginal incontinence pessaries, and penile compression devices. Other products are available for urine containment.

Toileting Programs

Behavioral interventions improve symptoms through teaching new skills or changing a person's habits and/or lifestyle choices that are contributing factors or triggers of LUTS. Toileting programs, commonly referred to as voiding regimens, have been the mainstay of treatment for decades for UI and symptoms of overactive bladder (OAB) in older adults (see Table 11.1). They include scheduled toileting regimens that most often rely on caregiver involvement or bladder training regimens that require the patient to resist urgency and delay voiding. Toileting programs are often combined with lifestyle modifications as described in Table 11.2 and are the cornerstone

D.K. Newman, D.N.P., F.A.A.N., B.C.B.-P.M.D. (✉)
Division of Urology, Department of Surgery, University of Pennsylvania Medical Center, 3rd Floor, West Pavilion, Perelman Center, 34th & Civic Center Blvd, Philadelphia, PA 19312 USA
e-mail: diane.newman@uphs.upenn.edu

K.L. Burgio, Ph.D. • A.D. Markland, D.O., M.Sc.
P.S. Goode, M.S.N., M.D.
Department of Medicine, Division of Gerontology, Geriatrics and Palliative Care, University of Alabama at Birmingham, Birmingham, AL, USA

Department of Veterans Affairs Medical Center, Birmingham/Atlanta Geriatric Research, Education, and Clinical Center (GRECC); VA Medical Center, GRECC/11G, 700 19th St S, Birmingham, AL 35233, USA
e-mail: kburgio@aging.uab.edu; amarkland@aging.uab.edu; pgoode@aging.uab.edu

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_11,

Table 11.1 Understanding toileting programs

Type	Key components
Scheduled or timed toileting	Fixed, predetermined time intervals between toileting The following is an example of a toileting program that can be used by institutions or caregivers that includes 8 times in a 24-h period or every 3 h • Day—upon awakening, after breakfast, midmorning, before lunch, and following an afternoon nap (midafternoon) • Evening—before dinner and at bedtime • Night—determine if the person wants to be awakened at night to void and identify times
Habit training	Using a bladder diary, incontinence and voiding pattern are identified, and the development of an individualized toileting schedule is developed. The voiding times preempt involuntary bladder emptying. In institutions such as nursing homes, a typical toileting schedule may be determined around daily events
Prompted voiding	Prompted voiding involves timed or scheduled toileting and promotes toileting behavior. Prompted voiding is most successful in individuals who can ask for assistance or void when prompted. The major elements of prompted voiding are: • Monitoring—the caregiver checks on a regular basis (use toileting schedule described in scheduled toileting) and person is asked to report verbally if wet or dry • Prompting—the person is asked if they need to void and assisted with voiding • Praise and encouragement—the caregiver provides if the person is continent
Bladder training	Promotes restoration of normal bladder function through education of urge inhibition techniques. Requires person to be able and willing to participate in active rehabilitation and education techniques Four primary components: 1. Education program that usually combines written, visual, and verbal instruction that addresses the physiology and pathophysiology of the lower urinary tract 2. Scheduled voiding with systematic delay of voiding that requires the ability to resist or inhibit the sensation of urgency to postpone voiding and to urinate according to a timetable rather than according to the urinary urge 3. Gradual increases in voiding interval 4. Reinforcement through consistent encouragement and positive feedback

Adapted from Newman DK. &Wein, AJ. (2009) *Managing and Treating Urinary Incontinence*. 2nd Ed. Baltimore: Health Professions Press:245–263

of continence care in cognitively impaired and mobility impaired persons.

In the older adult, interventions such as toileting programs can be categorized as "patient dependent" or "caregiver dependent." Bladder training and pelvic floor muscle training are "patient independent" interventions. These necessitate adequate function, learning capability, and motivation of the individual. Patient-dependent interventions, including scheduled voiding, habit training, and prompted voiding, are useful in people with functional disabilities. The success of these interventions is largely dependent on caregiver knowledge and motivation, rather than on the person's physical function and mental status. However, bladder training relies on the person's understanding of voiding habits and the ability to practice strategies to resist or delay voiding, often referred to as urgency suppression.

Several Cochrane Collaboration publications [2–7] and other systematic reviews [8, 9] have detailed the outcomes for toileting programs, including timed or scheduled voiding, habit training, prompted voiding, and bladder training. All toileting programs, excluding bladder training, are usually "caregiver dependent," which is defined as the need of a professional or family caregiver to assist with toileting [10]. These programs can be utilized to improve continence. The choice of program is determined by the cognitive and functional status of the individual, the variability of the voiding pattern, and the need for psychological reinforcement for adherence to the regimen [11].

Table 11.2 Guide on lifestyle modifications

Adequate fluid intake—individuals with urinary symptoms often limit fluids so as to decrease frequency. Individuals with urgency incontinence and who have a high fluid intake (>2,400 ccs/day) may show a reduction in incontinence episodes and voiding frequency by lowering fluid intake. Incontinent persons with low fluid intakes (<1,500 ccs/day) may benefit from increasing their fluid intake. Reducing fluid intake after 6 pm and concentrating fluid intake during morning and afternoon hours may decrease nighttime incontinence episodes
Stop smoking—nicotine in cigarettes can be irritating to the bladder muscle causing bladder contractions and urgency. A smoker's repeated and chronic coughing may cause urinary leakage. Smoking cessation may help to decrease urine leakage
Diet and medications Certain food and beverages can irritate the bladder and make symptoms worse. They are: • Alcoholic beverages • Citrus juices and fruits • Beer, wine • Highly spiced foods • Carbonated beverages • Sugar, honey • Milk/milk products • Corn syrup • Soft drinks with caffeine, tea, coffee even decaffeinated • Artificial sweetener—NutraSweet (Equal)
Also some over-the-counter medications and prescription drugs contain caffeine which can worsen bladder problems such as Excedrin, Midol, Anacin, Dristan, and Sinarest
Maintain a healthy weight—being overweight can put pressure on your bladder, which may cause leakage of urine when laughing or coughing. If you are overweight, losing some weight can lessen the pressure on your bladder
Keep healthy bowel habits—constipation and difficulty with defecation (e.g., straining) causes more pressure on the bladder leading to urinary urgency and urine leakage

The impact of a toileting regimen on caregivers can be significant. UI management has been rated as the third most troublesome caregiving task, behind a lack of time for their own needs and managing care recipient emotional and behavioral problems [12]. Caregivers do not feel prepared to deal with UI [12]. Engberg and colleagues [13] reported areas of caregiver strain in relation to incontinence, including odor (56 %), toileting (55 %), changing pads and clothing (53 %), UI-related costs for pads or briefs (53 %), wet clothing (50 %), and changing bed linens (44 %). Drennan [14] conducted a qualitative study of managing incontinence for people with dementia living at home and found that toilet prompting or reminding can lead to irritation and arguments, as persons perceive this as being treated like a child.

Timed Voiding

Timed voiding has also been called scheduled toileting, routine toileting, and fixed toileting. It provides toileting on a scheduled or fixed time basis such as every 3–4 h [3, 5]. This is a "passive" type of toileting program, as it takes place whether or not a sensation to void is present, but the schedule is usually only followed during waking hours [4]. The goal is to keep the person dry, and no effort is made to alter an individual's voiding pattern or to motivate the person to resist the urge to urinate. The premise of these programs is that if the person toilets on a preplanned schedule, the bladder will be emptied before incontinence occurs.

Prefixed times, such as every 2 h, have been adopted for toileting programs in many nursing homes, with the schedule usually determined by administrative staff. However, a more realistic schedule may be related to certain daily routines such as upon awakening, before or after meals, and at bedtime. If the individual self-toilets independently, then scheduled times are readjusted. Ideally, the schedule for toileting is based on some objective measure, such as a bladder diary, on data collected using a bladder volume recording instrument [15], or from an electronic device used to monitor and record incontinence episodes [16].

A timed voiding toileting program can be beneficial for toileting-dependent residents in nursing homes or individuals living at home who have an available and willing caregiver. These individuals may have mobility or cognitive impairment and

Table 11.3 Scheduled toileting: patient/caregiver handout[a]

When you have an overactive bladder that causes urinary urgency and frequency, it is very important to go to the bathroom on a regular schedule. It can help prevent leakage
One possible schedule:
1. Go to the bathroom first thing in the morning 2. Go to the bathroom before and after every meal 3. Go to the bathroom at bedtime
Another possible schedule:
1. Go to the bathroom first thing in the morning 2. Go to the bathroom every 2 h by the clock while you are awake (even or odd hours) 3. Go to the bathroom at bedtime
Go to the bathroom on these schedules, even though you don't think you need to urinate Waiting for urgency makes you more likely to get wet
Using a schedule can put you in control!

[a]Used with permission. © University of Alabama at Birmingham Continence Clinic

may need some assistance from at least one person but are able to cooperate with toileting. While fewer than 20 % of frail elders become completely dry with timed voiding, between 30 and 50 % of incontinent elders may improve, reducing the number and volume of incontinence episodes. This is probably also true in people being cared for in their homes. A sample patient and caregiver handout that can be used for scheduled or timed voiding is shown in Table 11.3.

Timed voiding can also be useful for cognitively intact elders who have developed bladder sensory impairment due to neurologic conditions. Voiding by the clock, instead of waiting for urgency, and before spontaneous bladder emptying occurs can prevent or reduce incontinence. A trial of timed voiding can determine if it will be successful for an individual. Voiding intervals can be guided by habit training described below.

Habit Training

Habit training is a toileting regimen that matches the person's voiding habits or needs based on their voiding pattern. The goal is for the person to follow a planned schedule that is shorter than the person's normal voiding pattern and is timed prior to a possible incontinence episode [6]. To successfully implement a habit training regimen, the caregiver will identify specific times the person is likely to void by tracking the voiding pattern for at least 3 days using a bladder diary. Based on the pattern observed and times identified, efforts are made to schedule toileting opportunities prior to these times. If the person is taking a diuretic, the toileting schedule may need to be altered, because the urine volume will be increased at the diuretic's peak action time.

Colling and colleagues [12] conducted a habit training program in caregiver-dependent homebound frail elders that combined electronic monitoring of UI episodes. The program was called Pattern Urge-Response Toileting (PURT). Three weeks of voiding patterns were obtained from electronic data loggers, individualized toileting schedules were identified based on each person's voiding pattern, and caregivers were taught when and how to toilet the care recipient. The PURT program reduced the number of incontinence episodes over 24 h by 18 %, decreased the mean number of daily episodes from 4.9 to 4.0, and reduced the volume of UI over 24 h by 39 %. In this study, caregivers were relatives, usually spouses providing care.

Prompted Voiding

Prompted voiding is a toileting program that combines scheduled voiding with "prompting" from a caregiver. It is used to teach people with or without cognitive impairment to initiate their own toileting through requests for help and positive reinforcement from caregivers when they do so [2, 10]. It has been used primarily in nursing home settings with cognitively and physically impaired older adults [17, 18]. Prompted voiding has been shown to reduce UI episodes by up to 33 % in nursing home residents with UI regardless of the type of UI or cognitive deficit. Prompted voiding has three components: (1) regular monitoring with encouragement to report continence status, (2) prompting of resident to toilet on a scheduled basis, and (3) praise with positive feedback when the resident is continent and tries to toilet [10]. For prompted voiding to be effective, the individual must be able to delay voiding and cooperate with toileting or have awareness of urge sensation of when there is a need to void. But prompted voiding has also been shown to be effective in residents with cognitive impairment.

Research in the area of prompted voiding has been conducted mostly in nursing homes and has shown that between 25 and 40 % of incontinent residents respond well to toileting assistance, while approximately 38 % cannot successfully toilet even when provided help by research assistants [19]. In one study of 191 incontinent residents in seven nursing facilities, 25–40 % responded well to prompted voiding during the day, with incontinence episodes decreasing from three or four during the day to one or none.

Combining prompted voiding with other activities of daily living, as part of a multicomponent intervention, may be an option in older adults with UI [20]. Ouslander and colleagues [21] employed a "designated" versus "integrated" nursing assistant role to combine restorative care including a walking program, exercise therapy, and continence care. Specifically, the Functional Incidental Training (FIT) intervention, which combines prompted voiding with functionally oriented low-intensity endurance and strength-training exercises, has repeatedly been noted to improve physical function and UI in nursing facility residents [21, 22]. Schnelle and colleagues [23] reported on a multicomponent program that combined prompted voiding with physical activity and fluid management which improved UI, frequency of bowel movements, and percent of bowel movements in toilet.

Nighttime Toileting

Nighttime voiding (nocturia) and nighttime UI (nocturnal enuresis) are bothersome problems for many older adults [24], especially in those with chronic medical conditions [25]. Nocturia is defined as "waking at night one or more times to void" where each void is preceded and followed by sleep [26]. Interrupted sleep caused by nocturia can impact many areas of an older person's daily life and care. It can cause daytime fatigue, poor concentration, memory impairment, and mood alterations with physical aggression and hostility [27]; increase the number of falls [28, 29]; and increase requests for pain medication and sedatives. Nocturia is a predictor of mortality, with higher mortality risk associated with an increased number of nightly voids [30].

In nursing homes, routine nighttime care involves frequent and routine awakenings for managing incontinence episodes, leading to interrupted sleep in most residents. Nighttime waking episodes lasting 4 min or longer are associated with noise, light, or incontinence care activities. This is despite the fact that most experts recommend toileting programs such as prompted voiding should not be followed during nighttime sleep hours [31, 32]. Instead, strategies to reduce nighttime urine volume and voiding should be adopted, and alternative measures, such as devices and absorbent incontinence products, should be used to manage the urine leakage (see Fig. 11.1). The goal is to follow strategies that promote an adequate sleep period (see Table 11.4).

Barriers to Implementing Toileting Programs

Although intervention studies of toileting programs have consistently demonstrated improvements in incontinence [17, 31–33], there are barriers and obstacles to translation of these evidence-based "best practices" in all care settings. Cognitive and functional impairments causing immobility are primary risk factors for UI, but not good predictors of a person's potential responsiveness to toileting programs. These can interfere with independent toileting and bladder training, so a comprehensive evaluation of cognition, functional ability, voiding behavior, and the person's environment is an important part of the initial assessment.

Cognitive and Functional Impairment

A cognitive assessment is important to determine the person's ability to understand instructions, motivation, and affect [34]. If the person can recognize a sensation of bladder fullness and an urge to void, then a bladder training program may be more successful. Recognizing the location of the

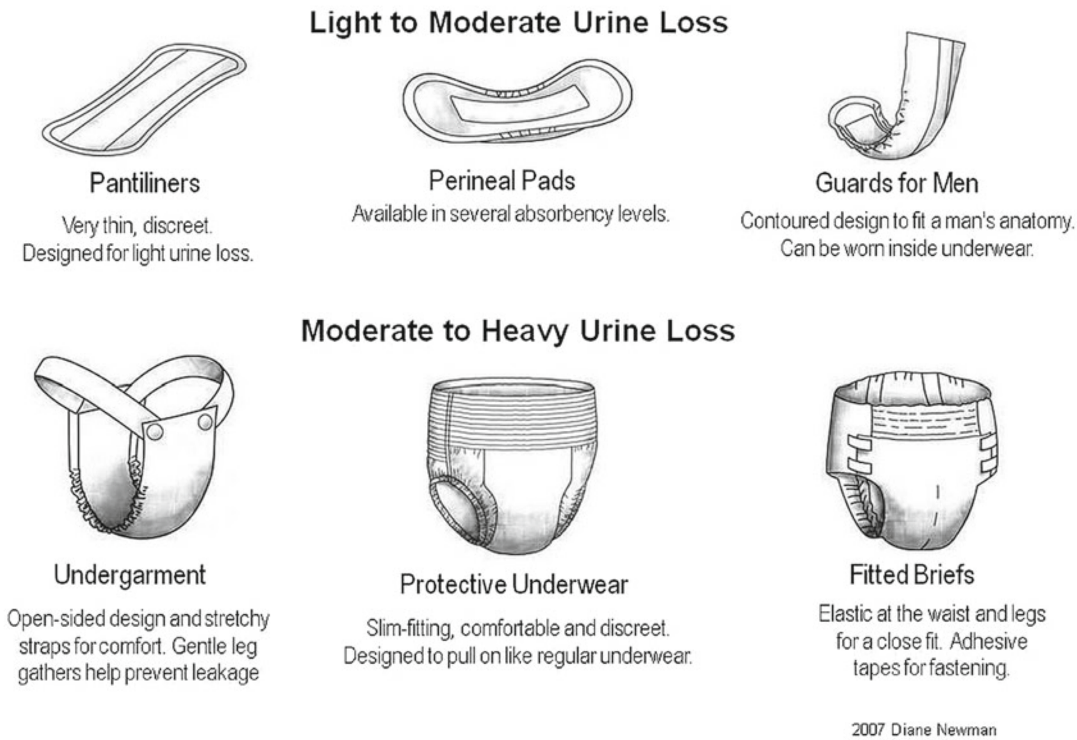


Fig. 11.1 Incontinence products and absorbency. Copyright 2007 Diane K Newman

toileting facility and bathrooms will aid independent toileting. In cognitively impaired individuals, observing body language for cues about the need to use the toilet such as fidgeting, nervousness, pacing, or increased anxiety can assist the caregiver in determining the voiding times [10].

In the frail elder, impaired mobility, balance, and physical function are associated with UI due to difficulties with reaching the toilet in time or having the manual dexterity to manage clothing [10, 35]. This is often a part of what is called "functional incontinence," which is due to contributing factors that are outside of the urinary tract. A functional ability assessment, including manual dexterity and ability to disrobe, should be performed to evaluate a person's capacity to accomplish toileting independently. Very few studies include interventions to improve functional impairments. Since functional impairments with gait speed, balance, and leg strength have been associated with UI in frail older adults, interventions targeting these factors may optimize continence status. An individual's fear of falling during toileting affects their independence in this activity of daily living [36]. Common chronic conditions such as osteoarthritis and joint pain can limit mobility [37] and thus contribute to difficulty in using the toilet. In addition, conditions such as a stroke can limit physical mobility. Chen et al. [38] found that of 138 in-hospital falls, 38 % of the falls occurred when patients tried to get to or from the toilet. Similarly, Tzeng [39] concluded that 45 % of falls in the acute care setting were related to toileting. Toilet-assisted technology, such as a standing lift, can be used to transfer the individual between beds, wheelchairs, or commodes. Functional Incidental Training (FIT), which combines mobility and transfer training with prompted voiding, has reduced UI in nursing home residents [21, 22] and can improve overall ADL abilities [40]. Research is needed regarding programs that combine physical activity and toileting regimens, and these should be tested outside the nursing home setting.

Table 11.4 Strategies that promote sleep hygiene and minimize nighttime voiding[a]

Ensure a conducive sleep environment that combines individualized nighttime incontinence care with a noise and light abatement program to reduce awakenings. Such a program including commonsense procedures, such as closing doors to rooms, fixing squeaky equipment and doors, turning off unattended TVs and radios, and using table lamps instead of overhead lights, should be followed other strategies include:

- Voiding at bedtime
- Use of appropriate absorbent incontinence products that will prevent skin problems
- Consider the appropriateness of a toileting assistive device such as a urinal or bedside commode or application of an external condom catheter in men
- Limiting fluid intake in the late afternoon and evening hours before bedtime so as to decrease nocturnal polyuria. This could be a helpful first step to reduce nocturnal enuresis. However, this does not mean that overall fluid intake should be reduced; rather, the person should be instructed to reduce fluid intake after 6 p.m. and shift intake toward the morning and afternoon
- In individuals with peripheral edema, promote daytime diuresis by elevation of lower extremities for several hours during the afternoon and using support stockings. Altering the administration time of certain medications. Taking diuretics midafternoon and calcium channel blockers in the morning rather than evening may help symptomatic patients

[a]Used with permission. © Diane K. Newman

Voiding Behavior

Optimal voiding behavior, posture, and position are important to ensure complete bladder emptying. If at all possible, the person should sit upright on a bathroom toilet seat or a bedside commode, rather than on a bedpan. Some women do not sit fully on the toilet seat, particularly in public restrooms, and instead "hover" over the toilet. This contracts the pelvic floor muscles and can inhibit adequate bladder evacuation [41]. Feet should be flat on the floor so the person can relax during voiding and easily move from sitting to standing. Making clothing easier to remove will encourage toileting independence. Suggest the use of underwear whenever possible, as this serves as a reminder for the person to stay dry, is a stimulus to use the toilet, and prompts one not to wet if it can be avoided.

Toileting Environment

Environmental factors such as difficulty reaching the toilet and availability of toileting equipment can affect continence. Adaptation of the physical environment to the individual's toileting needs can promote independent toileting and reduce adverse events including falls. A number of solutions can be sought to addressing environmental concerns [10]. For example, a bedside commode or urinal can be placed by the bed for ease of toileting overnight, and clothing can be chosen or altered for ease of use. Additionally, poor lighting, obstacles on the way to the toilet, and a low toilet without hand rails can make getting to the toilet difficult and create safety issues. If the person is utilizing a bathroom toilet, keep a clear, unobstructed, direct walking path to the bathroom; place night-lights along the path; and ensure privacy. In nursing homes, visual cues to indicate the location of the bathroom such as putting the word "toilet" on the outside of the bathroom door can be helpful. Making sure the toilet is easy to use and of the right height is important. Raised toilet seats and grab bars can be used for this purpose. Capezuti and colleagues [42] noted that toilet height for 45.2 % of nursing home residents was actually higher than the optimal height, defined as 100–120 % of the resident's lower leg length, which could consequently increase risk of falls and difficulty in toileting.

Staff and Care Models

In the long-term care setting, another barrier to quality continence care is nursing staff who lack an understating of the types of UI and are not aware of the effectiveness of toileting programs. The Centers for Medicare and Medicaid Service's Resident Assessment Instrument 3.0 Manual recommends that nursing home residents be given a trial of a toileting program both on admission or once UI is noted. This could include scheduled toileting, prompted voiding, or bladder training programs. Staff should document the type of toileting program, the resident's response to the trial program, and whether it continues. Education alone is insufficient to change continence care practices, but organizational and culture change [43] and an incentive payment program can be successful [44]. Nursing staff in care facilities have stated that barriers to implementation of toileting programs include lack of time and resources, lack of authority to change practice, and little support from the administration, physicians, and other staff [45]. Most would agree that it is difficult for staff to maintain toileting interventions after research staff leave [19, 46] and that proper follow-through with toileting care requires staff-management systems [17, 47]. Rahman and colleagues [48] advocate using a distance coaching course to facilitate adoption of evidence-based practice, although in their study, one-third of the nursing homes dropped out before or soon after the course started. Nursing staff have a difficult time providing resident-centered toileting because of the labor-intensive care needed by many nursing home residents [49]. So, a team approach is necessary. Medical directors in collaborative practice with advanced practice nurses such as nurse practitioners are ideally positioned to take up this challenge to improve the quality of care. Rantz and colleagues [50] recommend a continence "champion" who engages and encourages staff toward improvement and evidence-based practice. Over a 2-year period, these authors showed improvement in pressure ulcers and weight loss in residents in 29 facilities who received multilevel interventions with monthly on-site consultation from a geriatric advanced practice registered nurse.

Pelvic Floor Muscle Training and Exercise

Pelvic floor muscle training (PFMT) and exercise is a cornerstone of behavioral treatment for both men and women with UI. Originally it was designed to teach patients how to control periurethral muscles and exercise them daily to increase strength and reduce stress incontinence. Dr. Arnold Kegel, a gynecologist who first popularized this approach, proposed that stress incontinence was due to a lack of awareness of function and coordination of pelvic floor muscles [51]. He demonstrated that women could significantly reduce stress incontinence through PFMT and exercise [51, 52]. Over time, this intervention has evolved both as a behavior treatment and as a physical therapy, combining principles from both fields into a widely accepted nonsurgical treatment for stress, urgency, and mixed UI. It can also be useful in some patients with fecal urgency or fecal incontinence.

Teaching Pelvic Floor Muscle Control

The first step in training is to teach the patient to identify the pelvic floor muscles and to contract and relax them selectively, usually without increasing pressure on the bladder or pelvic floor. Not being able to identify the pelvic floor muscles or to exercise them correctly is probably the most common reason for poor outcomes with this treatment modality. Confirming that patients have identified and isolated the correct muscles is essential and often overlooked. Many clinicians teach pelvic floor muscle exercises by giving patients a pamphlet or brief verbal instructions to "lift the pelvic floor," to hold back the passage of flatus, or to interrupt the urinary stream. While this simple approach may be adequate for some patients, it does not ensure that they understand which muscles to use when they begin their exercises at home. Several techniques can be used to help patients learn to exercise correctly, including verbal feedback based on vaginal or anal palpation [53], biofeedback [54–56], or electrical stimulation [57]. Some clinicians use resistive devices or weighted vaginal cones to increase the patient's awareness of the pelvic floor or enhance the effects of exercise on strength, but there is little research to support these methods [58].

One problem that typically arises in PFMT is that patients tend to use other muscles, such as the rectus abdominis muscles or gluteal muscles, instead of or in addition to the pelvic floor muscles. Contracting some abdominal muscles can be counterproductive when it increases pressure on the bladder or pelvic floor. Therefore, it is important for clinicians to observe when patients are bearing down and help them to relax these abdominal muscles and exercise the pelvic floor muscles selectively. It is often helpful to remind patients not to hold their breath or to count out loud during pelvic floor muscle exercise.

Some clinicians and researchers have recommended coordinated training of transversus abdominis muscles, because it is believed that these muscles facilitate pelvic floor muscle contraction. However, this approach remains controversial, and a review of the literature has noted an absence of evidence for this type of training [59].

Daily Pelvic Floor Muscle Exercise

Once patients demonstrate the ability to properly contract and relax the pelvic floor muscles with the clinician, instructions for daily practice and exercise are provided. The purpose of daily exercise is not only to increase muscle strength but also to enhance motor skills through practice. Specific exercise regimens vary considerably in frequency and intensity, and the ideal exercise regimen has not yet been determined. However, good results have been achieved in many studies using 45–50 contractions per day paired with relaxations [60]. To avoid muscle fatigue, it is usually recommended that patients space the exercises across 2–5 sessions per day. Exercising in the supine position is often recommended at first, because it is the least challenging and facilitates patients' concentration during the learning phase. However, it is important for patients to progress to the more difficult sitting or standing positions with time, so they can become comfortable and skilled using their muscles to prevent incontinence in the positions they assume in daily life.

To increase muscle strength, contractions should be sustained for 2–10 s, depending on what the patient is able to do initially. Exercise regimens should be individualized for each patient, so they can succeed with a comfortable and achievable duration and gradually progress to 10 s. Each exercise consists of a muscle contraction followed by a period of relaxation using a 1:1 or 1:2 ratio [61]. The relaxation between contractions allows the muscles to recover, optimizes strength building, and reduces fatigue.

Strategies to Prevent Stress Incontinence

The goal of behavioral treatment for stress incontinence is to teach patients to occlude the urethra by consciously contracting pelvic floor muscles during coughing, sneezing, lifting, standing, or any other physical activities that precipitate urine leakage. Exercise alone can improve urethral pressure and structural support and reduce incontinence [62]. But in recent years, more emphasis has been placed on teaching patients the skill of contracting the pelvic floor muscles to increase urethral closure pressure during physical activities that cause stress incontinence [57, 63, 64]. This skill has been referred to as the "stress strategy" [63, 64], "counterbracing," "perineal co-contraction," "the Knack" [64], and "the perineal blockage before stress technique" [65]. As with any new skill, this requires the patient to be vigilant and make a conscious effort at first. With time and consistent practice, however, patients can develop the habit of using their muscles to occlude the urethra, and the behavior eventually becomes automatic. Table 11.5 shows a sample stress strategy handout to reinforce teaching.

Table 11.5 Stress strategies: patient handout[a]

Stress leakage occurs when the pressure pushing urine out is higher than the pressure holding it in, such as during coughing, sneezing, standing up, bending, or lifting. It is possible to squeeze your pelvic floor muscles during specific activities and prevent leakage. A bladder diary will help you identify activities that cause leakage

1. Remember: "**squeeze before you sneeze"**
2. Quickly squeeze your pelvic floor muscles (like trying to hold back gas) just before and during activities that normally cause you to leak (coughing, sneezing, bending, lifting, getting up from a chair)
3. If you forget to squeeze your muscles and urine leaks out, go ahead and squeeze your muscles right then. It won't prevent that accident but will help link squeezing the muscles with that activity
4. The stress strategy requires careful timing and practice. Don't get discouraged. Eventually, it will become automatic

[a]Adapted from Burgio KL, Pearce KL, Lucco AJ. Staying Dry: A Practical Guide to Bladder Control. Baltimore, MD: Johns Hopkins Press, 1989;67–100

Because most comprehensive PFMT programs include daily practice to increase strength as well as skill, little attention is paid to their relative contributions. It is important to note, however, that even those with weak muscles can benefit from simply learning how to control their muscles and use them actively to prevent incontinence. This has been shown clearly in a randomized trial that found reduced leakage after only 1 week of training among women taught to voluntarily contract their pelvic floor muscles before or during coughing [64].

The literature on PFMT and exercise has demonstrated that it is effective for reducing stress, urgency, and mixed UI in most outpatients who cooperate with training. Cochrane Database systematic reviews [66] and the International Consultation on Incontinence [60] concluded that there is grade A evidence for PFMT and that it should be offered as first-line treatment to women with stress, urgency, or mixed incontinence [60, 66, 67]. Less research has been conducted with men. However, a recent randomized trial of an exercise-based behavioral training program for men with persistent post-prostatectomy incontinence demonstrated a 51 % reduction in incontinence episodes, significantly greater than the 24 % reduction in the control group [68].

Urge Suppression Strategies

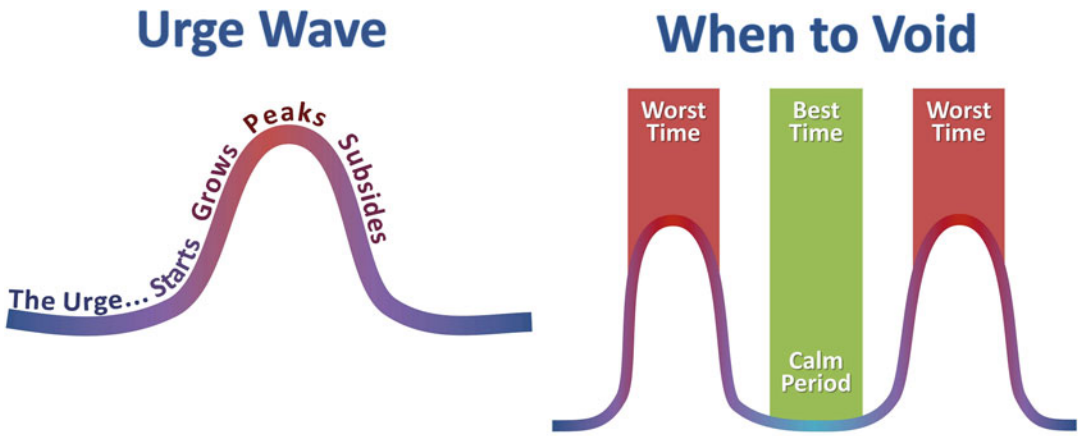
Although originally conceived for the treatment of stress incontinence, PFMT and exercise now plays a major role in behavioral training for urgency and urge incontinence, because pelvic floor muscle contractions can also be used to suppress detrusor contraction [55, 63, 69]. Muscle control and exercise is taught using the same methods available for treating stress UI. What differs is how patients with urge UI use their muscles to respond to urgency and prevent urge incontinence episodes. Not only do they use active pelvic floor muscle contraction to occlude the urethra during detrusor contraction, more importantly, they use volitional muscle contractions to inhibit or suppress the detrusor contraction.

The urge suppression strategy is an essential component in teaching patients a new and more adaptive way of responding to the sensation of urgency. Ordinarily, men and women with urge incontinence feel compelled to rush to the bathroom to avoid leaking when they feel the urge to void. In behavioral training, they learn how this natural reaction is actually counterproductive, because it increases physical pressure on the bladder, increases the feeling of fullness, and exacerbates urgency. Approaching the bathroom, they are also exposed to visual cues that can trigger urgency and detrusor contraction, increasing the risk of an incontinence episode.

Although patients may find it paradoxical at first, they can learn not to rush to the bathroom when they feel the urge to void. Instead, they are taught to stay away from the bathroom and to avoid exposure to cues that trigger urgency. They are encouraged to pause, sit down if possible, relax the entire body, and contract pelvic floor muscles repeatedly, without relaxing in between contractions, to diminish urgency, inhibit detrusor contraction, and prevent urine loss. As they wait for the urge to subside, they breathe evenly and focus on inhibiting the urge. Once the urge sensation subsides, they walk at a normal pace to the toilet. Patient instructions for using the urge suppression strategy are presented in Fig. 11.2.

In addition to daily pelvic floor muscle exercise, it is also helpful for patients with urge incontinence to interrupt or slow the urinary stream during voiding once per day. Not only does this provide practice in using muscles to occlude the urethra and interrupt detrusor contraction, it does so in the presence of the urge sensation, when they need it most. Some clinicians have expressed concern that repeated interruption of the urinary stream may interfere with complete bladder emptying in certain groups of patients. Therefore, caution is recommended when using this technique with patients who may be at risk for voiding dysfunction.

The effectiveness of behavioral training with urge suppression for urge incontinence has been demonstrated in several clinical series [55, 70–72] and in randomized controlled trials using intention-to-treat models. Mean reductions in frequency of incontinence episodes range from 60 to 80 % [53, 69]. The first randomized controlled trial of behavioral training used biofeedback to teach pelvic floor muscle control. Results showed that behavioral training reduced incontinence episodes significantly more than drug treatment and that patient perceptions of improvement and satisfaction with their progress were better [69]. A more recent trial demonstrated the



When the Urge Strikes...

- Stop and stay still. Sit down if you can.
- Squeeze your pelvic floor muscles quickly 3 to 5 times and repeat as needed – Don't relax muscles in between.
- Relax the rest of your body by taking several slow, deep breaths.
- Concentrate on suppressing the urgency and once it calms down, squeeze again as you stand up.
- Walk to the bathroom at a normal pace, do not rush or hurry.
- If the urge returns on the way to the bathroom, stop and squeeze away the urge again.

Fig. 11.2 Urge suppression strategy: patient handout. Burgio KL, Pearce KL, Lucco AJ. Staying Dry: A Practical Guide to Bladder Control. Baltimore, MD: Johns Hopkins Press, 1989; 67–100

effectiveness of PFMT and urge suppression strategies in men with overactive bladder with or without incontinence and without clinically demonstrable outlet obstruction [73]. Behavioral training led to reductions in voiding frequency that were statistically equivalent to those achieved with antimuscarinic drug therapy. Reductions in UI were also significant and similar to those seen with drug therapy.

Bladder Training and Delayed Voiding

Bladder training and other voiding schedules have been used for decades to treat urge incontinence [74–78]. Many patients who experience urgency incontinence or overactive bladder symptoms tend to void frequently. This provides immediate, short-term relief from the urgency sensation, but it sets the stage for more and more frequent voiding. Once this becomes a habit, it can be difficult to change and can lead to reduced functional bladder capacity, detrusor overactivity, and, in some cases, urge incontinence. Detrusor overactivity in turn produces urgency, completing a cycle of urgency and frequency, which is then perpetuated. This cycle can be broken by initiating a regular voiding schedule using bladder training or by using a program of progressive delayed voiding.

Bladder Training

The goal of the bladder training is to break the cycle of urgency and frequency using incremental voiding schedules to reduce voiding frequency, increase bladder capacity, and restore normal bladder function. Patients first complete a voiding diary to determine how often they typically void. The clinician reviews the diary with the patient and then selects a voiding interval that is comfortable for the patient based on the longest time interval between voids. The patient is advised to void at specific predetermined intervals, rather than in response to urgency. Instructions are given to void first thing in the morning, every time the selected interval passes, and before going to bed at night. Over time, the voiding interval is increased at comfortable intervals up to every 3–4 h.

When patients experience the sensation of urgency, they must resist the urge to void and postpone urination in order to comply with the voiding schedule. Several behavioral techniques have been used to help patients control these urges while they wait for their voiding interval to pass. A traditional approach has been to suggest techniques for relaxation or cognitive distraction [77, 78]. Patients are encouraged to get their minds off the bladder by engaging in a task that requires mental but not physical effort, such as calling a friend, reading, or making a to-do list. Affirming self-statements are also used, such as "I am in control of my bladder" or "I can wait." More recently, the urge suppression strategy using repeated contractions of the pelvic floor muscles without relaxing them in between, known as "quick flicks," has been used to help control urgency while the patient postpones urination until the next scheduled time. Table 11.6 shows a sample patient handout to guide urge suppression strategies.

Several studies have demonstrated the effectiveness of bladder training for treating urge incontinence [74–78]. The most definitive randomized clinical trial demonstrated a mean 57 % reduction in frequency of incontinence in older women [77]. In this study, bladder training not only reduced urgency incontinence but also stress UI. It is possible that this unanticipated finding could be explained by patients developing a greater awareness of bladder function or bladder habits in general or that postponing urination increased pelvic floor muscle activity. In another trial that compared bladder training to oxybutynin, 73 % of women in bladder training were reported to be "clinically cured" [76].

Table 11.6 Controlling bladder urgency and frequency: patient handout[a]

When you feel a sudden, urgent need to urinate, do not rush or try to hurry to the bathroom. Rushing will jiggle your bladder and increase the urge to go. You can take control over your urgency and frequency by using some simple strategies:

- *Focus on another body sensation*. Sit down and take five slow, deep breaths. Think about the air moving in and out of your lungs instead of how your bladder feels
- *Squeeze your pelvic floor muscles five times quickly and strongly*. These "quick flicks" will relax the bladder so that the feeling of urgency goes away. Or you could try holding one strong squeeze of your pelvic floor muscles. Try each way and see which one works best for you
- *Distract yourself* by focusing on a mental activity: Use mind games. Turn your attention to counting backward from 100 by 7 s or working on a crossword puzzle. Do a task that requires a lot of thought—for example, balance your checkbook, write a letter, and do handwork or some other activity that requires a great deal of attention
- *Use self-talk or good self-statements*. Tell yourself: "I am the boss, not my bladder." "I am in control." "I can beat this." Create a statement that fits your situation and personality the best. Keep saying this statement over and over until the feeling of urgency passes

After the urge goes away, try to wait at least several minutes longer and then go to the bathroom whether you feel you have to go or not. Never rush or run to the bathroom—walk slowly. It may take some practice with these strategies, but over time, you will see that you are gaining more control and experiencing fewer episodes of urgency

[a]Used with permission. © Diane K Newman

Delayed Voiding

Delayed voiding is another way to help patients improve bladder control by expanding the interval between voids [73]. It differs from bladder training in that patients do not follow a predetermined voiding schedule. Instead, they are instructed to use their urge suppression strategies to reduce any urgency they experience. Then, instead of going to the bathroom immediately after suppressing the urge, they are to postpone urination by 5 min before voiding. Once they are comfortable with a 5-min delay, the delay time can be increased gradually. Patients are often surprised to find that after a brief wait, the urge subsides or disappears altogether. This enhances their sense of control and confidence to gradually increase the delay time to achieve a normal frequency.

Table 11.7 Prevent leakage without warning: patient handout[a]

Do you stand up and urine comes out without warning?
To prevent this from happening:
1. Before you get out of a chair, squeeze your pelvic floor muscles (like trying to hold back gas) and hold them as you stand up
2. Before you get out of bed, squeeze your pelvic floor muscles before you move to sit on the side of the bed and then squeeze again as you stand up
3. Be sure your bladder/bowels are under control before you start walking (urgency gone)
4. Walk to the bathroom once you are in control
5. If the urge returns on the way to the bathroom or in the bathroom, STOP, stand still, and squeeze again until your bladder calms down

[a]Used with permission. © University of Alabama at Birmingham Continence Clinic

Strategies to Prevent Sudden Urine Loss Without Warning

Many elderly patients, particularly frail older adults, will complain that they lose urine as soon as they stand up from a chair or from their bed, often without any warning. With the sarcopenia that is common with advanced age, getting out of a chair or the bed is difficult for many frail older persons. They may suppress the urgency when sitting or lying still, but after struggling to get up, when their feet hit the floor, the urine flow starts. The strategy to prevent this is to contract pelvic floor muscles *every* time as they stand up. This can effectively prevent the detrusor instability that standing initiates. Table 11.7 shows a sample patient handout to reinforce this teaching concept.

Strategies to Prevent Post-void Dribbling

Post-void dribbling is a common complaint in both older men and women. This is often caused by a small amount of residual urine in the bladder neck or urethra. Pelvic floor muscle contraction can be used to prevent post-void dribbling in both men and women. Table 11.8 shows a sample patient handout for this technique in men. Women with persistent post-void dribbling should be examined for evidence of a urethral diverticulum. Common associated symptoms include dysuria caused by infection of urine trapped in the diverticulum and dyspareunia in sexually active women. Pelvic examination may show soft tissue bulging from the urethra. Cystoscopy can also be useful, and magnetic resonance imaging (MRI) of the pelvis can help to confirm the diagnosis. Surgical treatment may be required to excise the diverticulum and repair the urethra if this is discovered to be the cause of post-void dribbling.

Drug Therapy

Drug therapy (Table 11.9) is available to treat UI and other LUTS in older adults. The type of drug used depends on the underlying cause of the urinary symptoms. Comorbid conditions, including frailty and dementia, must be carefully considered. The most common drug categories for UI and LUTS include anticholinergic drugs, nonselective and selective alpha-antagonist agents and 5-alpha-reductase inhibitors in men, topical estrogens in women, and the newest category, beta-3 adrenoreceptor agonists.

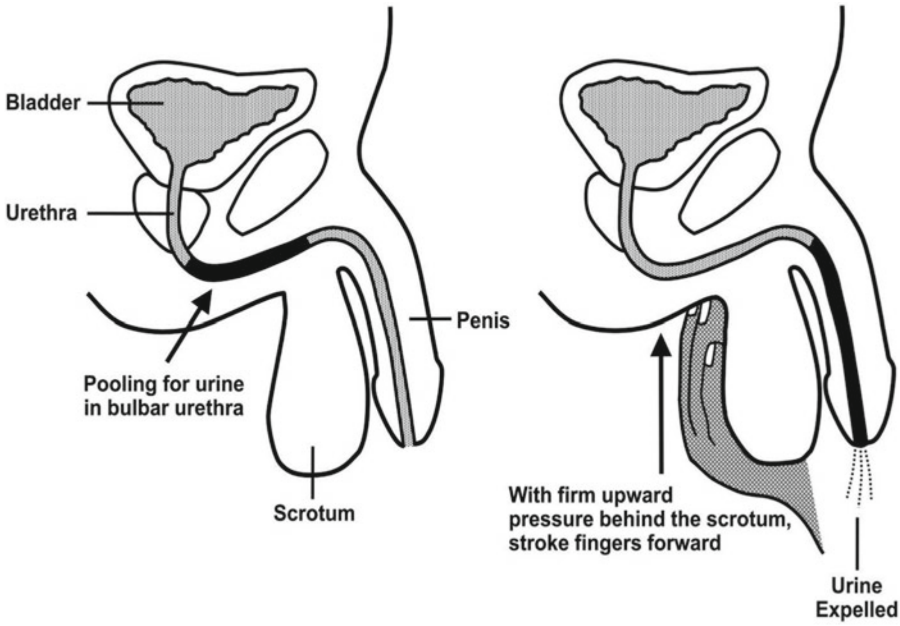
Anticholinergic drugs, which target the muscarinic receptors of bladder smooth muscle leading to bladder relaxation, are most often used to treat urgency or mixed incontinence [84, 85]. These antimuscarinic drugs can be used in men and women, and all have similar efficacy [86, 87]. Side effects of antimuscarinic therapy such as dry mouth and constipation are frequent [86–88] and can contribute to limited long-term adherence [89]. Patients who demonstrate incomplete bladder emptying should be monitored for significant urinary retention, generally accepted as a residual urine volume immediately post-void of ≥200 mL, while taking antimuscarinic agents.

Antimuscarinic drugs should be used with caution among older adults with liver and renal impairment (see Table 11.9). For all older patients, using the lowest possible effective dose is recommended. The potential for drug–drug and drug–food interactions also exist with the antimuscarinic drugs. The most common drug–drug interactions may occur with drugs that also require hepatic metabolism. Common food

Table 11.8 Dripping after you urinate: patient handout[a]

Sometimes after you urinate, urine continues to drip. This happens because the pelvic floor muscles are still relaxed. To help prevent this dripping:

1. After you urinate, squeeze your pelvic floor muscles tightly (like you are trying to hold back gas). Then do your final shake or wipe
2. If you sit to urinate, also squeeze those muscles as you stand up
3. Men can use the pads of your finger to exert a firm, upward pressure behind your scrotum. Move your fingers forward in a stroking motion. This will "milk out" the trapped urine and force it to the end of the urethra, where it can be removed by shaking or squeezing your penis



[a]Used with permission. © University of Alabama at Birmingham Continence Clinic
Illustration © Diane K. Newman

interactions include alcohol and grapefruit juice due to inhibition of the cytochrome P450 pathway. Use of these medications is also contraindicated in patients with a history of closed-angle glaucoma, also called narrow-angle glaucoma. Antimuscarinic medications can cause dangerous elevation of intraocular pressures in these patients. Older adults with open-angle glaucoma, which is the more common form of the disease, can usually use these medications without problems. If in doubt regarding the type of glaucoma, the healthcare provider should check with the patient's ophthalmologist or optometrist prior to prescribing any antimuscarinic medication.

Antimuscarinic agents can be used as single drug therapy in men with symptoms of urgency incontinence but are often prescribed in combination with drug treatments targeting symptoms associated with benign prostatic enlargement (BPE). Alpha-adrenergic antagonists and 5-alpha-reductase inhibitors are effective for LUTS associated with BPE which may include urgency incontinence [90, 91]. Patients using a selective alpha-adrenergic antagonist may have less risk of orthostatic hypotension compared to nonselective agents. However, titration of the dose and using the lowest effective dose may be easier with the nonselective alpha-adrenergic agents such as terazosin that have a wider range of dosages than the selective agents. Five-alpha-reductase inhibitors, when used for at least 1 year alone or in combination with an alpha-adrenergic antagonist, have been shown to reduce progression of urinary symptoms associated with BPE,

Table 11.9 Drug therapy for the treatment of urinary incontinence and other lower urinary tract symptoms

Drugs	Usual adult dose	Metabolizing liver enzyme	Hepatic impairment	Renal impairment	Food interaction	Comments
Drugs with predominantly antimuscarinic effects						
Darifenacin	7.5–15.0 mg daily orally	CYP3A4 CYP2D6 [a]mostly 3A4 in poor 2D6 metabolizers	Mild—no dose adjustment Moderate—7.5 mg daily Severe—do not use	No dose adjustment	Grapefruit (minor)	The drug is selective for the bladder muscarinic receptor and had fewer cognitive side effects than other agents in cognitively intact older adults [79]
Fesoterodine	4–8 mg daily orally	Hydrolysis CYP2D6 CYP3A4	Mild—no dose adjustment Moderate—4 mg daily Severe—do not use	GFR 30–80 mL/min—consider lower dose GFR < 30 mL/min—4 mg daily	Grapefruit (moderate)	This prodrug is easily converted to an active metabolite chemically identical to the active metabolite of tolterodine Demonstrated efficacy in frail older adults. May have low cognitive side effects in healthy vulnerable frail older adults [80, 81]
Oxybutynin[a]	2.5–5.0 mg 1–3 times daily orally (short acting) 5–30 mg daily orally (long acting) 3.9 mg over a 96-h period (transdermal) 10 % topical gel—½–1 g daily	CYP3A4	Not well studied—use with caution	Not well studied—use with caution	Alcohol (moderate)	Short-acting preparations can cause more side effects than long-acting and transdermal preparations The transdermal application can cause local skin irritation in some patients, the patch more than the gel
Solifenacin	5–10 mg daily orally	CYP3A4	Mild—no dose adjustment Moderate—5 mg daily Severe—do not use	GFR < 30 mL/min—5 mg daily	None noted	The drug is more selective for the bladder M3 muscarinic receptor over other muscarinic receptors
Tolterodine[a]	2–4 mg daily orally	CYP2D6: strong CYP3A4: weak	Use 2 mg daily with moderate/severe impairment	GFR < 30 mL/min—2 mg daily	Grapefruit (moderate) Alcohol (moderate)	The drug has relatively low lipophilicity with theoretically more limited ability to penetrate the blood–brain barrier and cause confusion
Trospium	20 mg twice daily orally 60 mg daily orally (long acting)	Negligible	Not well studied—use with caution; lower doses with moderate/severe impairment	GFR < 30 mL/min—20 mg daily (do not use longer-acting formulation)	Alcohol (moderate) Take on empty stomach or 1 h before meal	The agent is a quaternary ammonium compound, theoretically less likely to cross the blood–brain barrier

(continued)

Table 11.9 (continued)

Drugs	Usual adult dose	Metabolizing liver enzyme	Hepatic impairment	Renal impairment	Food interaction	Comments
Beta-3 adrenergic agonist						
Mirabegron	25 mg daily orally 50 mg daily orally	CYP3A4: strong CYP2D6: weak	Mild—no dose adjustment Moderate—25 mg daily Severe—do not use	GFR 30–80 mL/min—consider lower dose GFR < 30 mL/min—25 mg daily	May be taken with or without food	Key safety issues: cardiovascular (slight increases seen with heart rate and blood pressure, cardiovascular adverse events), neoplasms, hepatic, urinary tract-related diverse events, and hypersensitivity reactions
Topical vaginal estrogen (for women)						
	Approximately 0.5 g cream applied topically nightly for 2 weeks, then twice per week Estradiol ring, replaced every 90 days Estradiol, 1 vaginal tablet daily for 2 weeks, then 1 tablet twice a week	CYP3A4	Select dosage cautiously when on multiple other medications	Select dosage cautiously when on multiple other medications	Less interactions with topical than oral preparations	Local vaginal preparations are probably more effective for urgency related to local irritation than oral estrogen, but definitive data on effectiveness are lacking. Use is generally contraindicated in women with a personal history of breast or uterine cancers. Some women with a history of estrogen receptor negative breast cancer might be candidates if approved by their oncologist [82]
Serotonin and noradrenaline reuptake inhibitor						
Duloxetine	20–80 mg daily	CYP2D6 CYP1A2	Not recommended for use with hepatic insufficiency or substantial alcohol use	GFR 30–80 mL min—use lower dose GFR < 30 mL/min—do not use	Alcohol (moderate) Caffeine (moderate)	Not FDA approved in the USA for this indication; however, a systematic review of clinical trial data suggests improvement in stress UI [83]. Transient nausea is a common side effect
Alpha-adrenergic antagonists (for men) *Nonselective alpha-adrenergic antagonists*						
Doxazosin[a]	1–8 mg daily orally at bedtime		Use lower dose (≤4 mg daily), and when on multiple other medications, do not use with severe impairment	Use lower dose (≤4 mg) and when on multiple other medications	Alcohol (moderate)	Orthostatic hypotension can be a serious side effect
Prazosin	1–5 mg twice daily orally		Do not use with severe impairment	GFR 30–80 mL/min—1 mg twice daily GFR < 30 mL/min—1 mg daily	Alcohol (moderate)	Orthostatic hypotension can be a serious side effect Also used for post-traumatic stress disorder in men

Terazosin[a]	1–10 mg daily orally at bedtime		No specific dosage recommendations	No dosage adjustment needed; caution when on multiple other medications	Alcohol (moderate)	Orthostatic hypotension can be a serious side effect
Selective alpha-adrenergic antagonists						
Alfuzosin	10 mg daily orally	Oxidation in liver	Do not use with moderate/severe impairment	Use with caution with severe impairment	Alcohol (moderate) Give with or immediately after a meal	Orthostatic hypotension can be a serious side effect Doses of nonselective agents should be increased gradually to facilitate tolerance
Silodosin	4–8 mg daily orally	CYP3A4	Do not use with severe impairment	Reduce dose to 4 mg with GFR 30–50 mL/min Do not use with GFR <30 mL/min	Alcohol (moderate) Take with meal	Orthostatic hypotension can be a serious side effect
Tamsulosin[a]	0.4–0.8 mg daily orally	CYP enzymes (specific enzymes not identified)	No specific dosage recommendations	No dosage adjustment needed; caution when on multiple other medications	Alcohol (moderate) Give 30 min after a meal	Orthostatic hypotension can be a serious side effect, especially if taking a beta-blocking drug
5-alpha-reductase inhibitors (for men)						
Dutasteride	0.5 mg daily orally	CYP3A4 CYP3A5	No specific dosage recommendations	Dosage adjustment not required	None noted	Can lead to decreased libido and gynecomastia
Finasteride[a]	5 mg daily orally	CYP3A4 CYP3A5	Do not use with moderate/severe liver disease	Dosage adjustment not required	None noted	Can lead to decreased libido and gynecomastia

[a]Available as a generic Key: *GFR* glomerular filtration rate, *CYP* cytochrome P450 family

risk of acute urinary retention, and need for future invasive surgical therapy [92].

As of July 2012, a nonselective beta-3 adrenoreceptor agonist (beta 3-AR), mirabegron, was approved by the FDA as the first agent in this newest category of pharmaceutical treatment for overactive bladder and UI in men and women [93]. In placebo-controlled clinical trials, mirabegron reduced 24-h urinary frequency and UI episodes. Mirabegron was found to slightly increase heart rate and blood pressure in clinical trials, with greater increases seen with higher dosages. Improved efficacy may exist in the initial studies for older adults (65–80 years of age) compared to younger adults (<55 years of age). Reductions in dose (25 mg daily) are recommended for patients with liver and renal impairment. Mirabegron is not indicated for patients with severe liver impairment or uncontrolled hypertension.

No pharmacologic treatments are currently approved for the treatment of stress UI in the USA. However, duloxetine, a serotonin and norepinephrine reuptake inhibitor, has been evaluated in several randomized controlled trials, and a recent systematic review suggests it may be beneficial for treatment of mild stress incontinence in women [83].

Low-dose, topical vaginal estrogen can be effective to reduce urinary urgency, frequency, and urgency incontinence among older women [94]. Systemic absorption is low when using doses appropriate for treating urogenital atrophy, 0.5 g of estrogen cream three times a week. However, vaginal estrogen is generally considered to be contraindicated in women with a personal history of breast or uterine cancer. Some oncologists will permit use in select women with a history of breast cancer, particularly if the primary tumor was estrogen receptor negative [82]. Once the quality of the vaginal epithelium is restored, the dosing frequency of vaginal estrogen cream should be reduced. An intravaginal estradiol ring, which is changed every 90 days, may be a convenient method of treatment for many older women. If the patient is sexually active, the ring can be removed prior to intercourse and subsequently replaced.

Perineal skin irritation from incontinence or incontinence-associated dermatitis (IAD) should be treated with an antifungal cream if a fungal etiology exists and with a moisture barrier ointment for prevention, if indicated [95].

Urinary Incontinence in Frail Elders

Urinary incontinence in frail older patients requires special considerations. Dementia is common in these patients, so the index of suspicion should be high. A patient may seem to be cognitively intact when giving a history, but frail patients with dementia may not respond well to treatment protocols designed for younger patients. One clue of dementia can be that the patient denies any problems, while the caregiver is clear that incontinence is a problem. The following case study provides a typical example.

Case Study

Mr. J is an 88-year-old man who is brought to the urologist by his daughter who is his caregiver. He has begun having more frequent incontinence episodes which is quite burdensome to his daughter because he refuses to wear pads. She tells the urologist that her father just sits in his chair all day watching television. When he gets up to go to the bathroom, which he does about every 4–5 h, he walks very slowly due to his knee osteoarthritis, and urine starts to flow before he can get to the bathroom. This is happening several times a day. He uses a bedside urinal at night and stays dry.

His medical history includes hypertension, coronary artery disease, and degenerative joint disease. His medications are aspirin, metoprolol, lisinopril, hydrochlorothiazide, and donepezil. On physical examination, he is alert and pleasant but repeats himself a good bit. His physical examination is completely unremarkable; his pulse is 60 beats per minute, blood pressure 110/60 mmHg; rectal examination reveals a slightly enlarged but smooth and

(continued)

(continued)

symmetric prostate. His urinalysis is normal; his uroflow is 9 mL/s with a prolonged flow curve and voided volume of 350 mL; post-void residual is 80 mL.

You prescribe a selective alpha-1a adrenergic receptor antagonist and give him a return appointment in 3 months. The daughter calls you in a week and tells you her father has become much more unsteady on his feet and has fallen on the way to the bathroom twice. She is worried he will break a hip. His urine leakage might be a little better, but not much. What is the next step?

Despite the selective alpha-blocker, most likely Mr. J has developed symptomatic orthostatic hypotension. The potential morbidity and mortality associated with hip fracture are significant. Discontinuing the alpha-blocker is prudent. A clinician could prescribe an antimuscarinic medication, but most likely, it would make this frail man with dementia more confused, due to its anticholinergic effect. Also, anticholinergic medications are relatively contraindicated with acetylcholinesterase inhibitors such as donepezil. They have opposite effects on both the brain and the bladder. Donepezil allows acetylcholine to be present in the synapses longer and has been shown to help slow progression of dementia but can worsen detrusor overactivity and incontinence [96]. Most family members are reluctant to discontinue cholinesterase inhibitors due to the serious impact of dementia and the possibility that these medications are slowing dementia progression. However, a discussion with the family of the possible benefits of the cholinesterase inhibitors versus the burden of incontinence will help with the decision of whether the medication should be withdrawn to see if incontinence improves. Finally, once informed that antimuscarinic drugs can precipitate confusion and worsen constipation, most frail elderly and their caregivers wisely decline a trial. A beta-3 adrenoreceptor agonist might be a reasonable choice, but experience with this new class of agents in frail older persons is limited. Behavioral treatments would be the safest and most appropriate treatment for this older patient.

Behavioral Interventions in Frail Elders with Dementia

As with other older patients, behavioral measures can improve incontinence in frail, older adults with dementia. Tapering caffeine can reduce incontinence frequency and volume [97]. Prompted voiding is often an effective intervention in this population, as well [2]. An effective procedure for prompted voiding is for the caregiver to approach the patient every 2–3 h while awake and tell them, “It is time to go the bathroom,” and to assist them as necessary. This prevents the patient from saying, “No, I don’t need to go.” The caregiver can remind the patient that their urologist recommended regular trips to the bathroom for “bladder health.” A 3-day trial can determine whether prompted voiding will be effective [19]. If it decreases wetness and increases quality of life for the patient and caregiver, it can be continued. If not, a check and change strategy with absorbent pads or other products should be employed.

Fluid Intake

Encouraging intake of at least 6 eight-ounce glasses of liquids daily can help dilute the urine and reduce odor should leakage occur. Restricting fluids should be considered only for strategic purposes to enable certain activities, such as going to church or temple. Otherwise, it simply predisposes the patient to dehydration. More highly concentrated urine can actually increase urinary urgency by direct irritation of the bladder epithelium. Patients on a loop diuretic can delay administration until mid- to late afternoon to allow more daytime hours free of polyuria. The diuretic will wear off before bedtime, so it will not adversely affect nocturia.

Constipation

Chronic constipation can precipitate urinary retention and overflow incontinence and should be included in the differential diagnosis for frail older adults with new or worsened incontinence. The digital rectal exam and abdominal exam can be useful to uncover constipation that the patient may not be able to detect or communicate to the caregiver due to dementia [98]. Initiation of a bowel regimen to treat chronic constipation can also be useful with potential improvement in urinary symptoms.

Perineal Skin Irritation

Urinary incontinence can often cause skin irritation or breakdown. Perineal skin problems can also be diagnosed during physical examination. The caregiver may not be aware of the problem if the patient is still doing most of their own self-care. Antifungal cream should be prescribed if indicated and a moisture barrier ointment used to protect the skin while it heals and afterward to help prevent further irritation.

Asymptomatic Bacteriuria and Urinary Tract Infections

The relationship between Urinary Tract Infections (UTIs) and incontinence in patients with dementia is complex. UTIs can precipitate incontinence, but treating asymptomatic bacteriuria can result in antibiotic resistance and increase adverse events. A solid history of *new* or *worsened* incontinence in the setting of a positive urine culture may suggest that a trial of antibiotics is reasonable. After treatment, if the incontinence continues unchanged despite a negative urinalysis or repeat culture, a diagnosis of asymptomatic bacteriuria should be noted to prevent additional use of antibiotics in the absence of fever or other constitutional symptoms. One constitutional symptom common in patients with dementia is worsened mental status, so UTI is always in the differential diagnosis for patients with dementia and altered cognitive status or delirium.

Pharmacotherapy

For patients with dementia who fail prompted voiding and fluid and caffeine management and who do not have constipation or a UTI, medications such as selective alpha-blockers, antimuscarinics, or beta-3 adrenoreceptor agonists can be tried. Caution is advised to watch for potential adverse events as previously described. If improvement is not noted within a month or if the patient has a functional decline or intolerable side effects, the medication should be discontinued.

Devices

Devices for the treatment of incontinence include urethral inserts, intravaginal devices, and penile compression devices [99].

Intraurethral Devices

A catheter-like device can be inserted into the urethra to block leakage occurring in women with stress UI [100]. The current device available in the USA, the FemSoft® Insert, is a sterile disposable, single-use intraurethral device (see Fig. 11.3a, b). It consists of a narrow, silicone tube entirely enclosed in a soft, thin, mineral oil-filled silicone sleeve that forms a balloon on the tip of the device. As the insert is advanced into the urethra, oil in the balloon is transferred toward the external retainer to facilitate passage through the urethra. Once the tip of the insert has entered the bladder, the fluid returns to fill the balloon forming a mechanical barrier to retain urine within the bladder. To assist with insertion, the insert is supplied on a disposable applicator and with a lubricating gel. The insert has a string to facilitate removal. The device is easily removed for voiding and should be removed at least once every 6 h. It is available in three diameter sizes (16, 18, 20 French) and two lengths (3.5 cm, 4.5 cm) for each diameter. The insert must be properly sized to the woman's anatomy. Adverse events reported include hematuria, recurrent UTIs, and urethral discomfort.

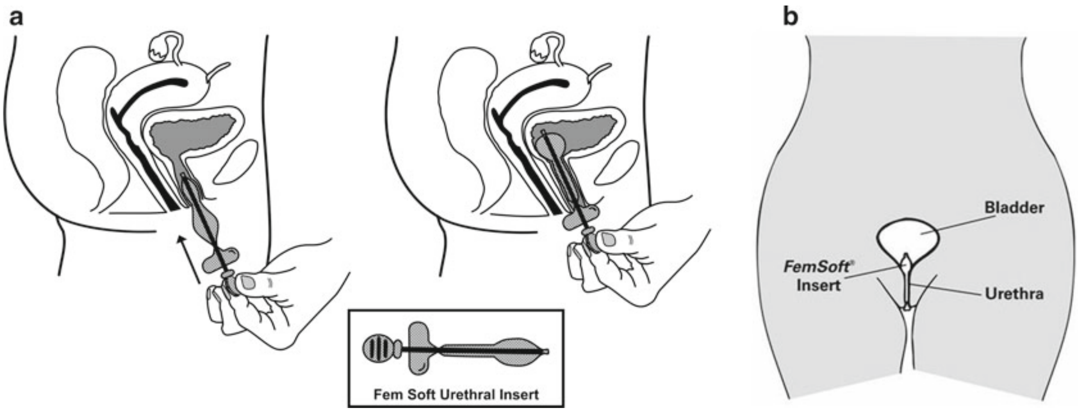


Fig. 11.3 (**a**) FemSoft insert (**b**) FemSoft urethral insert in place
Illustrations © Diane K. Newman

Intravaginal Devices

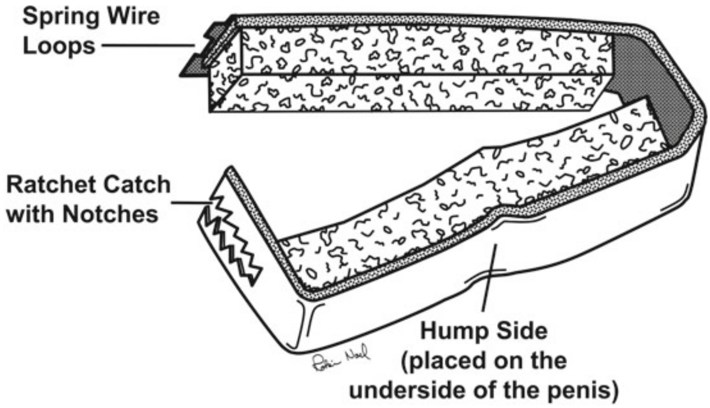
The use of an intravaginal incontinence pessary may also be effective in alleviating stress UI symptoms. This type of pessary is usually round, available with or without a support diaphragm in the center for pelvic organ prolapse, and has a knob, which adds a centimeter to the size of the pessary (see Fig. 11.4). The knob should be situated so it is suburethral behind the symphysis pubis, ideally at the level of the urethrovesical junction to stabilize and support the bladder neck and compress the urethra to prevent urine leakage during an increase in pressure from above. The ATLAS trial in women with stress incontinence treated with pessary, behavioral therapy, or combined therapy showed all three groups to be equally effective at 1 year, with 33–40 % of women reporting no bothersome stress incontinence symptoms and 50–54 % satisfied with treatment outcome [101].

Fig. 11.4 Incontinence dish with support pessary

Penile Compression Device

A penile compression or "clamp" device is an external occlusive device that is often used by men after prostate cancer surgery to stop stress UI or by men with continuous urine leakage [10]. These devices mechanically compress the soft tissue of the penis by applying external pressure to the urethra, thus preventing leakage (see Fig. 11.5). Used correctly, penile compression devices are one method of controlling UI in select men who are cognitively intact, have normal genital sensation, have intact penile skin, have adequate penile length, are aware of bladder filling, and have sufficient manual dexterity to open and close the device. Usually the device is placed halfway down the shaft of the penis and then tightened to a comfortable pressure to compress the urethra.

Fig. 11.5 Cunningham penile clamp Illustration © Diane K. Newman



Moore et al. [102] conducted a study to assess the safety, efficacy, comfort, and user satisfaction with three penile compression devices: the Cunningham Penile Clamp, C-3, and U-Tex. Subjects were men ($N=12$) who had undergone prostate cancer surgery in the past 6 months. Penile Doppler ultrasonography was performed to assess circulatory impedance with and without the compression device in place. Color flow assessment was made distal to the device. The results indicated that the Cunningham device was the most efficacious and most acceptable to users but also contributed to reduced systolic velocity in all men. None of the devices completely eliminated urine loss.

Potential complications including edema, urethral erosion, pain, and obstruction limit their use. Soft tissue damage by excess compression can occur with these clamps, and thus, their use is contraindicated in men with sensory impairment. Skin breakdown, swelling, and strictures (scarring) can occur inside the urethra if a clamp is left in place too long. If used properly and released every 1–2 h for bladder emptying, these devices can be very beneficial.

Products for Management of Urinary Incontinence

Incontinence products, such as absorbent products, external catheters, urinary and fecal pouches, and toilet substitutes (e.g., urinals and bedside commodes), can be effective ways to manage urine leakage for patients and their caregivers. They may be adjunctive management in addition to incontinence treatments or may be used in patients who have failed or are not candidates for certain interventions. These products contain urine leakage, maintain skin integrity, conceal the problem, and in many older adults improve quality of life [103].

Absorbent Products

The use of absorbent garments and pads can do much to contain incontinence, reduce caregiver burden, and preserve dignity. Perineal pads and pantiliners are commonly used by women to absorb mild to moderate urine leakage (see Fig. 11.1). Underwear substitution can be helpful in some patients who decline to wear adult briefs, such as Mr. J in the case study. Many patients with dementia, particularly women, will wear protective "pull-up"-type underwear if they are substituted for their regular underwear.

Continued advances in the design of disposable absorbent incontinence pads and products have helped them to become more fluid absorbent and can also help with odor control. Incontinence absorbent products have an upper layer through which moisture passes and one or more absorbent layers. Some pads incorporate a superabsorbent polymer that "locks" urine into a gel that holds much more urine for its weight than does fluff

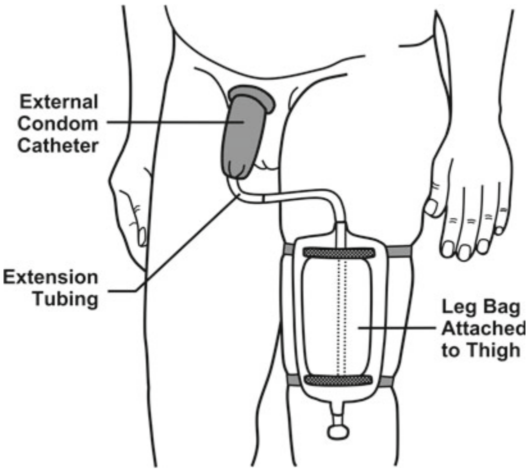


Fig. 11.6 External condom catheter
Illustration © Diane K. Newman

pulp (an absorbent pulp made from wood fiber) and retains it better. Reusable products are available, but they are not as popular with patients although they might be less expensive.

External Catheters and Pouches

External catheters are condom-type sheaths applied (usually rolled) over the penis and connected to a drainage bag (see Fig. 11.6). They are used primarily for urine collection in men who experience UI. The most commonly used external catheters are disposable and must be changed every 24–48 h (see Fig. 11.7a, b). There are reusable external catheter systems (see Fig. 11.8). Another external collection device is a flexible, plastic form-fitting pericup device placed over the urinary meatus (in men and women) to funnel urine away from the perineum into a drainage bag. Current pouches were modeled on ostomy pouches using similar synthetic adhesive. Problems with leakage persist because of poor adherence. These external devices use adhesive to adhere to the skin, and adverse events include local erythema, periurethral edema with removal, and urine leaking around the device if sizing is incorrect.

Toileting Assistive Devices

Handheld containers and devices, often referred to as "portable toilet substitutes," can be used by patients and caregivers to collect urine. There are two general categories: one includes commode seats or bedside commodes and the other handheld devices such as a bedpan or urinal. These devices can promote self-toileting especially if toilet facilities are inaccessible, doorways and bathrooms are too narrow for access (e.g., if using a walker, wheelchair), nocturnal frequency and urgency is a significant problem, and decreased mobility limits ambulation. Many different commodes exist which can ease toileting. Some have drop arms and adjustable heights to allow for tailoring the commode to the patient's needs. Other commodes are backless and can be placed on a toilet for quick adaptation in a bathroom. There are general areas that need consideration when selecting a commode, including:

- Height and weight of the person using the commode.
- A plastic seat with a large soft surface area may allow even distribution of body weight.
- Seats with grab bars on either side can prevent falling and provide assistance when rising.

Often the use of a fracture pan makes the patient more likely to be able to urinate without pain, especially in the period after a fracture or hip repair. Patients should not be left on the bedpan for more than 15–20 min, as this device does not allow correct positioning for complete bladder emptying.

Urinals have the potential to enable patients who experience difficulty accessing a toilet or bedside commode to regain continence. Also, they are useful for patients who have severe mobility restrictions or who are confined to bed or chair. Most urinals have handles, so they can be placed next to the patient; hung on a bedrail, wheelchair, or walker; or laid flat on the bed. Toilet-assisted technology, such as a standing lift, can be used to transfer the patient between beds, wheelchairs, and commodes. The lift is equipped with safety devices to prevent falls.

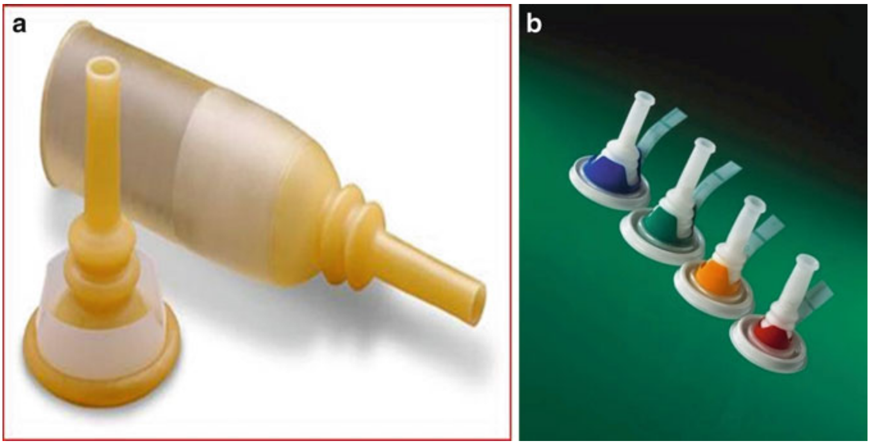


Fig. 11.7 Self-adhesive disposable external catheter. (**a**) Hollister, (**b**) Coloplast

Fig. 11.8 AlphaDry reusable external collection device in place

Summary

Urinary incontinence is a common clinical problem in both older men and women. A wide variety of nonsurgical treatment options are available that can address these conditions. In most cases, symptoms can be significantly improved, or sometimes completely resolved, by use of behavioral therapy, medications, devices, or combined therapies. This can have an enormous influence on both patients and their caregivers and can improve functional abilities and quality of life for many people. Additional research will likely lead to additional medications and other treatments in the future. Clinicians should work to incorporate these therapeutic options into their treatment armamentarium for older adults with incontinence, offering behavioral therapy as first-line treatment for incontinence.

References

1. Gormley EA, Lightner DJ, Burgio KL, Chai TC, Clemens JQ, Culkin DJ, Das AK, Foster HE, Scarpero HM, Tessier CD, Vasavada SP, American Urological Association (AUA) Guideline. Diagnosis and treatment of overactive bladder (non0neurogenic) in adults. AUA/SUFU GUIDELINE. Retrieved http://www.auanet.org/content/media/OAB_guideline.pdf
2. Eustice S, Roe B, Paterson J. Prompted voiding for the management of urinary incontinence in adults. Cochrane Database Syst Rev. 2000;(2):CD002113.
3. Ostaszkiewicz J, Roe B, Johnston L. Effects of timed voiding for the management of urinary incontinence in adults: systematic review. J Adv Nurs. 2005;52: 420–31.
4. Ostaszkiewicz J, Johnston L, Roe B. Timed voiding for the management of urinary incontinence in adults. J Urol. 2005;173(4):1262–3.

5. Ostaszkiewicz J, Johnston, L, Roe, B. Timed voiding for the management of urinary incontinence in adults. Cochrane Database Syst Rev. 2004a;(1): CD002802.
6. Ostaszkiewicz J, Johnston L, Roe B. Habit retraining for the management of urinary incontinence in adults. Cochrane Database Syst Rev. 2004b; (2):CD002801.
7. Roe B, Ostaszkiewicz J, Milne J, Wallace S. Systematic reviews of bladder training and voiding programmes in adults: a synopsis of findings from data analysis and outcomes using metastudy techniques. J Adv Nurs. 2007;57(1):15–31.
8. Roe B, Flanagan L, Jack B, Barrett J, Chung A, Shaw C, Williams K. Systematic review of the management of incontinence and promotion of continence in older people in care homes: descriptive studies with urinary incontinence as primary focus. J Adv Nurs. 2011;67(2):228–50.
9. Fink HA, Taylor BC, Tacklind JW, Rutks IR, Wilt TJ. Treatment interventions in nursing home residents with urinary incontinence: a systematic review of randomized trials. Mayo Clin Proc. 2008;83(12):1332–43.
10. Newman DK, Wein AJ. Managing and treating urinary incontinence. 2nd ed. Baltimore, MD: Health Professions Press; 2009. p. 245–306.
11. Lekan-Rutledge D, Colling J. Urinary incontinence in the frail elderly: even when it's too late to prevent a problem, you can still slow its progress. Am J Nurs. 2003; (Suppl):36–40.
12. Colling J, Owen TR, McCreedy M, Newman D. The effects of a continence program on frail community dwelling elderly persons. UrolNurs. 2003;23:117.22. 127e131.
13. Engberg SJ, Sereika SM, McDowell BJ, Weber E, Brodak I. Effectiveness of prompted voiding in treating urinary incontinence in cognitively impaired homebound older adults. J Wound Ostomy Continence Nurs. 2002;29:252–65.
14. Drennan VM, Cole L, Iliffe S. A taboo within a stigma? a qualitative study of managing incontinence with people with dementia living at home. BMC Geriatr. 2011;11:75.
15. Newman DK, Gaines T, Snare E. Innovation in bladder assessment: use of technology in extended care. J Gerontol Nurs. 2005;31(12):33–41.
16. Schnelle JF, Newman D, White M, Abbey J, Wallston KA, Fogarty T, Ory MG. Maintaining continence in nursing home residents through the application of industrial quality control. Gerontologist. 1993;33(1):114–21.
17. Burgio LD, McCormick KA, Scheve AS, et al. The effects of changing prompted voiding schedules in the treatment of incontinence in nursing home residents. J Am Geriatr Soc. 1994;42(3):315–20.
18. Schnelle JF, Traughber B, Sowell VA, Newman DR, Petrilli CO, Ory M. Prompted voiding treatment of urinary incontinence in nursing home patients: a behavior management approach for nursing home staff. J Am Geriatr Soc. 1989;37(11):1051–7.
19. Ouslander JG, Schnelle JF, Uman G, Fingold S, Nigam JG, Tuico E, Bates-Jensen B. Predictors of successful prompted voiding among incontinent nursing home residents. JAMA. 1995;273(17): 1366–70.
20. Sackley CM, Rodriguez NA, van den Berg M, et al. A phase II exploratory cluster randomised controlled trial of a group mobility training and staff education intervention to promote urinary continence in UK care homes. Clin Rehabil. 2008;22:714–21.
21. Ouslander JG, Griffiths PC, McConnell E, Riolo L, Kutner M, Schnelle J. Functional incidental training: a randomized, controlled, crossover trial in veterans affairs nursing homes. J Am Geriatr Soc. 2005;53: 1091–100.
22. Schnelle JF, MacRae PG, Ouslander JG, Simmons SF, Nitta M. Functional incidental training, mobility performance, and incontinence care with nursing home residents. J Am Geriatr Soc. 1995;43(12):1356–62.
23. Schnelle JF, Leung FW, Rao SS, Beuscher L, Keeler E, Clift JW, Simmons S. A controlled trial of an intervention to improve urinary and fecal incontinence and constipation. J Am Geriatr Soc. 2010;58(8):1504–11.
24. Bosch JL, Weiss JP. The prevalence and causes of nocturia. J Urol. 2010;184:440–6.
25. Plantinga L, Rao MN, Schillinger D. Prevalence of self-reported sleep problems among people with diabetes in the United States, 2005–2008. Prev Chronic Dis. 2012;9:E76.
26. Van Kerrebroeck P, Abrams P, Chaikin D, et al. The standardization of terminology in nocturia: report from the standardization subcommittee of the International Continence Society. BJU Int. 2002;90 Suppl 3:11–5.
27. Burgio KL, Johnson 2nd TM, Goode PS, et al. Prevalence and correlates of nocturia in community-dwelling older adults. J Am Geriatr Soc. 2010;58: 861–6.
28. Galizia G, Langellotto A, Cacciatore F, Mazzella F, Testa G, Della-Morte D, Gargiulo G, Ungar A, Ferrara N, Rengo F, Abete P. Association between nocturia and falls-related long-term mortality risk in the elderly. J Am Med Dir Assoc. 2012;13(7):640–4.
29. Asplund R. Hip fractures, nocturia, and nocturnal polyuria in the elderly. Arch Gerontol Geriatr. 2006;43:319–26.
30. Kupelian V, Fitzgerald MP, Kaplan SA, Norgaard JP, Chiu GR, Rosen RC. Association of nocturia and mortality: results from the Third National Health and Nutrition Examination Survey. J Urol. 2011;185:571–7.
31. Ouslander JG, Ai-Samarrai N, Schnelle JF. Prompted voiding for nighttime incontinence in nursing homes: is it effective? J Am Geriatr Soc. 2001;49(6):706–9.
32. Schnelle JF, Cruise PA, Alessi CA, et al. Individualizing nighttime incontinence care in nursing home residents. Nurs Res. 1998;47(4):197–204.

33. Schnelle JF, Kapur K, Alessi C, et al. Does an exercise and incontinence intervention save healthcare costs in a nursing home population? J Am Geriatr Soc. 2003;51(2):161–8.
34. Hägglund D. A systematic literature review of incontinence care for persons with dementia: the research evidence. J Clin Nurs. 2010;19(3–4): 303–12.
35. Wang J, Chang LH, Eberly LE, Virnig BA, Kane RL. Cognition moderates the relationship between facility characteristics, personal impairments, and nursing home residents' activities of daily living. J Am Geriatr Soc. 2010;58(12):2275–83.
36. Ko A, Nguyen HV, Chan L, Shen Q, Ding XM, Chan DL, Chan DK, Brock K, Clemson L. Developing a self-reported tool on fall risk based on toileting responses on in-hospital falls. Geriatr Nurs. 2012;33(1):9–16.
37. Gilmour H, Park J. Dependency, chronic conditions and pain in seniors. Health Rep. 2006;16(Suppl): 21–31.
38. Chen XL, Liu YH, Chan DK, Shen Q, Van Nguyen H. Characteristics associated with falls among the elderly within aged care wards in a tertiary hospital: a retrospective. Chin Med J (Engl). 2010;123(13): 1668–72.
39. Tzeng HM. Inpatient falls in adult acute care settings: influence of patients' mental status. J Adv Nurs. 2010;66(8):1741–6.
40. Vinsnes AG, Helbostad JL, Nyrønning S, Harkless GE, Granbo R, Seim A. Effect of physical training on urinary incontinence: a randomized parallel group trial in nursing homes. Clin Interv Aging. 2012;7:45–50.
41. Wang K, Palmer MH. Women's toileting behaviour related to urinary elimination: concept analysis. J Adv Nurs. 2010;66(8):1874–84.
42. Capezuti E, Wagner L, Brush BL, Boltz M, Renz S, Secic M. Bed and toilet height as potential environmental risk factors. Clin Nurs Res. 2008;17(1):50–66.
43. Lyons SS. How do people make continence care happen? An analysis of organizational culture in two nursing homes. Gerontologist. 2010;50(3):327–39.
44. Cooke V, Arling G, Lewis T, Abrahamson KA, Mueller C, Edstrom L. Minnesota's Nursing Facility Performance-Based Incentive Payment Program: an innovative model for promoting care quality. Gerontologist. 2010;50(4):556–63.
45. Etheridge F, Tannenbaum C, Couturier Y. A system-wide formula for continence care: overcoming barriers, clarifying solutions, and defining team members' roles. J Am Med Dir Assoc. 2008;9(3):178–89.
46. Schnelle JF, Alessi CA, Simmons SF, Al-Samarrai NR, Beck JC, Ouslander JG. Translating clinical research into practice: a randomized controlled trial of exercise and incontinence care with nursing home residents. J Am Geriatr Soc. 2002;50:1476–83.
47. Morgan C, Endozoa N, Paradiso C, McNamara M, McGuire M. Enhanced toileting program decreases incontinence in long term care. Jt Comm J Qual Patient Saf. 2008;34(4):206–8.
48. Rahman AN, Schnelle JF, Applebaum R, Lindabury K, Simmons S. Distance coursework and coaching to improve nursing home incontinence care: lessons learned. J Am Geriatr Soc. 2012;60(6):1157–64.
49. Simmons SF, Durkin DW, Rahman AN, Choi L, Beuscher L, Schnelle JF. Resident characteristics related to the lack of morning care provision in long-term care. Gerontologist. 2013;53(1):151–61.
50. Rantz MJ, Zwygart-Stauffacher M, Hicks L, Mehr D, Flesner M, Petroski GF, Madsen RW, Scott-Cawiezell J. Randomized multilevel intervention to improve outcomes of residents in nursing homes in need of improvement. J Am Med Dir Assoc. 2012;13(1):60–8.
51. Kegel AH. Progressive resistance exercise in the functional restoration of the perineal muscles. Am J Obstet Gynecol. 1948;56:238–48.
52. Kegel AH. Stress incontinence of urine in women: physiologic treatment. J Int Coll Surg. 1956;25: 487–99.
53. Burgio KL, Goode PS, Locher JL, Umlauf MG, Roth DL, Richter HE, et al. Behavioral training with and without biofeedback in the treatment of urge incontinence in older women: a randomized controlled trial. JAMA. 2002;288:2293–9.
54. Burns PA, Pranikoff K, Nochajski TH, Hadley EC, Levy KJ, Ory MG. A comparison of effectiveness of biofeedback and pelvic muscle exercise treatment of stress incontinence in older community-dwelling women. J Gerontol. 1993;48:167–74.
55. Burgio KL, Whitehead WE, Engel BT. Urinary incontinence in the elderly. Bladder-sphincter biofeedback and toileting skills training. Ann Intern Med. 1985;104:507–15.
56. Burgio KL, Robinson JC, Engel BT. The role of biofeedback in Kegel exercise training for stress urinary incontinence. Am J Obstet Gynecol. 1986;157:58–64.
57. Goode PS, Burgio KL, Locher JL, Roth DL, Umlauf MG, Richter HE, Varner RE, Lloyd LK. Effect of behavioral training with or without pelvic floor electrical stimulation on stress incontinence in women: a randomized controlled trial. JAMA. 2003;290:345–52.
58. Herbison GP, Dean N. Weighted vaginal cones for urinary incontinence. Cochrane Database Syst Rev. 2013;7:CD002114.
59. Bø K, Morkved S, Frawley H, Sherburn M. Evidence for benefit of transversus abdominus training alone or in combination with pelvic floor muscle training to treat female urinary incontinence: a systematic review. Neurourol Urodyn. 2009;28:368–73.
60. Moore K, Dumoulin C, Bradley C, et al. Adult conservative management. In: Abrams P, Cardozo L, Khoury S, Wein A, editors. Incontinence, 5th International Consultation on Incontinence. Paris, France: European Association of Urology; 2013. p. 1101–1227.

61. Kisner C, Colby LA. Therapeutic exercise. Foundations and techniques. 4th ed. Philadelphia, PA: FA Davis; 2003.
62. Bø K. Pelvic floor muscle exercise for the treatment of stress urinary incontinence: an exercise physiology perspective. Int Urogynecol J. 1995;6:282–91.
63. Burgio KL, Pearce KL, Lucco AJ. Staying dry: a practical guide to bladder control. Baltimore, MD: Johns Hopkins Press; 1989. p. 67–100.
64. Miller JM, Ashton-Miller JA, DeLancey JOL. A pelvic muscle precontraction can reduce cough-related urine loss in selected women with mild SUI. J Am Geriatr Soc. 1998;46:870–4.
65. Bourcier AP, Juras JC, Jacquetin B. Urinary incontinence in physically active and sportswomen. In: Appell RA, Bourcier AP, La Torre F, editors. Pelvic floor dysfunction: investigations and conservative treatment. Rome: C.E.S.I; 1999. p. 9–17.
66. Dumoulin C, Hay-Smith J. Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women. Cochrane Database Syst Rev. 2010;1:CC005654.
67. Shamliyan T, Wyman JF, Ramakrishnan R, Sainfort F, Kane RL. Systematic review: randomized, controlled trials of nonsurgical treatments for urinary incontinence in women. Ann Intern Med. 2008;148(6):459–73.
68. Goode PS, Burgio KL, Johnson TJ, et al. Behavioral therapy with or without biofeedback and pelvic floor electrical stimulation for persistent post-prostatectomy incontinence. JAMA. 2011;305: 151–9.
69. Burgio KL, Locher JL, Goode PS, Hardin JM, McDowell BJ, Dombrowski M, Candib D. Behavioral versus drug treatment for urge incontinence in older women: a randomized clinical trial. JAMA. 1998;23:1995–2000.
70. Rose MA, Baigis-Smith J, Smith D, Newman D. Behavioral management of urinary incontinence in homebound older adults. Home Healthc Nurse. 1990;8:10–5.
71. Baigis-Smith J, Smith DAJ, Rose M, Newman DK. Managing urinary incontinence in community-residing elderly persons. Gerontologist. 1989;229:33.
72. McDowell BJ, Burgio KL, Dombrowski M, Locher JL, Rodriguez E. Interdisciplinary approach to the assessment and behavioral treatment of urinary incontinence in geriatric outpatients. J Am Geriatr Soc. 1992;40:370–4.
73. Burgio K, Goode P, Johnson II TM, Hammontree L, Ouslander J, Markland A, et al. Behavioral versus drug treatment for overactive bladder in men: the male overactive bladder treatment in veterans (MOTIVE) trial. J Am Geriatr Soc. 2011;59:2209–16.
74. Jarvis GJ, Millar DR. Controlled trial of bladder drill for detrusor instability. Br Med J. 1980;281: 1322–3.
75. Pengelly AW, Booth CM. A prospective trial of bladder training as treatment for detrusor instability. Br J Urol. 1980;52(6):463–6.
76. Colombo M, Zanetta G, Scalambrino S, Milani R. Oxybutynin and bladder training in the management of female urinary urge incontinence: a randomized study. Int Urogynecol J. 1995;6:63–7.
77. Fantl JA, Wyman JF, McClish DK, et al. Efficacy of bladder training in older women with urinary incontinence. JAMA. 1991;265:609–13.
78. Wyman JF, Fantl JA, McClish DK, Bump RC, et al. Comparative efficacy of behavioral interventions in the management of female urinary incontinence. Am J Obstet Gynecol. 1998;179:999–1007.
79. Kay GG, Abou-Donia MB, Messer Jr WS, Murphy DG, Tsao JW, Ouslander JG. Antimuscarinic drugs for overactive bladder and their potential effects on cognitive function in older patients. J Am Geriatr Soc. 2005;53(12):2195–201.
80. Dubeau CE, Morrow JD, Kraus SR, Creanga D, Bavendam T. Efficacy and tolerability of fesoterodine versus tolterodine in older and younger subjects with overactive bladder: a post hoc, pooled analysis from two placebo-controlled trials. Neurourol Urodyn. 2012;31(8):1258–65.
81. Kay GG, Maruff P, Scholfield D, Malhotra B, Whelan L, Darekar A, Martire DL. Evaluation of cognitive function in healthy older subjects treated with fesoterodine. Postgrad Med. 2012;124(3):7–15.
82. Ponzone R, Biglia N, Jacomuzzi ME, et al. Vaginal oestrogen therapy after breast cancer: is it safe? Eur J Cancer. 2005;41:2673–81.
83. Mariappan P, Alhasso A, Ballantyne Z, et al. Duloxetine, a serotonin and noradrenaline reuptake inhibitor (SNRI) for the treatment of stress urinary incontinence: a systematic review. Eur Urol. 2007;51:67–74.
84. Ouslander JG. Management of overactive bladder. N Engl J Med. 2004;350:786–99.
85. Madhuvrata P, Cody JD, Ellis G, Herbison GP, Hay-Smith EJ. Which anticholinergic drug for overactive bladder symptoms in adults. Cochrane Database Syst Rev. 2012;1:CD005429.
86. Hay-Smith J, Herbison P, Ellis G, et al. Which anticholinergic drug for overactive bladder symptoms in adults. Cochrane Database Syst Rev. 2005:CD005429.
87. Hartmann K, PcPheeters M, Biller D, et al. Treatment of overactive bladder in women. Evidence Report/ Technology Assessment No.187 (Prepared by the Vanderbilt Evidence-based Practice Center under Contract No. 290-2007-10065-I) AHRQ Publication No. 09-E017. Rockville, MD: Agency for Healthcare Research and Quality; 2009.
88. Goode PS, Burgio KL, Richter HE, Markland AD. Incontinence in older women. JAMA. 2010;303: 2172–81.
89. Gopal M, Haynes K, Bellamy SL, et al. Discontinuation rates of anticholinergic medications used for the treatment of lower urinary tract symptoms. Obstet Gynecol. 2008;112:1311–8.
90. Kaplan SA, Roehrborn CG, Rovner ES, et al. Tolterodine and tamsulosin for treatment of men with lower urinary tract symptoms and overactive

bladder: a randomized controlled trial. JAMA. 2006;296:2319–28 [erratum appears in JAMA. 2007 Mar 21:297(11):1195].
91. McConnell JD, Roehrborn CG, Bautista OM, et al. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. N Engl J Med. 2003;349:2387–98.
92. Lepor H, Williford WO, Barry MJ, et al. The efficacy of terazosin, finasteride, or both in benign prostatic hyperplasia. Veterans Affairs Cooperative Studies Benign Prostatic Hyperplasia Study Group. N Engl J Med. 1996;335:533–9.
93. FDA News Release. FDA approves Myrbetriq for overactive bladder. Retrieved http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm310096.htm
94. Cardozo L, Bachmann G, McClish D, et al. Meta-analysis of estrogen therapy in the management of urogenital atrophy in postmenopausal women: second report of the Hormones and Urogenital Therapy Committee. Obstet Gynecol. 1998;92:722–7.
95. Gray M, Beeckman D, Bliss DZ, et al. Incontinence-associated dermatitis: a comprehensive review and update. J Wound Ostomy Continence Nurs. 2012;39(1):61–74.
96. Starr JM. Cholinesterase inhibitor treatment and urinary incontinence in Alzheimer's disease. J Am Geriatr Soc. 2007;55(5):800–1.
97. Bryant CM, Dowell CJ, Fairbrother G. Caffeine reduction education to improve urinary symptoms. Br J Nurs. 2002;11(8):560–5.
98. DuBeau CE, Ouslander JG, Palmer MH. Knowledge and attitudes of nursing home staff and surveyors about the revised federal guidance for incontinence care. Gerontologist. 2007;47(4):468–79.
99. Newman DK. Incontinence products and devices for the elderly. Urol Nurs. 2004;24:316–34.
100. Lipp A, Shaw C, Glavind K. Mechanical devices for urinary incontinence in women. Cochrane Database Syst Rev. 2011;7:CD001756.
101. Richter H, Burgio K, Brubaker L, et al. Continence pessary compared with behavioral therapy or combined therapy for stress incontinence: a randomized controlled trial. Obstet Gynecol. 2010;115: 609–17.
102. Moore KN, Schieman S, Ackerman T, Dzus HY, Metcalfe JB, Voaklander DC. Assessing comfort, safety, and patient satisfaction with three commonly used penile compression devices. Urology. 2004;63:150–4.
103. Newman DK, Fader M, Bliss DZ. Managing incontinence using technology, devices and products. Nurs Res. 2004;53(6 Suppl):S42–8.

12 Urinary Incontinence: Surgical Treatments

David James Osborn, Elizabeth B. Takacs, Karl J. Kreder, Melissa Kaufman, and Roger Dmochowski

Introduction

In 2009, an estimated 12.8 % of the US population was over the age of 65. Based on trends in US census data, this percentage of persons over 65 is expected to increase to 20 % by the year 2030 [1], equating to approximately 30 million US citizens. Such growth in the geriatric population will demand increased awareness by healthcare providers regarding common conditions afflicting this age group. One prominent, yet undertreated, condition associated with significant quality of life and financial burden is stress urinary incontinence (SUI). Overall, the prevalence of urinary incontinence in women over the age of 20 is 15.7 %, but in women 60–79, this prevalence increases to 23.3 % [2], with over one-third (31.7 %) of women over the age 80 affected.

In the USA, 51 % of women who seek care for SUI are greater than 70 years old [3]. Indeed, across all age groups, the most common form of incontinence is SUI; however, as women age, mixed urinary incontinence which encompasses urge incontinence and stress incontinence becomes more prevalent [4]. In a study of 200 women over the age of 55, Wells et al. found 35 %, 22 %, and 26 % rates of stress, mixed, and pure urge incontinence, respectively [5]. However, when looking only at patients older than 74 years, the rates of stress and mixed incontinence dropped to 19 and 15 %, whereas urge incontinence increased to 29 %. With a published rate of 61 %, mixed and urge incontinence are significantly more common in the institutionalized geriatric population [6]. This more prevalent urge component in older adults makes the treatment of SUI challenging, and this can often lead to frustration for the provider and the patient.

In addition, it is critical to appreciate the dramatic impact urinary incontinence can have on daily activities of living. For this reason, many clinicians refer to incontinence as a “social cancer” [7]. SUI is associated with depression and social isolation [8]. Besides the social issues, treatment of SUI is also important for elderly women because persistent urinary leakage can contribute to decubitus ulcers, dermatologic irritation, and urinary tract infections [9].

D.J. Osborn, M.D. • M. Kaufman, M.D.
Department of Urologic Surgery, Vanderbilt University Medical Center, 1301 Medical Center Dr Street 3823, Nashville, TN 37232, USA
e-mail: melissa.kaufman@vanderbilt.edu

E.B. Takacs, M.D. • K.J. Kreder, M.D., M.B.A.
Department of Urology, University of Iowa, 200 Hawkins Drive, 3 RCP, Iowa City, IA 52242, USA
e-mail: elizabeth-takacs@uiowa.edu; karl-kreder@uiowa.edu

R. Dmochowski, M.D., F.A.C.S. (✉)
Department of Urologic Surgery, Vanderbilt University Medical Center, Room A 3102 Medical Center North, Nashville, TN 37232, USA
e-mail: roger.dmochowski@vanderbilt.edu

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_12,

When considering surgical treatment for SUI, age should not be the primary determining factor. More important is the consideration of the patient's overall health or frailty. Goals of treatment are aimed not to increase longevity but to improve quality of life. Most elderly patients will achieve immediate benefit from treatment of SUI. However, elderly patients do have multiple comorbid conditions that contribute to their urinary leakage that must be factored when considering recommending medical or surgical treatment.

Evaluation

Evaluation of an elderly patient with SUI begins with a thorough history. Approaching the topic is often the determining factor with regard to initiation of treatment. Indeed, without the need for invasive diagnostics, a well-performed history and physical can lead to accurate diagnosis in the majority of patients. Only 65 % of elderly women will seek medical attention for urinary incontinence, and only 53 % of elderly women with SUI will mention this as their chief complaint when visiting a primary care physician [5]. Because of this well-documented reluctance in elderly patients to report urinary incontinence, performing a detailed review of systems on all patients may be the primary means of uncovering this symptom.

A focused physical exam and pelvic exam should be performed on any patient with complaints of SUI. In addition to the critical nature of uncovering physical findings of neurologic or musculoskeletal deficits which may contribute to the patient's incontinence symptoms, the pelvic exam should be performed to evaluate for any reversible conditions or anatomic abnormalities which can contribute to or result from urinary incontinence. Initially, the introitus and external genitalia should be examined. The most common significant finding during this part of the exam in the postmenopausal female population is atrophic vaginitis. Atrophic vaginitis is characterized by loss of the normal rugae and friability of the vaginal epithelium as a result of decreased physiologic estrogen. An estimated 40 % of postmenopausal women have atrophic vaginitis, and the percentage is much higher in elderly women [10]. This epithelium is often easily irritated by urine and thus can exacerbate the symptomatology of SUI. When examining the urethral meatus in older adults, it is common to see some purplish discoloration of the posterior meatus. This is usually the result of asymptomatic prolapse of some urethral mucosa and is commonly associated with estrogen loss and atrophic vaginitis. With a half speculum inserted into the vagina, the patient should be asked to Valsalva in order to reveal pelvic organ prolapse, urethral hypermobility, and stress incontinence. Though popularity of this test is waning, a Q-tip test can also be performed to assess abnormal mobility of the urethra. A patient is considered to have urethral hypermobility if a cotton swab inserted into the urethra moves more than 30° during abdominal straining [11].

Palpation of the lower abdomen is important to assess for intra-abdominal pathology; however, this rarely reveals a distended bladder. Therefore, measurement of post-void residual urine using a bladder scanner can be a straightforward adjunct in the evaluation of incontinence in the elderly population [12, 13]. A urinalysis is important in the evaluation of incontinence in the elderly woman and rules out several additional processes; however, a urine culture should only be performed if there is strong suspicion for a urinary tract infection or if there is evidence of pyuria or bacteria on the urinalysis. Asymptomatic bacteriuria is common in this age group, and antibiotic treatment may not be beneficial [14].

In addition, patients should also be asked to fill out a voiding diary for a time period of 48–72 h. A voiding diary can provide exceptional help to guide therapy and provide useful information such as fluid management, leakage frequency, and functional bladder capacity.

Urodynamic testing is not required for the initial evaluation of geriatric patients with incontinence; however, it is often useful in the patient with complex mixed symptoms or if a patient has failed empiric therapy. Unlike younger patients, if surgery is being considered, urodynamic testing

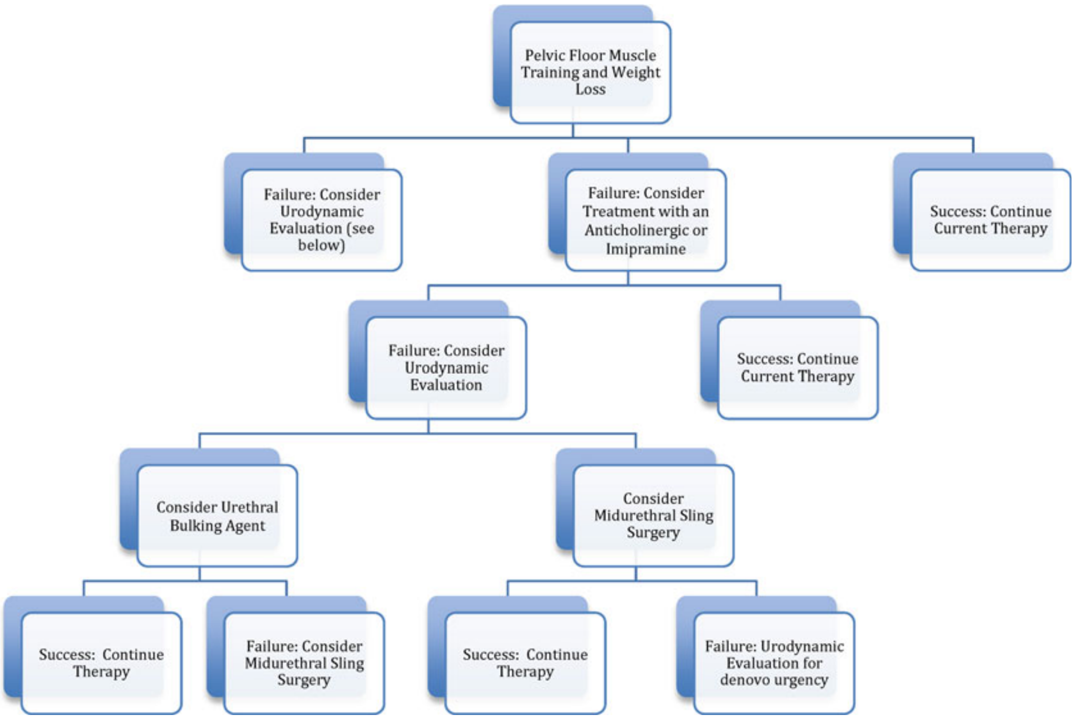


Fig. 12.1 Proposed treatment algorithm for SUI in elderly female patients using AUA guidelines

is recommended [6]. A suggested algorithm of evaluation and treatment options for elderly women with stress urinary incontinence is shown (Fig. 12.1).

Weight Loss

Even in the elderly population, obesity is increasing in prevalence. From 1991 to 2000, the rate of obesity in persons over the age of 70 increased by 36 % [15]. Fortunately, obesity is a reversible contributor to SUI. Multiple studies have demonstrated a clear relationship between weight loss from lifestyle modification and improved urinary incontinence. Subak et al. performed a randomized controlled trial of 338 obese women placed in one of two different weight loss programs [16]. After 6 months, the two programs showed an average of 8 and 1.6 kg weight loss with a corresponding significant 58 and 33 % reduction in SUI. Importantly, age was not associated with diminished outcome. A randomized controlled trial by Auwad et al. additionally demonstrated the positive effects of weight loss from lifestyle modification [17]. In this study, patients who had a 5 % or greater weight loss showed a statistically significant improvement in SUI.

Though possibly not safe for many elderly patients, it has also been clearly shown that surgically induced weight loss decreases stress urinary incontinence. In 46 obese women who achieved a ≥50 % excess body weight loss after bariatric surgery and completed the Pelvic Floor Distress Inventory (PFDI-20) and Pelvic Floor Impact Questionnaire (PFIQ-7), there was a significant reduction in total mean distress scores after surgery [18]. This reduction was mainly attributed to a significant decrease in SUI.

Pelvic Floor Muscle Training

Pelvic floor muscle training or Kegel exercises are theorized to help with pelvic floor muscle strength and coordination. Pelvic floor muscle training has been shown in multiple studies to improve SUI. Partially based on a Cochrane Review by Dumoulin et al. of 13 randomized and quasi-randomized trials, pelvic floor muscle training should be recommended to all patients with SUI [19]. Interestingly, a prospective study of 343 women looking at risk factors for pelvic floor dysfunction such as age, number of children delivered, and BMI found that elderly patients had the same ability to contract and relax the pelvic floor musculature as younger women [20]. Therefore, although more research is required, it appears that pelvic floor muscle training may be beneficial in the elderly population.

Periurethral Bulking Agents

The submucosal injection of periurethral bulking agents is a minimally invasive, moderately successful treatment for SUI. For years, bovine-derived cross-linked collagen was the most commonly used substance; however, safety concerns regarding its use have led to the adoption of several different synthetic agents. Both a *Cochrane Database Systemic Review* and a review by the Fourth International Consultation on Urinary Incontinence of periurethral bulking agents concluded that there was limited evidence for the benefit of these agents and that more research is needed [21, 22]. Unfortunately, it is difficult to find evidence to support the use of these agents in the geriatric population. However, even though the benefit of this type of treatment is unclear, there are minimal side effects, and periurethral bulking agents are a good option for many patients who are not candidates for a more invasive surgical procedure.

Pharmacologic Management

Although anticholinergic medications are not beneficial for pure SUI, they may be useful in patients with a component of mixed incontinence which includes urinary urgency, frequency, or urge urinary incontinence (UUI). Unfortunately, anticholinergic medications can have negative effects on cognitive functioning and are many times not well tolerated in the elderly population [23]. Imipramine is a medication that is sometimes used in patients with stress incontinence because it prevents reuptake of norepinephrine, which increases bladder outlet resistance [24]. However, it also has anticholinergic properties and concomitant side effects. Caution should be used whenever considering use of this type of medication in elderly patients. Duloxetine is similar to imipramine and may have benefit for women with mixed symptoms, but remains unavailable for this indication in the USA. Mirabegron, a β_3-adrenoceptor agonist, represents a promising novel treatment for the treatment of overactive bladder symptoms. β_3-adrenoceptors account for more than 95 % of all β-adrenoceptors mRNA in the human bladder and are thought to be the main β-adrenoceptors mediating human detrusor relaxation [25]. Because the side effect profile of β_3-adrenoceptor agonists is markedly different than anticholinergics, they may have increased utility in the elderly population. This is confirmed by a recent phase III clinical trial evaluating safety and efficacy of mirabegron in patients over the age of 65 years [26].

Changing Trends in Incontinence Surgery

If minimally invasive treatments such as bulking agents and conservative measures fail, surgical management may be considered in elderly women with SUI with a high likelihood of success. Predominately driven by the development of less invasive procedures, over the past 20 years, there has been a substantial increase in the use of surgery for stress incontinence, highlighted in multiple recent publications. First, in 2009, Anger et al. published a review of US Medicare beneficiary data from 1992 to 2001 [27]. During this time, the total number of procedures for treatment of SUI increased nearly 1.75-fold. In addition, in 1992, the needle suspension and anterior urethropexy were the two most common surgical procedures for stress incontinence. But by 1998, collagen injections had become the most frequently performed treatment for SUI and the use of the needle suspension had dropped substantially. Then, in 2001 the pubovaginal sling had surpassed all the other invasive surgical treatments and even collagen had a significant decline in utilization. Lastly, from 2001 to today, the use of midurethral slings has increased fourfold and they have become the most common surgical intervention for SUI [28].

Over this previously mentioned time period, the segment of the population that demonstrated the greatest increase in surgery for stress incontinence was geriatric patients. In a review of the US National Hospital Discharge Survey from 1979 to 2004, Oliphant et al. found that the mean age of patients having procedures for stress incontinence increased from 50 years old in 1979 to 58 years old in 2004 [29]. This similar trend is found elsewhere in the world. Lee et al. reviewed the Medicare data for Australia from 1994 to 2009 and found a 76 % increase in the total number of surgeries for female SUI [30]. The area of greatest proportional growth was in patients over the age of 65. Similar to the findings in the US Medicare data, there was a significant increase in the use of less invasive procedures such as midurethral slings and bulking agents.

Safety and Efficacy of Midurethral Slings

As mentioned earlier, geriatric patients are much more likely to undergo midurethral slings than any other form of open surgical management for SUI. There are several studies that specifically look at the efficacy of retropubic midurethral slings in the elderly population. In 2003, Sevestre et al. analyzed the outcomes of 76 patients with a mean age of 76 years who underwent Tension Free Vaginal Tape (TVT). In this study, there were no major postoperative complications, and the researchers found a 14 % rate of persistent SUI, an 18 % rate of de novo postoperative urge incontinence, and a 21 % rate of de novo urgency. This rate of persistent SUI is similar to the finding of multiple other recent studies looking at the outcome of TVT in patients of all ages [31–33]. The rate of de novo urge incontinence is similarly high in another study that looked at outcomes of TVT surgery in the elderly population by Gordon et al. [34]. In this study, the rate of de novo urge incontinence after TVT was 18 % in 157 women with an average age of 75 years and only 4 % in 303 younger women with an average age of 57 years. Therefore, most likely related to the pathophysiology of the aging bladder, elderly women may experience more voiding dysfunction characterized primarily by urgency following TVT sling surgery. Additional studies evaluating outcomes of TVT in the elderly population found a higher failure rate of TVT surgeries in the elderly population. Hellberg et al. demonstrated in his survey of 970 consecutive women after TVT surgery [35] that only 61.7 % of women ≥75 years were cured versus 76.8 % cured <75 years. Lastly, in a study of risk factors associated with failure 1 year after TVT and Transobturator Tape (TOT), age was associated with recurrent incontinence(adjusted OR 1.7; 95 % CI: 1.1–2.6 per decade) [36].

Indeed, in the majority of literature evaluating outcomes of transobturator midurethral sling surgery in elderly patients, age is a significant risk factor for a diminished outcome. In a prospective study of 54 women, Chen et al. found that the rate of persistent SUI after TOT sling was significantly greater in women ≥60 years old, compared with those younger than 60 years [37]. Groutz et al. compared 97 patients older than 70 years with 256 women younger than 70 years who underwent TOT. The incidence of subjective complaints of persistent SUI was the same in both age groups, but the rate of asymptomatic SUI on urodynamics was significantly higher in the elderly population (19 % vs. 4 %) [38]. In addition, as previously illustrated, the rates of de novo urgency and urge incontinence were significantly higher in elderly patients. The rate of postoperative UTI was additionally higher in the elderly population.

Overall it does appear that age is associated with a higher failure rate after midurethral sling surgery. This point is further illustrated by a review of 1,356 Medicare beneficiaries who underwent midurethral sling surgery between July 1999 and December 2000 [40]. In that study, there was a higher rate of treatment failure as defined by requiring a repeat procedure within the first year based on age. For patients younger than age 75, 7.2 % had a repeat procedure, and for patients >75 year old, 10.5 % had a repeat procedure ($P = 0.03$). A secondary analysis of the SISTEr trial comparing age <65 to >65 years regardless of treatment type concluded that older women (>65) were more likely to have a positive stress test postoperatively and more likely to have retreatment for SUI then women <65 years [39]. Lastly, in an analysis of Medicate data in 2007, Anger et al. found that patients >75 years were more likely to have treatment for outlet obstruction within 1 year of midurethral sling surgery [40]. Even though elderly women might have a slightly higher rate of persistent SUI and de novo urgency after midurethral sling surgery, it appears that both retropubic (TVT) and transobturator slings are safe and effective in this patient population and women should not be excluded from midurethral slings based on their age. As always, appropriate counselling regarding the risks of treatment and recurrence is essential such that outcomes match patient expectations.

The data regarding the use of single incision slings, also called mini-slings, in the elderly population is scarce. However, a recent prospective study looking at predictors of failure after the mini-sling TVT Secur® in 175 women found no association between failure of the procedure and age [41].

Non-Urologic Complications of Surgery

One of the greatest concerns for older patients undergoing surgical procedures is the risk of complications related to the anesthesia. Age and underlying medical conditions are critical considerations when deciding on the type of surgery and anesthesia in the elderly population. In 2008, Gerten et al. presented a review of these specific issues in older women undergoing surgery for prolapse and incontinence [42]. In the two studies reviewing anesthesia in elderly patients, the authors concluded that indeed the choice of anesthesia is determined by patient history and clinical and laboratory findings, in combination with the preference of the surgeon, anesthesiologist, and patient.

A single institution review of perioperative complications for incontinence surgery in elderly patients by Lambrou et al. demonstrated that relative to the results of the CREST (DEFINE) study, there was a higher incidence of thromboembolic events in geriatric patients [43]. The authors suggested that this may be related to longer operative time in the elderly population [43]. Gerten et al. recommend that in older women undergoing surgery for pelvic organ prolapse or urinary incontinence, there should be increased concern for thrombosis prevention and cardiac protection and appropriate perioperative prophylaxis should be used [42]. Overall, Gerten et al. concluded that older women should not avoid surgery based on age alone; however, consideration of conservative treatment modalities is recommended. He also found that patients who experienced a perioperative complication were twice as likely to be discharged to a care facility.

The American Urological Association (AUA) guidelines state that early ambulation is sufficient DVT prophylaxis in low-risk patients undergoing incontinence surgeries; however, based on the studies above, elderly individuals should probably be classified as moderate or high risk for DVT. Therefore, physicians treating elderly patients should utilize intermittent pneumatic compression devices and/or low molecular weight heparin [44].

In a review of the Medicare data for complications of sling surgery, Anger et al. reported an overall 9.1 % rate of cardiac complications, 2.6 % rate of thromboembolic complications, and a 15.3 % rate of pulmonary complications [45]. Patients >75 years old were significantly more likely to experience these non-urologic complications, and patients with a Charlson index of greater than 1 were 1.5 times more likely to experience a complication regardless of age. Conversely, in a review of prolapse and incontinence surgery in older women, Richter et al.

compared patients greater than 65 years old to patients less than 65 years old and found that there was no apparent difference in non-urologic perioperative adverse events [39].

Surgical Therapies for Urge Urinary Incontinence

For the older patient, urinary urgency, frequency, and UUI can be debilitating and is frequently a cause of social isolation or need for homebound status due to a fear of wetting pants in public and of odor. Risk factors for UUI include use of diuretics and underlying neurologic diseases such as Parkinson's disease or prior stroke. Treatment of UUI can be challenging due to the concern of potential cognitive side effects from anticholinergic medications. Many patients already suffer from dry mouth and constipation due to side effects of other medications which also limit compliance.

Prior to the introduction of neuromodulation, surgical management was often highly morbid for patients with refractory UUI and included surgical procedures such as autoaugmentation and augmentation enterocystoplasty. Neuromodulation modalities, including either sacral neuromodulation (InterStim®) or posterior tibial nerve stimulation (Urgent PC®), are much less invasive options.

As with any surgical procedure, patient selection is critical. Attention to conditions that may require MRIs is important because this form of imaging is generally contraindicated after device placement. Prior placement of other stimulating devices such as cardiac pacemakers also needs to be identified [46]. InterStim placement is not absolutely contraindicated in those with a cardiac pacemaker, but specific precautions need to be followed. The cardiac pacemaker needs to be fully interrogated during any surgical procedure for neuromodulator placement. Amudsen et al. prospectively evaluated 55 patients who had proceeded to generator implantation [47]. Overall, regardless of age, patients with three or more comorbid conditions had a reduced chance of improvement, and cure was also less. Beyond the physical health of the patient, it is important to consider if the patient is capable of understanding how the patient programmer works and actually manipulating it. Older patients may have cognitive impairment, limited experience, and lower comfort levels with technological devices [48].

The InterStim device has several positive features. It is a minimally invasive procedure, and postoperative morbidity is low. There is a trial period that allows for the patient to determine if improvement can be achieved, if they are satisfied with the clinical response, and if they like the device. If any of these expectations are not met, the device is removed.

White et al. reported that 17/19 (89.5 %) of patients age 70 or older compared to 165 of 170 (97.1 %) of nonelderly patients went onto implantable pulse generator (IPG) placement [49]. Wallace et al. reported on a small group of patients with neurologic diseases [50]. In this group, there were six patients with Parkinson's disease and two patients with prior cerebrovascular accident. Overall, 67 % and 100 %, respectively, had a successful test phase and went on to IPG implantation. Amudsen et al. first reported on a small group of 12 responders over the age of 55 who underwent full system implantation including the IPG [51]. In this study at a mean of 7.8 months, 2 patients (17 %) achieved total dryness, all patients had an 80 % decrease in heavy leakage, and pad use and urinary frequency decreased by about 40 %. The results translated into a statistically significant improvement in the Incontinence Impact Questionnaire. Amudsen et al. reported that the overall cure rate, defined as no daily leakage episodes, was lower overall among older patients, noting a greater proportion of patients being not cured over the age of 55 years [47]. It is important to remember that InterStim data post-implantation implies patients initially had achieved at least a 50 % improvement or greater during the test phase in order to proceed to IPG placement.

White et al. reported follow-up at a mean of 48.5 months in a small cohort of older patients [49]. Eleven of 17 (64.7 %) of the elderly patients had functional IPGs versus 86.7 % of the nonelderly patients. For the six elderly patients without a functional IPG, two had device removal without revision, four had a lack of efficacy confirmed by diary, and three had unsuccessful revision and subsequent device removal. Overall the elderly group had a higher device removal rate than the younger group ($P = 0.018$). Unfortunately, additional data examining the long-term efficacy and explantation results in elderly patients is not currently available.

Overall, for older patients with refractory urinary urge incontinence, the InterStim device is a viable option. There is data for this specific age group supporting its use. Elderly patients may have lower implantation rates and overall cure rates than younger patients; however, substantial improvement can be achieved for those patients in whom it has effect. There is minimal morbidity associated with the procedure, and it can be performed under local anesthesia with sedation thus avoiding complications often associated with general anesthesia.

Percutaneous tibial nerve stimulation is another form of neuromodulation. It offers the benefit of being performed in the outpatient clinic setting and does not require surgery. Treatments are generally performed about every 2 weeks. However, there is a general paucity of data specific to use or outcomes in geriatric patients. Booth et al. did recently examine the potential utility of percutaneous tibial nerve stimulation for urinary urgency and urge incontinence in the nursing home setting [52]. They found that use of this therapy appeared feasible for treatment of UUI and bowel symptoms even in older adults in residential care facilities.

Chemodenervation is another minimally invasive option for the surgical treatment of UUI. The most commonly used agent is onabotulinumtoxinA (Botox®) which acts as a pharmacologic neuromodulator. This inhibits presynaptic release of acetylcholine from efferent nerves and may inhibit sensory pathways as well. These changes help to reduce symptoms of overactive bladder and urinary urgency and urge incontinence. A phase II clinical trial demonstrated that it can be used safely at doses ranging from 100 to 300 units with good efficacy [53]. It has recently been approved by the US Food and Drug Administration (FDA) for use in both neurogenic and non-neurogenic forms of UUI. The procedure is attractive for use in older adults because it is performed via cystoscopy and does not require incision. The medication is injected into the detrusor muscle in approximately 20–30 sites across the body of the bladder. The trigone of the bladder is usually spared and not injected. It is an outpatient procedure and can be done with local anesthesia or intravenous sedation. One potential concern about this treatment is the potential risk for developing urinary retention and incomplete bladder emptying which could require at least a temporary course of clean intermittent catheterization. This is often temporary and may subside with time. However, it is difficult to predict who might develop problems with retention. Theoretically older adults might be at increased risk due to changes in bladder contractility due to structural changes in the wall of the bladder.

To date, there has been very little published data on the use of chemodenervation of the bladder for treatment of overactive bladder or urge incontinence in older adults. White et al. published a small case series on 21 elderly patients treated with this therapy [54]. This included 18 women and 3 men with a mean age of 81.2 years (range 75–92). They showed patients experienced a clinically significant reduction in the mean number of voids per day and also pad use, with 76 % reporting at least a 50 % reduction in symptoms following one injection procedure. Two patients who did not respond initially to the first treatment had clinically significant improvement with a repeat injection. Three additional patients did not have improvement after the second injection procedure. Mean duration of efficacy was 7.12 months with subsequent deterioration of symptoms. No treatment-related complications were observed. More recently, a phase III, placebo controlled clinical trial demonstrated good efficacy and quality of life outcomes with administration of 100 units of onabotulinumtoxinA [55]. Of the 280 subjects in the study treatment arm, 46 (16.4 %) were 75 years of age or older. The overall mean age in the treatment arm was 61.7 ± 12.7 years. Clinically significant reductions in bothersome voiding symptoms and improvements in health-related quality of life were noted in the treatment group compared to placebo. Although data were not fully stratified by age, no substantial differences were reported in the elderly patient subgroup. Additional research will be needed to more fully explore the role of chemodenervation for elderly patients with bothersome overactive bladder and UUI.

Conclusions

Because the elderly female population has a high prevalence of urinary incontinence, these patients often present for surgical evaluation. A review of the literature supports weight loss and lifestyle modification as primary treatment options in these patients. In general, the rate of persistent SUI following retropubic or transobturator midurethral slings is higher in the elderly population. In addition, the elderly population has a higher incidence of de novo urgency and urge incontinence after surgery. While there may be some initial increase in perioperative morbidity in the elderly population, surgical intervention does appear to be safe in the carefully screened individual. Surgical treatments such as neuromodulation or chemodenervation may also be useful in select elderly patients with UUI. Most of the surgical options for these conditions are minimally invasive. However, there is still limited data on the use and clinical outcomes of most of these therapies. Finally, while the literature is insufficient to support one anti-incontinence surgery over another for the elderly woman, it can be concluded that elderly women should not be excluded from potentially curative surgery based on their age alone.

References

1. United States - Age and Sex. American Community Survey 1-Year Estimates. United States Census Bureau. 2009. Available at: http://www.factfinder2.census.gov/faces/nav/jsf/pages/index.xhtml. Accessed 22 May 2013.
2. Nygaard I, Barber MD, Burgio KL, et al. Prevalence of symptomatic pelvic floor disorders in US women. JAMA. 2008;300:1311–6.
3. Abrams P, Cardozo L, Fall M, et al. The standardisation of terminology in lower urinary tract function: report from the standardisation sub-committee of the International Continence Society. Urology. 2003;61:37–49.
4. Hannestad YS, Rortveit G, Sandvik H, et al. A community-based epidemiological survey of female urinary incontinence: the Norwegian EPINCONT study. Epidemiology of Incontinence in the County of Nord-Trøndelag. J Clin Epidemiol. 2000;53:1150–7.
5. Wells TJ, Brink CA, Diokno AC. Urinary incontinence in elderly women: clinical findings. J Am Geriatr Soc. 1987;35:933–9.
6. Resnick NM, Yalla SV, Laurino E. The pathophysiology of urinary incontinence among institutionalized elderly persons. N Engl J Med. 1989;320:1–7.
7. McDougal WS, Wein AJ, Kavoussi LR, et al. Campbell-Walsh urology. 10th ed. Philadelphia, PA: Saunders; 2011.
8. Sims J, Browning C, Lundgren-Lindquist B, et al. Urinary incontinence in a community sample of older adults: prevalence and impact on quality of life. Disabil Rehabil. 2011;33:1389–98.
9. Long MA, Reed LA, Dunning K, et al. Incontinence-associated dermatitis in a long-term acute care facility. J Wound Ostomy Continence Nurs. 2012;39:318–27.
10. Bachmann GA, Nevadunsky NS. Diagnosis and treatment of atrophic vaginitis. Am Fam Physician. 2000;61:3090–6.
11. Bergman A, Bhatia NN. Urodynamic appraisal of the Marshall-Marchetti test in women with stress urinary incontinence. Urology. 1987;29:458–62.
12. Coombes GM, Millard RJ. The accuracy of portable ultrasound scanning in the measurement of residual urine volume. J Urol. 1994;152:2083–5.
13. Resnick B. A bladder scan trial in geriatric rehabilitation. Rehabil Nurs. 1995;20:194–6–203.
14. Boscia JA, Kobasa WD, Knight RA, et al. Therapy vs no therapy for bacteriuria in elderly ambulatory nonhospitalized women. JAMA. 1987;257:1067–71.
15. Villareal DT, Apovian CM, Kushner RF, et al. Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, The Obesity Society. Am J Clin Nutr. 2005;82:923–34.
16. Subak LL, Wing R, West DS, et al. Weight loss to treat urinary incontinence in overweight and obese women. N Engl J Med. 2009;360:481–90.
17. Auwad W, Steggles P, Bombieri L, et al. Moderate weight loss in obese women with urinary incontinence: a prospective longitudinal study. Int Urogynecol J Pelvic Floor Dysfunct. 2008;19:1251–9.
18. Wasserberg N, Petrone P, Haney M, et al. Effect of surgically induced weight loss on pelvic floor disorders in morbidly obese women. Ann Surg. 2009;249:72–6.
19. Dumoulin C, Hay-Smith J. Pelvic floor muscle training versus no treatment for urinary incontinence in women. A Cochrane systematic review. Eur J Phys Rehabil Med. 2008;44:47–63.

20. Talasz H, Himmer-Perschak G, Marth E, et al. Evaluation of pelvic floor muscle function in a random group of adult women in Austria. Int Urogynecol J Pelvic Floor Dysfunct. 2008;19:131–5.
21. Keegan PE, Atiemo K, Cody J, et al. Periurethral injection therapy for urinary incontinence in women. Cochrane Database Syst Rev. 2007;(3):CD003881.
22. Abrams P, Andersson KE, Birder L, et al. Fourth International Consultation on Incontinence Recommendations of the International Scientific Committee: Evaluation and treatment of urinary incontinence, pelvic organ prolapse, and fecal incontinence. Neurourol Urodyn. 2010;29:213–40.
23. Bottiggi KA, Salazar JC, Yu L, et al. Long-term cognitive impact of anticholinergic medications in older adults. Am J Geriatr Psychiatry. 2006;14:980–4.
24. Hunsballe JM, Djurhuus JC. Clinical options for imipramine in the management of urinary incontinence. Urol Res. 2001;29:118–25.
25. Takeda M, Obara K, Mizusawa T, et al. Evidence for beta3-adrenoceptor subtypes in relaxation of the human urinary bladder detrusor: analysis by molecular biological and pharmacological methods. J Pharmacol Exp Ther. 1999;288:1367–73.
26. Khullar V, Cambronero J, Angulo JC, et al. Age related efficacy of the selective beta-3 adrenoceptor agonist mirabegron for the treatment of overactive bladder: pooled analysis of three prospective, randomised phase III studies in patients >65 years. ICS Annual Meeting; 2012 Oct 15–19; Beijing, China. Abstr No 331.
27. Anger JT, Weinberg AE, Albo ME, et al. Trends in surgical management of stress urinary incontinence among female Medicare beneficiaries. Urology. 2009;74:283–7.
28. Suskind AM, Kaufman SR, Dunn RL, et al. Population-based trends in ambulatory surgery for urinary incontinence. Int Urogynecol J. 2013;24: 207–11.
29. Oliphant SS, Wang L, Bunker CH, et al. Trends in stress urinary incontinence inpatient procedures in the United States, 1979–2004. Am J Obstet Gynecol. 2009;200:521.e1–6.
30. Lee J, Dwyer PL. Age-related trends in female stress urinary incontinence surgery in Australia - Medicare data for 1994–2009. Aust N Z J Obstet Gynaecol. 2010;50:543–9.
31. Sivaslioglu AA, Unlubilgin E, Dolen I. A randomized comparison of polypropylene mesh surgery with site-specific surgery in the treatment of cystocoele. Int Urogynecol J Pelvic Floor Dysfunct. 2008;19: 467–71.
32. Hsiao S-M, Chang T-C, Lin H-H. Risk factors affecting cure after mid-urethral tape procedure for female urodynamic stress incontinence: comparison of retropubic and transobturator routes. Urology. 2009;73: 981–6.
33. Guerrero KL, Emery SJ, Wareham K, et al. A randomised controlled trial comparing TVT, Pelvicol and autologous fascial slings for the treatment of stress urinary incontinence in women. BJOG. 2010;117: 1493–502.
34. Gordon D, Gold R, Pauzner D, et al. Tension-free vaginal tape in the elderly: is it a safe procedure? Urology. 2005;65:479–82.
35. Hellberg D, Holmgren C, Lanner L, et al. The very obese woman and the very old woman: tension-free vaginal tape for the treatment of stress urinary incontinence. Int Urogynecol J Pelvic Floor Dysfunct. 2007;18:423–9.
36. Barber MD, Kleeman S, Karram MM, et al. Risk factors associated with failure 1 year after retropubic or transobturator midurethral slings. Am J Obstet Gynecol. 2008;199:666.e1–7.
37. Chen H-Y, Yeh L-S, Chang W-C, et al. Analysis of risk factors associated with surgical failure of inside-out transobturator vaginal tape for treating urodynamic stress incontinence. Int Urogynecol J Pelvic Floor Dysfunct. 2007;18:443–7.
38. Groutz A, Cohen A, Gold R, et al. The safety and efficacy of the “inside-out” trans-obturator TVT in elderly versus younger stress-incontinent women: a prospective study of 353 consecutive patients. Neurourol Urodyn. 2011;30:380–3.
39. Richter HE, Goode PS, Brubaker L, et al. Two-year outcomes after surgery for stress urinary incontinence in older compared with younger women. Obstet Gynecol. 2008;112:621–9.
40. Anger JT, Litwin MS, Wang Q, et al. The effect of age on outcomes of sling surgery for urinary incontinence. J Am Geriatr Soc. 2007;55:1927–31.
41. Hwang IS, Yu JH, Chung JY, et al. One-year outcomes of mid-urethral sling procedures for stress urinary incontinence according to body mass index. Korean J Urol. 2012;53:171–7.
42. Gerten KA, Markland AD, Lloyd LK, et al. Prolapse and incontinence surgery in older women. J Urol. 2008;179:2111–8.
43. Lambrou NC, Buller JL, Thompson JR, et al. Prevalence of perioperative complications among women undergoing reconstructive pelvic surgery. Am J Obstet Gynecol. 2000;183:1355–8. discussion 1359–60.
44. AUA Guidelines from AUA Website. Available at: https://www.auanet.org/education/aua-guidelines.cfm. Accessed 24 May 2013.
45. Anger JT, Litwin MS, Wang Q, et al. Complications of sling surgery among female Medicare beneficiaries. Obstet Gynecol. 2007;109:707–14.
46. Wallace PA, Lane FL, Noblett KL. Sacral nerve neuromodulation in patients with cardiac pacemakers. Am J Obstet Gynecol. 2007;197:94.e1–3.
47. Amundsen CL, Romero AA, Jamison MG, Webster GD. Sacral neuromodulation for intractable urge incontinence: are there factors associated with cure? Urology. 2005;66:746–50.
48. Griebling TL. Sacral nerve stimulation in the elderly. Int Urogynecol J. 2010;21 Suppl 2:485–9.
49. White WM, Mobley III JD, Doggweiler R, Dobmeyer-Dittrich C, Klein FA. Sacral nerve stimulation for refractory overactive bladder in the elderly population. J Urol. 2009;182:1449–52.

50. Wallace PA, Lane FL, Noblett KL. Sacral nerve neuromodulation in patients with underlying neurologic disease. Am J Obstet Gynecol. 2007;197:96.e1–5.
51. Amundsen CL, Webster GD. Sacral neuromodulation in an older, urge-incontinent population. Am J Obstet Gynecol. 2002;187:1462–5.
52. Booth J, Hagen S, McClurg D, Norton C, MacInnes C, Collins B, Donaldson C, Tolson D. A feasibility study of transcutaneous posterior tibial nerve stimulation for bladder and bowel dysfunction in elderly adults in residential care. J Am Med Dir Assoc. 2013;14:270–4.
53. Dmochowski R, Chapple C, Nitti VW, et al. Efficacy and safety of onabotulinumtoxinA for idiopathic overactive bladder: a double-blind, placebo controlled, randomized, dose ranging trial. J Urol. 2010; 184:2416–22.
54. White WM, Pickens RB, Doggweiler R, Klein FA. Short-term efficacy of botulinum toxin A for refractory overactive bladder in the elderly population. J Urol. 2008;180:2522–6.
55. Nitti VW, Dmochowski R, Herschorn S, et al. OnabotulinumtoxinA for the treatment of patients with overactive bladder and urinary incontinence: results of a phase III, randomized, placebo controlled trial. J Urol. 2013;189:2186–93.

Pelvic Organ Prolapse in Older Adults

13

Gregory Bales, Doreen Chung, and Katie Ballert

Introduction

This chapter will focus on the highly prevalent condition of pelvic organ prolapse (POP). POP is a leading cause of morbidity in aging female adults and has a variety of clinical presentations. Unfortunately, there is a lack of uniformity in the approaches to POP and there is much misinformation among patients and in the lay media. Recent concerns about some of the surgical treatments of POP with synthetic mesh have heightened awareness and drawn attention to this condition. This chapter will look at the epidemiology of POP and associated risk factors. The etiology of these conditions and diagnostic criteria will also be explored. Finally, the clinical evaluation will be outlined followed by a thorough analysis of both conservative therapies and surgical options in older women.

Epidemiology

Data on the prevalence of POP are highly variable mainly due to inconsistent definitions. Some studies use non-validated classification systems, while others define prolapse based on symptoms alone. The number of studies that use the Pelvic Organ Prolapse Quantification (POP-Q) system is very limited. In a study of 497 women ≥18 years of age undergoing routine gynecologic care, Swift et al. found that 43.3 % had stage I prolapse, 47.7 % had stage II prolapse, and 2.6 % had stage III prolapse based on the POP-Q classification. No patients in the study had grade 4 prolapse and only 6.4 % were classified as stage 0 with no prolapse [1]. In an ancillary study of the Women's Health Initiative, Nygaard et al. evaluated the prevalence of POP in older women using the POP-Q classification. Of 270 women with mean age 68.3 years, 2.3 % of women had stage 0 prolapse, 62.9 % had stage II, and 1.9 % had stage III prolapse [2]. The lifetime risk of surgical repair for POP or urinary incontinence by 80 years of age is 11.1 %. The incidence of POP and urinary incontinence was also found to increase with advanced age [3]. According to the United Nations World Population Aging 2009, the proportion of older people has been steadily rising since 1950. In 2009 the number of persons aged 60 or older had surpassed 700 million, and it has been projected that by 2050, more than two billion persons 60 years old or older will be alive. The fastest growing segment of the population is

G. Bales, M.D. (✉) • D. Chung, M.D., F.R.C.S.C.
Section of Urology, The University of Chicago School of Medicine, 5841 S. Maryland Avenue, MC 6038, Chicago, IL 60637, USA
e-mail: gbales@surgery.bsd.uchicago.edu; doreenchung@gmail.com

K. Ballert, M.D.
Department of Surgery, University of Kentucky College of Medicine, 800 Rose Street, Lexington, KY 40536, USA
e-mail: kballert@gmail.com

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_13,

actually those 80 years or older, and because women have a longer life expectancy, they outnumber older men. The population of women currently aged 80 years or older is nearly double that of men [4]. Luber et al. noted that women over the age of 60 are more likely to seek medical care for pelvic floor disorders and their research group predicted a 45 % increase in the demand for treatment of pelvic floor disorders including POP over the next 30 years [5].

Risk Factors

Age

Several studies have documented an increase in POP with aging [2, 5, 6]. In a cross-sectional analysis of women enrolled in the Women's Health Initiative Hormone Replacement Clinical Trial, Hendrix et al. found that older women had a higher risk of POP at all anatomic sites including anterior, posterior, and apical [6]. An Italian cross-sectional study also found increased age to be a risk factor for POP. When compared to women younger than 51 years of age, the odds ratio of uterovaginal prolapse was 1.3 for women aged 52–55 and 1.7 for those 56 years of age or older [7]. In a multicenter observational study, Swift et al. found that the odds ratio of POP increased by 1.38 per year [8]. Mant et al. noted an increased risk of POP with aging, but parity was noted to have the strongest correlation [9].

Race

Some studies have suggested that African-American women have a lower risk of developing POP. Hendrix et al. found that African-American women had the lowest risk of POP in all anatomic compartments. Hispanic women had the highest risk of uterine prolapse, while Asian women had the highest risk for cystocele and rectocele [6]. A study by Rortviet et al. found that white and Hispanic women were twice and three times as likely to have symptomatic POP as African-American women [10]. Swift et al. also noted an increased risk for POP in Hispanic women but did not find African-American race to be protective [8].

Parity

In the Oxford Family Planning Association Study, Mant et al. found an 11-fold increase in POP in mothers of four or more children compared to nulliparous women. The majority of the increased risk was noted after two deliveries [9]. Rortviet et al. also found that the number of vaginal deliveries was strongly associated with symptomatic POP [10]. In a study evaluating the natural history of POP in postmenopausal women, Bradley et al. found that women with a history of five or more vaginal deliveries were more likely to have progression of vaginal descent over the 3-year study period [11].

Obesity

Hendrix et al. found that overweight (BMI 25–30 kg/m^2) and obese (BMI >30 kg/m^2) women had an increased occurrence of prolapse in all anatomic compartments. Uterine prolapse increased 31 % and 40 %, respectively, in overweight and obese women. Occurrence of cystocele increased 39 % and 57 %, and rectocele occurrence increased 38 % and 75 %, respectively [6]. The Italian cross-sectional study found that women with higher BMI had an increased risk of uterine prolapse. Compared to women with BMI <23.8, those with a BMI of 23.8–27.2 and >27.2 had an odds ratio of 1.4 and 1.6, respectively [7]. Bradley et al. and Kudish et al. both noted that increased BMI was also a risk factor for POP progression [11, 12].

Other Potential Risk Factors

Constipation has been linked to POP both as a potential cause as well as a symptom of POP.

Spence-Jones et al. found that straining during bowel movements as a young adult prior to the onset of urogynecological symptoms was more common in women with uterovaginal prolapse (61 %) compared to controls (4 %) [13]. However, Blandon et al. did not find an association between POP repair and constipation in women post-hysterectomy. The study did find an increased risk for POP repair in patients with COPD [14]. Studies have also shown an association between prior gynecologic surgery and subsequent POP. Mant et al. found that the risk of prolapse requiring additional surgery in women post-hysterectomy increased in a linear fashion reaching 5 % at 15 years. The risk was also noted to be significantly higher if the indication for the hysterectomy was POP [9]. Swift et al. found that the risk of having severe prolapse increased by more than 200 % for women with a prior hysterectomy and by more than 500 % for those with a prior history of prolapse repair [15]. Some studies have suggested that women who perform strenuous manual labor for a living are at a higher risk for POP [16, 17]. Other studies have found no significant association with profession [2, 6, 11].

Etiology

The etiology of POP is poorly defined, but appears to be multifactorial. It likely involves injury to pelvic muscles, ligaments and nerves as well as genetic factors. The levator ani and endopelvic fascia are important for normal support of the pelvic organs. Both of these structures can be injured during pregnancy and delivery. Injury may be related to nerve damage, ischemia, or direct tearing. A study by Richardson et al. documented breaks in the endopelvic fascia in women with anterior POP and attributed them to obstetric trauma [18]. DeLancey et al. also demonstrated that women with POP were more likely to have levator ani defects. In addition, they found that women with POP generated less vaginal closure force during pelvic muscle contraction [19]. Stretching, tearing, and avulsion of the levators cause lengthening and widening of the urogenital hiatus [20]. A study by Delancey and Hurd documented that increased urogenital size is associated with POP [21]. Age-related weakening of connective tissue may also play a role in the development and/or progression of POP. Pelvic floor denervation and decreased neuropeptide activity have been proposed as factors contributing to the pathogenesis of POP [22]. Aging and childbirth are two major factors in pelvic floor denervation [23]. Other possible contributing factors include pelvic surgery and radiation.

An Italian study found that the risk of prolapse was higher in women with a family history of POP [17]. Rinne et al. found a 30 % familial incidence of POP in a group of Finnish women [24]. It has been suggested that the genetic determinants of POP are likely related to connective tissue metabolism and possibly variation in collagen subtypes [25]. However, data on the collagen content of pelvic floor and vaginal tissues in women with POP have been inconsistent [26]. Jackson et al. demonstrated a reduction in collagen content with an increase in collagenolytic activity in the vaginal tissue of women with POP [27]. Takano et al. found a reduction of collagen in the parametrium, but not the vaginal apex in women with uterine prolapse [28]. However, Maolli et al. found the total amount of collagen in the vaginal tissues of women with POP to be increased with the increase being primarily related to an increase in expression of type III collagen [29]. Some studies have found an increase in type III collagen expression relative to other collagen subtypes in the tissues of women with POP [29, 30], while other studies have not [27]. Connective tissue disorders such as Marfan's and Ehlers–Danlos syndrome have also been associated with the development of POP [31, 32]. Furthermore, aging has been associated with significant changes in collagen that are thought to be detrimental to its function [33].

Smooth muscle may also play a role in the development of POP. Boreham et al. demonstrated that the smooth muscle content of the vaginal wall was significantly decreased in women with anterior prolapse. The decrease did not appear to be age related [34]. Reisenauer et al.

also found that the smooth muscle component of the uterosacral ligament was impaired in women with POP [35]. Lastly, hormonal status has been suggested as a possible contributing factor in the pathogenesis of POP. Studies by Swift et al. and Moalli et al. revealed that postmenopausal women not taking hormone replacement were more likely to experience POP [15, 29].

Diagnosis and Classification

Patients with POP may present with a variety of symptoms including those related directly to the prolapse such as a vaginal bulge and vaginal or pelvic pressure, symptoms related to urinary incontinence and/or symptoms related to voiding, defecation, and sexual dysfunction. Unfortunately, there is somewhat limited data regarding the reliability of patients' symptoms to diagnose prolapse or to predict its severity. Ellerkmann et al. found that symptoms did not necessarily correspond with which compartment was affected and that increasing severity of prolapse was only weakly to moderately associated with symptoms. However, the majority of the patients in the study had only stage II prolapse [36]. Tan et al. found that the report of a bulge per vagina had an 81 % positive predictive value and a 76 % negative predictive value for POP [37]. Burrows et al. found that patients who required manual assistance during urination had more advanced POP, while those who had stress incontinence had less advanced POP [38].

The physical examination allows for more definitive diagnosis as well as classification of POP. The extent of prolapse is first evaluated with the patient in the dorsal lithotomy position. The presence of anterior, apical, and posterior prolapse should be assessed. A split speculum or the posterior speculum blade is used, and the patient is instructed to perform a Valsalva maneuver to evaluate the degree of prolapse in each compartment. To ascertain the full extent of the prolapse, the patient should also be examined in the standing position with one foot elevated on a stool.

There are several systems used to classify POP. The two most commonly used are the Baden–Walker classification [39] and the POP-Q system [40]. The Baden–Walker classification consists of grades 0–4 and is simple to use. The most dependent portion of the pelvic organs during straining is noted and graded as follows:

Grade 0: Normal
Grade 1: Descent halfway to hymen
Grade 2: Descent to hymen
Grade 3: Halfway through hymen
Grade 4: Maximal progression through hymen

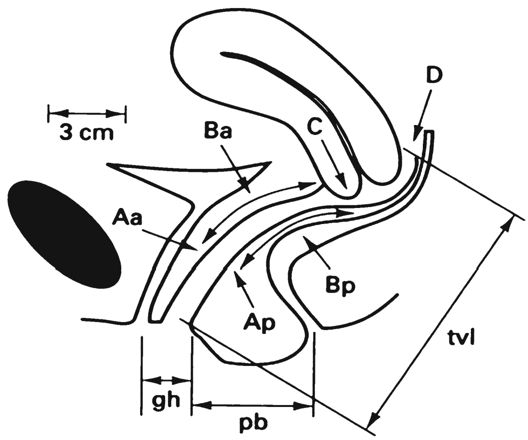


Fig. 13.1 POP-Q Points of Ref. [40]. (With permission. Bump RC, Mattiasson A, Bo K, et al. The standardization of terminology of female pelvic organ prolapse and pelvic floor dysfunction. Am J Obstet Gynecol 1996;175:10–7.)

The POP-Q system (Fig. 13.1) was developed to provide an objective system to quantitate and stage POP and was adopted by the International Continence Society (ICS) in 1995 [40]. It includes six vaginal points (Aa, Ba, C, D, Ap, and Bp) that are measured during a Valsalva maneuver. Measurements are made in relation to the hymen. Points above the hymen are negative and those below the hymen are positive. Point Aa is located in the midline of the anterior vaginal wall 3 cm proximal to the urethral meatus. Point Ba is the most distal position of the anterior vaginal wall. Point C is the most distal edge of the cervix or the vaginal cuff. If the cervix is present, point D is the location of the posterior fornix. Point Ap is 3 cm proximal to the hymen on the posterior vaginal wall. Bp is the most distal position of the posterior vaginal wall. In addition, the genital hiatus (gh) is the size of the vaginal opening, the perineal body (pb) is the distance from the posterior margin of the gh to the anus, and the total vaginal length (tvl) measures the depth of the vagina with the prolapse reduced.

The POP-Q system also includes staging criteria that are assigned based on the most severe portion of the prolapse [40]. The five stages are as follows:

Stage 0: No prolapse; Aa, Ap, Ba, and Bp at −3 cm and C or D ≤ −(tvl-2)cm

Stage I: Stage 0 criteria not met, but most distal portion of prolapse <−1 cm

Stage II: Most distal portion ≥−1 cm but ≤+1 cm

Stage III: Most distal portion >+1 cm but <+(tvl-2)cm

Stage IV: Complete eversion; Distal portion protrudes to ≥+(tvl-2)

Clinical Evaluation

History

Despite the lack of correlation between symptoms and prolapse severity, the history is extremely important in determining future treatment plans. It should include questions regarding the sensation of a vaginal bulge, pelvic or vaginal pressure, or discomfort. The history should ascertain symptoms of urinary obstruction including the sensation of incomplete emptying, the need to manually reduce the prolapse or change positions to void or defecate, hesitancy, intermittency, and straining to void. Women with POP may also have symptoms of overactive bladder including frequency, urgency, nocturia, or urge incontinence, and/or stress urinary incontinence (SUI). It is also important to ascertain whether the patient experienced SUI before the onset of the prolapse. Many patients will report symptomatic SUI that improved or resolved with the onset of the vaginal bulge. This is likely due to kinking of the urethra caused by the prolapse. Defecatory symptoms should also be carefully evaluated. These include constipation, difficulty with defecation, the need to perform vaginal or perineal splinting, fecal urgency or incontinence, and the sensation of incomplete evacuation. The correlation between POP and sexual symptoms is not well delineated; however, sexual function should also be evaluated in patients with POP. Information regarding sexual activity, dyspareunia, and urinary incontinence during intercourse should be obtained. Sexual function can also be assessed using the validated Prolapse and Incontinence Sexual Questionnaire [41]. Lastly, the impact of the prolapse on the patient's quality of life (QOL) should be assessed. How does the prolapse impact the patient's daily activities? Has the patient limited or changed her activity level or lifestyle because of the prolapse? The Pelvic Floor Impact Questionnaire is a validated questionnaire that allows quantification of the effects of POP on QOL [42]. This information is weighed against the risk associated with various treatment options when determining how to manage the prolapse.

A comprehensive medical and surgical history including medications should be ascertained. This may be especially pertinent in elderly patients who are more likely to have multiple medical comorbidities that can influence plans for treatment. Gynecologic and obstetric history should include information about gravity, parity, history of obstetrical trauma, and history of prior pelvic surgeries or radiation. Determination of hormonal status as well as use of exogenous hormones should also be included.

Physical Examination

A comprehensive physical examination should provide information regarding a patient's performance status and will help determine future treatment options. As previously outlined, each vaginal compartment should be assessed during pelvic examination both at rest and with Valsalva using a split speculum or posterior speculum blade. With the prolapse reduced, the patient is asked to cough and perform a Valsalva maneuver to evaluate for occult stress incontinence. The vaginal epithelium should be assessed for signs of atrophy. Urethral mobility should also be noted during cough and Valsalva. If desired, the Q-tip test can be used as a more objective measurement of urethral mobility. A sterile Q-tip is gently inserted into the urethra, and the patient is asked to cough or perform a Valsalva maneuver. The change in angulation of the Q-tip gives information about the degree of hypermobility of the urethra. A rectal examination should be performed to assess the perineal body and to evaluate anal sphincter tone. A basic neurologic examination should also be performed to evaluate gross lower sensory and motor function. Perineal sensation and pelvic floor muscle contraction should be assessed as part of the neurologic examination.

Additional Testing

Because POP can cause urethral obstruction, it can also result in incomplete bladder emptying. Post-void residual urine volume should be measured by either catheterization or bladder ultrasound. A urinalysis is recommended in patients with LUTS, incontinence, or incomplete emptying. Cystoscopy should be performed in patients with hematuria and considered in patients with lower urinary tract symptoms to rule out any additional urethral or bladder pathology.

Magnetic resonance imaging (MRI) has been recommended by some experts for evaluation of POP in patients with complex multicompartment defects or prior failed surgery [43, 44]. Dynamic MRI may also provide information for patients in whom the physical examination is limited. MRI provides excellent visualization of the pelvic organs and soft tissues and allows simultaneous evaluation of all three vaginal compartments (anterior, apical, posterior). Some have suggested that MRI is more accurate than physical examination alone in demonstrating cystocele, enterocele, uterine hypermobility, and vaginal vault prolapse [45]. However, others have found poor correlation between clinical and MRI findings when evaluating prolapse of the vaginal apex [46] as well as between MRI and operative findings when diagnosing rectoceles [47]. The significant costs associated with MRI should also be kept in mind prior to ordering this test as part of any POP assessment.

The role of urodynamics (UDS) in evaluating patients with POP has not yet been fully established. Many endorse the use of urodynamics prior to surgical intervention for POP especially in patients with urinary symptoms such as incontinence, OAB, voiding symptoms, or incomplete emptying as well as in those that have failed prior reconstructive surgery. Bai et al. reported a 63 % rate of coexisting SUI in women with POP [48]. In a study by Romanzi et al. 52 % of women with high-grade anterior POP (Grade 3 or 4) demonstrated detrusor overactivity on urodynamics. Women with high-grade prolapse were also much more likely to report voiding difficulties such as difficulty with initiation of stream, intermittent flow, weak stream, incomplete emptying, and urinary retention [49].

Elderly patients specifically may present with a complex array of urologic symptoms that can be further elucidated with urodynamic testing. Urodynamics allows for evaluation of incomplete emptying that may be related to obstruction or detrusor hypocontractility. It also allows for further evaluation of symptomatic urinary incontinence and may facilitate diagnosis of impaired compliance, detrusor overactivity, or occult SUI. An important thing to consider when performing urodynamics is how the findings may impact clinical decision-making or patient counseling. It is important to attempt to replicate a patient's typical voiding symptoms during the urodynamic evaluation.

Reduction of prolapse has been reported to unmask occult SUI in up to 36–80 % of clinically continent women with severe POP [50–52]. Furthermore, POP repair in clinically continent women has been shown to result in SUI postoperatively in 11–22 % [53, 54]. It is presumed that many of these women would have demonstrated occult SUI if tested prior to surgery. Currently there is no standardized method of prolapse reduction used to evaluate for occult SUI. The goal of prolapse reduction is to simulate the outcome after surgical repair and to determine if a woman is at risk for SUI postoperatively. Several methods have been used including a pessary, split speculum, cotton swab, vaginal packing, and ring forceps. Potential concerns with all of these methods are that they may not accurately simulate surgical repair and may result in overcorrection or cause urethral obstruction.

Various studies have proposed UDS as a means to determine the need for a simultaneous anti-incontinence procedure at the time of surgical repair for POP [55, 56]. However investigation of the predictive value of urodynamics has been limited because few studies have randomized patients to an anti-incontinence procedure versus no procedure. Brubaker et al. found that in women without clinical SUI, simultaneous Burch colposuspension at the time of sacrocolpopexy was beneficial regardless of the findings on preoperative urodynamics [57]. Visco et al. noted that women who demonstrated SUI on urodynamics prior to abdominal sacrocolpopexy were more likely to have postoperative SUI regardless of whether they underwent simultaneous Burch [58]. In a smaller retrospective study, Roovers et al. studied 76 patients who underwent transvaginal prolapse surgery and found that none of the preoperative urodynamic parameters predicted urinary incontinence postoperatively [59].

Defecography may be used to further evaluate patients with defecatory dysfunction and provides additional structural and functional information. These patients may also benefit from additional gastrointestional evaluation with ancillary tests including proctosigmoidoscopy or colonic transit studies. Some recommend the use of ultrasound to screen for hydronephrosis resulting from ureteral kinking in patients with "untreated severe prolapse" [60]. Others have suggested that routine imaging of the kidneys and ureters is unnecessary prior to surgical repair because it typically does not influence management [61].

Aging is associated with a progressive decline in the functional reserve in all organ systems, but the onset and extent of these changes varies based on the individual [62]. When surgical intervention is being considered for an elderly patient, the key is to determine her functional condition and comorbidities. It appears that the best predictor of postoperative level of function is preoperative level of function [63]. Elderly patients are often subjected to a myriad of preoperative evaluations including blood tests, electrocardiogram (ECG), and chest X-ray. However, based on their review of the literature, John et al. did not recommend routine preoperative laboratory testing based on age alone. Instead, they suggested that selective testing should be performed based on the history and physical examination as well as the specific surgical procedure being performed [63]. In patients over 70 years of age undergoing noncardiac surgery, Dzankic et al. found that the American Society of Anesthesiologists (ASA) 5-point classification system and surgical risk stratification (low, intermediate, and high) were the only independent predictors of adverse postoperative outcomes [64]. It has also been suggested that preoperative ECG and chest X-ray are not required based on age alone [65]. Tait et al. found that preoperative ECGs on patients without a prior history of cardiovascular disease were poor predictors of perioperative complications [66]. Furthermore, Liu et al. found that although abnormalities were commonly identified on preoperative ECGs in older adults, they were of limited value in predicting postoperative cardiac complications in patients undergoing noncardiac surgery [67]. The 2007 ACC/AHA guidelines provide recommendations regarding additional perioperative cardiovascular evaluation in specific situations [68].

Treatment of Pelvic Organ Prolapse

Introduction

A recent population-based study calculated that the lifetime risk of undergoing first-time POP surgery was 19 %, and several studies have shown that the peak incidence occurs between 70 and 79 years of age [3, 69, 70]. Hence, a significant proportion of patients undergoing surgery for POP are elderly. Waetjen et al. observed that 42 % of patients undergoing surgery for POP were over 60 years of age. The treatment of POP must be individualized according to patient needs. Because prolapse is mostly a QOL issue, in order to attain a successful treatment outcome one must consider the stage of prolapse, the nature and character of the patient's symptoms, and the degree to which the patient's QOL is affected [71]. Patient factors that are paramount to selecting treatment are age, cormorbidities, previous surgeries, performance status, and level of physical and sexual activity. Treatment can be classified as conservative, meaning nonsurgical, and surgical.

Conservative Management for Pelvic Organ Prolapse in Older Adults

Conservative management includes used of mechanical devices or behavioral therapies. Behavioral therapies include lifestyle changes and pelvic floor muscle training (PFMT). For many elderly patients with significant comorbidities, conservative management may be the only viable treatment option for POP.

A Cochrane Database review of conservative management and prevention of POP was recently published [72]. Due to a paucity of literature only six trials could be included. Of these, four trials had fewer than 25 women per arm. There was difficulty in comparing the trials because of different treatment outcome measures and different classifications of prolapse symptoms. Overall there appeared to be improvement in prolapse stage by 17 % in patients who underwent PFMT compared to controls who did not undergo PFMT. In addition 2 out of 3 trials that examined various urinary outcomes reported a positive difference between the groups in favor of PFMT.

Braekken et al. randomized 109 women with POP (stages I–III) to PFMT, with individual physical therapy sessions and home exercises, or control for 6 months [73]. Nineteen patients (17 %) had stage I prolapse, 65 patients (60 %) had stage II prolapse, and 24 patients (22 %) had stage III prolapse. The compartment of prolapse was not presented in the study. The mean age in this study was relatively young, 49 ± 12 years. Eleven of the women (19 %) in the PFMT group improved POP-Q stage compared to four of the controls (8 %) ($p = 0.035$). Significant improvements were also seen in frequency and bother of prolapse symptoms. Although this is the largest study to evaluate the utility of PFMT in the treatment of prolapse, the conclusions may not be applicable to the geriatric patients.

Estrogen therapy has been investigated as a potential management option for POP in postmenopausal women. Goldstein et al. reported on a secondary analysis of the effects of raloxifine, a selective estrogen receptor modulator (SERM) [74]. Although POP was not specifically evaluated in patients, there appeared to be a decreased number of postmenopausal women over age 60 who had prolapse surgery, considered an adverse effect, at 3 years in the treatment group. Separately, a Cochrane Database review was performed to assess the role of estrogens for the treatment or prevention of POP in postmenopausal women [75]. Only three trials and one meta-analysis were included. The review concluded that evidence from randomized controlled trials regarding the use of estrogens for prevention and management of POP was limited.

Pessaries are mechanical devices of varying size and shape which can be inserted into the vagina to reduce POP and alleviate symptoms (Fig. 13.2). The main limitation of this treatment is a high discontinuation rate due to the pessary falling out or other complications. Several larger studies have been published with varying outcomes [76–78].

Lone et al. studied a group of women who decided on treatment with a pessary for POP and had retained the pessary for a minimum of 4 weeks [77]. Of the original 246 women fitted with a pessary, 187 were able to retain the device for 4 weeks. One hundred thirty women used the pessary successfully over 5 years. Twelve percent of patients who used the pessary reported minor complications including pain or discomfort, excoriation or bleeding, and constipation.

Friedman et al. performed a retrospective study in 150 women who used a pessary for greater than 1 year to identify factors influencing long-term use [78]. One hundred fifteen women (77 %) successfully used the pessary for over 1 year. The main factor influencing success was older age at pessary insertion. Patients who had previously had a POP repair were more likely to discontinue use. No significant discontinuation differences were seen in patients with stress incontinence despite a trend toward higher discontinuation in this patient group.

Sarma et al. reported on the long-term discontinuation rates and incidence of adverse events associated with vaginal ring pessary use for a minimum of 6 years and noted lower success rates and higher complication rates than in other series [76]. Of the 273 women fitted with a ring pessary, 167 (61 %) were successfully using it at

Fig. 13.2 Examples of various types of pessaries

4 weeks. Of those 167 patients who continued pessary use, 93 patients (56 %) experienced complications including bleeding, extrusion, severe vaginal discharge, pain, and constipation. Twenty-three of 167 (14 %) continued with pessary use to the study endpoint with median duration of use being 7 years (interquartile range, 6–9 years; range, 2.25–13.9 years).

Surgery for Pelvic Organ Prolapse in Older Adults

When considering for surgery for POP in geriatric patients, one must carefully balance the probability of success from the surgical repair with comorbidity and potential complications. It is also important to note that recurrence rates increase with each subsequent attempt to surgically correct the defect [79]. Hence the best chance for anatomic success of a surgical repair is with the initial attempt.

Success may be assessed objectively or subjectively. Particularly for elderly patients, subjective success may be a more important goal than objective success. Objective success can be measured by staging of POP using either the Baden–Walker or POP-Q systems as previously discussed. Subjective success can be measured by various self-administered questionnaires such as the Urogenital Distress Inventory-6/short form (UDI-6), the Incontinence Impact Questionnaire-short form (IIQ-7), the Pelvic Floor Distress Inventory (PFDI), and the Pelvic Floor Impact Questionnaire (PFIQ) [80, 81].

Repairs can be classified according to the vaginal compartment as well as by the type of repair including obliterative, restorative, or compensatory procedures [82]. Obliterative procedures, such as colpocleisis, essentially involve sealing off the vaginal introitis by severely reducing the vaginal lumen. This can provide symptom relief with minimal surgical risk in elderly patients who are no longer sexually active. These types of procedures are contraindicated in patients who may wish to still engage in penetrative sexual activity. For patients with discrete defects in the fibromuscular layer of the endopelvic fascia, restorative repairs using a patient's own support structures are indicated [83]. Many elderly patients have weak native tissues and reconstructive compensatory procedures using grafts may provide a more successful outcome.

There are two main approaches for pelvic floor reconstruction: abdominal and vaginal. The abdominal approach may be performed through either an open or minimally invasive technique. Compared to the abdominal approach, there is evidence that the vaginal approach offers a lower complication rate, faster recovery time, and decreased operative time. These are important factors to consider when operating on geriatric patients [84, 85]. However, there is also evidence that the abdominal approach may have a more durable outcome and improved patient satisfaction [86, 87]. Surgeon experience is also a very important factor associated with surgical outcomes, operative time, and complication rates, and this should not be overlooked.

Preparing Geriatric Patients for Pelvic Organ Prolapse Surgery

Preoperative counseling is a very important factor that influences patient satisfaction following surgery. Studies show that prolapse patients who perceived they were more fully prepared for surgery were more likely to note improvement on questionnaires such as the Patient Global Impression of Improvement (PGI-I) scale and the Pelvic Organ Prolapse Distress Inventory (POPDI) [42, 88].

Preoperative investigations should always include a urinalysis and urine culture. Culture-specific antibiotics should be given to eradicate bacteriuria prior to surgery. There are also specific guidelines for perioperative antibiotic prophylaxis in patients undergoing procedures to correct POP [89, 90]. The American Urologic Association has published guidelines for vaginal surgery based on evidence pertaining to vaginal hysterectomy. First-choice agents are first- or second-generation cephalosporins, or for patients with penicillin allergy, an aminoglycoside with metronizadole or clindamycin can be used. Second-line agents include ampicillin/sulbactam or a fluoroquinolone. The recommended duration of therapy is $\leq$24 h [90]. No specific guidelines currently exist for antimicrobial prophylaxis in the setting of vaginal surgery with implantation of synthetic mesh.

Patients older than 60 years of age undergoing major surgery are considered high risk for deep vein thrombosis (DVT) [91]. Recommendations for these patients regarding DVT prophylaxis following surgery include anticoagulant medications as well as mechanical prophylaxis devices. For anticoagulant-based prophylaxis, heparin 5,000 units three times per day or low-molecular weight heparin are recommended choices. These should be administered with or without lower extremity sequential compression devices.

Vaginal estrogens are commonly recommended to patients prior to surgery in order to enhance incisional healing and prevent mesh complications [92]. Only one animal study exists addressing this practice [93]. Higgins et al. found no difference between mesh extrusion rates in rabbits that were or were not administered 8 weeks of vaginal estrogen following vaginal mesh repair. However increased collagen deposition was seen histologically in the rabbits in the estrogen group.

The Use of Grafts in Pelvic Organ Prolapse Surgery

Grafts can be classified as biologic or synthetic. The Food and Drug Administration (FDA) has issued an advisory warning pertaining to complications associated with the use of vaginal synthetic mesh. The first advisory was published in 2008, and this was updated in July 2011 [94]. Specifically, the FDA notes that serious complications from the use of vaginal synthetic mesh in POP repairs are not rare. It also cautions that there is no clear evidence that transvaginal prolapse repairs with mesh are more effective than traditional non-mesh repairs. However, there are some randomized studies that indicate mesh repairs may confer a better outcome [95]. Importantly, the FDA advisory does not pertain to the use of mesh for SUI procedures or for abdominal sacral colpopexy. As a consequence of this warning some surgeons have changed their practice with increased usage of biologic grafts [96].

Biologic Grafts

Biologic grafts can be categorized as autologous (same species, same individual), heterologous (same species, different individual), and xenogenic (different species). The most common donor sites for autologous grafts are rectus fascia and fascia lata. The advantages of autologous grafts are absence of potential for disease transmission and minimal risk of rejection and encapsulation. The main disadvantage is potential morbidity associated with graft harvest. Allografts and xenografts are commonly used to prevent this morbidity. However, the potential for disease transmission is the main drawback of allografts [97].

Xenograft materials currently available commercially include porcine subintestinal submucosa, porcine dermis, bovine dermis, and bovine pericardium. Their purported mechanism of action is to serve as a collagen-based scaffold to stimulate host tissue infiltration. The source animals for xenografts are strictly raised for medical purposes and production is very carefully regulated by the U.S. FDA [98]. Various processing techniques are used for xenografts. One such process is cross-linking which is done to delay reabsorption by collagen [99]. Encapsulation is a local complication that has been reported with the use of porcine dermis grafts [100]. Encapsulation can be concerning because it prevents appropriate tissue ingrowth leading to a weakened repair and subsequent early failure. Graft fenestrations may prevent this complication by enhancing ingrowth and angiogenesis [101].

Cross-linked porcine dermis (Pelvicol®, Bard Medical, Murray Hill, NJ) is an acellular collagen scaffold [102] that is one of the first xenografts to be studied for use in POP repairs. Porcine small intestine submucosa (Surgisis®, Cook Medical, Bloomington, IN) is an acellular graft that is not cross-linked and processed to keep the extracellular matrix and growth factors intact [103]. Xenform® Matrix (Boston Scientific Corp., Natick, Massachusetts, USA), is an acellular noncrosslinked collagen-based xenograft derived from fetal bovine dermis. This is designed to provide a molecular scaffold that is gradually reabsorbed and replaced by native connective tissue [104]. No published comparative studies have compared the available xenografts.

Type	Description
I	Macroporous monofilament (>75μm)
II	Microporous monofilament (<10μm)
III	Macroporous or microporous multifilament
IV	Submicroporous (<1μm)

Fig. 13.3 Amid classification of synthetic mesh

Synthetic Grafts

Synthetic grafts are either permanent or absorbable. The advantages of absorbable mesh include promotion of fibroblast activity, less infectious disease risk, and lack of rejection. The main disadvantage is that the resultant scar tissue may not be as strong as the original native tissue [105]. Two types of absorbable meshes are available: polyglycolic acid (Dexon®, Davis and Geck, American Cyanamid, Danbury, CT) and polyglactin 910 (Vicry®l, Ethicon, Somerville, NJ). They differ in the duration of time until absorption. Polyglactin 910 starts to hydrolyze by 21 days and loses its mechanical support by 30 days. Polyglycolic acid takes 90 days for absorption [92].

Synthetic meshes are also classified by pore size and monofilament versus multifilament design. The classification system most commonly used is the Amid system (Fig. 13.3) [106]. Macroporous mesh has a pore size >75 μm and microporous <10 μm. Most bacteria are <1 μm in diameter, while macrophages and granulocytes are >10 μm in diameter. The larger the pore size, the more flexible the mesh which may potentially decrease postoperative mesh extrusion rates [107, 108]. Multifilament meshes have pore sizes >75 μm, but the space between the fibers is <10 μm, theoretically leading to a greater risk of infection. The mesh with the most favorable characteristics for use in POP surgery is type I macroporous monofilament mesh, with the most commonly available product being polypropylene.

Outcomes of Surgery for POP in Older Adults

There is a paucity of literature specifically addressing outcomes of surgery for POP in geriatric patients. In addition, the specific age at which a person is classified as "geriatric" has not been standardized, and there is wide variation between published studies. There are several studies supporting the safety and efficacy of surgery for POP in elderly patients [109–111].

Ghezzi et al. published a retrospective series of 138 women age 75 or older who underwent surgery for POP, urinary incontinence, or both, with 116 undergoing surgery for prolapse [110]. The median age was 77 years and the mean follow-up was 12 months. One hundred and two patients (74 %) underwent vaginal hysterectomy, 106 (76.8 %) anterior repair, 36 (26 %) posterior repair, and nine (6.5 %) colpocleisis. No intraoperative complications were reported during prolapse repair. Five (4 %) postoperative complications were reported including vaginal bleeding, hematoma, and fever. No data were presented on hospital stay or blood loss. Anatomic success rate at 12 months was 87.6 %. No patients required additional procedures for correction of recurrence.

Tuschy et al. performed a retrospective study to evaluate the morbidity in elderly patients undergoing surgery for correction of POP [109]. Forty-eight patients aged 70 or older were included along with 65 controls aged 50–69 years undergoing similar surgical procedures during the same time period. There were no significant differences between study and control groups regarding operating time, duration of hospital stay, intraoperative and postoperative complications, and body mass index, although a significant difference was identified between the pre-existing comorbidities in the two patient groups.

Anterior Compartment

Anterior colporrhaphy was initially described by Kelly in 1913 [112]. In this repair the pubocervical fascia is plicated with absorbable sutures to repair the central defect (Fig. 13.4).

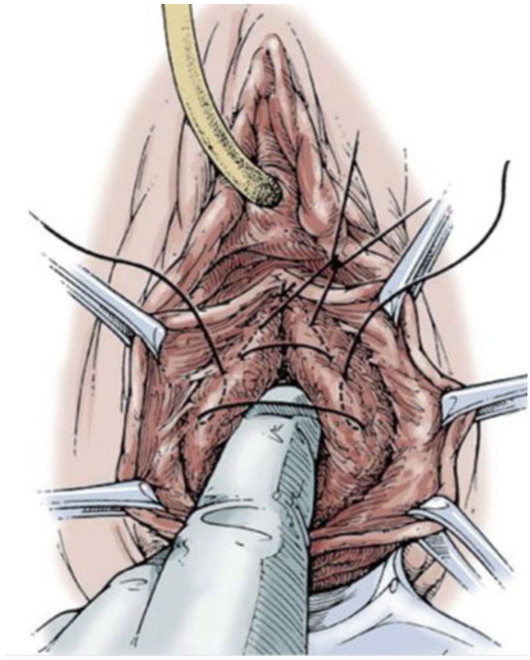


Fig. 13.4 Anterior colporrhaphy. The anterior submucosal layer is imbricated with absorbable continuous or interrupted suture. (*From Nicholas DH. Cystocele. In Nichols DH, editor. Gynecologic and obstetric surgery. St. Louis: CV Mosby; 1993. p. 334–62.*)

Porges and Smilen reported a success rate of 97 % in anterior colporrhaphy for 299 patients with a mean follow-up of 31 months [113]. However, the success rate in this series was highly subjective with recurrence being defined as symptomatic descent for which additional surgery was performed or recommended. More contemporary series using POP-Q scoring to define objective cure rate have demonstrated much lower success rates in the range of 60–70 %.

Weber et al. compared anterior colporrhaphy reinforced with polyglactin mesh to both traditional plication without tension using polydioxanone suture and "ultralateral" plication using both polydioxanone suture and tension [114]. One hundred and fourteen women with symptomatic cystoceles (93 % ≥ stage II POP-Q) were randomized between the three groups. With a mean follow-up of 23 months, there was no significant difference in the failure rate, defined as stage II or greater on the POP-Q, between the three groups. The failure rate was 30 % in those who underwent traditional plication (39 patients), 46 % in those who underwent “ultralateral” plication (35 patients), and 42 % in those who underwent traditional plication augmented with polyglactin mesh (35 patients). However, the study did not recruit enough women to achieve adequate statistical power to detect differences between the groups.

Sand et al. randomized 161 women to either anterior colporrhaphy with polyglactin suture or anterior colporrhaphy with a free polyglactin mesh inlay, which was placed underneath the trigone after plicating the pubocervical fascia. Approximately 40 % of patients in each group also underwent hysterectomy, and approximately the same proportion underwent concomitant vaginal vault suspension. After 1 year of follow-up, the women randomized to polyglactin mesh had a failure rate of 25 % compared to a 43 % failure rate in those women who underwent the plication with suture alone ($p = 0.02$). Complications of these types of repairs include voiding dysfunction such as de novo SUI, urinary retention, incomplete bladder emptying, and de novo detrusor overactivity. This is why a thorough preoperative evaluation of voiding symptoms prior to any POP repair is paramount. Other potential complications include significant bleeding, blood transfusion, bladder or ureteral injuries, vaginal shortening, and dyspareunia. Cystoscopy with the intravenous administration of indigo carmine should be routinely performed [92].

Vaginal Paravaginal Repair

George White first described the paravaginal repair in 1909 [115]. His repair involved suturing the lateral sulci of the vagina to the white line of the pelvic fascia. The main concept of this surgical procedure is to repair a lateral compartment defect by reattaching the pubocervical fascia to the arcus tendineus fascia pelvis (ATFP). This repair may be combined with anterior colporrhaphy (Fig. 13.4). Success rates of this repair vary and long-term results are not yet available. Shull et al. reported a 73 % success rate in 56 patients with mean follow-up of 19 months [116]. Young et al. published a retrospective series evaluating 100 patients with symptomatic grade 2 or higher prolapse of the anterior compartment with combined central and lateral cystoceles. All patients underwent both vaginal paravaginal repair and concomitant anterior colporrhaphy. With a mean follow-up of 11 months, the lateral cystocele recurrence rate was only 2 % and the central cystocele recurrence rate was 22 % [117]. Major complications were reported in 21 patients. There were three major intraoperative hemorrhages and two developed lower extremity neuropathy. Transfusion rates for the procedure have been reported up to 12 % [118].

Anterior Compartment Repairs Using Grafts

The use of grafts has expanded due to high recurrence rates of traditional repairs. This is understood to be secondary to placement of sutures through already weakened pubocervical fascia. Repairs using grafts can be classified as suture based or trocar based. In suture-based repairs, sutures are placed on the ATFP generally with a Capio Suture Capturing Device (Boston Scientific, Natick MA) (Fig. 13.5). In trocar-based repairs, trocars carrying mesh are brought through the ATFP. Many kits also incorporate sacrospinous uterine or vaginal vault suspension. Success rates for trocar-based kits are in the range of 75–95 % [119–122].

A Cochrane Database review for the surgical treatment of POP was recently updated [123]. The inclusion of new randomized controlled trials showed that the use of mesh at the time of anterior vaginal wall repair significantly reduced the risk of recurrent anterior vaginal wall prolapse on physical examination. For anterior vaginal wall prolapse, standard anterior repair was associated with more recurrent cystoceles than when supplemented with a polyglactin mesh inlay (RR 1.39, 95 % CI 1.02–1.90) or porcine dermis mesh inlay (RR 2.72, 95 % CI 1.20–6.14). However, data on morbidity and other clinical outcomes were lacking. Standard anterior repair

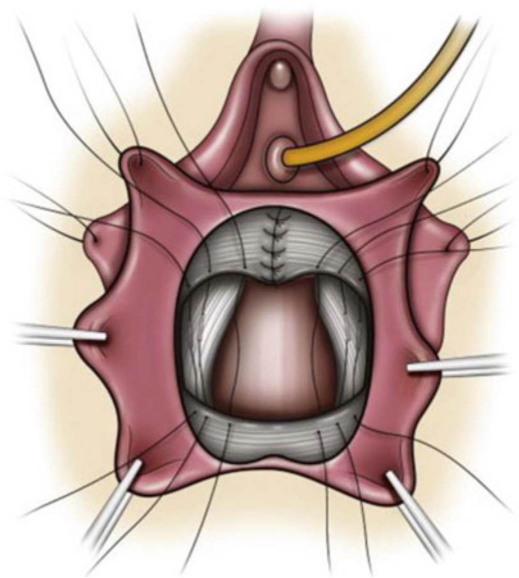


Fig. 13.5 High uterosacral ligament vaginal vault suspension. Three sutures are placed from lateral to medial in each uterosacral ligament. The sutures are brought through the vaginal muscularis anteriorly (pubocervical fascia) and posteriorly (rectovaginal fascia). (*From Walters M, Muir T. Surgical treatment of vaginal apex prolapse. In: Vasavada SP, Appell RA, Sand PK, Raz S, editors. Female urology, urogynecology, and voiding dysfunction. Boca Raton* [*FL*]*: Taylor & Francis; 2005, with permission.*)

was associated with more anterior compartment failures. However, this was not translated into improved functional or QOL outcomes. The document also concluded that adequately powered randomized controlled trials are needed and should particularly include women's perceptions of prolapse symptoms and functional outcome.

Nicita first demonstrated the efficacy and safety of polypropylene mesh for treatment of anterior vaginal wall prolapse in 1998 [124]. The technique was to suture the mesh to the ATFP using 3.0 polypropylene sutures. With 2 years of follow-up, there was a 93 % success rate in 44 patients. De Tayrac et al. published a series of 63 women with grade 3 and 4 cystoceles who underwent transvaginal placement of polypropylene mesh (Gynemesh; Ethicon, Somerville, NJ) with a tension-free approach without suture placement between 1999 and 2002 [125]. Mean follow-up was 37 months, and 49 women (89.1 %) had been cured, defined as POP-Q grade 0 or 1, at the time of follow-up. Three patients (5.5 %) reported local pain around an area of mesh shrinkage. Five patients (9.1 %) experienced vaginal mesh erosion. Seventeen percent of patients specifically questioned about dyspareunia (4/24) reported de novo dyspareunia.

Few randomized studies have been performed to compare traditional repairs to repairs using grafts. In a randomized controlled trial, Hiltunen et al. compared 97 subjects who underwent standard anterior colporrhaphy to 105 subjects who underwent the anterior colporrhaphy reinforced with low-weight polypropylene mesh [126]. There was a statistically significant lower chance of recurrent stage II or greater prolapse at 12 months. The success rate of repair at 12 months was 91 % in the mesh group versus 61 % for the anterior colporrhaphy group ($p<0.001$). Notwithstanding, no significant differences were seen between the groups with regard to symptomatic outcomes including pelvic pressure, vaginal bulging, or difficulty with bladder emptying. In the mesh group, 18 patients (17.3 %) had vaginal extrusion of the mesh with 4 of the 18 (22 %) self-reporting symptoms.

Altman et al. conducted a multicenter parallel-group randomized controlled trial comparing subjective and objective outcomes of a trocar-guided transvaginal polypropylene-mesh repair kit with traditional anterior colporrhaphy in women with cystoceles [95]. A total of 389 women were randomized to a treatment, with 200 undergoing prolapse repair with the transvaginal mesh kit and 189 undergoing traditional anterior colporrhaphy. The primary outcome was POP-Q stage 0 or I of the anterior vaginal wall and a negative response to question #16 on the UDI: "Do you experience a feeling of bulging or protrusion in the vaginal area?" Mean age was 65 ± 10 years in the colporrhaphy group and 64 ± 10 years in the mesh-repair group. Forty-two patients in the colporrhaphy group and 41 patients in the mesh-repair group were ≥ 72 years of age. One year after surgery, the success rate based on the primary outcome was significantly higher among patients in the mesh-repair group than among those in the colporrhaphy group (60.8 % vs. 34.5 %, $p<0.001$; adjusted odds radio, 3.6: 95 % CI 2.2–5.9).

Secondary analyses were performed to separately assess the success of each of the primary outcomes. Use of the transvaginal mesh kit demonstrated superiority over colporrhaphy with regard to the percentage of women in whom support of the anterior vaginal wall was restored to POP-Q stage 0 or I (82.3 % vs. 47.5 %, $p<0.001$), and also the percentage of those who had symptoms of vaginal bulging (75.4 % vs. 62.1 %, $p=0.008$) at 1 year. No significant differences were seen between groups with regard to urinary storage symptoms. New onset stress incontinence occurred in 6.2 % of subjects in the colporrhaphy group versus 12.4 % in the mesh repair group ($p=0.05$), although no details were given about formal preoperative testing for occult SUI. At 12 months, mean PISQ-12 (an instrument evaluating urinary control and sexual function) scores were modestly improved compared to baseline and were similar between the groups. When patients were asked how satisfied they were with their sexual relationships with their partners, 40 % of the colporrhaphy group and 48 % of the mesh-repair group answered “usually” or “always” ($p=0.37$) [41]. Compared to the colporrhaphy group, the mesh group had a significantly longer mean duration of surgery (52.6 vs. 33.5 min, $p<0.001$) and greater mean intraoperative blood loss (84.7 vs. 35.4 mL, $p<0.001$). At 2 months follow-up, five patients in the mesh-repair group reported severe pelvic pain compared to one patient in the colporrhaphy group ($p=0.22$). The pain had resolved spontaneously by the 12 month follow-up visit in all except one of these patients in the mesh-repair group. At 12 months, six patients (3.2 %) in the mesh-repair group had undergone vaginal wound revision to correct mesh exposure. One patient in the colporrhaphy group underwent a second anterior repair for prolapse recurrence.

Several studies have been published on the topic of age and repairs with synthetic mesh. Gabriel et al. analyzed a series of 62 women over 80 years of age who underwent vaginal synthetic mesh repair using a kit that included a trocar-based paravaginal repair and sacrospinous suspension [111]. Mean follow-up time was 6 months. The procedure was well tolerated with intraoperative complications occurring in 1.6 % of patients. One patient had blood loss >500 mL, but she did not require blood transfusion. Mean hospital stay was 4 days. Early postoperative complications included increased post-void residual urine volume (25.8 %), urinary tract infection (3.2 %), and moderate or severe pain (17.7 %). Five patients (8.3 %) developed prolapse recurrence, and mesh retraction was seen in six patients (10 %). Two (3.3 %) patients underwent reoperation, one for stress incontinence and the other for recurrent prolapse. There was no mesh erosion at short-term follow-up. These results suggest that vaginal mesh repair may be a safe alternative to colpocleisis for treatment of POP in older women. When Rzepka et al. compared 11 patients aged 75 years or older to 20 patients aged 60 years or younger who underwent vaginal mesh repair for prolapse, no differences were seen in surgical outcomes [127]. However, the sample size of this study was quite small.

Long et al. conducted a study to examine the changes in sexual function in 36 sexually active premenopausal and 32 postmenopausal women following vaginal mesh repair for POP [128]. Mean age was 42 ± 6 in the premenopausal group and 57 ± 6 in the postmenopausal group. Assessments included physical examination for POP-Q scoring and a personal interview with the Female Sexual Function Index (FSFI), UDI-6, and IIQ-7 questionnaires. There were significant improvements seen at POP-Q points Aa, Ba, C, Ap, and Bp ($p<0.001$) in both groups except for total vaginal length ($p>0.05$). The UDI-6 and IIQ-7 scores significantly decreased postoperatively ($p<0.01$). After surgery, the score of the dyspareunia domain decreased significantly in the premenopausal group ($p<0.01$) but not in the postmenopausal group ($p>0.05$). There were no significant changes in other domains or in the total scores in both groups ($p>0.05$). However, worsening of dyspareunia and total scores were noted in the premenopausal group following surgery in over one-third of these patients.

Biologic Grafts

Few studies have been published concerning the usage of biologic grafts in vaginal POP repairs. The majority of studies demonstrating the use of xenografts for POP have been conducted using porcine dermis. Gomelsky et al. did a retrospective review of 70 patients with high grade cystoceles who underwent repair using a 6×8 cm piece of porcine dermis sutured to the ATFP [129]. At a mean follow-up of 24 months, 61 patients (87 %) had no cystocele. Of the nine patients (13 %) with recurrence, none were symptomatic. One patient had a superficial vaginal wound separation which was treated with conservative measures.

Meschia et al. performed a prospective randomized controlled study to compare anterior colporrhaphy in 103 women using absorbable suture to the same repair in 98 women where the colporrhaphy was reinforced with a 4×7 cm piece of Pelvicol. All women had a POP-Q stage II or greater anterior vaginal wall prolapse [130]. At 1-year of follow-up, the failure rate of the Pelvicol group was 7 % versus 19 % in the anterior colporrhaphy group ($p=0.019$). One patient in the graft group experienced extrusion of the biologic material month after surgery. No differences were seen between the groups with regard to postoperative dyspareunia.

Apical Vaginal Compartment

Many pelvic surgeons believe that the cornerstone of vaginal support is the vaginal apex [92]. McCall et al. first described the landmark technique of posterior culdoplasty in 1957, which suspends the vaginal vault with sutures that bring the uterosacral ligaments together [131].

Uterosacral Ligament Suspension

There are various techniques of vaginal apical repairs using the uterosacral ligaments, and this procedure can be done with or without concomitant hysterectomy. The vaginal epithelium is dissected away from the peritoneum of the hernia sac. Once mobilized, the peritoneum is entered and the sac is excised (Fig. 13.5). Allis clamps are placed at the 5-o'clock and 7-o'clock positions of the vaginal apex in order to tent the uterosacral ligaments. Suspensory sutures in the uterosacral ligaments are then placed in the most apical portions of the pubocervical and rectovaginal fascia. The more distal sutures are placed most laterally in the fascia, and the highest sutures are sewn to the most medial portions. Cystoscopy with indigo carmine is essential because the course of the uterosacral ligaments is variable in relation to the ureters and injury is not uncommon [132]. The uterosacral ligaments may also be accessed transabdominally [133].

Overall series reporting on uterosacral ligament suspension are limited, usually having only a very small proportion of patients with stage II or higher apical prolapse or having a short duration of follow-up. Shull et al. reported on a series of 289 patients who underwent uterosacral ligament suspension who returned for at least one follow-up visit [132]. Eighty-seven percent had no recurrence; however, only 5 % of patients had grade 2 prolapse or greater. Ten patients developed grade 2 or 3 defects in the anterior compartment. One patient required ureteroneocystostomy and two patients required removal of suspensory sutures due to decreased urine flow from the affected ureter. Karram et al. reported on a series of 168 patients with an average age of 60 years who underwent vaginal vault suspension with uterosacral ligament suspension [134]. Uterosacral ligament suspension could not be performed in six patients because the enterocele sac could not be identified or exposure of the cul-de-sac could not be accomplished. Ten women underwent a repeat operation for recurrence of prolapse in one or more segments of the pelvic floor. There were five cases (2.4 %) of ureteral injury. One patient sustained an intraoperative small bowel injury and one patient developed a pelvic abscess requiring exploratory laparotomy and colostomy.

Sacrospinous Ligament Fixation

The sacrospinous ligament is a fibrous structure that attaches laterally to the ischial spine and medially to the lateral margin of the sacrum and coccyx. Important adjacent structures lying in close proximity include the pudendal nerves and vessels, the hypogastic plexus of veins, and the hemorrhoidal vessels. One of the main potential adverse consequences of sacrospinous ligament suspension is pudendal nerve entrapment which manifests as pain localized to the buttock or perineum. To avoid this complication, sutures should be placed 1.5–2.0 cm medial to the ischial spine, directly into the sacrospinous ligament [92].

The sacrospinous ligament may be approached through either an anterior or posterior vaginal approach. First a vaginal mucosal flap is created. The sacrospinous ligament is cleared off with blunt dissection. Sutures are then placed 1.5–2.0 cm medial to the ischial spine, usually one on each side. The sutures are brought through the vaginal epithelium or through the graft and tied down.

Anatomic success rates for sacrospinous ligament suspension are generally over 90 %, although most of the larger series are not contemporary. Nichols reported on a series of 163 patients who underwent sacrospinous ligament fixation, some with severe vaginal vault prolapse [135]. No recurrences were seen at follow-up, although nine patients perceived that their vaginas were too narrow postoperatively. Morley and DeLancey published a series of 100 patients who underwent sacrospinous ligament fixation, with 33 undergoing isolated apical treatment. Apical success was 95.7 %, with four patients developing prolapse in the anterior compartment. Complications included cystotomy, wound infection, voiding difficulty, and vaginal stenosis [84]. Sacrospinous ligament suspension also continues to be a major component of many vaginal mesh repair kits.

Abdominal Sacral Colpopexy

The benefits of abdominal sacral colpopexy are excellent proven long-term success and preservation of maximal vaginal length. The success rate in numerous series is greater than 90 % [136–138]. This procedure can be performed through an open abdominal, laparoscopic, or robotically assisted laparoscopic approach. However, due to increased morbidity, this repair may not be the best choice for many elderly patients. An update of the Cochrane Database review on the surgical management of POP was recently published [123]. While abdominal sacrocolpopexy had lower recurrent vault prolapse rates compared to sacrospinous suspension, there was a longer time to full return to the activities of daily life.

The key components of this procedure are the use of a type I, macroporous, monofilament permanent synthetic mesh, secure fixation of the graft to the sacral promontory and vaginal cuff, and complete enterocele reduction and culdoplasty [92]. An incision is made in the peritoneum over the sacral promontory extending inferior along the right lateral aspect of the sigmoid colon. The fatty tissue anteriorly is dissected free to expose the anterior surface of the sacral promontory. Care must be taken to avoid the presacral veins which can cause severe bleeding. The peritoneum over the vaginal cuff is excised and flaps are created anteriorly and posteriorly. Alternatively, if the uterus is still in place, the peritoneum is opened posterior to the uterus and the flap is dissected posteriorly between the rectum and the vagina. The Y-shaped mesh is secured to the vagina. Next the graft is fixed to the sacral promontory using non-absorbable sutures or a tacking device (see Fig. 13.6).

As previously mentioned, a Cochrane Database review was done to evaluate surgical management of POP [139]. The group found that three trials compared abdominal sacral colpopexy to vaginal sacrospinous colpopexy; however, the trials were quite heterogenous making analysis difficult. Abdominal sacral colpopexy had an advantage over vaginal sacrospinous colpopexy in terms of a lower rate of recurrent vault prolapse (RR 0.23, 95 %; CI 0.07–0.77) and less dyspareunia (RR 0.39, 95 % CI 0.18–0.86). However there was no statistically significant difference in reoperation rates for prolapse (RR 0.46, 95 %; CI 0.19–1.11). The vaginal sacrospinous colpopexy was quicker and less expensive to perform and women had an earlier return to activities of daily living.

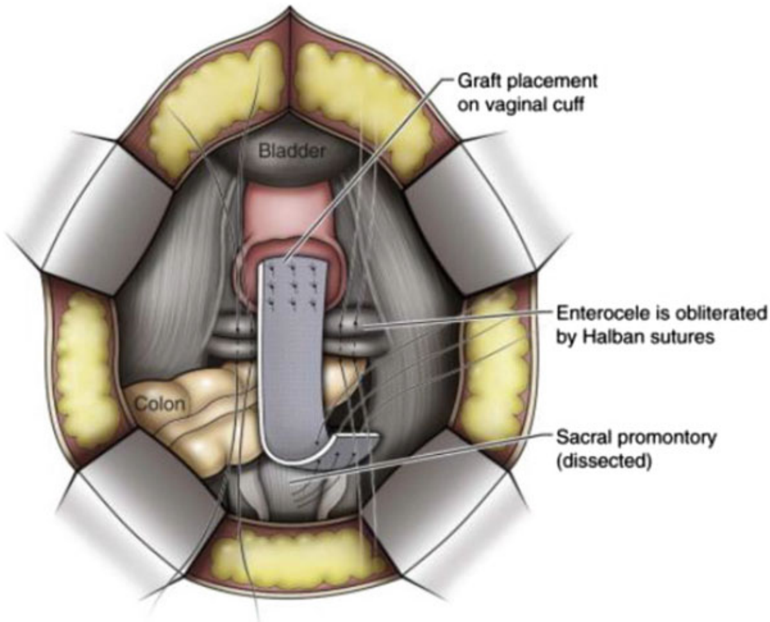


Fig. 13.6 Abdominal sacral colpopexy: Synthetic graft material is sutured securely to vaginal cuff using multiple interrupted permanent sutures. The peritoneal cul-de-sac is closed using linearly placed sutures to obliterate this potential space. (*From Winters J, Cespedes R, Vanlangendonck R. Abdominal sacrocolpopexy and abdominal enterocele repair in the treatment of vaginal vault prolapse. Urology 2000;56:55–63, with permission.*)

Maher et al. reported on a series of 108 patients with symptomatic stage ≥2 vault prolapse with 53 women randomized to laparoscopic sacral colpopexy and 55 women randomized to total vaginal mesh repairs [87]. Longer operative time was seen for the laparoscopic sacral colpopexy group. At 2-year review, the total objective success rate at all vaginal sites was 41 of 53 (77 %) for laparoscopic sacral colpopexy compared with 23 of 55 (43 %) in total vaginal mesh ($p<0.001$). No differences were seen between the groups in subjective outcomes. In the sacral colpopexy group, one patient developed a mesh-related complication compared to seven in the vaginal mesh group (p=0.006; OR 4.65, 95% CI 1.23-17.57).

Although sacral colpopexy has a very high success rate, there remains a postoperative risk of developing distal defects such as cystocele and rectocele [140]. Blanchard et al. reported on a series of 40 women with vault prolapse who underwent abdominal sacral colpopexy, culdoplasty, and paravaginal repair. Mean patient age was 67 years, and mean follow-up was 26 months. Eighteen (45 %) developed grade II or higher cystocele or rectocele which negatively influenced patient satisfaction.

Nygaard et al. reviewed complications of sacrocolpopexy [141]. The risk of transfusion or hemorrhage was 4 %, cystotomy 3 %, enterotomy 2 %, and ureteral injury 1 %. The risk of postoperative urinary tract infection was 11 %, wound infection 5 %, ileus 4 %, small bowel obstruction 1 %, and DVT or pulmonary embolus 3 %. The overall rate of mesh erosion was 3 %. Hence, although the abdominal sacral colpopexy procedure is highly successful, complications are not uncommon. One must carefully weigh the benefits and risks when considering this procedure in elderly patients with comorbidities.

Uterine Prolapse

Between 1988 and 1990, 16 % of all hysterectomies were done with an indication of POP. If the objective is to resolve a symptomatic prolapse, a vaginal vault suspension must be done concomitantly. In geriatric patients, due to increased morbidity, another option for correcting uterine prolapse is vaginal vault suspension. This can be accomplished using the sacrospinous ligament, the uterosacral ligaments, or by performing abdominal sacral colpopexy. Few studies have examined the effect of concomitant hysterectomy at the time of apical prolapse repair. Chu et al. compared outcomes of vaginal mesh reconstruction with and without concomitant hysterectomy in patients with POP-Q stage III and IV prolapse. Thirty-nine women underwent hysterectomy, and 52 had uterine preservation. Mean age of the hysterectomy group was 59 ± 10 years, which was significantly younger than in the uterine preservation group where mean age was 66 ± 8 years ($p = 0.003$). Operative time (129.3 vs. 97.2; $p < 0.001$), estimated blood loss (179.5 vs. 77.4; $p < 0.001$), and days of indwelling urinary catheter (2.7 vs. 2.4; $p = 0.006$) were significantly higher in the hysterectomy group compared to the uterine preservation group. One patient in the hysterectomy group required transfusion. There were no anatomical differences in outcome between the two groups other than a longer perineal body in the hysterectomy group ($p < 0.05$) and a longer total vaginal length in the uterine preservation group ($p < 0.05$). There were no significant differences for mesh extrusion, with 12.8 % in the hysterectomy group and 3.8 % in the uterine preservation group ($p = 0.134$).

Posterior Compartment

Patients with posterior compartment prolapse may complain of herniation symptoms, defecatory problems, and sexual dysfunction. Patients may also be completely asymptomatic. Because of this variability in bother, several groups have attempted to identify patient factors that predict who may benefit most from rectocele repair [142, 143]. These factors include sensation of vaginal mass or bulge, need for digital reduction to complete rectal evacuation, nonemptying or partial emptying on defecography, and presence of a large rectocele. In geriatric patients, unless a rectocele is bothersome and there is a high chance of patient satisfaction from repair, surgery may not be necessary. Hence, one must very carefully weigh the benefits and risks before undertaking surgery in elderly patients with posterior vaginal prolapse.

Posterior colporrhaphy is the mainstay of treatment for rectoceles and was originally described in the nineteenth century. An incision is made on the posterior vaginal epithelium. The rectovaginal fascia is separated from the vaginal epithelium. The dissection is carried lateral to expose the levator ani. The levator muscles are then plicated in the midline with interrupted or continuous 2–0 absorbable sutures. The excess vaginal mucosa is trimmed and a perineorrhaphy is done. Site-specific repairs have also been described with good success [144].

Anatomic success rates for posterior colporrhaphy in series range from 76 to 96 % [145, 146]. Paraiso et al. carried out a prospective study with patients with rectocele randomized to traditional posterior colporrhaphy using rectovaginal fascial plication, site-specific repair, or site-specific repair with porcine small intestinal submucosa graft [147]. They found that posterior colporrhaphy and site-specific rectocele repair had similar functional and anatomic outcomes. However, the addition of the porcine-derived graft did not improve anatomic outcomes. Rates of dyspareunia did not differ between the three groups. Abramov et al. did a retrospective review of patients with severe posterior prolapse comparing patients who underwent posterior repair to those who had site-specific repair [146]. Recurrence of posterior defects was higher in the site-specific group and rates of de novo dyspareunia and bowel symptoms were similar. Singh et al. published a prospective study of 42 women who underwent posterior colporrhaphy [148]. All subjects were evaluated for bowel, sexual, urinary, and prolapse symptoms as well as anatomic outcomes after fascial plication technique. At 6-week follow-up, 87 % had an improvement of bowel symptoms. At 18 months the estimated relief of vaginal symptoms was between 73 %

and 92 %. Sixty-five percent had improvement in their defecatory symptoms and 38 % had improvement in sexual discomfort. None of the patients reported de novo dyspareunia or bowel symptoms.

Synthetic and biologic grafts have been used in the posterior compartment with reasonable rates of success [149–151]. However, to date there is no evidence that the use of grafts improves anatomic outcomes when compared to a posterior repair without the use of a graft. Graft extrusion rates between 1 and 12 % have been reported [150, 151]. The most significant concern is the risk of dyspareunia from posterior repair with synthetic mesh. Some studies have suggested that the rate of dyspareunia can be as high as 60 % [152].

Obliterative Procedures

Colpocleisis refers to a vaginal procedure which obliterates the vaginal lumen. This procedure is commonly elected for the treatment of post-hysterectomy vaginal vault prolapse or severe uterine prolapse. It is only appropriate for patients who are no longer sexually active. In a study that surveyed older adults on their sexuality and health, researchers found that the prevalence of sexual activity among women aged 57–64, 65–74, and 75–85 years of age was 62 %, 40 %, and 17 %, respectively [153].

Potential benefits for geriatric patients include high success rates combined with minimal complications and reduced recuperative time [154, 155]. A total colpocleisis refers to removal of the vaginal epithelium to 0.5–2 cm from the urethral meatus with complete closure. In a Le Fort partial colpocleisis, used in cases of uterovaginal prolapse, lateral channels are created to allow uterine drainage.

For patients whose uterus is to be left in situ, preoperative evaluation should include a Papanicolaou smear, pelvic ultrasonography, and endometrial biopsy if indicated [92]. Performance of hysterectomy at the time of colpocleisis eliminates the risk of pyometra which is a serious complication of partial colpocleisis that may occur when the channels become obstructed [156]. However, most patients selected for colpocleisis are elderly and have significant comorbidities that would make the increased comorbidity from hysterectomy disadvantageous.

For a Le Fort partial colpocleisis, or Le Fort colpocleisis, the cervix is grasped with a tenaculum, and a rectangular segment of vaginal epithelium is marked anteriorly and posteriorly. The vaginal epithelium is excised from 3 cm from the urethral meatus to 3 cm from the cervix [155]. Starting at the leading edge of the prolapse, successive layers of 2–0 absorbable sutures are placed in transverse rows anteriorly and posteriorly until the prolapse is reduced. A high perineorrhaphy is performed by removing a triangular segment of vaginal epithelium posteriorly. The fibromuscular tissues of the perineal body are plicated together with absorbable sutures to narrow the introitus. Cystoscopy should be performed with administration of indigo carmine to confirm patency of the ureters. Success rates have been reported between 91 and 100 % with a follow-up of 180 months [157, 158]. Goldman et al. reported results on 118 women who underwent Le Fort partial colpocleisis. There were three recurrences that did not require additional operative management [157]. One patient developed a pulmonary embolus and one a urinary tract infection. Langmade and Oliver published a series of 102 patients who underwent partial colpocleisis with a mean follow-up of 35 months [158]. No recurrences were observed. Sixteen patients had transient postoperative urinary retention. No patients regretted their inability to engage in sexual intercourse.

In total colpocleisis lateral channels are not left in place. The vaginal vault is grasped and the entire epithelium is denuded from the apex to 3 cm proximal to the urethral meatus. Purse string 2.0 delayed absorbable sutures are placed beginning at the apex and are tied down until the entire prolapse is reduced (see Fig. 13.7). In multiple series the anatomic success rate of colpocleisis has been reported to be 97–100 % with follow-up to 5 years [154, 155, 159]. Von Pechmann et al. performed colpocleisis on 92 women [160]. Patients underwent physical examination at follow-up visits and were also interviewed by telephone. Although the ana-

Fig. 13.7 Total colpocleisis. (**a**) A circumferential incision is created at the base of the prolapse. (**b**) Purse-string sutures are placed in the prolapsed tissues to reduce it. (**c**) The vaginal epithelium is closed transversely. (*From Delancey JO, Morley GW. Total colpocleisis for vaginal eversion. Am J Obstet Gynecol 1997*;*176*:*1228–35*, *with permission*.)

tomic success rate was 98 % at 64 months, eight (13 %) patients expressed regret over loss of coital ability.

Fitzgerald et al. reported on a series of 152 patients with mean age 79 ± 6 years and POP-Q stage III or IV prolapse who underwent total (42 %) or partial (58 %) colpocleisis with follow-up to 12 months in 103 (68 %) patients [154]. Seventy-one (47 %) patients also underwent concomitant incontinence procedures. Intraoperative complications included one cystotomy and one urethral injury. During the year following the initial procedure, one patient required repeat colpocleisis and three patients required suburethral sling procedures for urinary incontinence. Twelve months after surgery, looking back on their decision to have vaginal closure, 125 (84 %) were very satisfied or satisfied. One patient was dissatisfied and one very dissatisfied.

Postoperative urinary retention and SUI may develop after colpocleisis [154, 158]. Hence it is recommended that all women be screened for occult stress incontinence prior to repair. Anti-incontinence procedures may be done concomitantly in women where it is indicated.

Conclusions

The prevalence of POP in older women is very high. In geriatric patients, a very thorough evaluation that includes assessment of objective vaginal prolapse, correlation with patient symptoms, and preoperative counseling about options is necessary before electing surgical treatment. Both conservative and surgical management are appropriate, but that choice depends on patient factors including comorbidity, sexual activity, and symptomatic bother. With proportional growth of the aging population, healthcare practitioners will need to remain highly attentive to prolapse. Hopefully continued research on causative factors and additional scientific study on treatment outcomes will enable physicians to address these conditions in our geriatric patients in an effective manner. Ultimately the QOL of our older female patients will be better maintained with appropriate and cost-efficient care.

References

1. Swift S, Tate S, Nicholas J. Correlation of symptoms with degree of prolapse organ support in a general population of women: what is pelvic organ prolapse? Am J Obstet Gynecol. 2003;189(2):372–7.
2. Nygaard I, Bradley C, Brandt D. Pelvic organ prolapse in older women: prevalence and risk factors. Obstet Gynecol. 2004;104(3):489–97.
3. Olsen A, Smith V, Bergstrom J, Colling J, Clark A. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. Obstet Gynecol. 1997;89:501–6.
4. Nations U. World population ageing. 2009. http://www.un.org/esa/population/publications/WPA2009. Accessed 5 Dec 2011.
5. Luber K, Boero S, Choe J. The demographics of pelvic floor disorders: current observations and future projections. Am J Obstet Gynecol. 2001;184:1496–501.

6. Hendrix S, Clark A, Nygaard I, Aragaki A, Barnabei V, et al. Pelvic organ prolapse in the women's health initiative: gravity and gravidity. Am J Obstet Gynecol. 2002;186(6):1160–6.
7. PMIS Group. Risk factors for genital prolapse in non-hysterectomized women around menopause. Results from a large cross-sectional study in menopausal clinics in Italy. Eur J Obstet Gynecol Reprod Biol. 2000;93:135–40.
8. Swift S, Woodman P, O'Boyle A, et al. Pelvic Organ Support Study (POSST): the distribution, clinical definition, and epidemiologic condition of pelvic organ support defects. Am J Obstet Gynecol. 2005;192(3):795–806.
9. Mant J, Painter R, Vessey M. Epidemiology of genital prolapse: observations from the Oxford Family Planning Association study. Br J Obstet Gynaecol. 1997;104(5):579–85.
10. Rortveit G, Brown J, Thom D, et al. Symptomatic pelvic organ prolapse: prevalence and risk factors in a population based, racially diverse cohort. Obstet Gynecol. 2007;109(4):848–54.
11. Bradley C, Zimmerman M, Qi Y, Nygaard I. Natural history of pelvic organ prolapse in postmenopausal women. Obstet Gynecol. 2007;109(6):1396–403.
12. Kudish B, Iglesia C, Sokol R, et al. Effect of weight change on natural history of pelvic organ prolapse. Obstet Gynecol. 2009;113(1):81–8.
13. Spence-Jones C, Kamm M, Henry M, et al. Bowel dysfunction: a pathogenic factor in uterovaginal prolapse and urinary stress incontinence. Br J Obstet Gynaecol. 1994;101:147–52.
14. Blandon R, Bharucha A, Melton 3rd LJ, et al. Risk factors for pelvic floor repair after hysterectomy. Obstet Gynecol. 2009;113(3):601–8.
15. Swift S, Pound T, Dias J. Case–control study of etiologic factors in the development of severe pelvic organ prolapse. Int Urogynecol J Pelvic Floor Dysfunct. 2001;12(3):187–92.
16. Woodman P, Swift S, O'Boyle A, et al. Prevalence of severe pelvic organ prolapse in relation to job description and socioeconomic status: a multicenter cross-sectional study. Int Urogynecol J Pelvic Floor Dysfunct. 2006;17(4):340–5.
17. Chiaffarino F, Chatenoud L, Dindelli M, et al. Reproductive factors, family history, occupation and risk of urogenital prolapse. Eur J Obstet Gynecol Reprod Biol. 1999;82(1):63–7.
18. Richardson A, Lyon J, Williams N. A new look at pelvic relaxation. Am J Obstet Gynecol. 1976; 126(50):568–73.
19. DeLancey J, Morgan D, Fenner D, Kearney R, Guire K, et al. Comparison of levator ani muscle defects and function in women with and without pelvic organ prolapse. Obstet Gynecol. 2007;109:295–302.
20. Chapple C, Milsom I. Urinary incontinence and pelvic prolapse: epidemiology and pathophyisiology. In: Wein A, editor. Campbell-walsh urology. 10th ed. Philadelphia, PA: WB Saunders; 2011. p. 1871–95.
21. Delancey J, Hurd W. Size of the urogenital hiatus in the levator ani muscles in normal women and women with pelvic organ prolapse. Obstet Gynecol. 1998;91:364–8.
22. Busacchi P, Perri R, Paradisi C, Oliverio D, Santini S, et al. Abnormalities of somatic peptide-containing nerves supplying the pelvic floor of women with genitourinary prolapse and stress urinary incontinence. Urology. 2004;63(3):591–5.
23. Smith A, Hosker G, Warrell D. The role of partial denervation of the pelvic floor in the etiology of genitourinary prolapse and stress urinary incontinence of urine. A neurophysiological study. Br J Obstet Gynaecol. 1989;96(1):24–8.
24. Rinne K, Kirkinen P. What predisposes young women to genital prolapse? Eur J Obstet Gynecol Reprod Biol. 1999;84:23.
25. Tinelli A, Malvasi A, Rahimi S, et al. Age-related pelvic floor modifications and prolapse risk factors in postmenopausal women. Menopause. 2010;17: 201–12.
26. Goh J. Biomechanical and biochemical assessments for pelvic organ prolapse. Curr Opin Obstet Gynecol. 2003;15(5):391–4.
27. Jackson S, Avery N, Tarlton J, Eckford S, Abrams P, Bailey A. Changes in metabolism of collagen in genitourinary prolapse. Lancet. 1996;15(347): 1658–61.
28. Takano C, Girao M, Sartori M, Castro R, Arruda R, et al. Analysis of collagen in parametrium and vaginal apex of women with and without uterine prolapse. Int Urogynecol J Pelvic Floor Dysfunct. 2002;13(6):342–5.
29. Maolli P, Shand S, Zyczynski H, Gordy S, Meyn L. Remodeling of vaginal connective tissue in patients with prolapse. Obstet Gynecol. 2005;106:952–63.
30. Gabriel B, Denschlag D, Gobel H, et al. Uterosacral ligament in postmenopausal women with or without pelvic organ prolapse. Int Urogynecol J Pelvic Floor Dysfunct. 2005;16:475–9.
31. Carley M, Schaffer J. Urinary incontinence and pelvic organ prolapse in women with Marfan's or Ehlers Danlos syndrome. Am J Obstet Gynecol. 2000;182: 1021–3.
32. McIntosh L, Mallett V, Frahm J, Richardson D, Evans M. Gynecologic disorders in women with Ehlers–Danlos syndrome. J Soc Gynecol Investig. 1995;2(3):559–64.
33. Bailey A, Paul R, Knott L. Mechanisms of maturation and ageing of collagen. Mech Ageing Dev. 1998;106:1–56.
34. Boreham M, Wai C, Miller R, et al. Morphometric analysis of smooth muscle in the anterior vaginal wall of women with pelvic organ prolapse. Am J Obstet Gynecol. 2002;187:56–63.
35. Reisenauer C, Shiozawa T, Oppitz M, et al. The role of smooth muscle in the pathogenesis of pelvic organ prolapse. An immunohistochemical and morphometric analysis of the cervical third of the utero-

sacral ligament. Int Urogynecol J Pelvic Floor Dysfunct. 2008;19:383–9.
36. Ellerkmann R, Cundiff G, Melick C, et al. Correlation of symptoms with location and severity of pelvic organ prolapse. Am J Obstet Gynecol. 2001;185:1332–8.
37. Tan J, Lukacz E, Menefee S, et al. Predictive value of prolapse symptoms: a large database study. Int Urogynecol J Pelvic Floor Dysfunct. 2005;16:203–9.
38. Burrows L, Meyn L, Walters M, Weber A. Pelvic symptoms in women with pelvic organ prolapse. Am J Obstet Gynecol. 2004;104:982–8.
39. Baden W, Walker T. Genesis of the vaginal profile: a correlated classification of vaginal relaxation. Clin Obstet Gynecol. 1972;15(4):1048–54.
40. Bump R, Mattiasson A, Bo K, et al. The standardization of terminology of female pelvic organ prolapse and pelvic floor dysfunction. Am J Obstet Gynecol. 1996;175(1):10–7.
41. Rogers R, Coates K, Kammerer-Doak D, et al. A short form of the pelvic organ prolapse/urinary incontinence sexual questionnaire (PISQ-12). Int Urogynecol J Pelvic Floor Dysfunct. 2003;14:164–8.
42. Barber M, Kuchibhatla M, Pieper C, Bump R. Psychometric evaluation of 2 comprehensive condition-specific quality of life instruments for women with pelvic floor disorders. Am J Obstet Gynecol. 2001;185:1388–95.
43. Boyadzhyan L, Raman S, Raz S. Role of static and dynamic MR imaging in surgical pelvic floor dysfunction. Radiographics. 2008;28(4):949–67.
44. Maubon A, Aubard Y, Berkane V, et al. Magnetic resonance imaging of the pelvic floor. Abdom Imaging. 2003;28:217–25.
45. Comiter C, Vasavada S, Barbaric Z, et al. Grading pelvic floor prolapse and pelvic floor relaxation using dynamic magnetic resonance imaging. Urology. 1999;54:454–7.
46. Cortes E, Reid W, Singh K, et al. Clinical examination and dynamic magnetic resonance imaging in vaginal vault prolapse. Obstet Gynecol. 2004;103:42–6.
47. Gousse A, Barbaric Z, Safir M, et al. Dynamic half Fourier acquisition, single shot turbo spin-echo magnetic resonance imaging for evaluating the female pelvis. J Urol. 2000;164(5):1606–13.
48. Bai S, Jeon M, Kim J, et al. Relationship between stress urinary incontinence and pelvic organ prolapse. Int Urogynecol J Pelvic Floor Dysfunct. 2002;13:256–60.
49. Romanzi L, Chaikin D, Blaivas J. The effect of genital prolapse on voiding. J Urol. 1999;161:581–6.
50. Bergman A, Koonings P, Ballard D. Predicting postoperative urinary incontinence development in women undergoing operation for genitourinary prolapse. Am J Obstet Gynecol. 1988;158:1171–5.
51. Chaikin D, Groutz A, Blaivas J. Predicting the need for anti-incontinence surgery in continent women undergoing repair of severe urogenital prolapse. J Urol. 2000;163:531–4.
52. Richardson D, Bent A, Ostergard D. The effect of uterovaginal prolapse on urethrovesical pressure dynamics. Am J Obstet Gynecol. 1983;15:901–5.
53. Stanton S, Hilton P, Norton C, et al. Clinical and urodynamic effects of anterior colporrhaphy and vaginal hysterectomy for prolapse with and without incontinence. Br J Obstet Gynaecol. 1982;89:459–63.
54. Borstad E, Rud T. The risk of developing urinary stress incontinence after vaginal repair in continent women: a clinical and urodynamic follow up study. Acta Obstet Gynecol Scand. 1989;68:545–9.
55. Ballert K, Biggs G, Isenalumhe AJ, et al. Managing the urethra at transvaginal pelvic organ prolapse repair: a urodynamic approach. J Urol. 2009;181(2):679–84.
56. Elser D, Moen M, Stanford E, et al. Abdominal sacrocolpopexy and urinary incontinence: surgical planning based on urodynamics. Am J Obstet Gynecol. 2010;202(4):375.e1–5.
57. Brubaker L, Cundiff G, Fine P, et al. Abdominal sacrocolpopexy with Burch colposuspension to reduce urinary stress incontinence. N Engl J Med. 2006;354(15):1557–66.
58. Visco A, Brubaker L, Nygaard I, Network PFD, et al. The role of preoperative urodynamic testing in stress-continent women undergoing sacrocolpopexy: the colpopexy and urinary reduction efforts (CARE) randomized surgical trial. Int Urogynecol J Pelvic Floor Dysfunct. 2008;19(5):607–14.
59. Roovers J, van Laar J, Loffeld C, et al. Does urodynamic investigation improve outcome in patients undergoing prolpase surgery? Neurourol Urodyn. 2007;26:170–5.
60. Kobashi K. Evaluation of patients with urinary incontinence and pelvic prolapse. In: Wein A, editor. Campbell-Walsh urology. 10th ed. Philadelphia, PA: WB Saunders; 2011. p. 1896–908.
61. Chen C, Walters M. Pelvic organ prolapse: clinical diagnosis and presentation. In: Raz S, Rodriguez LV, editors. Female urology. 3rd ed. Philadelphia, PA: WB Saunders; 2008. p. 556–3.
62. Sieber F, Pauldine R. Miller's anesthesia. 7th ed. Philadelphia, PA: Churchill Livingston; 2009.
63. John A, Sieber F. Age associated issues: geriatrics. Anesthesiol Clin North Am. 2004;22:45–58.
64. Dzankic S, Pastor D, Gonzalez C, et al. The prevalence and predictive value of abnormal laboratory test in elderly surgical patients. Anesth Analg. 2001;93:301–8.
65. Fischer S, Bader A, Sweitzer B. Preoperative evaluation. In: Miller R, editor. Miller's anesthesia. 7th ed. Philadelphia, PA: Churchill Livingston; 2009. p. 1001–66.
66. Tait A, Parr H, Tremper K. Evaluation of the efficacy of routine preoperative electrocardiogram. J Cardiothorac Vasc Anesth. 1997;11:752–5.
67. Liu L, Dzankic S, Leung J. Preoperative electrocardiogram abnormalities do not predict postoperative

cardiac complications in geriatric surgical patients. J Am Geriatr Soc. 2002;50:1186–91.
68. Fleisher L, Beckman J, Brown K, et al. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care noncardiac surgery: executive summary: a report of the American College of Cardiology/American heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Preoperative Cardiovascular Evaluation for Noncardiac Surgery). Circulation. 2007;116:1971–96.
69. Smith F, Holman D, Moorin R, Tsokos N. Lifetime risk of undergoing surgery for pelvic organ prolapse. Obstet Gynecol. 2010;116(5):1096–100.
70. Fialkow M, Newton K, Lentz G. Lifetime risk of surgical management for pelvic organ prolapse or urinary incontinence. Int Urogynecol J Pelvic Floor Dysfunct. 2008;19:437–40.
71. Novara G, Artibani W. Surgery for pelvic organ prolapse: current status and future perspectives. Curr Opin Urol. 2005;15:256–62.
72. Hagen S, Stark D. Conservative prevention and management of pelvic organ prolapse in women. Cochrane Database Syst Rev. 2011;12.
73. Braekken I, Majida M, Engh M, Bø K. Can pelvic floor muscle training reverse pelvic organ prolapse and reduce prolapse symptoms? An assessor-blinded, randomized, controlled trial. Am J Obstet Gynecol. 2010;203(2):170.e1–7.
74. Goldstein S, Neven P, Zhou L, Taylor Y, Ciaccia A. Raloxifene effect on frequency of surgery for pelvic floor relaxation. Obstet Gynecol. 2001;98: 91–6.
75. Ismail S, Bain C, Hagen S. Oestrogens for treatment or prevention of pelvic organ prolapse in postmenopausal women. Cochrane Database Syst Rev. 2010;9.
76. Sarma S, Ying T, Moore K. Long-term vaginal ring pessary use: discontinuation rates and adverse events. BJOG. 2009;116:1715–21.
77. Lone F, Thakar R, Sultan A, Karamalis G. A 5-year prospective study of vaginal pessary use for pelvic organ prolapse. Int J Gynaecol Obstet. 2011;114(1): 56–9.
78. Friedman S, Sandhu K, Wang C, Mikhail M, Banks E. Factors influencing long-term pessary use. Int Urogynecol J. 2010;21:673–8.
79. Maher C, Baessler K. Surgical management of anterior vaginal wall prolapse: an evidence based literature review. Int Urogynecol J Pelvic Floor Dysfunct. 2006;17:195–201.
80. Uebersax JS, Wyman J, Shumaker SA, McClish DK, Fantl JA, & the Continence Program for Women Research Group. Short forms to assess life quality and symptom distress for urinary incontinence in women: the Incontinence Impact Questionnaire and the Urogenital Distress Inventory. Neurology and 1995;14(2):131–9.
81. Barber MD, Walters MD, Bump RC. Short forms of two condition-specific quality of life questionnaires for women with pelvic floor disorder (PFDI-20 and PFIQ-7). Am J Ob Gyn. 2005;193:103–113.
82. Van Rooyen J, Cundiff G. Surgical management of pelvic organ prolapse. In: Cundiff G, Bent A, Ostergaard D, Swift S, editors. Ostergaard's urogynecology and pelvic floor dysfunction. Philadelphia, PA: Lippincott Williams & Wilkins; 2005.
83. Winters J, Togami J, Chermansky C. Vaginal and abdominal reconstructive surgery for pelvic organ prolapse. In: Wein AJ, editor. Campbell-walsh urology. Philadelphia, PA: Elsevier; 2011.
84. Morley G, DeLancey J. Sacrospinous ligament fixation for eversion of the vagina. Am J Obstet Gynecol. 1988;158:872–81.
85. Maher C, Qatawneh A, Dwyer P, Carey M, Cornish A, Schluter P. Abdominal sacral colpopexy or vaginal sacrospinous colpopexy for vaginal vault prolapse: a prospective randomized study. Am J Obstet Gynecol. 2004;190:20–6.
86. Benson J, Lucente V, McClellan E. Vaginal versus abdominal reconstructive surgery for the treatment of pelvic support defects: a prospective randomized study with long-term outcome evaluation. Am J Obstet Gynecol. 1996;175:1418–22.
87. Maher C, Feiner B, DeCuyper E, Nichlos C, Hickey K, O'Rourke P. Laparoscopic sacral colpopexy versus total vaginal mesh for vaginal vault prolapse: a randomized trial. Am J Obstet Gynecol. 2011:204:360.e1–7.
88. Kenton K, Pham T, Mueller E, Brubaker L. Patient preparedness: an important predictor of surgical outcome. Am J Obstet Gynecol. 2007;197(654):e1–6.
89. ACOG Committee on Practice Bulletins–Gynecology. ACOG practice bulletin No. 104: antibiotic prophylaxis for gynecologic procedures. Obstet Gynecol. 2009;113(5):1180–9.
90. Wolf J, Bennett C, Dmochowski R, Hollenbeck B, Pearle M, Schaeffer A, editors. Best practice policy statement on urologic surgery antimicrobial prophylaxis. Linthicum, MD: American Urological Association; 2011.
91. Geerts W, Pineo G, et al. Prevention of venous thromboembolism: the seventh ACCP conference on antithrombotic and thrombolytic therapy. Chest. 2004;126(3 Suppl):338S–400.
92. Winters J, Togami J, Chermansky C. Vaginal and abdominal reconstructive surgery for pelvic organ prolapse. In: Wein A, editor. Campbell-Walsh urology, vol. 3. Philadelphia, PA: Elsevier; 2012. p. 2069–114.
93. Higgins E, Rao A, Baumann S, et al. Effect of estrogen replacement on the histologic response to polypropylene mesh implanted in the rabbit vagina model. Am J Obstet Gynecol. 2009;201(5):505.e1–9.
94. Administration FUSFaD: FDA public health notification: serious complications associated with transvaginal placement of surgical mesh in repair of pelvic organ prolapse and stress urinary incontinence. 2011. http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm262435.htm. Accessed 18 Dec 2011.
95. Altman D, Väyrynen T, Engh M, Axelsen S, Falconer C, Group. NTM. Anterior colporrhaphy

versus transvaginal mesh for pelvic-organ prolapse. N Engl J Med. 2011;364(19):1826–36.
96. Togami J, Krilin R, Winters J. Graft materials in prolapse surgery. AUA Update Series. 2008;27(31): 1764–71.
97. Choe J, Bell T. Genetic material is present in cadaveric dermis and cadaveric fascia lata. J Urol. 2001;166:122–4.
98. Deprest J, Zheng F, Konstantinovic M, et al. The biology behind fascial defects and the use of implants in pelvic organ prolapse repair. Int Urogynecol J Pelvic Floor Dysfunct. 2006;17:S16–25.
99. Badylak S, Kokini K, Tullius B, Simmons-Byrd A, Morff R. Morphologic study of small intestinal submucosa as a body wall repair device. J Surg Res. 2002;103:190–202.
100. Cole E, Gomelsky A, Dmochowski R. Encapsulation of a porcine dermis pubovaginal sling. J Urol. 2003;170:1950.
101. Taylor G, Moore R, Miklos J, Mattox T. Posterior repair with perforated porcine dermal graft. Int Braz J Urol. 2008;34:84–90.
102. Medical B. 2011. http://www.bardmedical.com/PELVICOLAcellularCollagenMatrix. Accessed 18 Dec 2011.
103. Medical C. 2011. http://www.cookmedical.com/uro/dataSheet.do?id=5165. Accessed 18 Dec 2011.
104. Goldstein HB, Maccarone J, Naughton MJ, Aguirre OA, Patel RC. A multicenter prospective trial evaluating fetal bovine dermal graft (Xenform® Matrix) for pelvic reconstructive surgery. BMC Urol. 2010; 10(21):1–5.
105. Klinge U, Schumpelick V, Klosterhalfen B. Functional assessment and tissue response of short- and long-term absorbable surgical meshes. Biomaterials. 2001;22(11):1415–24.
106. Amid P. Classification of biomaterials and their related complications in abdominal wall hernia surgery. Hernia. 1997;1:15–21.
107. Dietz H, Vancaillie P, Svehla M, Walsh W, Steensma A, Vancaillie T. Mechanical properties of urogynecologic implant materials. Int Urogynecol J Pelvic Floor Dysfunct. 2003;14(4):239–43.
108. Birch C. The use of prosthetics in pelvic reconstructive surgery. Best Pract Res Clin Obstet Gynaecol. 2005;19:979–91.
109. Tuschy B, Berlit S, Hornemann A, Sütterlin M, Bussen S. Morbidity in elderly women undergoing gynaecological pelvic floor surgery. Arch Gynecol Obstet. 2011;285(5):1295–300.
110. Ghezzi F, Uccella S, Cromi A, Bogani A. Surgical treatment for pelvic floor disorders in women 75 years or older: a single-center experience. Menopause. 2011;18(3):314–8.
111. Gabriel B, Rubod C, Córdova L, Lucot J, Cosson M. Prolapse surgery in women of 80 years and older using the Prolift™ technique. Int Urogynecol J. 2010;12:1463–70.
112. Kelly HA. Incontinence of urine in women. Urol Cutaneous Rev. 1913;17:291–93.
113. Porges R, Smilen S. Long-term analysis of the surgical management of pelvic support defects. Am J Obstet Gynecol. 1994;171:1518–26.
114. Weber A, Walters M, Piedmonte M, Ballard L. Anterior colporrhaphy: a randomized trial of three surgical techniques. Am J Obstet Gynecol. 2001;185(6):1299–304.
115. White GR. Cystocele. A radical cure by suturing lateral sulci of vagina to white line of pelvic fascia. JAMA 1909;80(21):1707–10.
116. Shull B, Benn S, Kuehl T. Surgical management of prolapse of the anterior vaginal segment: an analysis of support defects, operative morbidity, and anatomic outcome. Am J Obstet Gynecol. 1994;171(6): 1429–36.
117. Young S, Daman J, Bony L. Vaginal paravaginal repair: one-year outcomes. Am J Obstet Gynecol. 2001;185:1360–7.
118. Elkins T, et al. Transvaginal paravaginal repair: a useful adjunctive procedure in pelvic relaxation surgery. J Pelvic Surg. 2000;6:11–5.
119. Fatton B, Amblard J, Debodinance P, Cosson M, Jacquetin B. Transvaginal repair of genital prolapse: preliminary results of a new tension-free vaginal mesh (Prolift technique)—a case series multicentric study. Int Urogynecol J Pelvic Floor Dysfunct. 2007;18(7):743–52.
120. Elmér C, Altman D, Engh M, Axelsen S, Vayrynen T, Falconer C. Trocar-guided transvaginal mesh repair of pelvic organ prolapse. Obstet Gynecol. 2009;113:117–26.
121. Abdel-Fattah M, Ramsay I. Retrospective multicentre study of the new minimally invasive mesh repair devices for pelvic organ prolapse. BJOG. 2008;115: 22–30.
122. Feiner B, Jelovsek J, Maher C. Efficacy and safety of transvaginal mesh kits in the treatment of prolapse of the vaginal apex: a systematic review. BJOG. 2009;116:15–24.
123. Maher C, Feiner B, Baessler K, Glazener C. Surgical management of pelvic organ prolapse in women: the updated summary Cochrane review. Int Urogynecol J. 2011;22:1445–57.
124. Nicita G. A new operation for genitourinary prolapse. J Urol. 1998;160:741–5.
125. de Tayrac R, Deffieux X, Gervaise A, Chauveaud-Lambling A, Fernandez H. Long-term anatomical and functional assessment of trans-vaginal cystocele repair using a tension-free polypropylene mesh. Int Urogynecol J Pelvic Floor Dysfunct. 2006;17(5): 483–8.
126. Hiltunen R, Nieminen K, Takala T, et al. Low-weight polypropylene mesh for anterior vaginal wall prolapse: a randomized controlled trial. Obstet Gynecol. 2007;110(2 Pt 2):455–62.
127. Rzepka J, Brocker K, Alt C, Corteville C, Sohn C, Lenz F. Pelvic organ prolapse: does the postoperative course of mesh-repair surgery differ in elderly women when compared with younger patients? J Obstet Gynaecol. 2010;30(8):852–6.

128. Long C, Hsu C, Wu M, Lo T, Liu C, Tsai E. Comparison of the changes in sexual function of premenopausal and postmenopausal women following transvaginal mesh surgery. J Sex Med. 2011;8(7): 2009–16.
129. Gomelsky A, Rudy D, Dmchowski R. Porcine dermis interposition graft for repair of high grade anterior compartment defects with or without concomitant pelvic organ prolapse procedures. J Urol. 2004;171:1581–4.
130. Meschia M, Pifarotti P, Bernasconi F, Magatti F, Riva D, Kocjancic E. Porcine skin collagen implants to prevent anterior vaginal wall prolapsed recurrence: a multicenter, randomized study. J Urol. 2007;177:192–5.
131. McCall M. Posterior culdoplasty. Obstet Gynecol. 1957;10:595–602.
132. Shull B, Bachofen C, Coates K, Kuehl T. A transvaginal approach to repair of apical and other associated sites of pelvic organ prolapse with uterosacral ligaments. Am J Obstet Gynecol. 2000;183: 1365–74.
133. Lowenstein L, Fitz A, Kenton K, FitzGerald M, Mueller E, Brubaker L. Transabdominal uterosacral suspension: outcomes and complications. Am J Obstet Gynecol. 2009;200(6):656.e1–5.
134. Karram M, Goldwasser S, Kleeman S, Steele A, Vassallo B, Walsh P. High uterosacral vaginal vault suspension with fascial reconstruction for vaginal repair of enterocele and vaginal vault prolapse. Am J Obstet Gynecol. 2001;185(6):1339–42.
135. Nichols D. Sacro-spinous fixation for massive eversion of the vagina. Am J Obstet Gynecol. 1982;142:901–4.
136. Snyder T, Krantz K. Abdominal-retroperitoneal sacral colpopexy for the correction of vaginal prolapse. Obstet Gynecol. 1991;77:944–9.
137. Daneshgari F, Paraiso M, et al. Robotic and laparoscopic female pelvic floor reconstruction. BJU Int. 2006;98 Suppl 1:62–8.
138. Menefee S, et al. Results of abdominal sacral colpopexy using polyester mesh in the treatment of posthysterectomy vaginal vault prolapse and enterocele. Obstet Gynecol. 1999;154:563–5.
139. Maher C, Feiner B, Baessler K, Glazener C. Surgical management of pelvic organ prolapse in women. Cochrane Database Syst Rev. 2010;4.
140. Blanchard K, Vanlangendonck R, Winters J. Recurrent pelvic floor defects after abdominal sacral colpopexy. J Urol. 2006;175(3 Pt 1):1010–3.
141. Nygaard I, McCreery R, Brubaker L, et al. Abdominal sacrocolpopexy: a comprehensive review. Obstet Gynecol. 2004;104(4):805–23.
142. Murthy V, et al. Excellent outcome using selective criteria for rectocele repair. Dis Colon Rectum. 1996;39:374–8.
143. Watson S, Loder P, Halligan S, et al. Transperineal repair of symptomatic rectocele with Marlex mesh: a clinical, physiological and radiologic assessment of treatment. J Am Coll Surg. 1996;183:257–61.
144. Richardson A. The rectovaginal septum revisited: its relationship to rectocele and its importance in rectocele repair. Clin Obstet Gynecol. 1993;36:976–83.
145. Khan M, Stanton S. Posterior colporrhaphy: its effects on bowel and sexual function. Br J Obstet Gynaecol. 1997;104:882–6.
146. Abramov Y, et al. Site-specific rectocele repair compared with standard posterior colporrhaphy. Obstet Gynecol. 2005;105:314–8.
147. Paraiso M, et al. Rectocele repair: a randomized trial of three surgical techniques including graft augmentation. Am J Obstet Gynecol. 2006;195:1762–71.
148. Singh K, et al. Evaluation of the fascial technique for surgical repair of isolated posterior vaginal wall prolapse. Obstet Gynecol. 2003;101:320–4.
149. Kohli N, Miklos J. Dermal graft-augmented rectocele repair. Int Urogynecol J Pelvic Floor Dysfunct. 2003;14:146–9.
150. Kobashi K, Leach G, Frederick R, et al. Initial experience with rectocele repair using nonfrozen cadaveric fascia lata interposition. Urology. 2005;66:1203–8.
151. de Tayrac R, Picone O, Chauveaud-Lambling A, Fernandez H. A 2-year anatomical and functional assessment of transvaginal rectocele repair using a polypropylene mesh. Int J Gynecol Obstet. 2006;17: 100–5.
152. Milani R, Salvatore S, et al. Functional and anatomical outcome of anterior and posterior vaginal prolapse repair with Prolene mesh. Br J Obstet Gynaecol. 2005;112:107–11.
153. Lindau S, Schumm L, Laumann E, et al. A study of sexuality and health among older adults in the United States. N Engl J Med. 2007;357:762–74.
154. Fitzgerald M, Richter H, Bradley C, et al. Pelvic support, pelvic symptoms, and patient satisfaction after colpocleisis. Int Urogynecol J Pelvic Floor Dysfunct. 2008;19(12):1603–9.
155. Cespedes R, Winters J, Ferguson K. Colpocleisis for the treatment of vaginal vault prolapse. Tech Urol. 2001;7(2):152–60.
156. Shayya R, Weinstein M, Lukacz E. Pyometra after Le Fort colpocleisis resolved with interventional radiology drainage. Obstet Gynecol. 2009;113(2 Pt 2):566–8.
157. Goldman J, Ovadia J, Feldberg D. The Neugebauer-Le Fort operation: a review of 118 partial colpocleisis. Eur J Obstet Gynecol Reprod Biol. 1981;12:31–5.
158. Langmade C, Oliver JJ. Partial colpocleisis. Am J Obstet Gynecol. 1986;154:1200–5.
159. DeLancey J, Morley G. Total colpocleisis for vaginal eversion. Am J Obstet Gynecol. 1997;176:1228–35.
160. von Pechmann W, Mutone M, Fyffe J, Hale D. Total colpocleisis with high levator plication for the treatment of advanced pelvic organ prolapse. Am J Obstet Gynecol. 2003;189:121–6.

Urinary Tract Infections in Older Adults

14

Tracey Small Wilson and Alayne D. Markland

Introduction

Urinary tract infection (UTI) and asymptomatic bacteriuria are common infectious illnesses in adults aged 65 and over [1]. The incidence rate approaches 10 % in women and 5.3 % in men over the age of 80 (ratio 2:1, women to men). Asymptomatic bacteriuria occurs in up to 6–16 % of women in the community and 25–50 % of women in nursing homes, with a frequency in men about half those numbers. With the use of chronic catheters, rates are even higher at about 85 % for condom catheters and nearly 100 % for indwelling catheters. Increasing antibiotic resistance among urinary tract-specific organisms is a problem, especially among older adults in nursing home settings. Gram-negative bacilli including *Escherichia coli*, *Enterobacter spp*., *Klebsiella spp*., and *Proteus spp*. remain the most common organisms associated with UTIs in older adults, but more resistant isolates such as *Pseudomonas aeruginosa*, gram-positive organisms including *Enterococcus fecalis* and *Enterococcus faecium*, coagulase-negative staphylococci, and Group B *Streptococcus agalactiae* are increasing, when compared to young adults. A significant amount of morbidity and mortality, as well high healthcare costs, are associated with UTIs in community-dwelling and nursing home populations.

Infections often present in subtle fashion in older adults. In addition to the frequent lack of fever, infections in older adults may be associated with a nonspecific decline in baseline functional status such as increased confusion, falling, and anorexia. Cognitive impairment further contributes to the atypical presentation of infections in older adults, reducing the capacity to communicate symptoms. Often, healthcare providers should evaluate objective assessments such as laboratory and radiologic evaluations in older adults suspected of having symptoms of an infection in cognitively impaired patients, unless advanced directives and goals of care indicate otherwise.

Healthcare providers who treat UTIs in older adults often face a difficult determination: what defines "symptomatic" in frail, often cognitively impaired older adults in community and various healthcare settings? Diagnosis of a UTI in an older adult relies on clinical signs and symptoms, supported by laboratory data. Urine cultures in infected older adults may have lower colony counts of 10^2–10^3 compared to standard criteria of 10^5 in younger patients [2]. Therapeutic antibi-

T.S. Wilson, M.D., F.A.C.S.
Department of Urology, University of Alabama at Birmingham, Birmingham, AL, USA
e-mail: traceywilson@uabmc.edu

A.D. Markland, D.O., M.Sc. (✉)
Department of Medicine, Division of Gerontology, Geriatrics and Palliative Care, University of Alabama at Birmingham, Birmingham, AL, USA

Department of Veterans Affairs Medical Center, Birmingham/Atlanta Geriatric Research, Education, and Clinical Center (GRECC); VA Medical Center, GRECC/11G, 700 19th St S, Birmingham, AL 35233, USA
e-mail: amarkland@aging.uab.edu

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_14,

Table 14.1 Type and definition of UTIs in older adults

Type of UTI	Definition	Population	Diagnostic criteria	Special considerations in older adults
Asymptomatic bacteriuria	Isolation of a specified quantitative count of bacteria in an appropriately collected urine specimen from an individual without symptoms or signs	Occurs more often in older women and in nursing home populations	Women: two separate urine cultures with the same organism with quantitative counts $\geq 10^5$ Men: one urine culture with counts $\geq 10^5$	Women: ≥ 10 leukocytes/mm^3 of uncentrifuged urine is not enough to diagnose a UTI Men: rare to have contaminated urine samples
Uncomplicated UTI	Isolation of a specified quantitative count of bacteria from a woman with a structurally and functionally normal urinary tract	Mostly younger women, some older women	10^5 cfu/mL on a voided, midstream sample Culture may be omitted if patient is symptomatic and dipstick is + for leukocyte esterase and nitrites	Check for negative culture after therapy to prevent partial treatment or resistance.
Complicated UTI	Isolation of a specified quantitative count of bacteria from an immunocompromised patient, or one with an abnormal urinary tract. *OR* the isolate has increased virulence or antimicrobial resistance	All men and most elderly women	Specific criteria are variable and may be associated with patient characteristics	Have low threshold for imaging studies or cystoscopy to rule out urinary stasis and/or stones
Recurrent UTI	UTIs recur over a specific time period after sufficient antibiotic treatment	More likely to occur in older women	Three or more culture proven infections within 12 months or two culture proven infections within 6 months	Need to distinguish between relapse (persistence) and reinfection
CAUTI	UTI that occurs in a symptomatic adult when the catheter is present or removed within the previous 48 h	Equal in both genders	One urine culture with ≥ 1 organism with quantitative counts $\geq 10^3$	Replace catheter prior to starting antibiotics, especially if present for > 2 weeks

otic "trials" are not recommended to avoid possible drug toxicity, drug–drug interaction, and antimicrobial resistance.

Clinical practice guidelines have been developed and recently updated for the evaluation and treatment of asymptomatic bacteriuria, complicated and uncomplicated UTIs, and catheter-associated UTIs (CAUTI). In this chapter, we will discuss these guidelines and mention important aspects of the evaluation and treatment of UTIs in older adults [3–6]. When a documented urinary tract infection meets the guideline criteria for treatment, therapy is based on the location of infection in the upper versus lower tract, complicated and uncomplicated individuals, and likely causative agent. Lower tract UTIs with acute cystitis, are characterized by dysuria, frequency, and urgency. Fever usually indicates upper tract disease with pyelonephritis. Fever is absent in 30–50 % of frail, older adults, even in the setting of serious infections and can limit the distinction between upper and lower UTIs. Complicated UTIs occur in individuals with structural or functional abnormalities which may further increase susceptibility to uropathogens and/or decrease therapeutic efficacy.

Table 14.1 summarizes the different types of UTIs and factors that may be unique to the older population that can influence therapy.

UTIs may necessitate different treatment in older women and men compared to younger patients. UTIs in men are frequently caused by concomitant prostate disease, primarily benign prostatic hyperplasia, or functional bladder impairment, such as poor bladder emptying due to diabetes with peripheral neuropathy. Thus, UTIs in men are considered complicated UTIs and short-course therapy in the older male is inappropriate. UTIs in men are discussed in greater detail in a later section of this chapter.

Asymptomatic Bacteriuria in Older Adults

Asymptomatic bacteriuria is defined as isolation of a specified quantitative count of bacteria in an appropriately collected urine specimen from an individual without symptoms or signs of urinary tract infection. Asymptomatic bacteriuria is not associated with long-term adverse outcomes such as chronic kidney disease or increased mortality [7].

The prevalence of asymptomatic bacteriuria among healthy women increases with advancing age. It reaches >20 % among women over 80 years residing in the community [7–10]. In older women, asymptomatic bacteriuria may last for long periods of time, even several weeks, and can reoccur, thus treatment can contribute to antibiotic-resistant organisms. Among community-dwelling men over 75 years, prevalence is 6–15 % [9]. Older adults in healthcare facilities, such as nursing homes or long-term care settings, have much higher rates of asymptomatic bacteriuria, approaching 50 % of women and 15–40 % of men [10].

Risk factors for asymptomatic bacteriuria in community-dwelling adults include previous UTIs, presence of a urinary catheter, and female gender. The presence of diabetes has been identified as a risk factor only in women, but not in men [9]. Prevalence of asymptomatic bacteriuria among diabetic women is 8–14 % and is usually correlated with duration and presence of long-term complications of diabetes, rather than with metabolic parameters of diabetes control [11]. Diabetic men do not appear to have a higher prevalence of bacteriuria than nondiabetic men.

Because of the difficulty in obtaining uncontaminated voided midstream urine specimens, quantitative thresholds have been established to distinguish bladder bacteriuria from urethral contamination. Asymptomatic bacteriuria is defined as isolation of a specified quantitative count of bacteria in an appropriately collected urine specimen from an individual without symptoms or signs of urinary tract infection. The quantitative thresholds are different for voided clean catch specimens and catheterized specimens. The presence of pyuria with ≥10 leukocytes/mm^3 of uncentrifuged urine is not sufficient for diagnosis of bacteriuria [8]. This was illustrated in a study of urine samples from asymptomatic elderly women, where 60 % of samples with pyuria had no bacteriuria [12].

Diagnostic criteria for clean-catch specimens including number of specimens and minimum quantitative bacteria counts are outlined for women and men in Table 14.1. Asymptomatic bacteriuria in women is defined by the 2005 Infectious Diseases Society of America (IDSA) guidelines as two consecutive clean-catch voided urine specimens with isolation of the same organism in quantitative counts of ≥10 cfu/mL [4]. A bacterial count of ≥10^5 cfu/mL in a catheterized specimen was confirmed by a repeat catheterized specimen in >95 % of cases among women. On the other hand, ≥10^5 cfu/mL documented in an initial voided urine specimen was confirmed in a second voided specimen in 80 % of cases. Two consecutive positive cultures predicted a third positive culture with 95 % confidence. Therefore, two consecutive voided specimens were needed to predict bladder bacteriuria with the same degree of accuracy as a single urine specimen obtained through a catheter in women.

Asymptomatic bacteriuria in men is defined as a single clean-catch voided urine specimen with isolation of a single organism in quantitative counts of ≥10^5 cfu/mL [4]. External contamination with a voided urine specimen among men is an unlikely cause of significant bacteriuria.

In asymptomatic catheterized men or women, bacteriuria is defined by the IDSA guidelines as a single catheterized specimen with isolation of a single organism in quantitative counts of ≥10^2 cfu/mL [4]. Catheterized specimens are less likely to be contaminated than voided specimens. Therefore, positive cultures of catheterized specimens are more likely to reflect true bladder bacteriuria even with low colony counts.

Table 14.2 Minimum criteria for the initiation of antibiotics for urinary tract infection in long-term care residents

With indwelling catheter
At least one of the following
Fever (>37.9 °C/100 °F or 1.5 °C/2.4 °F above baseline)
New CVA tenderness
New onset delirium
Without indwelling catheter
Acute dysuria *OR*
Fever (>37.9 °C/100 °F or 1.5 °C/2.4 °F above baseline) AND
At least one of the following
New or worsening urgency
Frequency
Suprapubic pain
Gross hematuria
CVA tenderness
Urinary incontinence

There have been no comparisons of culture yields from urethral catheterized specimens and suprapubic aspiration specimens.

Clinical guidelines from the Infectious Diseases Society of America for evaluation of infection in older residents of long-term care facilities advise that urinalysis and urine cultures should not be ordered for asymptomatic individuals [5]. Diagnostic testing and the initiation of antibiotics should be reserved for residents with fever, dysuria, gross hematuria, worsening urinary frequency and incontinence, costovertebral angle tenderness, or suspected bacteremia. Altered mental status or delirium is no longer part of the recommended evaluation for a possible UTI. However, if a long-term care resident has an indwelling catheter and delirium, along with fever and signs of systemic infection, initiation of antibiotics for a UTI are indicated by current practice guidelines. Evidence also suggests that treating asymptomatic bacteruria in long-term care patients who have stable incontinence does not improve incontinence in the short term [13]. See Table 14.2 for additional details.

The absence of symptoms in patients with asymptomatic bacteriuria could reflect characteristics specific to the pathogen, the host, or both. The microbiology of asymptomatic bacteriuria is similar to that of cystitis and pyelonephritis, although some strains capable of producing asymptomatic bacteriuria may have subtle adaptations. For example, attachment of bacteria via fimbrial adhesins is thought to be important for the establishment and persistence of symptomatic infection. Some bacterial strains with reduced capability for fimbriae expression appear to have the capacity for relatively rapid growth that allows them to cause asymptomatic bacteriuria [14]. Alternatively, strains implicated in asymptomatic bacteriuria may be less virulent and therefore may not necessarily be true pathogens [14].

Numerous studies suggest that there is no clinical benefit when asymptomatic bacteriuria is treated, but treatment can lead to significant side effects, expense, and potential for selection of resistant organisms [4, 15]. Thus, treatment is not recommended, even in the presence of white blood cells in the urine. There is also no role for screening for bacteriuria in older women, diabetic patients, patients with spinal cord injuries, patients with indwelling urinary catheters, or nursing home residents.

In certain situations, asymptomatic bacteriuria does need to be treated. For example, in patients undergoing specific urologic procedures, such as transurethral resection of the prostate and cystoscopy, there is a need for treatment of asymptomatic bacteriuria because of the risk of mucosal injury. Also, consideration should be given to older adults with asymptomatic bacteruria prior to hip arthroplasty. There are no specific large trials that have evaluated treatment of asymptomatic bacteriuria in these situations.

Case 1

Introduction. A 76-year-old woman presents to a urologist upon the referral of her primary care physician for evaluation of recurrent UTIs. She reports at least three infections detected in the last 6 months for which she has received antibiotics. Her antibiotic courses are usually 7–10 days. She does not like to take the antibiotics because she usually experiences GI upset and/or diarrhea. She does not recall symptoms of UTIs and states that she is usually

(continued)

(continued)

informed of these infections when she visits her doctor for routine visits regarding the management of her type II diabetes mellitus. She denies symptoms of a UTI including dysuria, urgency, or fever, but reports her baseline symptoms of urinary frequency and two episodes of nocturia. She will occasionally experience dysuria that resolves spontaneously and denies hematuria. She has mild urgency urinary incontinence requiring the use of three thin panty liners per day. She is not bothered by these symptoms and they persist while on antibiotics. She denies fecal incontinence but admits to constipation, reporting two bowel movements per week. Other comorbidities include hypertension, osteoarthritis, and hypothyroidism. She has a sulfa allergy.

Objective findings. She is alert and afebrile with stable vital signs. Her abdomen is non-tender, non-distended, and there is no costovertebral angle tenderness. The perineum is within normal limits without evidence of skin breakdown or fecal soiling. There is severe vaginal atrophy and no evidence of pelvic organ prolapse. Urine dipstick of a voided specimen reveals 2+ leukocytes, negative blood, positive for leukocyte esterase, and is positive for nitrites. Her post void residual urine volume is 50 mL. Review of her outside records indicates that she had two positive urine cultures for *Escherichia coli* with colony counts greater than 10^5 cfu/mL. However, she received antibiotics on four separate occasions over the last 6 months, including two courses of empiric treatment, always a 10-day course of nitrofurantoin. The organism was initially resistant to penicillins but sensitive to sulfa, nitrofurantoin, cephalosporins, and fluoroquinolones. On the most recent culture, the organism has developed resistance to nitrofurantoin.

Intervention. The provider elects not to order a urine culture since she is asymptomatic. She is given a prescription for vaginal estrogen cream to treat her atrophic vaginitis which is likely contributing to her occasional dysuria. She is instructed to discontinue the consumption of fluids 2 h prior to bedtime. She is asked to consume more water during the day and is given fiber supplements.

Follow up. The patient is evaluated 2 months later. She has not had any recurrent episodes of dysuria, her nocturia has resolved, and she is now having a bowel movement daily. Her urine dipstick remains positive for leukocytes, leukocyte esterase, and nitrites.

Uncomplicated UTI

Uncomplicated UTI describes an infection in an otherwise healthy patient with a structurally and functionally normal urinary tract. The majority of these patients are healthy, young women. However, some elderly female patients may be classified in this category although this is rare because so many of these patients experience recurrent episodes or have comorbidities. These factors would justify reclassifying them as having complicated UTIs. The clinical presentation of an uncomplicated UTI in a premenopausal woman differs from that in a postmenopausal woman [16]. Most younger patients present with local symptoms such as dysuria with or without frequency, urgency, suprapubic pain, or hematuria. Older women may present with unspecified symptoms such as abdominal pain, low back pain, constipation, cold chills, and nausea. These generalized symptoms are very important because they can lead to a delay in diagnosis and treatment of UTIs in older adults.

Acute uncomplicated cystitis rarely progresses to severe disease, even if untreated. The primary goal of therapy is to ameliorate symptoms. Uropathogenic *Escherichia coli* is the predominant pathogen in uncomplicated UTIs causing 75–95 % of episodes. However, there is a significant increase in the incidence of *Proteus*, *Klebsiella*, *Enterobacter*, *Serratia*, and *Pseudomonas* species, as well as enterococci. Bacteriuria due to gram-positive organisms is more common in elderly men than elderly women [17]. Polymicrobial bacteriuria is more common in geriatric patients [18].

Older adults are more susceptible than younger patients to the toxic and adverse effects of antimicrobial therapy because metabolism and excretion of antimicrobial agents may be impaired and the resulting increased serum levels can further damage renal function. Interactions with other medications are also of major concern. Additionally, the safety margin between therapeutic and toxic levels is significantly narrowed. Antimicrobials should be used judiciously in this population and drug levels monitored carefully when indicated. Patients with uncomplicated UTIs who present with lower urinary tract symptoms can usually be treated with a short course of 5–7 days of antimicrobial therapy. For patients with fever or a more severe systemic infection, 10–14 days of therapy is recommended. Again, the goal in this population is to eliminate symptoms, not sterilize the urine [19]. The choice of an antimicrobial agent should be individualized on the basis of the patient's allergy and compliance history, local practice patterns, the prevalence of resistance in the local community and in specific healthcare settings, availability, cost, and the patient and provider threshold for failure [6]. Trimethoprim–sulfamethoxazole (TMP-SMX), nitrofurantoin, and fosfomycin (used in European countries) are considered first-line agents for cystitis. Trimethoprim–sulfamethoxazole has been the most widely used antimicrobial agent for the treatment of acute UTI. TMP alone or in combination with SMX is effective against most common uropathogens, except *Enterococcus* and *Pseudomonas* species [20]. Nitrofurantoin is also effective against most uropathogens, but is not effective against *Pseudomonas* and *Proteus* species [21]. It is rapidly excreted from the urine but does not attain therapeutic levels in most body tissues, including the gastrointestinal tract. Therefore it is not useful for upper tract and complicated UTIs. However, if none of these are appropriate choices, fluoroquinolones or beta lactams are reasonable alternatives.

Fluoroquinolones are effective in the older population and the side effects are not more apparent than in the younger population. However, fluoroquinolones can cause QT interval prolongation and should be avoided in patients with a prolonged QT interval, uncorrected hypokalemia or hypomagnesemia, and in some patients receiving some anti-arrhythmics [22].

Complicated UTI

A complicated infection is one associated with factors that increase the chance of acquiring bacteria and decrease the efficacy of therapy (Table 14.3). The urinary tract may be functionally or structurally impaired, the host compromised, and/or the bacteria have increased virulence or antimicrobial resistance. Most older patients are considered to have complicated UTIs because they may be immunocompromised, have poor renal function affecting therapeutic choice, be hospitalized, or have acquired anomalies of the

Table 14.3 Factors that complicate urinary tract infections

General
Male gender
Pregnancy
Diabetes mellitus
Immunosuppression
Renal insufficiency
Urological
Nosocomial urinary tract infection
Foreign body
Intubated urinary tract
Urolithiasis
Anatomical abnormalities
Polycystic kidney disease
Medullary sponge kidney
Diverticula: calyceal, bladder, urethral
Vesicoureteral reflux
Ureteral or urethral obstruction
Renal artery stenosis or thrombosis
Voiding dysfunction
Surgery of the urinary tract
Antimicrobial resistance

urinary tract resulting in some form of urinary stasis. Common sources of urinary stasis in geriatric patients include hydronephrosis, bladder diverticulae, and urinary retention. Stone formation may occur in any of these locations secondary to stasis. Thus, older patients with characteristics of a complicated UTI should be evaluated with post-void residual determination, upper tract imaging with either renal ultrasound or CT scan, and possible cystoscopy. Cystoscopy should always be done in patients with persistent hematuria after microbial therapy or hematuria associated with other risk factors. In cases of complicated UTIs that are not associated with an indwelling catheter, the underlying urinary tract abnormality should be corrected, as UTIs associated with structural abnormalities including obstruction or hydronephrosis, or systemic disease such as severe diabetes mellitus can promptly lead to renal damage or sepsis in the older population. Although urinary retention is a source of stasis, research results are conflicted regarding the association of post-void residual volume and infection. If there is any association at all, it is likely population specific or only relevant at high volumes [23]. Nonetheless, urinary retention is oftentimes treated with an indwelling urethral catheter, which is a major associated cause of complicated UTIs.

A urethral catheter facilitates entry of bacteria or yeast into the bladder through several mechanisms. The most common route is ascension of bacterial biofilm along the tubing and catheter, with acquisition of bladder bacteriuria correlated with duration of catheterization [24]. Other modes of infection related to catheter use include inoculation of periurethral organisms into the bladder at the catheter insertion site, a problem sometimes seen in patients performing intermittent catheterization, or reflux of contaminated urine from the drainage bag or tubing that occurs when a catheter is mismanaged. Patients with a chronic indwelling catheter have a prevalence of bacteriuria or funguria of 100 %, but the incidence of acquisition of new organisms is 3–7 % per day that a catheter is left in place. Eighty percent of healthcare-acquired infections are attributed to an indwelling urinary catheters [23], and catheter acquired urinary infection (CAUTI) is the most common cause of bacteremia in long-term care facilities. If the prevalence of bacteruria or funguria is 100 % in patients with an indwelling catheter, the diagnosis of a UTI in these individuals can be challenging. The following section will address catheter-associated UTIs in detail.

Catheter-Associated Urinary Tract Infection

Catheter-associated urinary tract infection (CAUTI) in patients with indwelling urethral, suprapubic, or intermittent catheterization is defined by the presence of symptoms or signs compatible with UTI with no other identifiable source of infection, together with $\geq 10^3$ cfu/mL of ≥ 1 bacterial species in a single-catheterized urine specimen. In a patient whose urethral, suprapubic, or condom catheter has been removed within the previous 48 h, similar clinical parameters and culture results define the condition [3]. For patients in whom the catheter has been recently removed, the usual localizing symptoms of cystitis include frequency, urgency, and dysuria. However, the presentation is more subtle in the patient with an indwelling catheter, making the diagnosis one of exclusion. Localizing signs and symptoms that may be present include catheter obstruction, hematuria, costovertebral angle tenderness, urethritis, periurethral abscesses, epididymo-orchitis, and prostatitis.

Fever is a hallmark sign. More than 50 % of febrile episodes in individuals with chronic indwelling catheters are from a urinary source. Episodes of fever occur more frequently in long-term care facility residents with indwelling catheters than those without a catheter [10]. Additionally, the urinary tract is the source of bacteremia in patients with indwelling catheters who reside in long-term care facilities. Bacteremia is reported to be 3–39 times more common in residents with chronic indwelling catheters [25].

The best mode of defense against CAUTI is reducing the use of indwelling urinary catheters and removal of them as soon as they are no longer clinically necessary. An indwelling catheter

Table 14.4 Indications for indwelling catheter use by the Healthcare Infection Control Practices Advisory Committee

Acute urinary retention
Accurate measurement of urine output in critically ill patients
Selected perioperative use
Urologic or genitourinary surgery
Prolonged duration of surgery
Large-volume infusions or diuretics during surgery
Intraoperative monitoring of urine output
Assist in healing open sacral or perineal wounds for incontinent patients
Prolonged immobilization for spine or pelvic fractures
Comfort for end-of-life care

Table 14.5 Minimum criteria for the initiation of antibiotics for urinary tract infection in long-term care residents

With indwelling catheter
At least one of the following:
Fever (>37.9 °C/100 °F or 1.5 °C/2.4 °F above baseline)
New CVA tenderness
New onset delirium
Without indwelling catheter
Acute dysuria OR
Fever (>37.9 °C/100 °F or 1.5 °C/2.4 °F above baseline) AND
At least one of the following
New or worsening urgency
Frequency
Suprapubic pain
Gross hematuria
CVA tenderness
Urinary incontinence

should be inserted only for approved indications (Table 14.4) [23]. Insertion of an indwelling catheter should be avoided for the management of urinary incontinence alone. Alternate methods of bladder drainage that avoid an indwelling catheter such as intermittent catheterization or condom catheters for men should be considered whenever possible. There are no randomized comparative trials of intermittent catheterization versus an indwelling catheter, but multiple case studies support a decreased occurrence of symptomatic UTI with use of intermittent catheterization. In addition, a prospective randomized trial of condom or indwelling catheter use for men in a Veterans Administration hospital reported a significantly improved composite outcome of bacteruria, symptomatic infection or death, and improved patient comfort with the condom catheter [26].

In addition to the catheter avoidance approach, various other prevention strategies generally fall under the heading of different types of catheters, different catheter materials, or alternatives to indwelling catheters. Catheters have been coated with different antimicrobial materials including silver oxide (no longer available), silver alloy, and nitrofurazone. There is no evidence to date to support clinical benefit to the use of coated catheters and thus their routine use is not recommended.

Minimum criteria for the initiation of antibiotics for UTIs in long-term care residents, with and without a urinary catheter, have been proposed by the Infectious Disease Society of America and are shown in Table 14.5 [27]. An indwelling catheter should be removed and replaced before initiating antibiotics, especially if the catheter has been present for more than 7 days. The urine sample for culture should be obtained upon insertion of the new catheter. This allows better sampling of the bacteria within the bladder, avoiding biofilm adherent to the catheter lumen. There is no optimal duration of therapy; however, if there is good clinical response, the antibiotics should be administered for only 7 days, reducing the risk of reinfection with resistant organisms.

True infection of the upper urinary tract can be confirmed by localizing studies such as bladder washout or ureteral catheterization. However, these studies are rarely indicated, so the diagnosis of acute pyelonephritis is usually made clinically. The classic presentation is an abrupt onset of chills, fever of 100 ° F or greater, and unilateral or bilateral flank pain and/or costovertebral tenderness. These upper tract signs are often accompanied by lower urinary tract symptoms including dysuria, increased urinary frequency, and urgency. In the geriatric population, the symptoms and signs may be more subtle or even absent because concomitant disease can mask or mimic them. In fact, even severe upper tract infection may not be associated with leukocytosis and/or fever [28]. In addition, urine cultures may be negative in the presence of acute pyelonephritis if the involved renal unit is obstructed. Thus, one should have a high clinical suspicion and a low threshold for conducting upper tract imaging, especially in geriatric patients.

Upper tract imaging can consist of ultrasonography, CT scan, or MRI. Ultrasound has the added benefit of being noninvasive, easy to perform, and is without radiation exposure. In addition, patients with cognitive impairment are able to cooperate more easily than with CT or MRI. Ultrasound is capable of identifying stones, hydronephrosis, or perinephric abscesses. However, it does have limitations and should be combined with abdominal X-ray when looking for ureteral calculi. Additionally it is affected by patient body habitus, is operator dependent, and can be fairly subjective.

On the other hand, CT and MRI offer the best anatomic detail and are more sensitive than excretory urography or ultrasound in the diagnosis of bacterial nephritis and renal and perirenal abscesses. However, because both should be done with contrast when evaluating the upper tracts for pathology, renal function is important and therefore may be contraindicated in the older patient with renal insufficiency. These studies should be reserved for those patients with abnormalities seen on ultrasound that may require further investigation.

Recurrent UTI

UTIs are classified as recurrent when three or more culture-proven infections develop within 12 months or two culture-proven infections develop within 6 months. Recurrent UTI (rUTI) needs to be distinguished from relapse defined as a persistent or incompletely treated infection and reinfection. For example, reinfection may exist if the uropathogen is a different species than the original, a negative urine culture is obtained between infection, or if the infection occurs more than 2 weeks after successful treatment. Relapse occurs when a UTI occurs within 2 weeks of the initial treatment and the uropathogen is identical to the original organism. Recurrent UTIs are always associated with symptoms.

A paucity of data exists for the true prevalence and incidence rates for rUTIs. Estimate from population-based studies exist for UTIs, but not for rUTIs. In younger women followed prospectively, the rate of rUTI may be as high as 44 % within a year after the initial culture-proven UTI, and 5 % had more than three UTIs during the 1-year period [29].

The pathogenesis of rUTI was once believed to be due to ascent from extra urinary sources including the rectum and vagina. However, studies with uropathogenic *E. coli* suggest that these organisms may invade urothelial cells and remain dormant. After dormancy, these organisms may resurge and cause recurrent infection.

Women, especially older women, are at the highest risk for rUTI. Risk factors for rUTI include biologic and genetic factors, behavioral factors, anatomical factors, and postmenopausal status [30, 31]. See Table 14.3 for a summary of the specific factors by category that may predispose an individual to having rUTIs.

Women with rUTI compared to women without rUTIs may have an increased susceptibility to vaginal colonization with specific uropathogens [32]. Genetic determinants, such as the nonsecretor and the P1 phenotypes, may be overrepresented among women with rUTIs [33]. Specifically, women who are nonsecretors of the ABH blood group antigens show enhanced adherence of uropathogenic *E. coli* to cells compared with those that are secretors [34]. Interleukin (IL)-8 receptors may also play a role in the development of rUTIs. IL-8 is an inflammatory cytokine that aids in neutrophil migration across urothelium that is infected. IL-8 case–control studies have been done in children with pyelonephritis and their families [35].

Independent behavioral factors that may predispose younger women and potentially older women, to rUTIs include recent sexual intercourse, intercourse with a new partner, diaphragm or condom–spermicide use, and a history of rUTIs. Recent antimicrobial use that can affect the vaginal flora is also associated with an increased risk of UTIs and rUTIs. Most of the studies that evaluate rUTIs have been done in younger women. However, some of the same factors may also apply to older women who are sexually active [36]. Factors that have been evaluated in younger women, but have not been associated with rUTIs include pre- and postcoital voiding

Table 14.6 Categories and specific risk factors for recurrent UTIs in adults [5, 23]

Biologic/genetic factors	Behavioral factors (studied in premenopausal women)	Anatomical factors (studied in premenopausal women)	Postmenopausal women
Vaginal colonization with uropathogens	Sexual intercourse	Short perineal anatomic measurements	Urinary incontinence
Nonsecretor and P1 Phenotypes	Spermicide use	Elevated post-void residual volume	Cystocele
ABH blood group antigens	History of rUTIs—before the age of 15 years and a maternal history of UTIs		Vaginal atrophy
Interleukin-8 receptor variations	Recent antimicrobial use		Elevated post void residual volume

patterns, frequency of urination, delayed voiding habits, wiping patterns, douching, use of hot tubs, frequent use of pantyhose or tights, or elevated body mass index. Family history may be less important among older women for having rUTIs in comparison to younger women with rUTIs. Additionally, anatomical factors specific to perineal measurements have not been studied in older women, but may play a role. Among younger women in a case–control study, having a shorter mean distance from the urethra to the anus was found to be a significant factor for rUTIs [31].

Risk factors for rUTI have been studied in healthy postmenopausal women and differ from those factors found in premenopausal women (Table 14.6). In a case–control study among 149 healthy older, postmenopausal women cases compared to 53 age-matched controls, urologic risk factors for rUTI were having urinary incontinence, presence of a cystocele, and elevated post-void residual volumes [37]. In multivariable analysis from this study, having urinary incontinence, a history of UTI prior to menopause, and being a nonsecretor were associated with rUTI in the cases. Few controls had cystoceles or elevated post-void residual volumes and were excluded from the multivariable analysis. In addition, treating vaginal atrophy with topical estrogen has been associated with improvement in UTIs and rUTIs rates among postmenopausal women [37].

Diagnosis of rUTIs

All patients with recurrent UTIs are symptomatic. Thus the diagnosis and management of recurrent UTIs relies upon careful evaluation of the patient and urine samples with the onset of symptoms. Pertinent findings in the patient's history include baseline habits such as daily fluid intake including type and quantity; toileting habits including frequency, urgency, dysuria, and either urinary or fecal incontinence; and associated symptoms such as cystitis, pyelonephritis, microscopic or gross hematuria; the presence or absence of constitutional symptoms such as nausea, vomiting, fevers, or chills, and any history of stone disease. Temporal associations such as sexual activity, menopausal status, use of spermicides, vaginal lubricants, and antibiotics also need to be assessed. Physical examination findings of importance include the presence or absence of costovertebral angle tenderness, the quality of the vaginal tissues, and the presence or absence of pelvic organ prolapse. The urethra should be carefully inspected in both men and women for meatal stenosis and palpated for the presence of a diverticulum. Determination of post-void residual volume is also important, especially in males.

Additional urologic investigations, such as upper tract imaging and cystoscopy, are generally unnecessary during initial diagnostic testing. However, because older patients may have more subtle symptoms of a UTI or have an altered mental status, the threshold for conducting these studies may be lowered. When the history or physical examination is suggestive of complicating factors, further evaluation of the urinary tract is justified. Although guidelines do not exist for the evaluation of complicated rUTIs, it is reasonable to start with a post-void residual volume determination, renal ultrasonography, and possible cystoscopy. Cystoscopy should always be done in patients with persistent hematuria after antimicrobial therapy or hematuria associated with other risk factors. If there is no evidence of urinary stasis and the patient has a functionally and structurally normal urinary tract, then management may involve behavioral modifications and/or antimicrobial therapy.

Many times, especially in the older population, the etiology of the infections can be elucidated from the patient's history and review of their voiding habits. Three strong urologic risk factors associated with recurrent UTIs in the older population include incontinence, presence of a cystocele, and elevated post-void residual volumes [37]. It is unclear exactly how incontinence predisposes to rUTIs; however, it is conceivable that a continuously damp perineum and introitus may facilitate uropathogen colonization and ascent into the urinary tract. In addition, patients may restrict fluid intake to improve or prevent their incontinence. Many patients in this population are already dehydrated and this restriction can further predispose them to UTIs. Adjustment of fluid intake, toileting habits, and other behavioral modifications are discussed in detail below with prevention strategies.

Treatment of rUTIs

Antimicrobial therapy for rUTIs is very similar to that of uncomplicated UTIs. Empiric therapy should be avoided until a clear pattern of rUTI has been established. Self-start therapy is a reasonable option in younger adults; however, this form of therapy must be used with caution in the older person. Studies have documented the ability of younger patients to self-diagnose (88–92 %) and effectively treat rUTIs with short 1–3 day courses of antibiotics [38–40]. However, other studies have questioned the ability of the older patient to self-diagnose because the presenting symptoms may be nonspecific [16].

Prevention Strategies for rUTI

Many prevention strategies have been studied and adequately tested for rUTI prevention. Patients and providers often hold strong beliefs and biases about effectiveness. In order to decrease antibiotic exposure and avoid worsening resistance among uropathogens, prevention strategies could be considered in a step-wise approach in older adults. Current categories for preventive strategies include behavioral modifications, cranberry, methenamine salts, estrogen, probiotics, specific drugs aimed at uropathogenic bacteria, and antimicrobial prophylaxis.

Behavioral strategies for preventing rUTIs have not been rigorously tested in controlled studies among women. Reasonable considerations that are unlikely to be harmful may include postcoital voiding and liberal fluid intake. Specific intake of cranberry products in either juice or pill formulations has undergone more rigorous testing than other fluid and behavioral strategies. The mechanism for cranberries to improve UTIs and rUTIs may involve decreasing adherence of uropathogens to uroepithelial cells. One randomized controlled trial did not demonstrate efficacy of cranberry juice for either prevention of UTI or decreasing the 6-month incidence rates of rUTIs compared to drinking a placebo juice in young, college women [41]. Another recent study compared cranberry tablets to using antibiotics for rUTI prevention in premenopausal women and found that antibiotics were superior to cranberry tablets for prevention of rUTIs within a 12-month period [42]. In a recent meta-analysis among four high quality studies identified out of ten total in a Cochrane review, cranberry interventions were found to be more effective in younger adult females with rUTIs than in older adults [43]. Some concern has been raised for the use of cranberry products with warfarin anticoagulation, but recent studies suggest that there is no significant interaction.

Methenamine salts have also been used for rUTI prevention. In urine, methenamine salts are hydrolyzed to ammonia and formaldehyde, which is bacteriostatic. Although these agents have broad-spectrum antimicrobial activity, lack antimicrobial resistance, and have limited side effects, clinical evidence supporting their efficacy for rUTI is limited [44]. In a Cochrane review, methenamine hippurate may be effective for short-term prevention in patients with neurogenic bladder or UTI abnormalities, but data are still needed regarding longer term use [44].

Estrogen replacement with intravaginal creams has been systematically reviewed and evidence exists for efficacy and safety of use for rUTIs among postmenopausal women with signs and symptoms of vaginal atrophy [45]. Intravaginal estrogens were found to be effective, whereas oral estrogens do not have appeared to be efficacious for rUTIs and have more side effects. Vaginal estrogen rings may also be used in older women with hand dexterity problems or poor compliance with using vaginal estrogen creams.

When all other preventive measures have been utilized, antimicrobials can be used to reduce rUTIs. Evidence from systematic reviews exists for the efficacy of antibiotics prophylaxis for 6–12 months for reducing rUTIs [46]. The number needed to treat to prevent one symptomatic UTI was 1.85 (95 % CI 1.6, 2.2) by microbiological criteria and 2.2 (95 % CI 1.8, 2.8) by clinical criteria for UTI. Once the antimicrobial prophylaxis was discontinued these differences were no longer observed. Side effects including oral and vaginal candidiasis and gastrointestinal symptoms were more common in patients taking prophylactic antimicrobials. No clear differences were found for selecting the type of antimicrobial agent for use, the frequency of use, and the duration of use. Individual characteristics and local antimicrobial resistance patterns are important considerations when choosing an antimicrobial agent. Prophylaxis should only be initiated in the setting of a negative urine culture after a symptomatic UTI. Most clinicians recommend starting a 6-month trial of antimicrobials administered nightly, followed with active surveillance for further infection. If rUTIs reoccur after prophylaxis treatment for 6 months, longer treatment periods of 1–2 years could be considered. However, benefits and risks should be discussed in detail with the patient. Weekly prophylaxis appears to be better than monthly prophylaxis doses, but no clinical studies exist to compare these schedules [46].

In older adults, chronic kidney disease is an important consideration for the choice of antimicrobial treatment. Nitrofurantoin is contraindicated for older patients with a creatinine clearance of <60 mL/min. Additionally, long-term treatment with nitrofurantoin has been associated with pulmonary disease, chronic hepatitis, and neuropathy and should be avoided.

Other strategies, such as use of probiotics and vaccines, could be considered for the prevention of rUTIs. Probiotics with live cultures may protect the vagina from colonization by uropathogens through different mechanisms. Some of these mechanisms include blocking sites of attachment, production of hydrogen peroxide which acts as a microbicidal, lowering the pH of the vaginal environment, and induction of anti-inflammatory cytokine responses. Although randomized controlled trials exist using probiotics, larger clinical trials are needed to determine efficacy. Vaccine strategies have also been developed to prevent uropathogenic *E. coli* infections. Monovalent vaccines have been studied, but no licensed vaccines currently exist in the USA. Two other immunoactive agents including a daily pill and a vaginal suppository containing several strains of *E. coli* that are available in Europe have been studied for the prevention of uropathogenic recurrence [47].

UTIs in Men

The incidence of acute cystitis in males is much lower than in females owing to a drier periurethral environment, a longer urethra, and antibacterial substances in prostatic fluid. By convention, all UTIs in men are considered complicated because the majority are associated with urinary tract abnormalities, the most common being benign prostatic hyperplasia (BPH). Symptoms of urinary tract infection in men are often similar to those of women; however, the diagnosis in males may be delayed and attributed to prostatic enlargement. Normal voiding is the most important defense against urinary tract infection, therefore, it is common to find prostate enlargement as the etiology of UTIs in men. BPH causes urethral obstruction and turbulent urinary flow, which facilitates ascension of organisms into the bladder. The high voiding pressure created by BPH contributes to UTI development via several mechanisms. Reduction of blood flow to the bladder results in impaired immune and host responses. Disruption of the uromucoid layer allows increased bacterial adherence and colonization. Development of cellules, diverticula, and/or vesicoureteral reflux can all lead to incomplete bladder emptying and possible renal insufficiency [48]. Additionally, bacteria established in the prostate of older men may persist indefinitely because of poor penetration of antimicrobials into the prostate gland and the frequent presence of bacteria within prostatic stones [10].

Men may present with urinary frequency, urgency, nocturia, dysuria, and gross hematuria which are the same symptoms associated with BPH. Therefore, evaluation of the male patient presenting with symptoms of a UTI should include an abdominal examination, genitourinary evaluation, as well as a prostate examination. Analysis of an unspun midstream sample is also valuable in the diagnosis of a UTI because the presence of pyuria with > 10 leukocytes/HPF is almost always diagnostic of acute cystitis or pyelonephritis. Absence of pyuria usually indicates an alternate etiology. The presence of white blood cell casts is indicative of upper tract infection. Hematuria is also present in cystitis but usually absent in urethritis. A midstream urine culture should be obtained in all men suspected of having a UTI, utilizing a colony count criterion of 10^4 CFU/mL [49]. The differential diagnosis of a male presenting with irritative LUTS should include prostatitis, urethritis, and interstitial cystitis or bladder pain syndrome (IC/BPS).

Prostatitis

Acute bacterial prostatitis is another lower urinary tract infection that has a similar presentation to that of a bladder infection. It is characterized by irritative and obstructive voiding symptoms and may be associated with the acute onset of pelvic pain and manifestations of a systemic febrile illness. Typical complaints include urgency, frequency, dysuria, hesitancy, poor force of stream, stranguria, and possibly acute urinary retention. Systemic symptoms may include fever, chills, malaise, nausea, vomiting, and possibly septicemia with hypotension. On physical examination, the prostate is often described as being hot, boggy, and exquisitely tender. The expression of prostatic fluid is usually not necessary in this setting and can possibly be harmful.

Depending upon the seriousness of the infection, parenteral antibiotics may be indicated in the acute setting followed by oral agents with wide-spectrum antimicrobial activity. The most common drugs suggested for initial therapy include a combination of a penicillin and an aminoglycoside, a second- or third-generation cephalosporin, or a fluoroquinolone. Once the acute infection has improved, oral therapy with TMP-SMX or an oral fluoroquinolone is indicated. The optimal duration of treatment is unknown, but 2–4 weeks of therapy has been recommended. If the patient is not clinically improving, a transrectal ultrasound or CT scan of the pelvis is indicated to rule out the presence of a prostatic abscess. Because urinary obstruction is a common symptom associated with acute prostatitis, it is recommended that the patient have a short 12-h of Foley catheter drainage with a small-caliber catheter, intermittent catheterization, or insertion of a suprapubic catheter. Long-term Foley catheter drainage should be avoided due to potential blockage of the urethral ducts, resulting in the potential for prostatic abscess development. The traditional route of drainage of a prostatic abscess has been transurethral incision. However, transperineal drainage must be considered when the abscess has penetrated through the levator ani muscles. More recently it has been suggested that percutaneous drainage is most effective and less morbid [50].

Case 2

Introduction. A 78-year-old male with moderate cognitive impairment due to Alzheimer's disease, chronic kidney disease with baseline clearance of 55 mL/min, and a history of benign prostatic enlargement for which he takes tamsulosin and finasteride, presents to his specialist appointment for a

(continued)

(continued)

routine follow-up for his prostate symptoms. The patient reports having worsening urinary frequency and urinary incontinence when he cannot make it to the toilet with urgency, along with nocturia. Although he lives alone, he depends on his two sons for some of his instrumental activities of daily living. His sons assist him with driving to his appointments, helping setup medications, providing meals, and assisting with managing his finances. He appears to be a little more confused today in comparison to his last appointment 6 months ago, although he has not been sleeping for the past three nights due to his nocturia. He has not been started on any diuretics and has not taken any over-the-counter sleep medications. He is not taking warfarin.

Objective Findings. He is afebrile. His weight and blood pressure are stable compared to his prior visits documented in the electronic medical record. He has no abdominal fullness or tenderness and no lower extremity edema. After urinating 150 mL, he is found to have an elevated post-void residual volume of 300 mL. His dipstick urine testing shows a large amount of leukocyte esterase, positive nitrates, and 50 white blood cells per high power field.

Intervention. The provider elects to treat him with empiric antibiotics for a urinary tract infection. The urine is sent for a culture given that the local hospital and clinical resistance patterns for *E. coli* have been higher in the past year at 12–15 %. Since he has not been hospitalized in the last 3 months and has not been on any other antibiotics, the provider chooses trimethoprim–sulfamethoxazole (TMP–SMX) twice daily for 7 days. The dose is appropriately adjusted for his chronic kidney disease.

Follow-up. Two days later, you get an electronic alert regarding the results of his urine culture and culture sensitivities. The culture is positive for *E. coli*, $>10^5$ CFU/mL. The *E. coli* organism on the culture report is sensitive to the trimethoprim–sulfamethoxazole. Your staff calls the patient and his sons to let them know that he should complete the 7 days of the antibiotics. Upon completion of the antibiotic course, the patient reports that he is sleeping much better and no longer has urinary leakage when trying to toilet. One of his sons notes that he appears less confused and is back to his baseline mental status.

Summary

Urinary tract infections are one of the most common clinical conditions diagnosed in the geriatric patient population. A variety of presentations and conditions occur ranging from acute cystitis to urosepsis. Chronic and recurrent UTIs are common. Older adults may not manifest the traditional symptoms of fever and dysuria. Clinicians treating older adults need to be aware of subtle signs and symptoms that may be indicators of an underlying urinary tract infection. Prevention methods may help to reduce the incidence and prevalence of UTIs in many older adults. Treatment of underlying risk factors such as stone disease may also be beneficial. Asymptomatic bacteriuria is also very common in older adults, but generally does not require antibiotic therapy. Clinicians should also be aware of antibiotic resistance profiles and trends in their regional community and adjust antibiotic treatment accordingly based on culture results.

References

1. Juthani-Mehta M. Asymptomatic bacteriuria and urinary tract infection in older adults. Clin Geriatr Med. 2007;23(3):585–94. vii.
2. Wilson ML, Gaido L. Laboratory diagnosis of urinary tract infections in adult patients. Clin Infect Dis. 2004;38(8):1150–8.

3. Hooton TM, Bradley SF, Cardenas DD, Colgan R, Geerlings SE, Rice JC, et al. Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America. Clin Infect Dis. 2010;50(5): 625–63.
4. Nicolle LE, Bradley S, Colgan R, Rice JC, Schaeffer A, Hooton TM, et al. Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. Clin Infect Dis. 2005;40(5):643–54.
5. High KP, Bradley SF, Gravenstein S, Mehr DR, Quagliarello VJ, Richards C, et al. Clinical practice guideline for the evaluation of fever and infection in older adult residents of long-term care facilities: 2008 update by the Infectious Diseases Society of America. J Am Geriatr Soc. 2009;57(3):375–94.
6. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis. 2011;52(5):e103–20.
7. Bengtsson C, Bengtsson U, Björkelund C, Lincoln K, Sigurdsson JA. Bacteriuria in a population sample of women: 24-year follow-up study. Results from the prospective population-based study of women in Gothenburg, Sweden. Scand J Urol Nephrol. 1998; 32(4):284–9.
8. Hooton TM, Scholes D, Hughes JP, Winter C, Roberts PL, Stapleton AE, et al. A prospective study of risk factors for symptomatic urinary tract infection in young women. N Engl J Med. 1996;335(7):468–74.
9. Nicolle LE. Asymptomatic bacteriuria: when to screen and when to treat. Infect Dis Clin North Am. 2003;17(2):367–94.
10. Nicolle LE. Urinary tract infections in the elderly. Clin Geriatr Med. 2009;25(3):423–36.
11. Nicolle LE. Urinary tract infection in diabetes. Curr Opin Infect Dis. 2005;18(1):49–53.
12. Boscia JA, Abrutyn E, Kaye D. Asymptomatic bacteriuria in elderly persons: treat or do not treat? Ann Intern Med. 1987;106(5):764–6.
13. Ouslander JG, Schapira M, Schnelle JF, Fingold S. Pyuria among chronically incontinent but otherwise asymptomatic nursing home residents. J Am Geriatr Soc. 1996;44(4):420–3.
14. Roos V, Schembri MA, Ulett GC, Klemm P. Asymptomatic bacteriuria Escherichia coli strain 83972 carries mutations in the foc locus and is unable to express F1C fimbriae. Microbiology. 2006;152 (Pt 6):1799–806.
15. Abrutyn E, Mossey J, Berlin JA, Boscia J, Levison M, Pitsakis P, et al. Does asymptomatic bacteriuria predict mortality and does antimicrobial treatment reduce mortality in elderly ambulatory women? Ann Intern Med. 1994;120(10):827–33.
16. Arinzon Z, Shabat S, Peisakh A, Berner Y. Clinical presentation of urinary tract infection (UTI) differs with aging in women. Arch Gerontol Geriatr. 2012;55(1):145–7.
17. Jackson GG, Arana-Sialer JA, Andersen B, Grieble HG, Mc CW. Profiles of pyelonephritis. Arch Intern Med. 1962;110:63–75.
18. Nicolle LE, Ronald AR. Recurrent urinary tract infection in adult women: diagnosis and treatment. Infect Dis Clin North Am. 1987;1(4):793–806.
19. McMurdo ME, Gillespie ND. Urinary tract infection in old age: over-diagnosed and over-treated. Age Ageing. 2000;29(4):297–8.
20. Cockerill FR, Edson RS. Trimethoprim-sulfamethoxazole. Mayo Clin Proc. 1991;66(12): 1260–9.
21. Iravani A. Advances in the understanding and treatment of urinary tract infections in young women. Urology. 1991;37(6):503–11.
22. Stahlmann R, Lode H. Fluoroquinolones in the elderly: safety considerations. Drugs Aging. 2003;20(4):289–302.
23. Nicolle LE. Urinary catheter-associated infections. Infect Dis Clin North Am. 2012;26(1):13–27.
24. Saint S, Chenowith CE. Biofilms and catheter-associated urinary tract infections. Infect Dis Clin North Am. 2003;17:411–32.
25. Rudman D, Hontanosas A, Cohen Z. Clinical correlates of bacteruria in a Veterans Administration extended care facility. J Am Geriatr Soc. 1998;36: 726–32.
26. Saint A, Kaufman SR, Rogers MA. Condom vs indwelling urinary catheters: a randomized trial. J Am Geriatr Soc. 2006;54:1055–61.
27. Loeb M, Bentley DW, Bradely S, et al. Minimum criteria for the initiation of antibiotics for urinary tract infection in long-term care residents. Infect Control Hosp Epidemiol. 2001;22:120–4.
28. Baldassarre JS, Kaye D. Special problems of urinary tract infection in the elderly. Med Clin North Am. 1991;75:375–90.
29. Ikäheimo R, Siitonen A, Heiskanen T, Kärkkäinen U, Kuosmanen P, Lipponen P, et al. Recurrence of urinary tract infection in a primary care setting: analysis of a 1-year follow-up of 179 women. Clin Infect Dis. 1996;22(1):91–9.
30. Beveridge LA, Davey PG, Phillips G, McMurdo ME. Optimal management of urinary tract infections in older people. Clin Interv Aging. 2011;6:173–80.
31. Hooton TM. Recurrent urinary tract infection in women. Int J Antimicrob Agents. 2001;17(4): 259–68.
32. Schaeffer AJ. Urinary tract infections in the elderly. Eur Urol. 1991;19 Suppl 1:2–6.
33. Stapleton A, Hooton TM, Fennell C, Roberts PL, Stamm WE. Effect of secretor status on vaginal and rectal colonization with fimbriated Escherichia coli in women with and without recurrent urinary tract infection. J Infect Dis. 1995;171(3):717–20.

34. Sheinfeld J, Schaeffer AJ, Cordon-Cardo C, Rogatko A, Fair WR. Association of the Lewis blood-group phenotype with recurrent urinary tract infections in women. N Engl J Med. 1989;320(12):773–7.
35. Lundstedt AC, Leijonhufvud I, Ragnarsdottir B, Karpman D, Andersson B, Svanborg C. Inherited susceptibility to acute pyelonephritis: a family study of urinary tract infection. J Infect Dis. 2007;195(8):1227–34.
36. Scholes D, Hooton TM, Roberts PL, Stapleton AE, Gupta K, Stamm WE. Risk factors for recurrent urinary tract infection in young women. J Infect Dis. 2000;182(4):1177–82.
37. Raz R, Gennesin Y, Wasser J, Stoler Z, Rosenfeld S, Rottensterich E, et al. Recurrent urinary tract infections in postmenopausal women. Clin Infect Dis. 2000;30(1):152–6.
38. Wong ES, McKevitt M, Running K, Counts GW, Turck M, Stamm WE. Management of recurrent urinary tract infections with patient-administered single-dose therapy. Ann Intern Med. 1985;102(3):302–7.
39. Schaeffer AJ, Stuppy BA. Efficacy and safety of self-start therapy in women with recurrent urinary tract infections. J Urol. 1999;161(1):207–11.
40. Gupta K, Hooton TM, Roberts PL, Stamm WE. Patient-initiated treatment of uncomplicated recurrent urinary tract infections in young women. Ann Intern Med. 2001;135(1):9–16.
41. Barbosa-Cesnik C, Brown MB, Buxton M, Zhang L, DeBusscher J, Foxman B. Cranberry juice fails to prevent recurrent urinary tract infection: results from a randomized placebo-controlled trial. Clin Infect Dis. 2011;52(1):23–30.
42. Beerepoot MA, ter Riet G, Nys S, van der Wal WM, de Borgie CA, de Reijke TM, et al. Cranberries vs antibiotics to prevent urinary tract infections: a randomized double-blind noninferiority trial in premenopausal women. Arch Intern Med. 2011;171(14):1270–8.
43. Jepson RG, Craig JC. A systematic review of the evidence for cranberries and blueberries in UTI prevention. Mol Nutr Food Res. 2007;51(6):738–45.
44. Lee BB, Simpson JM, Craig JC, Bhuta T. Methenamine hippurate for preventing urinary tract infections. Cochrane Database Syst Rev. 2007(4):CD003265.
45. Perrotta C, Aznar M, Mejia R, Albert X, Ng CW. Oestrogens for preventing recurrent urinary tract infection in postmenopausal women. Cochrane Database Syst Rev. 2008(2):CD005131.
46. Albert X, Huertas I, Pereiró II, Sanfélix J, Gosalbes V, Perrota C. Antibiotics for preventing recurrent urinary tract infection in non-pregnant women. Cochrane Database Syst Rev. 2004(3):CD001209.
47. Naber KG, Cho YH, Matsumoto T, Schaeffer AJ. Immunoactive prophylaxis of recurrent urinary tract infections: a meta-analysis. Int J Antimicrob Agents. 2009;33(2):111–9.
48. Neal D. Complicated urinary tract infections. Urol Clin North Am. 2008;35:13–22.
49. Rubin RH, Shapiro ED, Andriole VT, et al. Evaluation of new anti-infective drugs for the treatment of urinary tract infection. Infectious Diseases Society of America and the Food and Drug Administration. Clin Infec Dis. 1992;15 Suppl 1:S216.
50. Varkarakis J, Sebe P, Pinggera GM, Bartsch G, Strasser H. Three-dimensional ultrasound guidance for percutaneous drainage of prostatic abscesses. Urology. 2004;63(6):1017–20. discussion 20.

Nocturia

15

Kari A.O. Tikkinen, Theodore M. Johnson II, and Jeffrey P. Weiss

Introduction

Early epidemiological research on urinary symptoms focused on stress urinary incontinence in women and on lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH) in men. Nocturia has more recently been recognized as a clinical entity in its own right [1, 2] leading to a proliferation of research on this topic [3].

The definition of nocturia is a critical factor in evaluating its epidemiology [4]. The International Continence Society (ICS) classifies nocturia as one of the urinary storage symptoms and defines nocturia as "the complaint that the individual has to wake at night one or more times to void…each void is preceded and followed by sleep" [2]. Several other definitions with subtle differences have also been published [5, 6]. Having to return to sleep following an awakening to void would seem not to be necessary for the awakening to be disruptive. If the definition needs to address the issue of sleep following the void, perhaps it is the intention of going back to sleep after voiding which might be more clinically relevant [7]. Overall, these idealized definitions are conceptually not difficult to use, but their detailed specificity makes them challenging to apply in practice. Furthermore, these definitions do not consider the bother, impact, or severity, and they provide no information as to when nocturia becomes clinically meaningful and worthy of evaluation and treatment [8, 9]. A single nighttime void would meet the criteria for nocturia by these definitions [2, 5, 6], and yet there is a lack of evidence that it is a suitable criterion for clinical purposes [10].

Prevalence

Estimates of nocturia prevalence have varied, mainly due to methodological differences in symptom assessment and definitions, populations, and data collection methods [4, 11]. Most, but not all, earlier studies conducted among elderly men [12–20] found that nocturia is a very common symptom in the elderly population, and the prevalence increases with age. Recently, this finding have been confirmed in comparative

K.A.O. Tikkinen, M.D., Ph.D. (✉)
Department of Urology, Helsinki University Central Hospital and University of Helsinki, Helsinki, Finland

Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, ON, Canada
e-mail: kari.tikkinen@fimnet.fi

T.M. Johnson II, M.D., M.P.H.
Emory Division of General Medicine and Geriatrics, Department of Medicine, Atlanta VA Medical Center, 1670 Clairmont Road, Mailstop:11B, Decatur, GA 30033, USA
e-mail: ted.johnson@va.gov

J.P. Weiss, M.D., F.A.C.S.
Department of Urology, SUNY Downstate College of Medicine, Brooklyn, NY, USA
e-mail: jeffrey.weiss@downstate.edu

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_15,

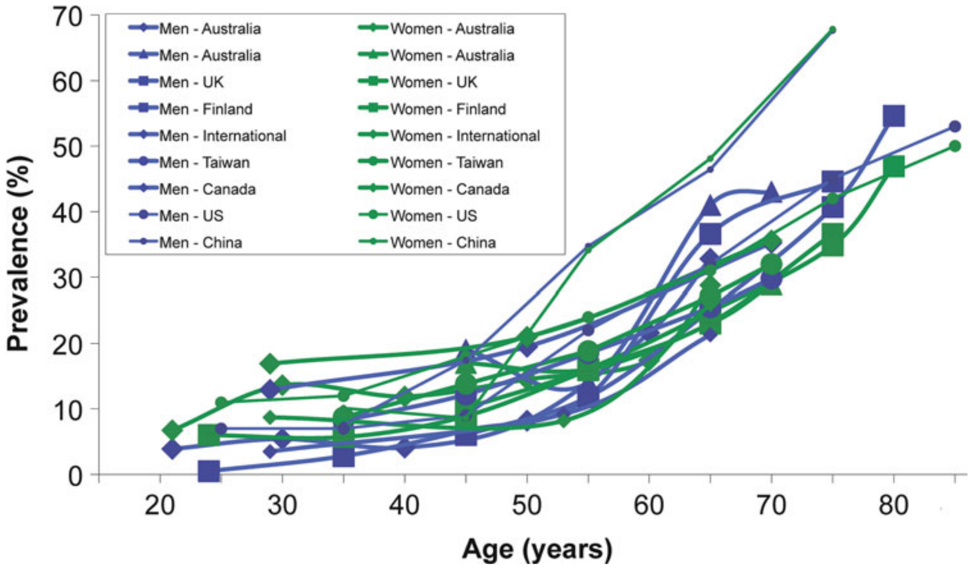


Fig. 15.1 Prevalence of at least two voids per night across age groups by sex in population-based studies conducted among both sexes with wide age range [8, 21, 27–33] All population-based studies assessing prevalence of nocturia in adults of both sexes were reviewed. To identify these studies, a PubMed search (English language articles published before April 2012) was carried out on with the strategy ((nocturia.mp)) and ((prevalence.mp)). Non-population-based studies, studies not conducted among both sexes of adults, studies with narrow age range (less than 40 years), and studies with percentage data unavailable were not included

studies conducted in both sexes with a wide age range [8, 21–31] (Fig. 15.1).

In the population-based Finnish National Nocturia and Overactive Bladder (FINNO) Study of both sexes aged 18–79, approximately one out of eight men and women reported at least two voids per night. In addition, one third reported one void per night [8]. Young women clearly reported more nocturia than young men. Prevalence of nocturia in men and women equalized only in the sixth to seventh decade of life, and in older age groups men had more nocturia than women [8]. Among those aged 60–69, approximately 37 % of men and 22 % of women voided at least twice per night. At ages 70–79 years, approximately 44 % of men and 34 % of women voided at least twice per night [11]. Many other recent studies have supported these findings of a higher prevalence of nocturia among young women than young men and an equalization of prevalence in middle age [27–30, 32, 34]. As the gender difference has been found across different continents including Europe, Asia, Australia, and North America, it is probably not due to specific country, lifestyle, climate, or culture (Fig. 15.1) [8, 11, 21, 27–30, 32–34]. The reasons for the excess of nocturia among older men remain unknown, but prostatic enlargement is likely to be the predominant factor.

The community-based Krimpen study conducted in the Netherlands among elderly men [35] is one of the few studies where nocturia was longitudinally assessed by voiding diaries and frequency volume charts. One and a half (1.5) or more voids/night, averaged from information on 2–3 nights, were present in 60 % of men aged 70–78 years, whereas at least 2.5 voids per night was present in 20 %, respectively. These estimations are comparable to questionnaire studies. Most elderly people void at least once per night [9] (Fig. 15.1).

Incidence

There is a paucity of data on the incidence and natural history of nocturia [3]. This is not only due to the fact that longitudinal studies are more difficult to fund and perform than are cross-sectional studies but also due to the relative youth of "nocturia research" [2], uncertainty about the definition of "incident nocturia" [36–38], and uncertainty about the appropriate time interval for repeated sampling [39]. Further, it has been found that nocturia "resolves" in a significant number of men or at least decreased in severity, a factor which creates difficulty in analysis of incidence [40]. Indeed, since nocturia is known to have a night-to-night variation, repeated surveys often measure short-term variability rather than the overall long-term trend (i.e., nocturia is more prevalent in older populations and therefore is a likely incident with time as individuals age).

In a community-based study among adults over 60 in the USA [41], participants were seen in their homes in 1983–1984, and nocturia was ascertained during the baseline and first and second year follow-ups. Incidence of nocturia was defined by following those with no nocturia at baseline (0 or 1 episodes) to year two. Of the 738 individuals with no nocturia at baseline, 34.6 % reported having nocturia (2 or more) at follow-up or an incidence rate of 213/1,000 person–years. Of the 357 individuals who had 2 or more episodes at baseline, 66.3 % reported 1 or fewer at follow-up, for a remittance rate of 497/1,000 person–years. These estimates were not calculated with adjustment for age or gender, and the exact number of days between date at baseline and date at follow-up were not determined [38].

In a population-based study conducted in one Finnish county, questionnaires were mailed in 1994, 1999, and 2004 to elderly men [42]. The DAN-PSS nocturia question with response categories of 0, 1–2, 3–4, and 5 or more (times per night) was used. The crude incidence of nocturia for men from 0 to 1 or more was 75 new cases per 1,000 person–years during the first 5-year period and 126 during the second period. Younger cohorts (50-year-olds) had a lower incidence (61 cases/1,000 person–years) than did the two older cohorts (60 and 70 year cohorts, 91 and 93 cases/1,000 person–years, respectively). Interestingly, for all age cohorts the observed incidence during the second 5-year period was higher than during the first: 102, 168, and 167 per 1,000 person–years, respectively. The incidence of nocturia to three or more times (from 0 or 1–2 times) was less across all age groups (3, 12, and 16/1,000 person–years, respectively, for the age cohorts). Interestingly, prevalence for 60-year-olds was higher at 10-year follow-up than was prevalence for 70-year-olds at baseline. However, this study is difficult to compare to other studies as no information on incidence of nocturia from ≤1 episode to ≥2 or more is available [42].

In a study conducted in the city of Gothenburg, Sweden, questionnaires were mailed in 1992 to 10,456 men (aged 45–99) [43]. Follow-up was performed in 2003 when 3,257 men replied (3,000 men had died and 691 had emigrated or were no longer available in the register). The authors presented prevalence data at two time points. Nocturia prevalence increased from 12.8 % to 50.1 % (2 or more voids/night) over the roughly 11-year period between the time points for participants in this study. Incidence and remission estimates remained unreported [43].

In the Krimpen study conducted in the 1990s among elderly men in a Dutch municipality [35], frequency volume charts were used for assessment of nocturia incidence. The overall incidence and remission rates (nocturia defined as ≥ 2 voids/night) were 23.9 % and 36.7 % after 2.1 years [40]. The incidence was highest among the oldest and lowest among the youngest men. As the absolute number of men with incident nocturia was higher, the prevalence rate increased over time. The authors concluded that "due to this fluctuation it is almost impossible to provide reliable incidence rates of nocturia in community dwelling older men" [40].

In a separate study in Denmark [44, 45], 305 women of child-bearing age were followed after their first pregnancy including 278 women who responded at 5 years and 242 at 12 years. Of 157 women who had no nocturia (2 or more voids/night) during pregnancy, not a single one developed it at 3 months. Of those having no nocturia at 3-month follow-up, 2.7 % developed nocturia by 5 years, and 5.9 % of those who had no nocturia at 5 years developed nocturia at 12 years. Nocturia resolved in 98.6 % of women (68/69) who experienced it during pregnancy at 3 months postpartum [44].

Impact

Bother and Impact on Quality of Life

Disturbed sleep is associated with negative effects on health, mood, morbidity, and ultimately also on mortality [46–48]. Nocturia is associated with sleep disorders and increased daytime fatigue [49]. Bother of nocturia is related to sleep [50–52], both with respect to difficulty initiating sleep [53] and difficulty returning to sleep after an awakening [53, 54]. Nocturia was the most important reason for nocturnal awakenings in some studies [55–57]. However, a sleep center study in the United States found that events during sleep including snoring, leg movements, and apnea episodes occurred surrounding the time when patients awoke to void [58].

The point at which nocturia becomes "too often" is a meaningful practical and theoretical question. Although more frequent nocturia causes more bother, the relationship is not perfectly correlated [10, 22, 25, 29, 59–63]. Does nocturia become abnormal with one or two episodes, or should that number be three?

The population-based FINNO Study examined the bother and quality of life impact of nocturia by age and sex, the relationship between nocturia frequency and bother, and nocturia frequency and quality of life [10]. Most respondents reported any degree of bother from nocturia with 2 or more episodes per night and moderate bother only with 3 or more nocturia episodes. Those with two nocturia episodes also reported substantially impaired health-related quality of life (HRQL) compared to those with no nocturia. Having at least three episodes of nocturia resulted in further impairment of similar magnitude [10]. Hence, the FINNO Study findings indicated that two episodes of nocturia constitute meaningful nocturia affecting well-being and perceived health, whereas one void per night does not identify subjects with interference from nocturia [10]. Several other studies concur with this finding [29, 60, 64]. How much reduction in nocturia is needed to be clinically important has not been answered.

While more frequent nocturia results in greater bother and poorer HRQL, many studies have shown that not all bother from nocturia is explained by the number of nocturia episodes. Nocturia may also be associated with other factors causing impaired HRQL, rather than directly affecting self-rated health [11]. In the FINNO Study, nocturia was associated with impaired HRQL not only within closely related domains including urination, defecation, and sexual activity but also ostensibly unrelated areas including moving, seeing, and hearing [10]. Furthermore, comorbidities were strongly associated with impaired HRQL and nocturia, indicating confounding of variables. Hence, treatment of nocturia episodes may not relieve all impairment among subjects with nocturia [11].

Impact on Falls, Fractures, and Mortality

Falls constitute the greatest risk factor for fractures among older adults [65]. Nocturia is associated with an increased risk of both falls and fractures [66–72]. Furthermore, studies [30, 72–74] have reported a relation between nocturia and mortality. In a Japanese study among older adults [72], at least 2 voids/night was associated with a doubled risk of fractures and mortality. In one US study, nocturia of at least 2 voids/night increased mortality risk 49 % for men and 32 % for women [30]. However, in another US study, the risk of falls due to nocturia defined as 3 or more voids/night was more modest, with an increased risk of falls of 28 % [71]. Whether nocturia is just an indicator of frailty, or if in fact falls, fractures, and increased mortality are actually caused by nocturia and its consequences, is not yet clear.

Risk Factors

Our aim in this section is to summarize the risk factors, in alphabetical order, identified as being associated with nocturia. However, the causes and risk factors of nocturia are not well understood [3, 4], and a remarkable proportion of our current understanding of nocturia is based mainly upon *expert opinions* rather than *scientific evidence* [75, 76]. Additionally, not all risk factors such as age or gender are modifiable.

Conditions

Benign Prostatic Hyperplasia

LUTS are especially common in elderly men with nocturia but can also occur in many other individuals. In men these symptoms are most often attributed to benign prostatic hyperplasia (BPH) sometimes with bladder outlet obstruction (BOO) [1]. Overall, LUTS suggestive of BPH constitute a well-recognized risk factor for nocturia [35, 77, 78]. In the FINNO Study [78], half of the subjects with physician-diagnosed BPH reported at least two voids per night; however, only a third of the men with nocturia reported BPH. Indeed, the impact of BPH may be overestimated. Nocturic men probably are more likely to be diagnosed with BPH than men without nocturia, and women do not have substantially less nocturia despite not having prostates. Nocturia was the least specific LUTS associated with BOO, and treatment to relieve BOO had less effect on nocturia than on other LUTS in Japanese studies [79, 80]. Furthermore, in a Veterans Affairs study on men with bothersome LUTS, those receiving doxazosin had very modest net reductions in nocturia, while finasteride had an effect indistinguishable from placebo [81]. Further, nocturia has been reported as one of the most, if not the single most, persistent LUTS following prostate surgery [82, 83].

Depression

In a Swedish population-based study [84], subjects with major depression, assessed using the Major Depression Inventory [85], reported substantially more nocturia than those without depression. The association was especially strong among men (OR 6.5, 95 % CI 2.6–15.6 for men, and OR 2.8, 95 % CI 1.3–6.3 for women, adjusted for age and somatic health). However, in a subsequent analysis from the same database [86], the authors reported that both major depression (OR 4.6, 95 % CI 2.8–7.5) and taking an SSRI (OR 2.2; 95 % CI 1.1–4.5) were associated with increased prevalence of nocturia. Gender was deleted by the logistic regression model. In the TAMUS cohort study of men aged 50 years or older, those with depressive symptoms at study entry were at 2.8 times higher risk (95 % CI 1.5–5.2) for moderate or severe nocturia (defined as at least three voids/night) than those without depressive symptoms. Nocturia had no effect on depressive symptoms during 5-year follow-up. In the FINNO Study [78], nocturia was associated with antidepressant use only in men (OR 3.2, 95 % CI: 1.3–7.7). Depression itself was not associated with nocturia after adjustment for other factors despite associations in the age-adjusted analyses (OR 2.8, 95 % CI: 1.6, 5.0 for men, and OR 2.0, 95 % CI: 1.2, 3.3 for women). In the Boston Area Community Health (BACH) survey, nocturia was associated with both depression (defined as score of 5 or more by the Center for Epidemiological Studies Depression Scale) and use of antidepressants in both genders, especially in younger age groups. While 10.1 % of men and 15.6 % of women reported depression among those without nocturia, corresponding figures were 15.6 % and 30.0 % for those with nocturia [64].

Hypertension and Coronary Artery Disease

The connection between nocturia and hypertension is not clear. It has been suggested that essential hypertension and nocturnal polyuria are part of the same pathophysiological process [87]. In a Japanese study [26] and in US [38, 88] studies, hypertension was associated with nocturia, although effect sizes were modest (ORs between 1.5 and 1.6). However, in studies conducted in Europe [24, 35, 78], neither nocturnal polyuria nor nocturia was associated with hypertension. In a secondary analysis from the BACH survey [89], nocturia was not generally associated with antihypertensives. However, monotherapy with calcium channel blockers in women (OR 2.65, 95 % CI 1.04–6.74) and combination therapy with loop diuretics in men (OR 2.55, 95 % CI 1.26–5.14) were associated with nocturia [89]. No other significant associations for nocturia with angiotensin-converting enzyme inhibitors, beta blockers, calcium channel blockers, or loop and thiazide diuretics were found [89]. While the treatment for hypertension may cause [1, 89, 90] or alleviate nocturia [91] in some cases, appropriate analytic methods are of particular importance when assessing this relationship.

Earlier studies in men [24, 26, 35] did not find a relation between nocturia and cardiac disease. However, in these studies [24, 26, 35], an association between cardiac symptoms and/or disease and nocturia was found in the preliminary analyses before multivariate models. In more recent studies [74, 78, 92, 93], coronary disease has been shown to be associated with nocturia. In the FINNO Study, coronary artery disease was associated with nocturia in the age-adjusted analyses in both sexes, but after adjustment for other factors, the association persisted only for women (OR 3.1, 95 % CI 1.5–6.6) [78].

Neurological Diseases

Most patients with multiple sclerosis have bladder dysfunction, which can also lead to nocturia [94, 95]. In studies conducted among elderly people, nocturia was associated with stroke and cerebrovascular disease [92, 96]. Moreover, in a study among Parkinson's patients, severity of disease was also associated with increased nocturia. The mean number of nocturia episodes was 1.8 in the mild and 2.9 in the severe Parkinson groups [97]. A relationship of nocturia with restless legs syndrome was found in the FINNO Study [78]. Subjects of both sexes with restless legs syndrome had almost triple the risk of having nocturia compared to those without this condition. However, only 1 of 8 with nocturia had restless legs syndrome. Increased risk of nocturia in patients with restless legs syndrome may relate to disturbed sleep [98]. Furthermore, restless legs syndrome patients use antidepressants, gastrointestinal medications, and asthma and allergy drugs more frequently than subjects free of them [99].

Menopause and Hormone Therapy

In the FINNO Study, the postmenopausal period was associated with increased nocturia (OR 2.3, 95 % CI 1.2–4.4; compared to premenopausal women) [100], consistent with a population-based study conducted on middle-aged women in Denmark (OR 2.4, 95 % CI 1.1–5.2) [101]. Two other studies also reported increased nocturia in the postmenopausal period [102, 103], whereas another attributed this to aging rather than to menopausal transition [104]. The menopausal period is often associated with sleep disturbances for other reasons including hot flashes, mood disorders, and increased sleep-disordered breathing [105]. Therefore, individuals reporting nocturia may be awakening due to non-bladder causes. There are few studies evaluating the effect of menopausal hormone therapy on nocturia. In Finnish and Swedish population-based studies, there were indications of increased nocturia among women with menopausal hormone therapy, but the findings were statistically insignificant in the multivariate analysis [100, 102]. In a small randomized trial [106], those with menopausal hormone therapy did not report more or less nocturia than those with placebo. This finding was confirmed in randomized, controlled trials of an estradiol vaginal ring [107] and vaginal estradiol on urinary storage symptoms after sling surgery for the treatment of stress urinary incontinence [108].

Nocturnal Polyuria

The ICS defines nocturnal polyuria as an increased proportion of the 24-h output of urine volume occurring at night [109]. However, there is a paucity of research providing reference values. In the Krimpen study, average nocturnal urine production was slightly more than 60 mL/h. The authors suggested that nocturnal urine production exceeding 90 mL/h is abnormal [35, 110]. However, authors concluded that "nocturnal urine production as an explanatory variable for nocturnal voiding frequency is of little value" [110]. What is the fundamental pathogenesis of nocturnal polyuria? Congestive heart failure, "third spacing" due to venous insufficiency or nephrosis, or late-night diuretic administration are potential underlying causes. Using bioelectric impedance analysis, nocturnal urine volume has been shown to correlate with the difference in fluid volume in the legs ($r=0.53$, $p=0.002$) and extracellular fluid volume ($r=0.38$, $p=0.02$) between the morning and evening [111]. This is indirectly supported by the results of a nonrandomized study where the number of nocturia episodes decreased significantly from 3.3 to 1.9 after 8 weeks of walking exercise in elderly men [112]. Possible other pathways to nocturnal polyuria include impaired renal concentrating capacity, diminished sodium conserving ability, dysfunction of antidiuretic hormone secretion, and increased secretion of atrial natriuretic hormone, often due to sleep apnea, leading to increased nighttime urine production [113–115]. The pathophysiology of nocturnal polyuria merits additional research.

Obesity and Diabetes

Several studies have shown the relation of overweight/obesity and nocturia. Obesity was associated with more than threefold risk of nocturia in a Swedish study among middle-aged women [116] and with more than twofold risk in the FINNO Study [8]. Confirmatory findings have been reported [88, 93, 117, 118]. In the longitudinal TAMUS study among men aged 50 or older [119], obese men were at higher risk for mild nocturia, and especially for moderate or severe nocturia (RR 2.3, 1.1–4.7), compared with normal-weight men. The frequency of nocturia at baseline did not increase the incidence of obesity at follow-up [119]. An association between diabetes and nocturia has been identified in most [26, 77, 78, 92, 93, 96, 118, 120–122], but not all, reports [24, 35]. Nocturia was associated with a doubled risk of diabetes in the BACH survey (OR 1.7, 95 % CI 1.2–2.3) [93] and in a Danish study (OR 2.0, 95 % CI 1.3–3.0) that included subjects aged 60–80 years [118]. In the FINNO Study [78], diabetes was associated with nocturia in the age-adjusted analyses in both sexes, but after adjustment for other factors, the association persisted only for women (OR 2.7, 95 % CI 1.4–5.2).

Overactive Bladder and Detrusor Overactivity

According to the ICS, overactive bladder syndrome (OAB) is a symptom-defined condition characterized by urinary urgency, with or without urgency incontinence, usually with increased daytime frequency and nocturia [109, 123]. It is commonly proposed that urinary urgency is the primary driver of all symptoms of the OAB constellation including increased nocturia [124]. Recent evidence using nocturnal cystometrograms has confirmed a temporal relationship between nocturnal detrusor overactivity and nocturic voids in some nocturia patients [125]. Urinary urgency was a clear risk factor for nocturia in the FINNO Study (OR 7.4, 95 % CI 4.5–12, for men and OR 4.9, 95 % CI 3.2–7.7 for women) [78]. However, while half of subjects with urgency also reported at least two voids per night, only one in three with nocturia reported urgency [126]. As most people with nocturia do not report frequent urgency (Fig. 15.2), it is not surprising that the treatment of nocturia with bladder relaxants and antimuscarinics is often unsuccessful [127].

Pelvic Surgery, Hysterectomy, and Stress Urinary Incontinence Operations

Results are inconsistent regarding nocturia and hysterectomy, with hysterectomy variously being associated with decreased prevalence [128–130], increased prevalence [101], or no association with nocturia [131, 132]. In the FINNO Study, women who had undergone hysterectomy had an OR of 1.8 for nocturia, with borderline statistical significance (OR 1.8, 95 % CI 0.9–3.6), whereas surgery for stress urinary incontinence was not associated with nocturia (OR 0.9, 95 % CI 0.4–2.5) despite association of urgency with stress incontinence surgery (OR 2.5, 95 % CI 1.0–6.1) [100]. However, statistical power was limited regarding analyses on stress incontinence surgery in this study.

Prostate Cancer

Many men with LUTS express a fear of prostate cancer [133]; however, whether LUTS, including nocturia, really are suggestive of prostate cancer is not well known [134]. In the large HUNT-2 study [135], LUTS severity was positively associated with the subsequent diagnosis of localized prostate cancer but not with advanced or fatal disease. In the FINNO Study [78], more than 70 % of men with physician-diagnosed prostate cancer reported at least two voids/night, while 7 % of men with nocturia reported prostate cancer. Are men with nocturia more vulnerable to be diagnosed with prostate cancer due to the use of prostate-specific antigen testing among men with LUTS? Or does prostate cancer really cause

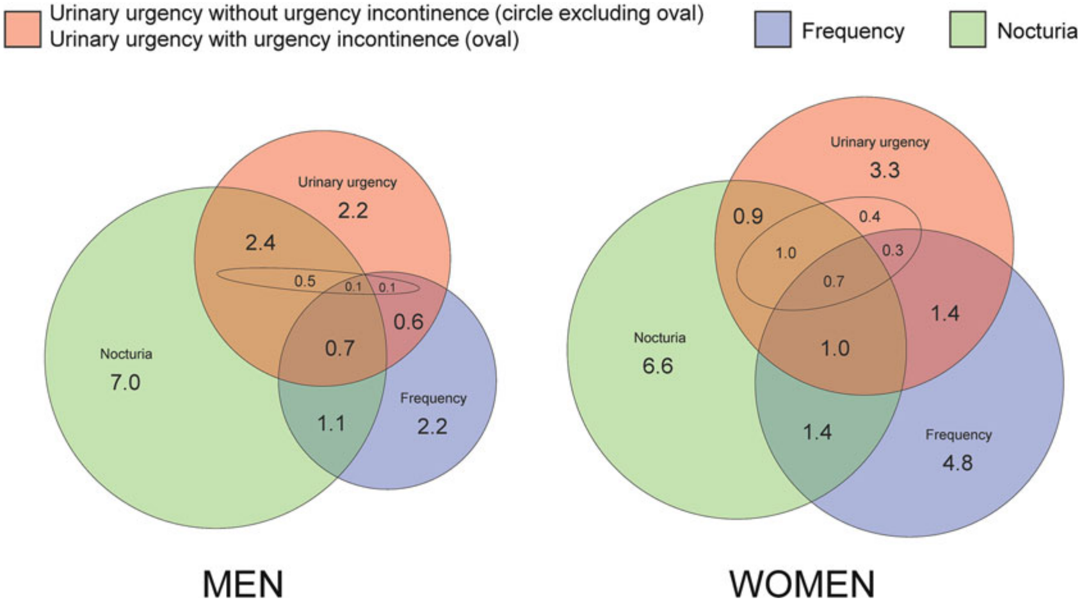


Fig. 15.2 Age-standardized prevalence of nocturia, urinary urgency (with or without urgency incontinence), and urinary frequency among Finnish people aged 18–79 years. The *red circle* represents individuals with urinary urgency (often or always in scale: never-rarely-often-always) without urgency incontinence (often or always in scale: never-rarely-often-always) excluding the area of the red oval representing individuals with urinary urgency with urgency incontinence. The *blue circle* represents individuals with urinary frequency (defined as more than eight voids/day) and the *green circle* nocturia (defined as at least two voids/night). Age standardization performed using the age structure of Finland. Modified from [126]

nocturia? Or is nocturia a side effect of various prostate cancer treatments [10, 136]? Following radical prostatectomy, more stress urinary incontinence and less obstructive symptoms have been reported, whereas the impact on nocturia has been either neutral or negative with increased nocturia [137–139].

Lifestyle

Coffee and Alcohol

Nocturia treatment guidelines usually recommend decreasing fluid intake around bedtime, especially for coffee and alcohol. However, most studies have not demonstrated a relation between nocturia and consumption of nighttime fluids [38], alcohol [22, 26, 38, 78, 118, 140], or coffee/caffeine [20, 78, 116, 119, 141]. In some studies moderate alcohol consumers had less nocturia than abstainers [92, 119, 142]. These findings could be explained by either a *systematic misclassification error* (people decrease or cease alcohol intake due to ill health) [143, 144] or *residual confounding* (moderate drinkers have many favoring social and lifestyle factors) [145, 146], although there could theoretically be several biological factors behind this association.

Smoking

Most studies have not found an association between nocturia and smoking [20, 74, 78, 110, 118, 119, 140, 141]. However, some conflicting results have also been reported. In a Swedish study [116] smoking was associated with increased nocturia but in Austrian [22] and Japanese [26] studies, it was associated with decreased nocturia.

Physical Activity

Physical activity has been reported to be protective against LUTS in men [147–149] and against nocturia specifically in women [116]. In an Austrian health-screening study [22], no relation was found between physical activity and nocturia. However, as exercise programs appear to improve nocturia [150], these effects deserve to be explored through additional research.

Race, Ethnicity, and Socioeconomic Status

In several US studies, it has been consistently noted that African American males are approximately twice as likely to report nocturia compared to other ethnic groups [88, 151, 152]. This effect persisted, although attenuated [88, 151], after adjusting for comorbidities and socioeconomic status. Similar effects were reported for women participating in the Boston Area Community Health Survey (BACH) [93] and the Penn Ovarian Aging Study [152], with black women being almost twice as likely to report nocturia even after multivariable adjustment. In addition to these population-based studies, reports from secondary-care populations [153, 154] have also suggested in a population seeking care that black women commonly reported more nocturia. However, conflicting results were found in a Kaiser Permanente study [155]. Less is known about the relationship between ethnicity and nocturia outside the United States. In small studies in Taiwan [156, 157] and Scotland [158], associations between nocturia and ethnicity have been found. In the Scottish study, the prevalence of nocturnal polyuria was significantly higher in the 200 Caucasian men compared to 93 Asian men. Overall, the underlying mechanisms for the possible association of nocturia with race/ethnicity remain unknown. In most studies, many of the risk factors for nocturia such as sleep apnea remained unmeasured.

Summary Points Regarding the Epidemiology of Nocturia

- Nocturia is one of the most, if not the most, common lower urinary tract symptoms with similar overall prevalence in both genders.
- The prevalence of nocturia is higher among young women than young men, but the prevalence increases more strongly with age in men.
- The literature on the incidence of nocturia remains relatively sparse. Incidence of nocturia has been shown to increase with age, but significant short-term fluctuation in nocturia makes studies on incidence challenging.
- Two episodes of nocturia constitute clinically meaningful nocturia, affecting quality of life and perceived health, while a single episode does not.
- Nocturia has been suggested to be associated with an increased risk of falls, fractures, and death.
- Risk factors for nocturia include conditions of the lower urinary tract, but also a range of systemic conditions, including but not limited to prostatic hyperplasia, urinary urgency, obesity, sleep apnea, parity, and postmenopausal periods.

Evaluation and Classification

Questionnaires About Nocturia and/or Sleep Quality

A number of validated instruments have been used to assess the impact of nocturia in affected patients (Table 15.1). Two [50, 159] of the instruments have been specifically designed for assessment of nocturia and its impact. Many others [160–164] have been originally designed for assessment of lower urinary tract symptom assessment suggestive of BPH. Generic quality of life instruments [165–168] have also been used in nocturia research. Generally, condition-specific measures are more responsive to small changes. On the other hand, global measures provided by a generic quality of life instrument can be more robust and give an indication of the impact on everyday activities and overall well-being compared to narrower information from a condition-specific instrument [169].

The International Consultation on Incontinence Nocturia-specific Quality of Life Questionnaire (N-QOL) is a condition-specific questionnaire for nocturia [50]. The N-QOL is a 13-item instrument, available in 17 languages, and takes approximately 5 min to complete [170]. After initial evaluation and psychometric

Table 15.1 Questionnaires employed in the study of nocturia

Questionnaire (see text)	Use in genders	Comments
ICIQ-NQOL	Both	Nocturia specific
NNES-Q	Both	Nocturia specific, validated in elderly subjects only
DAN-PSS	Both	Assesses not only nocturia severity but also bother; validated in men; nocturia questions seem not gender specific
AUA-SI/IPSS	Both	Assesses nocturia severity
BF-LUTS	Both	Assesses nocturia severity; validated in women; nocturia question seems not gender specific
ICS QoL	Men	Six questions as part of the ICS "BPH" questionnaire
BPH impact Index/ symptom Problem index	Men	Does not assess nocturia but questions on health feeling with and social implications of LUTS
EuroQoL-5D, SF-36, RAND-36, 15D	Both	Generic health-related quality of life instruments

validation in small focus groups, reproducibility and validity of the total score and subscale scores have been demonstrated. Subscales that have been identified within this score include sleep/energy and bother/concern, both of which have high loading factors for nocturia impact. N-QOL scores were shown to correlate with sleep quality measured by the Pittsburgh Sleep Quality Index (PSQI) [171] and energy/vitality and social functioning measured by the SF-36 Health Survey (SF-36) [166]. The N-QOL has been shown to demonstrate discriminant validity in relation to variation in scores among patients with nocturia times one, two, and three times per night. In a Taiwanese study [62], the validity of N-QOL was also confirmed among women. A qualitative study in adult men and women with many participants over 65 years of age showed that the N-QOL contained all of the relevant domains except for "fear of falling" and "nocturia makes me feel old" [51]. Still, responsiveness treatment needs to be assessed in an intervention study. The N-QOL represents the first questionnaire to have been specifically developed to assess the impact of nocturia on quality of life. Another instrument specifically validated for assessment of the impact of nocturia is the Nocturia, Nocturnal Enuresis and Sleep-Interruption Questionnaire (NNES-Q) [159]. It has been validated in a mailed questionnaire study among elderly people. The NNES-Q includes 12 questions on nocturia, nocturnal enuresis, sleep-interruptions, treatment, and physical function. This instrument remains to be validated in a younger population and in clinical practice.

Attempts have been made to correlate scales assessing LUTS with the impact of nocturia. A Dutch study [172] assessed 1,000 men and women using the Bristol Female Lower Urinary Tract Symptoms Questionnaire (BF-LUTS) [162], the Sleep Wake Experience List (SWEL) [173], and the RAND-36 scales [167]. They noted nocturia effects mediated by sleep problems having statistically significant effects on BF-LUTS subscales, SWEL, and RAND-36 scores [162, 167, 173]. Similarly, the BPH Impact Index [164], ICS QoL [163], BPH survey [174], Veterans Affairs Questionnaire [175], and the Olmstead County Questionnaire [176] have all been used to capture the impact of nocturia in men. The Incontinence Impact Questionnaire (IIQ) [177] and King's Health Questionnaire [178] have been used in women for assessment of this symptom [179]. A Swedish study assessed the relationship between two generic QOL instruments, the EQ-5D (EuroQol) [165] and the SF-36 [166] (specifically the vitality and energy domains) and the short quantitative Work Productivity and Activity Impairment (WPAI) [180] in a group of nocturic patients compared with controls. Nocturia resulted in significantly lower vitality and utility as aspects of quality of life [181]. Furthermore, increasing nocturia was related with impaired work productivity. In the population-based FINNO Study [10], the DAN-PSS [160] and the 15D [168] were used. In both genders, two voids per night, but not just one, were related to bother and clinically importantly impair quality of life.

In summary, it appears that the N-QOL [50] has the most robust validation for baseline and follow-up of nocturia therapy and would be the instrument of choice until other clinically validated options become available.

Initial Evaluation

Evaluation of nocturia begins with a history and physical examination which focuses on comorbidities including cardiac, pulmonary, or renal diseases, factors which may cause peripheral edema, fluid intake, prior lower urinary tract surgery, day versus nighttime urinary complaints, detrusor overactivity, or abnormal bladder sensory function. In addition, patients should be asked about snoring, sleep quality, type and timing of various medications, and other conditions that might account for excessive nocturnal urine output. The mainstay of evaluation and diagnosis of nocturia is the frequency volume chart (FVC). This requires patients to record the volume, timing, and degree of urgency perception and/or incontinence of daytime and nighttime voids, for 1–3 days. Based upon analysis of the 24-h FVC, the patient may be categorized as having any of the following: (1) polyuria (nocturnal and/or 24-h (global) urine overproduction), (2) low bladder capacity (nocturnal and/or 24 h), and (3) mixed (a combination of polyuria and low global or nocturnal bladder capacity (NBC)). Each category is associated with a differential of several contributing medical conditions (Table 15.2). Despite appropriate evaluation, clearly identifiable remediable conditions are not found in many patients. In these cases, nocturia may be judged to be idiopathic, thereby requiring an empiric approach to treatment. Questionnaires such as the DAN-PSS, AUA-SI, or BF-LUTS should be used as part of the initial evaluation of nocturia and can be useful to gauge responsiveness to various therapeutic interventions. The general advantage of questionnaires over FVCs is that the former do not suffer from a training effect: however, a disadvantage is potential recall bias.

Table 15.2 Diary-based categorization of nocturia and respective underlying medical conditions

Nocturia category	Underlying medical conditions
Nocturnal polyuria	• Congestive heart failure • Diabetes mellitus • Obstructive sleep apnea • Peripheral edema • Excessive nighttime fluid intake • Idiopathic
Diminished global or nocturnal bladder capacity	• Prostatic obstruction • Nocturnal detrusor overactivity • Neurogenic bladder • Cancer of the bladder, prostate, or urethra • Learned voiding dysfunction • Anxiety disorders • Pharmacologic agents • Bladder, ureteral calculi
Polyuria (global, 24 h)	• Uncontrolled diabetes mellitus • Diabetes insipidus • Primary polydipsia

Nocturnal Polyuria

Normally, urine is produced in a circadian pattern that is less pronounced with age. For a long time, it has been known that among healthy people, urine production is greater during the day than during the night [182] and that electrolyte excretion is reduced at night [183]. Healthy elderly people have been shown to excrete a higher proportion of urinary water, sodium, potassium, and solute output at night compared to young people [184]. In this study [184], among young people less than 25 years of age, the mean proportion of urine produced during the hours of sleep (nocturnal polyuria index, NPi) was 0.14 compared to 0.34 among older people (age > 65 years). The International Continence Society has defined NP to exist when 24-h urine production is within normal limits and NPi > 0.33 [2]. Several other definitions of nocturnal polyuria have been used. They include NUV greater than 6.4 mL/kg and nocturnal urine output > 0.9 mL/min (54 mL/h) or higher [185] and > 90 mL/h [186].

In regard to the latter definition arising from analysis of the Krimpen study, where urine production was computed using the method described by Van Mastrigt and Eijskoot [187], urine production was assumed constant between two voidings, and hourly urine production was estimated as the volume of each micturition divided by the number of hours that passed since the previous micturition. Nocturnal urine production (NUP) per hour was estimated as the mean between 1 am and 6 am, because 90 % of the men were asleep during this period. The mean nocturnal urine production in mL/h for the age strata 50–54, 55–59, 60–64, 65–69, and 70–78 years were 53.4, 54.2, 58.3, 62.8, and 66.6 mL/h, respectively. Mean nocturnal urine production was significantly higher at 100.9 mL/h in men with 24-h polyuria (>2,500 mL per 24 h). Bosch and coworkers suggested in accordance with the analysis of the Krimpen database that nocturnal urine production exceeding 90 mL/h is abnormal. However, in their study, about one third of the men with "increased" nocturnal urine production had 24-h polyuria [186].

Thus, regardless of the cut points determined for specific populations of men or women with nocturnal polyuria, for an "average" 70 kg person who sleeps about 8 h, the upper limit of urine excreted during the hours of sleep may be between 450 and 720 mL. The differential diagnosis of nocturnal polyuria includes excessive evening fluid intake, third spacing due to venous disease of the legs or cardiac dysfunction, and obstructive sleep apnea (Table 15.2).

Decreased Bladder Capacity

The two types of nocturia due to diminished bladder capacity are global (24 h) decrease in bladder capacity as expressed by low maximum voided volume and decreased nocturnal bladder capacity. In both conditions nocturnal urinary volume exceeds bladder capacity and the patient is awakened by the need to void because the bladder does not hold enough. Urological causes of low bladder capacity include infravesical obstruction, idiopathic nocturnal detrusor overactivity, neurogenic bladder, cystitis, bladder calculi, ureteral calculi, and neoplasms of the bladder, prostate, or urethra (Table 15.2). Urological evaluation for etiology of diminished bladder capacity includes cystoscopic examination and urodynamic techniques for diagnosing these disorders. Timing of medication intake should be carefully sought during the history-taking interview. Medications that pharmacologically decrease bladder capacity such as beta blockers may cause nocturia if taken just prior to retiring to bed. While urological causes for low bladder capacity may be found, it is often difficult to distinguish the causes of global from nocturnal decreases in bladder capacity. Thus, treatment of low bladder capacity may benefit patients during the day but not night or vice versa. Follow-up of therapy targeting the bladder is necessary in order to measure the benefit in regard to nocturia.

Mixed Nocturia

The etiology of nocturia in many patients is multifactorial. Diminished NBC appears to play a greater role in the pathogenesis of nocturia in younger patients, whereas in older patients nocturnal urine overproduction assumes relatively greater importance [188]. In view of emerging evidence of the manifold causes of nocturia [78], the "mixed" category is particularly relevant, in that treatment yielding clinically satisfying outcomes will likely require institution of multiple incremental additive therapies.

Polyuria

Polyuria has been defined as a 24-h urine output > 40 mL/kg [2], causing daytime urinary frequency and nocturia associated with a general increase in urine output, outstripping even normal bladder capacity [189]. Inappropriate excretion of water in cases of polyuria leads to polydipsia in order to maintain homeostasis. Causes of global polyuria include uncontrolled diabetes mellitus, diabetes insipidus, and primary polydipsia (Table 15.2). Diabetes insipidus (DI) is a disorder of water balance caused by inappropriate secretion or action of serum antidiuretic hormone (ADH). As opposed to diabetes mellitus, where the urine is hypertonic and sweet (mellitus means honey in Greek), DI is defined as having urine that is hypotonic and bland, in the setting of polyuria. There are various mechanisms of pathogenesis of DI, all leading to the same clinical manifestation. In cases where the disorder is due to inadequate secretion of ADH, the disorder is termed central DI. In contrast, when the disease is a result of renal insensitivity to ADH, the disease is termed nephrogenic DI. In cases where polyuria is due to vast amounts of ingested fluids driven primarily by behavioral or thirst disorders, it is called primary polydipsia. Overall, DI is a rare condition. It has been estimated that prevalence of DI is 3 per 100,000 in the general population [190].

ADH, a nonapeptide also known as arginine vasopressin (AVP), is produced in the supraoptic and paraventricular nuclei of the hypothalamus. ADH secretion is principally controlled by changes in serum osmolality [191]. In cases of both severe hypovolemia (normally stimulating ADH release) and hyponatremia (normally inhibitory to ADH release), the usual inhibition of ADH by osmoreceptors is overridden by the baroreceptor input and ADH is released despite the hyponatremia [189]. ADH's role in osmolality control is exerted through its influence on the kidney. ADH causes the kidney to reabsorb water in the collecting ducts and connecting tubules and decreases plasma osmolality.

Many exogenous conditions and medications may contribute to polyuria and result in the complaint of nocturia [192]. Medications can cause polyuria by increasing water intake (polydipsia), by interfering in renal ability to concentrate urine (diabetes insipidus), by causing venous stasis, or via unknown mechanisms. Inhibitors of vasopressin secretion include alcohol, phenytoin, morphine, glucocorticoids, fluphenazine, haloperidol, promethazine, oxilorphan, and butorphanol [192].

Drugs causing hypercalcemia can produce polyuria and secondary nocturia. Chronic hypercalcemia leads to a defect in the concentrating ability that may induce polyuria and polydipsia [192]. Hypervitaminosis A [193], hypervitaminosis D [194], and thiazide diuretics can result in hypercalcemia, attendant polyuria, and symptomatic nocturia.

Summary Points Regarding Evaluation and Classification of Nocturia

- Diagnosis of the etiology of nocturia utilizes an office-based approach focusing upon history and physical examination followed by analysis of 24-h frequency volume charts and questionnaires.
- Nocturia may be classified as being due to nocturnal polyuria, diminished bladder capacity, global polyuria, or combinations of factors.
- Each of the above categories leads to a set of potential medical conditions which may underlie the pathogenesis of nocturia in individual patients.
- It is currently thought that treatment of each underlying condition in a “cause-specific” manner should lead to improvement in both nocturia and related sleep disturbance and quality of life.
- The value of such evaluation in improving outcomes requires future verification.

Treatment

Goals of Care

The greater the number of nightly episodes of nocturia, the greater the risk of accidental falls and fractures [66–72] and the higher the degree of bother and quality of life disturbance [10, 29, 60, 64]. One might therefore imagine that the goal of treatment for nocturia would be to eliminate all nighttime voiding or to dramatically reduce the total number of episodes per night. This framework of greatly diminishing or curing nocturia is often the target goal of treatment. But in some ways, this sets the patient up for disappointment and unnecessarily limits potentially useful treatment options. Why is this?

First, rarely do treated patients have complete resolution of their nocturia, and in many cases, the average reduction of nocturia episodes from therapy might be perceived as rather low. Second, while the majority of disruption from nocturia is largely due to the number of nightly episodes, the number of episodes alone does not completely predict the degree of bother from nocturia [10]. One example is that older individuals are bothered by the variability and unpredictability of nocturia from night to night [52]. Since the range of time spent in bed by older adults might vary from 5 to 12 h, the impact of three episodes of nocturia might be very different at the extremes. Also, the number of nocturia episodes is adjusted by the hours spent in bed. Because sleep patterns may vary considerably in older persons, three interruptions to 5 h of sleep would likely be different from the impact of those episodes on 12 h of sleep [195]. Third, other non-bladder factors are likely meaningful potential targets for treatment. Since many older adults with nocturia are concerned with nighttime falls, minimizing risk may be useful [51, 52]. This could include using bedside commodes or urinals, minimizing the distance necessary to reach a toilet, and providing a safe, adequately lit path to the toilet. Also, one recent study showed that among individuals with similar number of episodes of nocturia, those with the greatest degree of bother were those with difficulty returning to sleep and those who reported daytime fatigue [53]. Addressing issues related to nocturia such as sleep quality might be a specific target for intervention. However, there has been a paucity of clinical trials specifically demonstrating this approach.

In most clinical trials, the primary outcome is usually a reduction in mean nocturia episodes. Nocturia episodes can be measured by voiding diary recordings or by a recalled, self-reported, average number of nocturia events occurring within a given period of time, usually ascertained with the use of a questionnaire. Because those with a higher number of episodes at baseline frequently have greater reduction, nocturia reduction may be reported as a percentage decline from baseline. Some clinical trials have reported the percent of participants achieving a 33 % [196] or 50 % [81, 197–200] reduction in nocturia from the baseline.

While some trials may report net statistical significance for reduction in nocturia, the clinical meaningfulness of these changes is suspect [201]. Many treatments offer what could be considered to be small reductions of nocturia, with most ranging from 0 to 0.8 fewer episodes of nocturia. The net reduction of an intervention, calculated as the effect of the active drug over baseline minus the effect of the placebo over baseline, can be even smaller because the placebo response is frequently in the same range. Given these facts, deciding what level of reduction is meaningful is very important. There is not perfect agreement on the number of episodes of nocturia reduction that is meaningful. Most trials examining nocturia reduction were performed prior to the validation testing the ICIQ-NQOL [50]. In several studies, the percent of individuals having a reduction equal to 1.0 fewer mean nightly episodes of nocturia [197, 199, 200] has been used, as a full nocturia episode reduction would likely be clinically meaningful [10].

An additional perspective on goal setting for treatment of nocturia would be to focus not solely on the episode reduction itself but rather also on the elimination of the negative impact of nocturia. Example targets might include reduction in reported bother from the condition, improvement in sleep, or eliminating the chance of falls. This holistic approach considers that nocturia takes place within an overall context. An additional important target for therapy is reduction in bother due to nocturia.

Overall Approach and Rationale for Combination Therapies

Guideline and review articles suggest identifying and targeting a "primary" or "principal" cause of nocturia such as nocturnal polyuria [2, 202, 203]. Because most older adults with nocturia have multiple potential causes, treatment will often require combination therapy. While many clinical investigations are trials of single agents, it has also been argued [195] that treatment of nocturia in elderly patients should be based on a holistic approach informed by identification of multiple potential underlying causes. Unfortunately, there is little high quality evidence for most treatments, and certainly with respect to combined treatments, for nocturia in this age group. One case series in older men showed benefit of an individualized and tailored intervention that combined behavioral strategies including improved sleep hygiene, therapy for medical comorbidities including diabetes mellitus, peripheral edema, and congestive heart failure, drug treatment for sleep maintenance, and bladder and prostate directed drug therapy [204]. Recommendations to use specific behavioral strategies for nocturia in older persons such as altering fluid intake, reducing sodium intake, and leg elevation for edema have largely been made on the basis of expert opinion. Another case series with 56 participants aged 59–85 (mean age 74.5, 84 % male) demonstrated that a combined intervention of fluid restriction, sleep hygiene, reducing excess bed hours, moderate daily exercise, and keeping warm in bed reduced nocturia from 3.6 episodes per night to 2.7 [150]. Yet at the same time, many older adults express that their own attempts to manage nocturia through such self-management techniques have been ineffective [52].

Approaches Found to be Efficacious in the Treatment of Nocturia

Behavioral and Exercise-Based Approaches

Some more recent information on multicomponent interventions including specific training has shown statistical benefit on nocturia reduction. A recent randomized, controlled trial (behavior with pelvic floor muscle exercises and urge suppression strategies vs. a titrated dose of oxybutynin vs. placebo) for women with urge-predominant urinary incontinence was analyzed post hoc for effect on nocturia [197]. The median reduction of 0.5 episodes per night achieved with behavioral strategies was greater than that achieved with antimuscarinic treatment (0.3 episodes) or placebo (no reduction). An additional secondary data analysis of an RCT that did not show benefit with respect to the primary endpoint of urge incontinence in women (mean age 55) did not show benefit of behavioral therapy when added to extended-release tolterodine 4 mg for nocturia [205]. An additional RCT examined the impact of the addition of either titrated bladder relaxant therapy (extended-release oxybutynin 5–30 mg) versus behavioral therapy with pelvic floor muscle exercise in men (mean age 64 years) whose 24-h urinary frequency was not resolved with alpha-blocker therapy. In this study of men with urinary frequency, defined as ≥ 9 total day and night voids, and urinary urgency, the behavioral group showed greater reductions in nocturia (mean = −0.70 episodes/night), compared to those treated with medication (mean = −0.32 episodes/night) ($p = 0.05$) [206]. Unfortunately, there are not yet published trials of pelvic floor muscle exercises or urgency suppression strategies in either men or women where nocturia was the criterion for study admission and the main outcome measure. This would be an important development, because although most patients with OAB do have nocturia, most patients with nocturia do not have OAB [126, 207].

Medications Potentially Useful in the Treatment of the Elderly Person with Nocturia

There are several pharmacological approaches for elderly patients with nocturia.

Antimuscarinic Therapy

A number of clinical trials have examined the effect of antimuscarinics for nocturia reduction, including studies of oxybutynin immediate release [197], solifenacin [208], and tolterodine [209, 210]. Overall, results of antimuscarinic treatment trials of nocturia have not been very promising. When therapy has sometimes yielded statistically significant reductions in nocturia, the net benefit has only been 0.0–0.3 episodes fewer. Four recent trials have compared placebo to active drug for nocturia without statistical improvement [211–214]. A recent "positive" trial showed a statistical advantage of solifenacin 10 mg over placebo of a net difference of −0.12 episodes per night [215]. Tolterodine demonstrated statistical reduction in nocturia accompanied by urinary urgency, but not for overall nocturia [210]. These agents may be used effectively in combination with other therapies [209] rather than as single modality therapy. Since one category of agents used for the treatment of dementia are effectively "pro-cholinergic agents," it is perhaps not surprising that drugs used for either the bladder or the brain might worsen or cause symptoms of the other [216].

While antimuscarinics are not usually efficacious for nocturia, they may be effective for nocturnal voids due to urgency [207]. Patients will often complain about the bother of a pressing need to get to the bathroom quickly upon awakening, but this outcome of *nocturnal urgency* is not well established within the literature.

Agents Directed Towards Benign Prostatic Obstruction

Alpha-adrenergic antagonists (alpha-blockers) have been shown to offer statistical reductions in nocturia in clinical trials in patients with symptoms suggestive of benign prostatic obstruction (BPO) [198, 217]. In a 1-year trial of patients presumed to have BPO treated in a Department of Veterans Affairs study, reductions from terazosin were 0.7 episodes/night; however, the net benefit compared to the effect of placebo was only 0.3 episodes/night [81, 198]. In a 4-year study with doxazosin, the reduction in nocturia was 0.5 episodes/night at 1 year, with a net benefit of 0.2 episodes compared to the effect of placebo. These results persisted out to 4 years, with a remaining statistical superiority of doxazosin versus placebo. In a subgroup analysis of those over 70 years of age, the results were similar. Nocturia response to alpha-blockers is significantly less than the response of other BPH-related symptoms [80]. This relatively small effect in research trials with populations selected to have the best chance for benefit and carefully monitored for compliance suggests that nocturia response in the general population could be even smaller.

Finasteride, which is a 5-alpha reductase inhibitor, and saw palmetto (*Serenoa repens*, saw palmetto berry extract) appear to be even less effective for nocturia than do the alpha-blockers [198, 218]. Finasteride is shown to be roughly equivalent to placebo in effect [81, 198]. In one study where a subset of participants aged ≥70 years had statistical benefit of <0.2 net fewer nocturia episodes over placebo at 1 year from finasteride 5 mg daily [81], the effect of placebo was unusually small (−0.11 episodes/night) and the net difference did not persist beyond the 1-year time point.

Treatments Addressing Sleep Problems

There are few studies that have treated nocturia by focusing on addressing the sleep disturbance. One RCT evaluated melatonin for treatment of nocturia in 20 older men with urodynamically demonstrated BPO (mean age 72 years, range 60–81 years) [219]. While melatonin showed some reductions in nocturia compared to placebo (−0.32 for melatonin vs. −0.05 episodes for placebo), this difference favoring melatonin was not statistically significant. There was, however, a significant reduction favoring melatonin in reported bother from nocturia. An unblinded, randomized trial compared the addition of either melatonin or the sedative hypnotic rilmazafone to older men and women (mean age 72) who were already taking a medication for nocturia. This study found that the addition of either treatment further reduced nocturia an additional episode, from 3.5 to 2.5 per night in both groups [220]. Treating sleep apnea with continuous positive airway pressure (CPAP) can reduce nocturia severity [121, 221]. However, these studies have not focused on frail or older populations, and this makes the generalization of results to these populations difficult. While treatment with very short-acting benzodiazepines for patients with primary insomnia and with dopaminergic agonists for patients with restless leg syndrome may improve sleep quality, there are no data to support these approaches for reducing nocturia.

Antidiuresis Treatment

Over the last 15 years, a large number of studies have examined the potential role of exogenous AVP (desmopressin or DDAVP) for the treatment of nocturia in older patients [196, 199, 200, 222–236]. DDAVP is an approved intervention for nocturia in approximately 80 countries worldwide including many in Europe and Asia but remains an off-label treatment for nocturia in the USA. In countries where DDAVP is approved for nocturia, it is not indicated for use in adults 65 years of age or older, based upon the age-related risks of hyponatremia [237]. The medication, given at night prior to bedtime, causes the kidneys to produce more highly concentrated urine that will have a reduced volume. Most older patients with nocturia do in fact have an increased nocturnal urine output, termed nocturnal polyuria, when compared to younger patients [188]. However, classifying individuals according to the *presence* or *absence* of nocturnal polyuria does not predict response to desmopressin [238]. The desired effect from DDAVP is that the production of a concentrated urine will only happen during sleep and that upon awakening, the patient will then not have a medication effect and will produce a more dilute urine, thereby equilibrating water and salt balance. The major concern related to DDAVP treatment in elderly patients is fluid retention, which can exacerbate underlying cardiovascular disease and hyponatremia. Consequences of hyponatremia can be severe and even life threatening. There is a need for the provider to have a proper knowledge of the mechanism of action of efficacy and harm. As well, the patient must strictly adhere to the proper timing of the dosage without altering the amount or adding a morning dosage. Monitoring with blood tests to make sure that there is not a drop in the serum sodium is very important, especially during the first 3–7 days of treatment.

The first two large randomized clinical trials using oral DDAVP employed essentially identical designs, with one conducted in men [200] and the other in women [199]. While many participants were older than 75, the mean age was 65 for the men and 57 for the women. These trial results both demonstrated significant reductions in nocturia and a longer initial period of sleep until first awakening. Some elements of the trial design likely have enhanced the effect size including an open-label run-in and eliminated from randomization those who did not experience >20 % reduction in nocturnal urine volume. As well, most individuals in these trials [199, 200] were titrated up to a higher dosage of DDAVP if any nocturia persisted during titration and therefore ended up on an oral dosage of 0.4 mg [199, 200]. Many older patients can have a significant reduction in nighttime urine with lower doses of oral DDAVP, such as 0.1 or 0.2 mg, thereby reducing the overall incidence of hyponatremia [231, 232, 239].

Even with diligence during the initial dosage period, in one research study where 57 individuals were randomized to 0.1 mg DDAVP for a year, one participant was described as having developed a "consciousness disturbance due to hyponatremia (116 mmol/L)" that left him unable to continue on with the study [231]. There are also concerns with the many older persons who may have preexistent hyponatremia due to a variety of medical conditions. Those who develop congestive heart failure or renal insufficiency while on DDAVP should have the drug stopped. The absolute frequency of hyponatremia is unclear but was 0 %–9 %, depending on definition, in one review [203]. Gender, age, and baseline sodium appear to be important predictors of adverse events. Pharmacodynamic studies in men aged 55–70 years found that DDAVP had a prolonged half-life, which was in part responsible for hyponatremia [240]. One review of pooled trial results broke down the incidence of hyponatremia by age and baseline sodium. For subjects with normal baseline sodium, the incidence of hyponatremia was approximately 1 % (3/336 subjects) in persons < 65 years old and 8 % (22/260) in those ≥65 years old. In older patients with a low baseline serum sodium, the incidence was as high as 75 % (6/8) [241]. Because so few frail elderly subjects were included in these trials, the actual incidence of clinically significant hyponatremia from DDAVP that might occur with monitoring outside of a clinical trial is unknown. One pilot study of DDAVP for nighttime urinary incontinence and/or nocturia was conducted in nursing home residents (mean age 82.5, range 74–96). Of the ten participants, four had a significant reduction in nocturnal polyuria. However, there was no meaningful reduction in nighttime urinary accidents with 0.84 fewer times found wet, from a baseline of 5.4 times wet per night. Also, 2 of 10 participants developed low serum sodium values of 126 and 127 mmol/L [239].

Antidiuretic therapy does reduce nighttime urinary output, but achieving this without the side effect of hyponatremia has been difficult. For elderly individuals, antidiuretic therapy via DDAVP orally absorbable tablets still has a narrow therapeutic window where the dosage that allows for efficacy in the absence of meaningful and potentially serious side effects may be difficult to find. Approaches to emphasize the efficacy and reduce the side effects have focused on the method of administration including a tablet to swallow, nasal spray, and oral lozenges; reducing or targeting the dosage; and changing the nature of the chemical used. Both a peptide analogue and a vasopressin-2-receptor agonist have been tested to better achieve the desirable half-life and pharmacokinetic profile [196].

Recently, data about the efficacy and safety of an orally disintegrating tablet formulation of DDAVP have been published [196]. The study evaluated co-primary outcomes of a decrease in nighttime voids from baseline versus placebo and the ability to achieve a 33 % decline in nocturia compared to baseline. Participants were stratified by age < 65 and ≥ 65 years, and there were 500 older individuals in the study with safety endpoints. At enrollment, all participants needed to have a serum sodium of >135 mmol/L; an estimated creatinine clearance of greater than 60 L/min (the largest single reason for exclusion during screening at 15 %); a post void residual of less than 150 mL; and, for men only, a peak uroflow of > 5 mL/s. The results showed that for men, the minimal effective dosage was 100 mcg (−1.38 mean nocturia change vs. −0.84 for placebo), and for women it was 25 mcg (−1.22 mean nocturia change vs. −0.88 for placebo). Side effects appeared in a dose-dependent fashion with higher dosages resulting in more hyponatremia. This differed by age, with older individuals having a higher rate of side effects, and by gender with women having more side effects. For those over 65 years of age dosed at 100 mcg prior to bedtime, 14.1 % had a serum sodium between 125 and 130 mmol/L and 4.7 % had < 125 mmol/L after 4 weeks. For lower dosages of 50 and 25 mcg, rates of hyponatremia with serum sodium levels of 125–130 mmol/L were 6.6 % and 2.6 %, respectively, or <125 mmol/L were 2.6 % and 0 %, respectively. The reasons for hyponatremia in women were not fully explained by pharmacokinetic profiles [242].

There have also been trials with combined usage of diuretics and antidiuretics. In this case, furosemide was given 6 h prior to bedtime, followed by a bedtime dosage of oral DDAVP after dosage was optimized during the open-label run-in [233] in a 3-week trial. Participants were excluded if they had serum sodium levels below the normal range; moderate renal insufficiency, defined as a clearance below 50 mL/min; or cardiac insufficiency. There were 204 patients screened and 122 participants over the age of 60 who enrolled. Again, only responders who achieved no voids per night or a decrease in nocturnal urine production of ≥20 % during open-label titration were enrolled in the trial. The study included 82 participants (mean age 67) who were subsequently randomized. The mean reduction of nocturia was from 3.5 to 2.0 in the treatment group and 3.3 to 3.0 in the placebo, for a net benefit of 1.2 episode reductions. Of the participants who completed the dosage titration and randomization, there were six episodes of hyponatremia, defined as <130 mmol/L.

Other Medications

Among postmenopausal women, one uncontrolled trial of estradiol in combination with a progestational agent showed a dramatic reduction in nocturia over 6 months [243]. However, in a randomized trial [106], those receiving menopausal hormone therapy did not report less or more nocturia than those taking placebo. Furthermore, no differences from placebo were found in randomized trials of an estradiol vaginal ring [107] or other estradiol preparations on urinary storage symptoms after sling surgery for stress urinary incontinence [108].

Reducing volume overload associated with lower extremity venous insufficiency or congestive heart failure with a late-afternoon dose of a rapid-acting diuretic may be helpful in reducing nocturnal polyuria and nocturia in selected patients [91, 244]. While the trial data supporting the use of diuretics in the treatment of nocturia have been small-scale randomized, controlled clinical trials, these results have been consistent and positive [245].

Surgical and Other Invasive Treatments

Posterior tibial nerve stimulation has been evaluated in OAB trials and may be effective for the treatment of nocturia. A recent trial [246] in 214 individuals demonstrated a favorable outcome for nocturia reduction in the active treatment group, dropping from 2.9 episodes/night at baseline to 2.1 with treatment. This was statistically superior to the effect of sham, with reduction from 2.9 to 2.6, yielding a net benefit of −0.4 episodes/night reduction. Of note, there were more individuals over 65 years of age (50 %) compared to the sham group (41 %) biasing against demonstrating benefit if it were true that older adults responded less well. Whether or not these gains are maintained without ongoing treatment is unknown [247].

Surgical approaches for BOO in order to treat nocturia are effective, yet nocturia specifically appears to be less responsive when compared to other LUTS [248–250]. In general, those with the most severe symptoms benefit the most from transurethral resection of the prostate (TURP) [248]. In one study, a consecutive group of 56 patients (mean age 69 years) was treated with either TURP or radical prostatectomy for persistent symptoms despite 6 months of medical therapy. The researchers monitored postoperative nocturia counts, hours of undisturbed sleep, and the ICIQ-NQOL, which were compared to baseline measurements. In this uncontrolled series, patients had significant improvements in all measured domains, including a 0.8 episode reduction per night [251]. The N-QOL outcome measure was most favorable in individuals with the greatest reductions in nocturia or the most uninterrupted sleep. Another study used a retrospective evaluation of 298 patients (mean age 70 years) over a 10-year period and found that younger men with lower preoperative urinary peak flow rates had the best postoperative results [250]. In a rare surgical versus medical treatment RCT, 66 treatment-naïve men aged 52–81 years (mean age 69, range 52–81) with nocturia believed solely due to BPH were randomized in a 1:1 fashion to either alpha-blocker therapy (tamsulosin 0.4 mg/day) or TURP. The prostate volumes and baseline nocturia nearly differed in a statistically significant manner at baseline (51 cm^3 and 2.0 mean nocturia episodes for tamsulosin group vs. 59 cm^3 and 2.4 mean nocturia episodes for the TURP group). Both groups had a reduction of nocturia to 1.5 episodes/night at 3 months and 1.4 at 6 months, as well as statistical improvements in the ICIQ-NQOL. Neither treatment was superior, but both were statistically improved from baseline [252].

Summary Points Regarding Treatment of Nocturia

- Very few older individuals achieve complete elimination of nocturia from treatment.
- Older adults are more likely to have nocturia and frequently experience greater side effects of treatment. With regard to specific therapeutic agents, older adults seem to derive similar benefit from treatment.
- Late-afternoon administration of a diuretic may reduce nocturia in persons with lower extremity venous insufficiency or congestive heart failure unresponsive to other interventions.
- Among treatment options for BPO, the alpha-blocker agents appear to be more effective for nocturia than finasteride.
- While nearly all patients with OAB have nocturia, a minority of individuals with nocturia have OAB. If OAB, DO, and/or urgency UI are felt to be major contributors to nocturia, antimuscarinic agents can be considered.
- There is limited evidence showing that dysfunctional sleep can be an appropriate target for reducing bother from nocturia. If nocturia appears due to insomnia alone, then a very short-acting sedative hypnotic may be considered.
- DDAVP should not be used in the frail elderly population because of the risk of

hyponatremia. The therapeutic window, defined as the dose at which there is efficacy, yet absence of side effects, may be quite narrow. It might be difficult to find the right dosage in any one older adult. Age, baseline serum sodium, and gender appear to affect the incidence rate of hyponatremia.

Conclusions

Nocturia is a common condition that occurs with increasing incidence and prevalence among older adults. The cause is usually multifactorial and evaluation and management can be challenging for clinicians who work with older adults. Successful treatment can help to improve clinical outcomes and quality of life for affected older adults.

References

1. Weiss JP, Blaivas JG. Nocturia. J Urol. 2000; 163(1):5–12.
2. van Kerrebroeck P, Abrams P, Chaikin D, Donovan J, Fonda D, Jackson S, et al. The standardisation of terminology in nocturia: report from the Standardisation Sub-committee of the International Continence Society. Neurourol Urodyn. 2002; 21(2):179–83.
3. Tikkinen KAO, Johnson TM, Cartwright R. Epidemiology of nocturia: evaluation of prevalence, incidence, impact and risk factors. In: Weiss JP, Blaivas JG, van Kerrebroeck PEV, Wein AJ, editors. Nocturia: causes, consequences and clinical approaches. New York, NY: Springer; 2011. p. 77–108.
4. Hunskaar S. Epidemiology of nocturia. BJU Int. 2005;96 Suppl 1:4–7.
5. Weber AM, Abrams P, Brubaker L, Cundiff G, Davis G, Dmochowski RR, et al. The standardization of terminology for researchers in female pelvic floor disorders. Int Urogynecol J Pelvic Floor Dysfunct. 2001;12(3):178–86.
6. Haylen BT, de Ridder D, Freeman RM, Swift SE, Berghmans B, Lee J, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. Neurourol Urodyn. 2010;29(1):4–20.
7. Weiss JP, Wein AJ, van Kerrebroeck P, Dmochowski R, Fitzgerald MP, Tikkinen KAO, et al. Nocturia: new directions ICI-RS Think Tank 2010. Neurourol Urodyn. 2011;30(5):723–8.
8. Tikkinen KA, Tammela TL, Huhtala H, Auvinen A. Is nocturia equally common among men and women? A population based study in Finland. J Urol. 2006;175(2):596–600.
9. Bosch JL, Weiss JP. The prevalence and causes of nocturia. J Urol. 2010;184(2):440–6.
10. Tikkinen KA, Johnson TM, Tammela TL, Sintonen H, Haukka J, Huhtala H, et al. Nocturia frequency, bother, and quality of life: how often is too often? A population-based study in Finland. Eur Urol. 2010;7(3):488–96.
11. Tikkinen KAO. Epidemiology of Nocturia—Results from the FINNO Study [dissertation]. Tampere, Finland: Tampere University Press; 2010. Available at http://acta.uta.fi/pdf/978-951-44-8020-1.pdf
12. Britton JP, Dowell AC, Whelan P. Prevalence of urinary symptoms in men aged over 60. Br J Urol. 1990;66(2):175–6.
13. Garraway WM, Collins GN, Lee RJ. High prevalence of benign prostatic hypertrophy in the community. Lancet. 1991;338(8765):469–71.
14. Chute CG, Panser LA, Girman CJ, Oesterling JE, Guess HA, Jacobsen SJ, et al. The prevalence of prostatism: a population-based survey of urinary symptoms. J Urol. 1993;150(1):85–9.
15. Sagnier PP, MacFarlane G, Richard F, Botto H, Teillac P, Boyle P. Results of an epidemiological survey using a modified American Urological Association symptom index for benign prostatic hyperplasia in France. J Urol. 1994;151(5):1266–70.
16. Homma Y, Imajo C, Takahashi S, Kawabe K, Aso Y. Urinary symptoms and urodynamics in a normal elderly population. Scand J Urol Nephrol Suppl. 1994;157:27–30.
17. Malmsten UG, Milsom I, Molander U, Norlen LJ. Urinary incontinence and lower urinary tract symptoms: an epidemiological study of men aged 45 to 99 years. J Urol. 1997;158(5):1733–7.
18. Sommer P, Nielsen KK, Bauer T, Kristensen ES, Hermann GG, Steven K, et al. Voiding patterns in men evaluated by a questionnaire survey. Br J Urol. 1990;65(2):155–60.
19. Brieger GM, Yip SK, Hin LY, Chung TK. The prevalence of urinary dysfunction in Hong Kong Chinese women. Obstet Gynecol. 1996;88(6):1041–4.
20. Samuelsson E, Victor A, Tibblin G. A population study of urinary incontinence and nocturia among women aged 20-59 years. Prevalence, well-being and wish for treatment. Acta Obstet Gynecol Scand. 1997;76(1):74–80.
21. Pinnock C, Marshall VR. Troublesome lower urinary tract symptoms in the community: a prevalence study. Med J Aust. 1997;167(2):72–5.
22. Schatzl G, Temml C, Schmidbauer J, Dolezal B, Haidinger G, Madersbacher S. Cross-sectional study of nocturia in both sexes: analysis of a voluntary health screening project. Urology. 2000;56(1):71–5.
23. van Dijk L, Kooij DG, Schellevis FG. Nocturia in the Dutch adult population. BJU Int. 2002;90(7):644–8.

24. Rembratt A, Norgaard JP, Andersson KE. Nocturia and associated morbidity in a community-dwelling elderly population. BJU Int. 2003;92(7):726–30.
25. Coyne KS, Zhou Z, Bhattacharyya SK, Thompson CL, Dhawan R, Versi E. The prevalence of nocturia and its effect on health-related quality of life and sleep in a community sample in the USA. BJU Int. 2003;92(9):948–54.
26. Yoshimura K, Terada N, Matsui Y, Terai A, Kinukawa N, Arai Y. Prevalence of and risk factors for nocturia: analysis of a health screening program. Int J Urol. 2004;11(5):282–7.
27. Irwin DE, Milsom I, Hunskaar S, Reilly K, Kopp Z, Herschorn S, et al. Population-based survey of urinary incontinence, overactive bladder, and other lower urinary tract symptoms in five countries: results of the EPIC Study. Eur Urol. 2006;50(6):1306–15.
28. Herschorn S, Gajewski J, Schulz J, Corcos J. A population-based study of urinary symptoms and incontinence: the Canadian Urinary Bladder Survey. BJU Int. 2008;101(1):52–8.
29. Choo MS, Ku JH, Park CH, Lee YS, Lee KS, Lee JG, et al. Prevalence of nocturia in a Korean population aged 40 to 89 years. Neurourol Urodyn. 2008;27(1):60–4.
30. Kupelian V, Fitzgerald MP, Kaplan SA, Norgaard JP, Chiu GR, Rosen RC. Association of nocturia and mortality: results from the Third National Health and Nutrition Examination Survey. J Urol. 2011;185(2):571–7.
31. Zhang X, Zhang J, Chen J, Zhang C, Li Q, Xu T, et al. Prevalence and risk factors of nocturia and nocturia-related quality of life in the Chinese population. Urol Int. 2011;86(2):173–8.
32. McGrother CW, Donaldson MM, Shaw C, Matthews RJ, Hayward TA, Dallosso HM, et al. Storage symptoms of the bladder: prevalence, incidence and need for services in the UK. BJU Int. 2004;93(6):763–9.
33. Muscatello DJ, Rissel C, Szonyi G. Urinary symptoms and incontinence in an urban community: prevalence and associated factors in older men and women. Intern Med J. 2001;31(3):151–60.
34. Parsons M, Tissot W, Cardozo L, Diokno A, Amundsen CL, Coats AC, et al. Normative bladder diary measurements: night versus day. Neurourol Urodyn. 2007;26(4):465–73.
35. Blanker MH, Bohnen AM, Groeneveld FP, Bernsen RM, Prins A, Ruud Bosch JL. Normal voiding patterns and determinants of increased diurnal and nocturnal voiding frequency in elderly men. J Urol. 2000;164(4):1201–5.
36. Hunskaar S. Fluctuations in lower urinary tract symptoms in women. Reassurance and watchful waiting can prevent overtreatment BMJ. 2000;320(7247):1418–9.
37. Moller LA, Lose G, Jorgensen T. Incidence and remission rates of lower urinary tract symptoms at one year in women aged 40-60: longitudinal study. BMJ. 2000;320(7247):1429–32.
38. Johnson TM, Sattin RW, Parmelee P, Fultz NH, Ouslander JG. Evaluating potentially modifiable risk factors for prevalent and incident nocturia in older adults. J Am Geriatr Soc. 2005;53(6):1011–6.
39. Yoshimura K, Kamoto T, Tsukamoto T, Oshiro K, Kinukawa N, Ogawa O. Seasonal alterations in nocturia and other storage symptoms in three Japanese communities. Urology. 2007;69(5):864–70.
40. van Doorn B, Blanker MH, Kok ET, Westers P, Bosch JL. Once nocturia, always nocturia? Natural history of nocturia in older men based on frequency-volume charts: the Krimpen study. J Urol. 2011;186(5):1956–61.
41. Herzog AR, Fultz NH. Prevalence and incidence of urinary incontinence in community-dwelling populations. J Am Geriatr Soc. 1990;38(3):273–81.
42. Hakkinen JT, Hakama M, Shiri R, Auvinen A, Tammela TL, Koskimaki J. Incidence of nocturia in 50 to 80-year-old Finnish men. J Urol. 2006;176(6 Pt 1):2541–5. discussion 2545.
43. Malmsten UG, Molander U, Peeker R, Irwin DE, Milsom I. Urinary incontinence, overactive bladder, and other lower urinary tract symptoms: a longitudinal population-based survey in men aged 45-103 years. Eur Urol. 2010;58(1):149–56.
44. Viktrup L. The risk of lower urinary tract symptoms five years after the first delivery. Neurourol Urodyn. 2002;21(1):2–29.
45. Viktrup L, Lose G. Incidence and remission of lower urinary tract symptoms during 12 years after the first delivery: a cohort study. J Urol. 2008;180(3):992–7.
46. Paunio T, Korhonen T, Hublin C, Partinen M, Kivimaki M, Koskenvuo M, et al. Longitudinal study on poor sleep and life dissatisfaction in a nationwide cohort of twins. Am J Epidemiol. 2009;169(2):206–13.
47. King CR, Knutson KL, Rathouz PJ, Sidney S, Liu K, Lauderdale DS. Short sleep duration and incident coronary artery calcification. JAMA. 2008;300(24):2859–66.
48. Hublin C, Partinen M, Koskenvuo M, Kaprio J. Sleep and mortality: a population-based 22-year follow-up study. Sleep. 2007;30(10):1245–53.
49. Asplund R, Aberg H. Health of the elderly with regard to sleep and nocturnal micturition. Scand J Prim Health Care. 1992;10(2):98–104.
50. Abraham L, Hareendran A, Mills IW, Martin ML, Abrams P, Drake MJ, et al. Development and validation of a quality-of-life measure for men with nocturia. Urology. 2004;63(3):481–6.
51. Mock LL, Parmelee PA, Kutner N, Scott J, Johnson TM. Content validation of symptom-specific nocturia quality-of-life instrument developed in men: issues expressed by women, as well as men. Urology. 2008;72(4):736–42.
52. Booth JM, Lawrence M, O'Neill K, McMillan L. Exploring older peoples' experiences of nocturia: a poorly recognised urinary condition that limits participation. Disabil Rehabil. 2010;32(9):765–74.

53. Vaughan CP, Eisenstein R, Bliwise DL, Endeshaw YK, Nagamia ZJ, Wolf RA, et al. Self-rated sleep characteristics and bother from nocturia. Int J Clin Pract. 2012;66(4):369–73.
54. Endeshaw Y. Correlates of self-reported nocturia among community-dwelling older adults. J Gerontol A Biol Sci Med Sci. 2009;64(1):142–8.
55. Middelkoop HA, den Smilde-van den Doel DA, Neven AK, Kamphuisen HA, Springer CP. Subjective sleep characteristics of 1,485 males and females aged 50-93: effects of sex and age, and factors related to self-evaluated quality of sleep. J Gerontol A Biol Sci Med Sci. 1996;51(3): M108–15.
56. Bing MH, Moller LA, Jennum P, Mortensen S, Skovgaard LT, Lose G. Prevalence and bother of nocturia, and causes of sleep interruption in a Danish population of men and women aged 60-80 years. BJU Int. 2006;98(3):599–604.
57. Bliwise DL, Foley DJ, Vitiello MV, Ansari FP, Ancoli-Israel S, Walsh JK. Nocturia and disturbed sleep in the elderly. Sleep Med. 2009;10(5):540–8.
58. Pressman MR, Figueroa WG, Kendrick-Mohamed J, Greenspon LW, Peterson DD. Nocturia. A rarely recognized symptom of sleep apnea and other occult sleep disorders Arch Intern Med. 1996; 156(5):545–50.
59. Sagnier PP, MacFarlane G, Teillac P, Botto H, Richard F, Boyle P. Impact of symptoms of prostatism on level of bother and quality of life of men in the French community. J Urol. 1995;153(3 Pt 1): 669–73.
60. Fiske J, Scarpero HM, Xue X, Nitti VW. Degree of bother caused by nocturia in women. Neurourol Urodyn. 2004;23(2):130–3.
61. Liew LC, Tiong HY, Wong ML, Png DC, Tan JK. A population study of nocturia in Singapore. BJU Int. 2006;97(1):109–12.
62. Yu HJ, Chen FY, Huang PC, Chen TH, Chie WC, Liu CY. Impact of nocturia on symptom-specific quality of life among community-dwelling adults aged 40 years and older. Urology. 2006;67(4):713–8.
63. Lowenstein L, Brubaker L, Kenton K, Kramer H, Shott S, FitzGerald MP. Prevalence and impact of nocturia in a urogynecologic population. Int Urogynecol J Pelvic Floor Dysfunct. 2007;18(9): 1049–52.
64. Kupelian V, Wei JT, O'Leary MP, Norgaard JP, Rosen RC, McKinlay JB. Nocturia and quality of life: results from the Boston Area Community Health Survey. Eur Urol. 2012;61(1):78–84.
65. Jarvinen TL, Sievanen H, Khan KM, Heinonen A, Kannus P. Shifting the focus in fracture prevention from osteoporosis to falls. BMJ. 2008;336(7636): 124–6.
66. Stewart RB, Moore MT, May FE, Marks RG, Hale WE. Nocturia: a risk factor for falls in the elderly. J Am Geriatr Soc. 1992;40(12):1217–20.
67. Brown JS, Vittinghoff E, Wyman JF, Stone KL, Nevitt MC, Ensrud KE, et al. Urinary incontinence: does it increase risk for falls and fractures? Study of Osteoporotic Fractures Research Group. J Am Geriatr Soc. 2000;48(7):721–5.
68. Temml C, Ponholzer A, Gutjahr G, Berger I, Marszalek M, Madersbacher S. Nocturia is an age-independent risk factor for hip-fractures in men. Neurourol Urodyn. 2009;28(8):949–52.
69. Asplund R. Hip fractures, nocturia, and nocturnal polyuria in the elderly. Arch Gerontol Geriatr. 2006;43(3):319–26.
70. Parsons JK, Mougey J, Lambert L, Wilt TJ, Fink HA, Garzotto M, et al. Lower urinary tract symptoms increase the risk of falls in older men. BJU Int. 2009;104(1):63–8.
71. Vaughan CP, Brown CJ, Goode PS, Burgio KL, Allman RM, Johnson TM. The association of nocturia with incident falls in an elderly community-dwelling cohort. Int J Clin Pract. 2010;64(5): 577–83.
72. Nakagawa H, Niu K, Hozawa A, Ikeda Y, Kaiho Y, Ohmori-Matsuda K, et al. Impact of nocturia on bone fracture and mortality in older individuals: a Japanese longitudinal cohort study. J Urol. 2010;184(4):1413–8.
73. Asplund R. Mortality in the elderly in relation to nocturnal micturition. BJU Int. 1999;84(3): 297–301.
74. Bursztyn M, Jacob J, Stessman J. Usefulness of nocturia as a mortality risk factor for coronary heart disease among persons born in 1920 or 1921. Am J Cardiol. 2006;98(10):1311–5.
75. Guyatt GH, Sackett DL, Sinclair JC, Hayward R, Cook DJ, Cook RJ. Users' guides to the medical literature IX. A method for grading health care recommendations. Evidence-Based Medicine Working Group. JAMA. 1995;274(22):1800–4.
76. Schunemann HJ, Oxman AD, Brozek J, Glasziou P, Jaeschke R, Vist GE, et al. Grading quality of evidence and strength of recommendations for diagnostic tests and strategies. BMJ. 2008;336(7653): 1106–10.
77. Yu HJ, Chen TH, Chie WC, Liu CY, Tung TH, Huang SW. Prevalence and associated factors of nocturia among adult residents of the Matsu area of Taiwan. J Formos Med Assoc. 2005;104(6):444–7.
78. Tikkinen KA, Auvinen A, Johnson TM, Weiss JP, Keranen T, Tiitinen A, et al. A systematic evaluation of factors associated with nocturia–the population-based FINNO study. Am J Epidemiol. 2009; 170(3):361–8.
79. Homma Y, Yamaguchi T, Kondo Y, Horie S, Takahashi S, Kitamura T. Significance of nocturia in the International Prostate Symptom Score for benign prostatic hyperplasia. J Urol. 2002;167(1):172–6.
80. Yoshimura K, Ohara H, Ichioka K, Terada N, Matsui Y, Terai A, et al. Nocturia and benign prostatic hyperplasia. Urology. 2003;61(4):786–90.
81. Johnson TM, Burrows PK, Kusek JW, Nyberg LM, Tenover JL, Lepor H, et al. The effect of doxazosin, finasteride and combination therapy on nocturia in

men with benign prostatic hyperplasia. J Urol. 2007;78(5):2045. discussion 2050-1.
82. Abrams PH, Farrar DJ, Turner-Warwick RT, Whiteside CG, Feneley RC. The results of prostatectomy: a symptomatic and urodynamic analysis of 152 patients. J Urol. 1979;121(5):640–2.
83. Bruskewitz RC, Larsen EH, Madsen PO, Dorflinger T. 3-year follow-up of urinary symptoms after transurethral resection of the prostate. J Urol. 1986;136(3): 613–5.
84. Asplund R, Henriksson S, Johansson S, Isacsson G. Nocturia and depression. BJU Int. 2004;93(9):1253–6.
85. Bech P, Rasmussen NA, Olsen LR, Noerholm V, Abildgaard W. The sensitivity and specificity of the Major Depression Inventory, using the Present State Examination as the index of diagnostic validity. J Affect Disord. 2001;66(2–3):159–64.
86. Asplund R, Johansson S, Henriksson S, Isacsson G. Nocturia, depression and antidepressant medication. BJU Int. 2005;95(6):820–3.
87. McKeigue PM, Reynard JM. Relation of nocturnal polyuria of the elderly to essential hypertension. Lancet. 2000;355(9202):486–8.
88. Burgio KL, Johnson TM, Goode PS, Markland AD, Richter HE, Roth DL, et al. Prevalence and correlates of nocturia in community-dwelling older adults. J Am Geriatr Soc. 2010;58(5):861–6.
89. Hall SA, Chiu GR, Kaufman DW, Wittert GA, Link CL, McKinlay JB (2011) Commonly used antihypertensives and lower urinary tract symptoms: results from the Boston Area Community Health (BACH) Survey. BJU Int. 2012;109(11):1676–84.
90. Bulpitt CJ, Connor M, Schulte M, Fletcher AE. Bisoprolol and nifedipine retard in elderly hypertensive patients: effect on quality of life. J Hum Hypertens. 2000;14(3):205–12.
91. Reynard JM, Cannon A, Yang Q, Abrams P. A novel therapy for nocturnal polyuria: a double-blind randomized trial of frusemide against placebo. Br J Urol. 1998;81(2):215–8.
92. Gourova LW, van de Beek C, Spigt MG, Nieman FH, van Kerrebroeck PE. Predictive factors for nocturia in elderly men: a cross-sectional study in 21 general practices. BJU Int. 2006;97(3):528–32.
93. Fitzgerald MP, Litman HJ, Link CL, McKinlay JB. BACH Survey Investigators. The association of nocturia with cardiac disease, diabetes, body mass index, age and diuretic use: results from the BACH survey. J Urol. 2007;177(4):1385–9.
94. Compston A, Coles A. Multiple sclerosis. Lancet. 2002;359(9313):1221–31.
95. DasGupta R, Fowler CJ. Bladder, bowel and sexual dysfunction in multiple sclerosis: management strategies. Drugs. 2003;63(2):153–66.
96. Asplund R. Nocturia in relation to sleep, somatic diseases and medical treatment in the elderly. BJU Int. 2002;90(6):533–6.
97. Young A, Home M, Churchward T, Freezer N, Holmes P, Ho M. Comparison of sleep disturbance in mild versus severe Parkinson's disease. Sleep. 2002;25(5):573–7.
98. Hornyak M, Kopasz M, Berger M, Riemann D, Voderholzer U. Impact of sleep-related complaints on depressive symptoms in patients with restless legs syndrome. J Clin Psychiatry. 2005;66(9):1139–45.
99. Pearson VE, Gamaldo CE, Allen RP, Lesage S, Hening WA, Earley CJ. Medication use in patients with restless legs syndrome compared with a control population. Eur J Neurol. 2008;15(1):16–21.
100. Tikkinen KA, Auvinen A, Tiitinen A, Valpas A, Johnson TM, Tammela TL. Reproductive factors associated with nocturia and urinary urgency in women – a population-based study in Finland. Am J Obstet Gynecol. 2008;199(2):153.e1-12.
101. Alling Moller L, Lose G, Jorgensen T. Risk factors for lower urinary tract symptoms in women 40 to 60 years of age. Obstet Gynecol. 2000;96(3):446–51.
102. Asplund R, Aberg HE. Development of nocturia in relation to health, age and the menopause. Maturitas. 2005;51(4):358–62.
103. Rekers H, Drogendijk AC, Valkenburg HA, Riphagen F. The menopause, urinary incontinence and other symptoms of the genitourinary tract. Maturitas. 1992;15(2):101–11.
104. Lin TL, Ng SC, Chen YC, Hu SW, Chen GD. What affects the occurrence of nocturia more: menopause or age? Maturitas. 2005;50(2):71–7.
105. Moline ML, Broch L, Zak R, Gross V. Sleep in women across the life cycle from adulthood through menopause. Sleep Med Rev. 2003;7(2):155–77.
106. Cardozo L, Rekers H, Tapp A, Barnick C, Shepherd A, Schussler B, et al. Oestriol in the treatment of postmenopausal urgency: a multicentre study. Maturitas. 1993;18(1):47–53.
107. Lose G, Englev E. Oestradiol-releasing vaginal ring versus oestriol vaginal pessaries in the treatment of bothersome lower urinary tract symptoms. BJOG. 2000;107(8):1029–34.
108. Liapis A, Bakas P, Georgantopoulou C, Creatsas G. The use of oestradiol therapy in postmenopausal women after TVT-O anti-incontinence surgery. Maturitas. 2010;66(1):101–6.
109. Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, et al. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. Neurourol Urodyn. 2002; 21(2):167–78.
110. Blanker MH, Bernsen RM, Ruud Bosch JL, Thomas S, Groeneveld FP, Prins A, et al. Normal values and determinants of circadian urine production in older men: a population based study. J Urol. 2002;168 (4 Pt 1):1453–7.
111. Torimoto K, Hirayama A, Samma S, Yoshida K, Fujimoto K, Hirao Y. The relationship between nocturnal polyuria and the distribution of body fluid: assessment by bioelectric impedance analysis. J Urol. 2009;181(1):219,24. discussion 224.

112. Sugaya K, Nishijima S, Owan T, Oda M, Miyazato M, Ogawa Y. Effects of walking exercise on nocturia in the elderly. Biomed Res. 2007;28(2):101–5.
113. Asplund R. The nocturnal polyuria syndrome (NPS). Gen Pharmacol. 1995;26(6):1203–9.
114. Miller M. Nocturnal polyuria in older people: pathophysiology and clinical implications. J Am Geriatr Soc. 2000;48(10):1321–9.
115. Weiss JP, Blaivas JG. Nocturnal polyuria versus overactive bladder in nocturia. Urology. 2002;60(5 Suppl 1):28,32. discussion 32.
116. Asplund R, Aberg HE. Nocturia in relation to body mass index, smoking and some other life-style factors in women. Climacteric. 2004;7(3):267–73.
117. Laven BA, Orsini N, Andersson SO, Johansson JE, Gerber GS, Wolk A. Birth weight, abdominal obesity and the risk of lower urinary tract symptoms in a population based study of Swedish men. J Urol. 2008;179(5):1891,5. discussion 1895-6.
118. Bing MH, Moller LA, Jennum P, Mortensen S, Lose G. Nocturia and associated morbidity in a Danish population of men and women aged 60-80 years. BJU Int. 2008 Sep;102(7):808–14. discussion 814-5.
119. Shiri R, Hakama M, Hakkinen J, Auvinen A, Huhtala H, Tammela TL, et al. The effects of lifestyle factors on the incidence of nocturia. J Urol. 2008;180(5): 2059–62.
120. Lee WC, Wu HP, Tai TY, Liu SP, Chen J, Yu HJ. Effects of diabetes on female voiding behavior. J Urol. 2004;172(3):989–92.
121. Fitzgerald MP, Mulligan M, Parthasarathy S. Nocturic frequency is related to severity of obstructive sleep apnea, improves with continuous positive airways treatment. Am J Obstet Gynecol. 2006; 194(5):1399–403.
122. Sarma AV, Burke JP, Jacobson DJ, McGree ME, St Sauver J, Girman CJ, et al. Associations between diabetes and clinical markers of benign prostatic hyperplasia among community-dwelling Black and White men. Diabetes Care. 2008;31(3):476–82.
123. Abrams P, Artibani W, Cardozo L, Dmochowski R, van Kerrebroeck P, Sand P, et al. Reviewing the ICS 2002 terminology report: the ongoing debate. Neurourol Urodyn. 2009;28(4):287.
124. Wein AJ, Rackley RR. Overactive bladder: a better understanding of pathophysiology, diagnosis and management. J Urol. 2006;175(3 Pt 2):S5–S10.
125. Krystal AD, Preud'homme XA, Amundsen CL, Webster GD. Detrusor overactivity persisting at night and preceding nocturia in patients with overactive bladder syndrome: a nocturnal cystometrogram and polysomnogram study. J Urol. 2010;184(2):623–8.
126. Tikkinen KA, Tammela TL, Rissanen AM, Valpas A, Huhtala H, Auvinen A. Is the prevalence of overactive bladder overestimated? A population-based study in Finland. PLoS ONE. 2007;2:e195.
127. Michel MC, de la Rosette JJ. Role of muscarinic receptor antagonists in urgency and nocturia. BJU Int. 2005;96 Suppl 1:37–42.
128. Thakar R, Ayers S, Clarkson P, Stanton S, Manyonda I. Outcomes after total versus subtotal abdominal hysterectomy. N Engl J Med. 2002;347(17): 1318–25.
129. Vervest HA, Kiewiet de Jonge M, Vervest TM, Barents JW, Haspels AA. Micturition symptoms and urinary incontinence after non-radical hysterectomy. Acta Obstet Gynecol Scand. 1988;67(2):141–6.
130. Virtanen H, Makinen J, Tenho T, Kiilholma P, Pitkanen Y, Hirvonen T. Effects of abdominal hysterectomy on urinary and sexual symptoms. Br J Urol. 1993;72(6):868–72.
131. Altman D, Lopez A, Falconer C, Zetterstrom J. The impact of hysterectomy on lower urinary tract symptoms. Int Urogynecol J Pelvic Floor Dysfunct. 2003;14(6):418–23.
132. Prasad M, Sadhukhan M, Tom B, Al-Taher H. The effect of hysterectomy on urinary symptoms and residual bladder volume. J Obstet Gynaecol. 2002; 22(5):544–7.
133. Brown CT, O'Flynn E, Van Der Meulen J, Newman S, Mundy AR, Emberton M. The fear of prostate cancer in men with lower urinary tract symptoms: should symptomatic men be screened? BJU Int. 2003; 91(1):30–2.
134. Young JM, Muscatello DJ, Ward JE. Are men with lower urinary tract symptoms at increased risk of prostate cancer? A systematic review and critique of the available evidence. BJU Int. 2000;85(9): 1037–48.
135. Martin RM, Vatten L, Gunnell D, Romundstad P, Nilsen TI. Lower urinary tract symptoms and risk of prostate cancer: the HUNT 2 Cohort. Norway Int J Cancer. 2008;123(8):1924–8.
136. Damber JE, Aus G. Prostate cancer. Lancet. 2008;371(9625):1710–21.
137. Sanda MG, Dunn RL, Michalski J, Sandler HM, Northouse L, Hembroff L, et al. Quality of life and satisfaction with outcome among prostate-cancer survivors. N Engl J Med. 2008;358(12):1250–61.
138. Namiki S, Saito S, Ishidoya S, Tochigi T, Ioritani N, Yoshimura K, et al. Adverse effect of radical prostatectomy on nocturia and voiding frequency symptoms. Urology. 2005;66(1):147–51.
139. Namiki S, Ishidoya S, Saito S, Satoh M, Tochigi T, Ioritani N, et al. Natural history of voiding function after radical retropubic prostatectomy. Urology. 2006;68(1):142–7.
140. Hsieh CH, Chen HY, Hsu CS, Chang ST, Chiang CD. Risk factors for nocturia in Taiwanese women aged 20-59 years. Taiwan J Obstet Gynecol. 2007; 46(2):166–70.
141. Klein BE, Klein R, Lee KE, Bruskewitz RC. Correlates of urinary symptom scores in men. Am J Public Health. 1999;89(11):1745–8.
142. Kang D, Andriole GL, Van De Vooren RC, Crawford D, Chia D, Urban DA, et al. Risk behaviours and benign prostatic hyperplasia. BJU Int. 2004;93(9): 1241–5.

143. Shaper AG, Wannamethee G, Walker M. Alcohol and mortality in British men: explaining the U-shaped curve. Lancet. 1988;2(8623):1267–73.
144. Fillmore KM, Stockwell T, Chikritzhs T, Bostrom A, Kerr W. Moderate alcohol use and reduced mortality risk: systematic error in prospective studies and new hypotheses. Ann Epidemiol. 2007;17(5 Suppl):S16–23.
145. Naimi TS, Brown DW, Brewer RD, Giles WH, Mensah G, Serdula MK, et al. Cardiovascular risk factors and confounders among nondrinking and moderate-drinking U.S. adults. Am J Prev Med. 2005;28(4):369–73.
146. Jackson R, Broad J, Connor J, Wells S. Alcohol and ischaemic heart disease: probably no free lunch. Lancet. 2005;366(9501):1911–2.
147. Platz EA, Kawachi I, Rimm EB, Colditz GA, Stampfer MJ, Willett WC, et al. Physical activity and benign prostatic hyperplasia. Arch Intern Med. 1998;158(21):2349–56.
148. Prezioso D, Catuogno C, Galassi P, D'Andrea G, Castello G, Pirritano D. Life-style in patients with LUTS suggestive of BPH. Eur Urol. 2001;40 Suppl 1:9–12.
149. Rohrmann S, Crespo CJ, Weber JR, Smit E, Giovannucci E, Platz EA. Association of cigarette smoking, alcohol consumption and physical activity with lower urinary tract symptoms in older American men: findings from the third National Health And Nutrition Examination Survey. BJU Int. 2005;96(1):77–82.
150. Soda T, Masui K, Okuno H, Terai A, Ogawa O, Yoshimura K. Efficacy of nondrug lifestyle measures for the treatment of nocturia. J Urol. 2010;184(3): 1000–4.
151. Kupelian V, Link CL, Hall SA, McKinlay JB. Are racial/ethnic disparities in the prevalence of nocturia due to socioeconomic status? Results of the BACH Survey. J Urol. 2009;181(4):1756–63.
152. Markland AD, Vaughan CP, Johnson TM, Goode PS, Redden DT, Burgio KL. Prevalence of nocturia in United States men: results from the National Health and Nutrition Examination Survey. J Urol. 2011;185(3):998–1002.
152. Gopal M, Sammel MD, Pien G, Gracia C, Freeman EW, Lin H, et al. Investigating the associations between nocturia and sleep disorders in perimenopausal women. J Urol. 2008;180(5):2063–7.
153. Munro-Faure AD, Beilin LJ, Bulpitt CJ, Coles EC, Dollery CT, Gear JS, et al. Comparison of black and white patients attending hypertension clinics in England. Br Med J. 1979;1(6170):1044–7.
154. Sze EH, Jones WP, Ferguson JL, Barker CD, Dolezal JM. Prevalence of urinary incontinence symptoms among black, white, and Hispanic women. Obstet Gynecol. 2002;99(4):572–5.
155. Lukacz ES, Whitcomb EL, Lawrence JM, Nager CW, Luber KM. Urinary frequency in community-dwelling women: what is normal? Am J Obstet Gynecol. 2009;200(5):552.e1. 552.e7.
156. Kuo HC. Prevalence of lower urinary tract symptoms in male Aborigines and non-Aborigines in eastern Taiwan. J Formos Med Assoc. 2008;107(9): 728–35.
157. Chuang FC, Kuo HC. Prevalence of lower urinary tract symptoms in indigenous and non-indigenous women in Eastern Taiwan. J Formos Med Assoc. 2010;109(3):228–36.
158. Mariappan P, Turner KJ, Sothilingam S, Rajan P, Sundram M, Stewart LH. Nocturia, nocturia indices and variables from frequency-volume charts are significantly different in Asian and Caucasian men with lower urinary tract symptoms: a prospective comparison study. BJU Int. 2007;100(2):332–6.
159. Bing MH, Moller LA, Jennum P, Mortensen S, Lose G. Validity and reliability of a questionnaire for evaluating nocturia, nocturnal enuresis and sleep-interruptions in an elderly population. Eur Urol. 2006;49(4):710–9.
160. Schou J, Poulsen AL, Nordling J. The value of a new symptom score (DAN-PSS) in diagnosing urodynamic infravesical obstruction in BPH. Scand J Urol Nephrol. 1993;27(4):489–92.
161. Barry MJ, Fowler Jr FJ, O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK, et al. The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. J Urol. 1992;148(5):1549. 1557, discussion 1564.
162. Jackson S, Donovan J, Brookes S, Eckford S, Swithinbank L, Abrams P. The Bristol Female Lower Urinary Tract Symptoms questionnaire: development and psychometric testing. Br J Urol. 1996;77(6):805–12.
163. Donovan JL, Kay HE, Peters TJ, Abrams P, Coast J, Matos-Ferreira A, et al. Using the ICSOoL to measure the impact of lower urinary tract symptoms on quality of life: evidence from the ICS-'BPH' Study. International Continence Society–Benign Prostatic Hyperplasia. Br J Urol. 1997;80(5):712–21.
164. Barry MJ, Fowler Jr FJ, O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK. Measuring disease-specific health status in men with benign prostatic hyperplasia. Measurement Committee of The American Urological Association. Med Care. 1995;33(4 Suppl):AS145–55.
165. The EuroQol Group. EuroQol–a new facility for the measurement of health-related quality of life. Health Policy. 1990;16(3):199–208.
166. Brazier JE, Harper R, Jones NM, O'Cathain A, Thomas KJ, Usherwood T, et al. Validating the SF-36 health survey questionnaire: new outcome measure for primary care. BMJ. 1992;305(6846):160–4.
167. Hays RD, Sherbourne CD. The RAND 36-Item Health Survey 1.0. Health Econ. 1993;2(3):217–27.
168. Sintonen H. The 15D instrument of health-related quality of life: properties and applications. Ann Med. 2001;33(5):328–36.
169. Osoba D. Guidelines for measuring quality of life in clinical trials. In: Staquet MJ, Hays RD, Fayers PM, editors. Quality of Life assessment in clinical trials. Oxford: Oxford University Press; 1998.

170. McKown S, Abraham L, Coyne K, Gawlicki M, Piault E, Vats V. Linguistic validation of the N-QOL (ICIQ), OAB-q (ICIQ), PPBC, OAB-S and ICIQ-MLUTSsex questionnaires in 16 languages. Int J Clin Pract. 2010;64(12):1643–52.
171. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989;28(2):193–213.
172. van Dijk L, Kooij DG, Schellevis FG, Kaptein AA, Boon TA, Wooning M. Nocturia: impact on quality of life in a Dutch adult population. BJU Int. 2004;93(7):1001–4.
173. van Diest R, Appels WP. Sleep physiological characteristics of exhausted men. Psychosom Med. 1994;56(1):28–35.
174. Epstein RS, Deverka PA, Chute CG, Panser L, Oesterling JE, Lieber MM, et al. Validation of a new quality of life questionnaire for benign prostatic hyperplasia. J Clin Epidemiol. 1992;45(12): 1431–45.
175. A comparison of quality of life with patient reported symptoms and objective findings in men with benign prostatic hyperplasia. The Department of Veterans Affairs Cooperative Study of transurethral resection for benign prostatic hyperplasia. J Urol 1993;150(5 Pt 2):1696–7000
176. Girman CJ, Epstein RS, Jacobsen SJ, Guess HA, Panser LA, Oesterling JE, et al. Natural history of prostatism: impact of urinary symptoms on quality of life in 2115 randomly selected community men. Urology. 1994;44(6):825–31.
177. Shumaker SA, Wyman JF, Uebersax JS, McClish D, Fantl JA. Health-related quality of life measures for women with urinary incontinence: the Incontinence Impact Questionnaire and the Urogenital Distress Inventory. Continence Program in Women (CPW) Research Group. Qual Life Res. 1994;3(5):291–306.
178. Kelleher CJ, Cardozo LD, Khullar V, Salvatore S. A new questionnaire to assess the quality of life of urinary incontinent women. Br J Obstet Gynaecol. 1997;104(12):1374–9.
179. Donovan JL. Measuring the impact of nocturia on quality of life. BJU Int. 1999;84 Suppl 1:21–5.
180. Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. Pharmacoeconomics. 1993;4(5):353–65.
181. Kobelt G, Borgstrom F, Mattiasson A. Productivity, vitality and utility in a group of healthy professionally active individuals with nocturia. BJU Int. 2003;91(3):190–5.
182. Roberts W (1860) Observations on some of the daily changes of the urine. 5:817–825,906–923
183. Norn M (1929) Über Schwankungen der Kalium-, Natrium- und Chloridausscheidung durch die Niere im Laufe des Tages [Fluctuations of the potassium, sodium and chloride excretion by the kidney in the course of the day] 55:184–210
184. Kirkland JL, Lye M, Levy DW, Banerjee AK. Patterns of urine flow and electrolyte excretion in healthy elderly people. Br Med J (Clin Res Ed). 1983;287(6406):1665–7.
185. Matthiesen TB, Rittig S, Norgaard JP, Pedersen EB, Djurhuus JC. Nocturnal polyuria and natriuresis in male patients with nocturia and lower urinary tract symptoms. J Urol. 1996;156(4):1292–9.
186. Blanker MH, Bernsen RM, Bosch JL, Thomas S, Groeneveld FP, Prins A, et al. Relation between nocturnal voiding frequency and nocturnal urine production in older men: a population-based study. Urology. 2002;60(4):612–6.
187. van Mastrigt R, Eijskoot F. Analysis of voided urine volumes measured using a small electronic pocket balance. Scand J Urol Nephrol. 1996;30(4):257–63.
188. Weiss JP, Blaivas JG, Jones M, Wang JT, Guan Z. 037 Study Group. Age related pathogenesis of nocturia in patients with overactive bladder. J Urol. 2007;178(2):548,51.
189. Karet FE. Disorders of water and acid-base homeostasis. Nephron Physiol. 2011;118(1):28–34.
190. Saborio P, Tipton GA, Chan JC. Diabetes insipidus. Pediatr Rev. 2000;21(4):122. quiz 129.
191. Thrasher TN. Baroreceptor regulation of vasopressin and renin secretion: low-pressure versus high-pressure receptors. Front Neuroendocrinol. 1994; 15(2):157–96.
192. Weiss JP, Bosch JL, Drake M, Dmochowski RR, Hashim H, Hijaz A, et al. Nocturia Think Tank: focus on nocturnal polyuria: ICI-RS 2011. Neurourol Urodyn. 2012;31(3):330–9.
193. Penniston KL, Tanumihardjo SA. The acute and chronic toxic effects of vitamin A. Am J Clin Nutr. 2006;83(2):191–201.
194. Bringhurst R, Demay MB, Kronenberg HM. Hormones and disorders of mineral metabolism. Williams Textbook of Endocrinology. 11th ed. Philadelphia, PA: Saunders Elsevier; 2008.
195. Dubeau CE, Tsui JF. Nocturia in the elderly. In: Weiss JP, Blaivas JG, van Kerrebroeck PEV, Wein AJ, editors. Nocturia: causes, consequences, and clinical approaches New York. NY: Springer; 2012. p. 147–55.
196. Weiss JP, Zinner NR, Klein BM, Norgaard JP. Desmopressin orally disintegrating tablet effectively reduces nocturia: results of a randomized, double-blind, placebo-controlled trial. Neurourol Urodyn. 2012;31(4):441–7.
197. Johnson TM, Burgio KL, Redden DT, Wright KC, Goode PS. Effects of behavioral and drug therapy on nocturia in older incontinent women. J Am Geriatr Soc. 2005;53(5):846–50.
198. Johnson TM, Jones K, Williford WO, Kutner MH, Issa MM, Lepor H. Changes in nocturia from medical treatment of benign prostatic hyperplasia: secondary analysis of the Department of Veterans Affairs Cooperative Study Trial. J Urol. 2003; 170(1):145–8.

199. Lose G, Lalos O, Freeman RM, van Kerrebroeck P, Nocturia Study Group. Efficacy of desmopressin (Minirin) in the treatment of nocturia: a double-blind placebo-controlled study in women. Am J Obstet Gynecol. 2003;189(4):1106–13.
200. Mattiasson A, Abrams P, Van Kerrebroeck P, Walter S, Weiss J. Efficacy of desmopressin in the treatment of nocturia: a double-blind placebo-controlled study in men. BJU Int. 2002;89(9):855–62.
201. Smith AL, Wein AJ. Outcomes of pharmacological management of nocturia with non-antidiuretic agents: does statistically significant equal clinically significant? BJU Int. 2011;107(10):1550–4.
202. Weiss JP, Blaivas JG, Stember DS, Brooks MM. Nocturia in adults: etiology and classification. Neurourol Urodyn. 1998;17(5):467–72.
203. Weatherall M, Arnold T. New Zealand Nocturia Guideline Committee. Nocturia in adults: draft New Zealand guidelines for its assessment and management in primary care. N Z Med J. 2006; 119(1234):U1976.
204. Vaughan CP, Endeshaw Y, Nagamia Z, Ouslander JG, Johnson TM. A multicomponent behavioural and drug intervention for nocturia in elderly men: rationale and pilot results. BJU Int. 2009;104(1): 69–74.
205. Fitzgerald MP, Lemack G, Wheeler T, Litman HJ. Urinary incontinence treatment network. Nocturia, nocturnal incontinence prevalence, and response to anticholinergic and behavioral therapy. Int Urogynecol J Pelvic Floor Dysfunct. 2008;19(11): 1545–50.
206. Burgio KL, Goode PS, Johnson TM, Hammontree L, Ouslander JG, Markland AD, et al. Behavioral versus drug treatment for overactive bladder in men: the Male Overactive Bladder Treatment in Veterans (MOTIVE) Trial. J Am Geriatr Soc. 2011;59(12): 2209–16.
207. Weiss JP, Blaivas JG, Bliwise DL, Dmochowski RR, Dubeau CE, Lowe FC, et al. The evaluation and treatment of nocturia: a consensus statement. BJU Int. 2011;108(1):6–21.
208. Wagg A, Wyndaele JJ, Sieber P. Efficacy and tolerability of solifenacin in elderly subjects with overactive bladder syndrome: a pooled analysis. Am J Geriatr Pharmacother. 2006;4(1):14–24.
209. Kaplan SA, Roehrborn CG, Rovner ES, Carlsson M, Bavendam T, Guan Z. Tolterodine and tamsulosin for treatment of men with lower urinary tract symptoms and overactive bladder: a randomized controlled trial. JAMA. 2006;296(19):2319–28.
210. Rackley R, Weiss JP, Rovner ES, Wang JT, Guan Z. 037 STUDY GROUP. Nighttime dosing with tolterodine reduces overactive bladder-related nocturnal micturitions in patients with overactive bladder and nocturia. Urology. 2006;67(4):731,6.
211. Vardy MD, Mitcheson HD, Samuels TA, Wegenke JD, Forero-Schwanhaeuser S, Marshall TS, et al. Effects of solifenacin on overactive bladder symptoms, symptom bother and other patient-reported outcomes: results from VIBRANT - a double-blind, placebo-controlled trial. Int J Clin Pract. 2009;63(12):1702–14.
212. Chapple C, Steers W, Norton P, Millard R, Kralidis G, Glavind K, et al. A pooled analysis of three phase III studies to investigate the efficacy, tolerability and safety of darifenacin, a muscarinic M3 selective receptor antagonist, in the treatment of overactive bladder. BJU Int. 2005;95(7):993–1001.
213. Nitti VW, Dmochowski R, Appell RA, Wang JT, Bavendam T, Guan Z, et al. Efficacy and tolerability of tolterodine extended-release in continent patients with overactive bladder and nocturia. BJU Int. 2006;97(6):1262–6.
214. Herschorn S, Stothers L, Carlson K, Egerdie B, Gajewski JB, Pommerville P, et al. Tolerability of 5 mg solifenacin once daily versus 5 mg oxybutynin immediate release 3 times daily: results of the VECTOR trial. J Urol. 2010;183(5):1892–8.
215. Yokoyama O, Yamaguchi O, Kakizaki H, Itoh N, Yokota T, Okada H, et al. Efficacy of solifenacin on nocturia in Japanese patients with overactive bladder: impact on sleep evaluated by bladder diary. J Urol. 2011;186(1):170–4.
216. Gill SS, Mamdani M, Naglie G, Streiner DL, Bronskill SE, Kopp A, et al. A prescribing cascade involving cholinesterase inhibitors and anticholinergic drugs. Arch Intern Med. 2005;165(7):808–13.
217. Chapple CR, Montorsi F, Tammela TL, Wirth M, Koldewijn E, Fernandez Fernandez E, et al. Silodosin therapy for lower urinary tract symptoms in men with suspected benign prostatic hyperplasia: results of an international, randomized, double-blind, placebo- and active-controlled clinical trial performed in Europe. Eur Urol. 2011;59(3):342–52.
218. Barry MJ, Meleth S, Lee JY, Kreder KJ, Avins AL, Nickel JC, et al. Effect of increasing doses of saw palmetto extract on lower urinary tract symptoms: a randomized trial. JAMA. 2011;306(12):1344–51.
219. Drake MJ, Mills IW, Noble JG. Melatonin pharmacotherapy for nocturia in men with benign prostatic enlargement. J Urol. 2004;171(3):1199–202.
220. Sugaya K, Nishijima S, Miyazato M, Kadekawa K, Ogawa Y. Effects of melatonin and rilmazafone on nocturia in the elderly. J Int Med Res. 2007; 35(5):685–91.
221. Lowenstein L, Kenton K, Brubaker L, Pillar G, Undevia N, Mueller ER, et al. The relationship between obstructive sleep apnea, nocturia, and daytime overactive bladder syndrome in women. Am J Obstet Gynecol. 2008;198(5):598.e1. 598.e5.
222. Seiler WO, Stahelin HB, Hefti U. Desmopressin reduces night urine volume in geriatric patients: implication for treatment of the nocturnal incontinence. Clin Investig. 1992;70(7):619.
223. Asplund R, Aberg H. Desmopressin in elderly subjects with increased nocturnal diuresis. A two-month treatment study. Scand J Urol Nephrol. 1993;27(1): 77–82.
224. Asplund R, Aberg H. Desmopressin in elderly women with increased nocturnal diuresis. A short-term study. Br J Urol. 1993;72(1):42–5.

225. Asplund R, Sundberg B, Bengtsson P. Oral desmopressin for nocturnal polyuria in elderly subjects: a double-blind, placebo-controlled randomized exploratory study. BJU Int. 1999;83(6):591–5.
226. Assassa RP, Osborn DE, Castleden CM. Male lower urinary tract symptoms: is surgery always necessary? Gerontology. 1998;44(2):61–6.
227. Cannon A, Carter PG, McConnell AA, Abrams P. Desmopressin in the treatment of nocturnal polyuria in the male. BJU Int. 1999;84(1):20–4.
228. Chancellor MB, Atan A, Rivas DA, Watanabe T, Tai HL, Kumon H. Beneficial effect of intranasal desmopressin for men with benign prostatic hyperplasia and nocturia: preliminary results. Tech Urol. 1999; 5(4):191–4.
229. Kuo HC. Efficacy of desmopressin in treatment of refractory nocturia in patients older than 65 years. Urology. 2002;59(4):485–9.
230. Rembratt A, Norgaard JP, Andersson KE. Desmopressin in elderly patients with nocturia: short-term safety and effects on urine output, sleep and voiding patterns. BJU Int. 2003;91(7):642–6.
231. Wang CJ, Lin YN, Huang SW, Chang CH. Low dose oral desmopressin for nocturnal polyuria in patients with benign prostatic hyperplasia: a double-blind, placebo controlled, randomized study. J Urol. 2011;185(1):219–23.
232. Rezakhaniha B, Arianpour N, Siroosbakhat S. Efficacy of desmopressin in treatment of nocturia in elderly men. J Res Med Sci. 2011;16(4):516–23.
233. Fu FG, Lavery HJ, Wu DL. Reducing nocturia in the elderly: a randomized placebo-controlled trial of staggered furosemide and desmopressin. Neurourol Urodyn. 2011;30(3):312–6.
234. van Kerrebroeck P, Rezapour M, Cortesse A, Thuroff J, Riis A, Norgaard JP. Desmopressin in the treatment of nocturia: a double-blind, placebo-controlled study. Eur Urol. 2007;52(1):221–9.
235. Johnson TM, Burridge A, Issa MM, Miller M, Tang T, Ouslander JG. The relationship between the action of arginine vasopressin and responsiveness to oral desmopressin in older men: a pilot study. J Am Geriatr Soc. 2007;55(4):562–9.
236. Bae JH, Oh MM, Shim KS, Cheon J, Lee JG, Kim JJ, et al. The effects of long-term administration of oral desmopressin on the baseline secretion of antidiuretic hormone and serum sodium concentration for the treatment of nocturia: a circadian study. J Urol. 2007;178(1):200–3.
237. Weatherall M. The risk of hyponatremia in older adults using desmopressin for nocturia: a systematic review and meta-analysis. Neurourol Urodyn. 2004; 23(4):302–5.
238. Weiss JP, Wein AJ, van Kerrebroeck P, Dmochowski R, Fitzgerald M, Tikkinen KA, et al. Nocturia: new directions. Neurourol Urodyn. 2011;30(5):700–3.
239. Johnson TM, Miller M, Tang T, Pillion DJ, Ouslander JG. Oral ddAVP for nighttime urinary incontinence in characterized nursing home residents: a pilot study. J Am Med Dir Assoc. 2006;7(1):6–11.
240. Rembratt A, Graugaard-Jensen C, Senderovitz T, Norgaard JP, Djurhuus JC. Pharmacokinetics and pharmacodynamics of desmopressin administered orally versus intravenously at daytime versus nighttime in healthy men aged 55-70 years. Eur J Clin Pharmacol. 2004;60(6):397–402.
241. Rembratt A, Riis A, Norgaard JP. Desmopressin treatment in nocturia; an analysis of risk factors for hyponatremia. Neurourol Urodyn. 2006;25(2):105–9.
242. Juul KV, Klein BM, Sandstrom R, Erichsen L, Norgaard JP. Gender difference in antidiuretic response to desmopressin. Am J Physiol Renal Physiol. 2011;300(5):F1116–22.
243. Kok AL, Burger CW, van de Weijer PH, Voetberg GA, Peters-Muller ER, Kenemans P. Micturition complaints in postmenopausal women treated with continuously combined hormone replacement therapy: a prospective study. Maturitas. 1999;31(2):143–9.
244. Pedersen PA, Johansen PB. Prophylactic treatment of adult nocturia with bumetanide. Br J Urol. 1988;62(2):145–7.
245. (2010) Committee for establishment of the clinical guidelines for Nocturia of the Neurogenic Bladder Society. Clinical guidelines for nocturia. Int J Urol 17(5):397–409.
246. Peters KM, Carrico DJ, Perez-Marrero RA, Khan AU, Wooldridge LS, Davis GL, et al. Randomized trial of percutaneous tibial nerve stimulation versus sham efficacy in the treatment of overactive bladder syndrome: results from the SUMIT trial. J Urol. 2010;183(4):1438–43.
247. MacDiarmid SA, Peters KM, Shobeiri SA, Wooldridge LS, Rovner ES, Leong FC, et al. Long-term durability of percutaneous tibial nerve stimulation for the treatment of overactive bladder. J Urol. 2010;183(1):234–40.
248. Hakenberg OW, Pinnock CB, Marshall VR. Does evaluation with the International Prostate Symptom Score predict the outcome of transurethral resection of the prostate? J Urol. 1997;158(1):94–9.
249. Meyhoff HH, Nordling J. Long term results of transurethral and transvesical prostatectomy. A randomized study. Scand J Urol Nephrol. 1986;20(1):27–33.
250. Seki N, Yuki K, Takei M, Yamaguchi A, Naito S. Analysis of the prognostic factors for overactive bladder symptoms following surgical treatment in patients with benign prostatic obstruction. Neurourol Urodyn. 2009;28(3):197–201.
251. Margel D, Lifshitz D, Brown N, Lask D, Livne PM, Tal R. Predictors of nocturia quality of life before and shortly after prostatectomy. Urology. 2007;70(3): 493–7.
252. Simaioforidis V, Papatsoris AG, Chrisofos M, Chrisafis M, Koritsiadis S, Deliveliotis C. Tamsulosin versus transurethral resection of the prostate: effect on nocturia as a result of benign prostatic hyperplasia. Int J Urol. 2011;18(3):243–8.

Lower Urinary Tract Symptoms and Benign Prostate Diseases in Older Men

16

Omer Onur Cakir and Kevin T. McVary

Introduction

Currently, 17 % of the USA's population is over 65 years old. By 2030, it is estimated more than 20 % (almost 72 million) of the population will be over 65. Globally, one of every ten persons is older than 60. In 2050, the estimated number will be double (one in five persons) [1]. Additionally, the life expectancy rates are getting higher each year. According to data collected in 2004, the median life expectancy for people older than 65 and 75 are 17.1 and 10.7 years, respectively [2, 3].

Urologic diseases increase in elderly men, and the frequency of pathologic diseases affecting the genitourinary tract increases as men age. The rising prevalence of lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) and erectile dysfunction (ED) is among the most important urologic changes of the aging man.

According to the National Institutes of Health (2012), the number of patients from the USA who visit physicians for LUTS/BPH increases with aging [4].

O.O. Cakir, M.D.
Department of Urology, Northwestern University Feinberg School of Medicine, 303 East Chicago Avenue, Tarry 16-703, Chicago, IL 60611-3008, USA

K.T. McVary, M.D., F.A.C.S. (✉)
Division of Urology, Department of Surgery, Southern Illinois University School of Medicine, 301 North 8th Street, PO Box 19665, Springfield, IL 62794-8860, USA
e-mail: kmcvary@siumed.edu

Total number of visits between 2002 and 2007: 22,828,855.

Age	6-year count
40–44	468,040
45–54	2,130,417
55–64	5,115,891
65–74	6,449,945
75–84	6,880,298
85+	1,784,264

BPH is diagnosed through histological tests; however, it becomes a clinical entity when associated with LUTS, prostatic enlargement, and/or bladder outlet obstruction (BOO). LUTS are the most prevalent diseases of elderly men caused primarily by BPH. Incidence of BPH and LUTS increases with each decade of life [3]. Ninety percent of men between 45 and 80 years of age suffer some type of LUTS. The pathogenesis of these conditions is caused by several factors including age-related changes in the nervous system and neuroregulatory factors [5].

Classically, the enlarged prostate causes LUTS through at least two mechanisms: (1) static component, direct bladder outlet obstruction and (2) dynamic component, increased smooth muscle tone and resistance. The prostate is not the only organ that causes these symptoms. In the management of LUTS, physicians need to be cognoscente of the complex interactions of the bladder, the bladder neck, the prostate, and the urethra. These symptoms may result from interactions between these organs and various components of the central nervous system [6].

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_16,

Several systemic factors likely play an important and underappreciated role in the etiology of LUTS.

The severity and the prevalence of LUTS increase progressively in the aging male. The American Urological Association (AUA) Symptom Index (SI) defines moderate-to-severe LUTS with a score of ≥7 [4]. The Olmsted County Study determined that a progressive increase of the prevalence of moderate-to-severe LUTS rises to approximately 50 % by the eighth decade of life. The presence of moderate-to-severe LUTS was also associated with the development of acute urinary retention (AUR) as a symptom of BPH progression. The AUR prevalence increases from 6.8 episodes per 1,000 patients to a high of 34.7 episodes in 70 years and older men with moderate-to-severe LUTS [5]. While the number of aging individuals and incidences of LUTS is increasing, the number of surgeries is decreasing due to alternative methods of treatment [7].

LUTS in the aging male can have an important impact on both individual and social health. Although LUTS are not often life threatening, they cause potential impairment of the quality of life (QoL) of elderly men [6]. LUTS associate with other disorders like depression and anxiety [4], but a causal connection is not manifest. LUTS and these disorders together may cause morbidity and affect the daily lives and self-concept of elderly men [8]. Lack of exercise, weight gain, obesity, and other lifestyle factors also have an impact on LUTS. These risk factors appear to increase with the aging of the male population. Traditionally, the primary treatment goal has been to alleviate LUTS, but more recently, treatment has addressed the prevention of disease progression [6].

Diagnosis

Lower urinary tract symptoms (LUTS) are not specific for BPH or bladder outlet obstruction (BOO). A variety of pathologic disorders of the aging men's urinary tract may exhibit similar LUTS. The goal of the initial diagnosis of these elderly men should be establishing if these symptoms are the result of BPH. The initial examination should focus on whether or not BOO is the cause of the symptoms. History, physical examination, and urinalysis can exclude some non-prostatic causes of LUTS in some of these men. In most patients, non-prostatic causes of LUTS can be ruled out by taking a patient history and performing a physical examination and a urinalysis test. If the initial evaluation is not definitive, then additional tests are necessary for these elderly patients.

Table 16.1 Male Lower Urinary Tract Symptoms (LUTS)

Storage Symptoms	Voiding Symptoms	Postmicturition Symptoms
Urgency	Hesitancy	Post-void dribble
Frequency	Poor flow	Sense of incomplete emptying
Nocturia	Intermittency	
Urgency incontinence	Straining	
Other incontinence	Terminal dribble	

There are three broad categories of male LUTS according to the International Continence Society: storage (irritative) symptoms, voiding (obstructive) symptoms, and postmicturition symptoms (Table 16.1) [9]. Determining what type of LUTS is present and bothering the patient can provide clues as to the etiology of the complaint(s).

Basic Management

Diagnostic tests are classified into two groups according to the basic management algorithm: recommended tests and optional tests. Recommended tests are those a primary care physician or a urologist should perform on every patient during the initial evaluation. Optional tests are those that should be performed by a urologist for patients exhibiting complicated LUTS during the detailed management of selected elderly patients. LUTS are defined as complicated symptoms if they are associated with a digital rectal examination (DRE) suspicious for prostate cancer, palpable bladder, abnormal prostate-specific antigen (PSA) levels, hematuria, recurrent urinary tract infection (UTI), history/risk of urethral stricture,

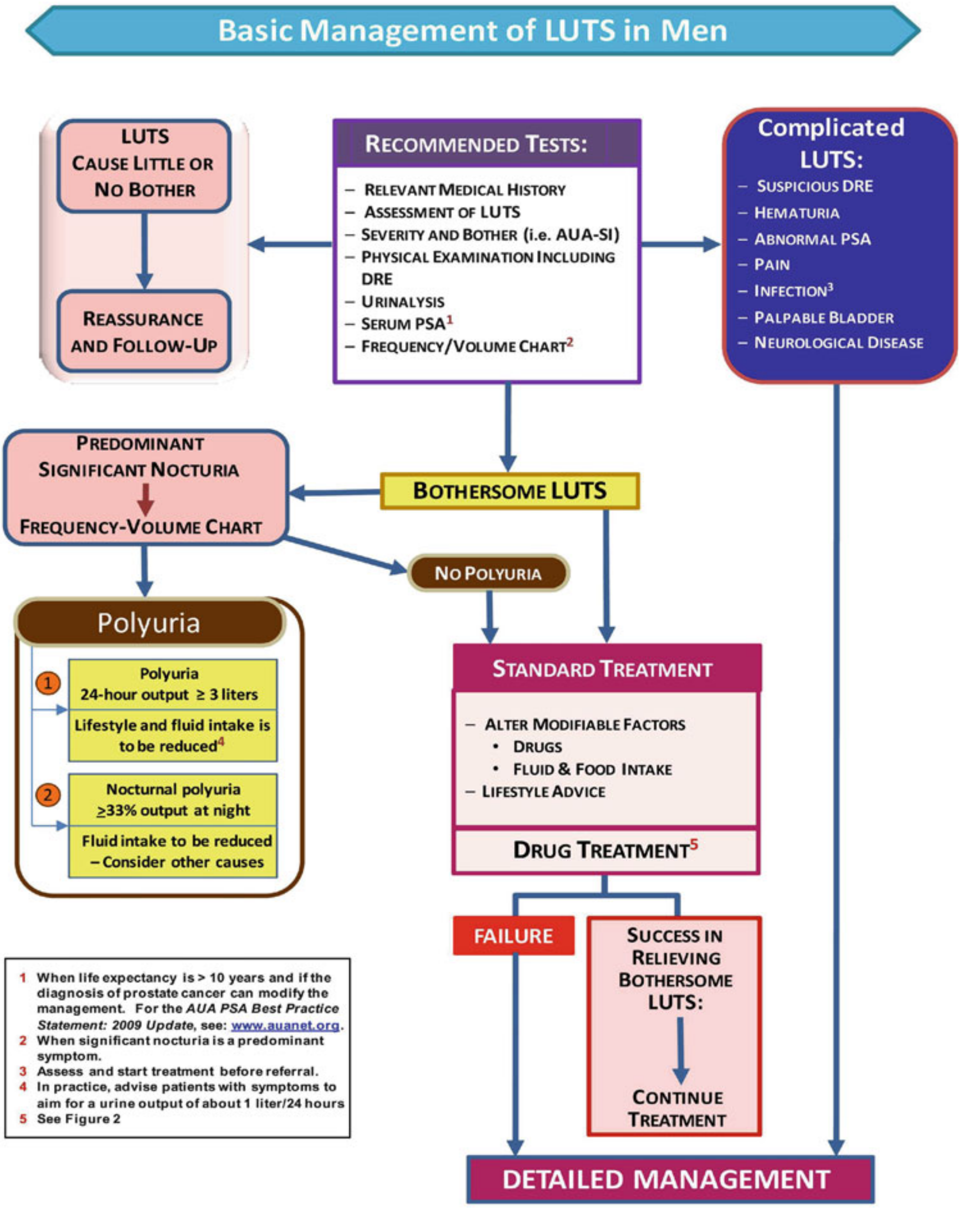


Fig. 16.1 Basic management of lower urinary tract symptoms in men

or neurological disease which can affect the bladder function. In these circumstances, the urologist should include these optional tests. Although baseline renal insufficiency is no more common in men with BPH than in men without BPH of the same age group, the urologist should consider monitoring the renal function of elderly patients with high post-voiding residual urine volumes [6] (Fig. 16.1).

Medical History

A detailed medical history should be obtained from geriatric patients concerning the nature and duration of the urinary symptoms to potentially identify other causes of voiding dysfunction. A detailed history is important for determining the effects of the comorbidities on the chosen therapy. The occurrence of hematuria, UTI, urethral stricture, urinary retention, sexual function history, general health issues, diabetes, nervous system diseases like Parkinson disease, and stroke should be elucidated in the patient history. In addition, urethral or bladder neck stricture can be caused by previous surgical operations of the lower urinary tract and display symptoms similar to those caused by BOO and BPH [10]. Elderly urologic patients require an additional assessment that includes determining a list of their medications that could possibly cause these symptoms, because 40 % of people over 65 use at least five medications. A comprehensive assessment of the functional ability and the frailty of geriatric men is very important. According to the Cardiovascular Health Study report, there are five different variables which cause the frailty phenotype of the geriatric population: recent weight loss, weakness, poor endurance, low physical activity, and slowness of gait [5]. The same study determined an association between frailty and the adverse outcomes for the elderly population. These adverse outcomes are increased hospitalization, falls, worsening disability, worsening activities of daily living, and death [3].

Assessment of Symptoms

The International Prostate Symptom Score (IPSS) is strongly recommended for assessing the grade of severity of LUTS and to determine the degree of bother (Table 16.2) [9]. Each question on the IPSS can yield 0–5 points, producing a total symptom score that can range from 0 to 35 [10]. Symptoms can be classified as mild (0–7), moderate (8–19), or severe (20–35) according to the score of the system. Error is inherent in this score since patients are not equally bothered by similar symptoms. The quality of life questions' scores can range from 0 to 6 points [9]. This questionnaire should be given to the patient during each visit. The answers to the survey monitor the effectiveness of the treatment and are reflected in varying scores. The IPSS should also be the

Table 16.2 International Prostate Symptoms Score (IPSS)

Urinary symptoms	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always
1. In 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
2. In 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
3. In the past month, how often have you found you stopped and started again several times while urinating?	0	1	2	3	4	5
4. In the past month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5
5. In the past month, how often have you had to weak urinary stream?	0	1	2	3	4	5
6. In the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5
7. In the past month, how many times did you typically get up to urinate from the time you went to bed until the time you got up in the morning?	Never 0	1 time 1	2 times 2	3 times 3	4 times 4	5 or more times 5
Total for urinary symptoms						

From Barry MJ, Fowler FJ Jr, O'Leary MP, et al. The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. J Urol 1992;148(5): 1549–57 [discussion:1564]; with permission primary determinant of treatment response or disease progression in the follow-up period and especially for elderly men managed by watchful waiting. The questionnaire is recommended as "self-administered," however, many elderly men benefit from having the questions explained by the examiner.

Physical Examination

Since neurologic problems are common among older adults, one may mistake neurologic symptoms for LUTS. Therefore, a focused neurologic examination should be conducted to evaluate the motor and sensory functions of the perineum and lower limbs. A physical examination of the abdomen and the suprapubic area is necessary to exclude bladder distention. In addition, a thorough examination of the external genitalia of elderly men is indicated to rule out meatal stenosis or a palpable urethral mass. A digital rectal examination (DRE) should be performed to evaluate the prostate gland and the tone of the anal sphincter. DRE establishes the approximate size, consistency, and shape of the prostate gland. The DRE is useful to detect the abnormalities suggestive of prostate cancer [9].

Urinalysis

Hematuria, proteinuria, glucosuria, pyuria, and UTI can be monitored by either a dipstick test or microscopic examination of the sediment. If the dipstick procedure is preferred, the detection of pyuria and bacteriuria can be tested with a leukocyte esterase and a nitrite test. If the result of these tests is abnormal, a urine culture should be conducted. UTIs and bladder cancer resulting from BPH can be monitored with urinalysis. Urine cytology should always be requested in men with severe irritable symptoms and dysuria, especially if they have a history of smoking [10].

Serum Prostate-Specific Antigen

Prostate cancer can lead to LUTS like BPH can lead to LUTS. In most men with a 10-year or longer life span, the knowledge of concomitant prostate cancer may well alter management of the BPH component. A PSA test combined with DRE increases the detection rate of prostate cancer in comparison to just the DRE alone. Therefore, measurement of the serum PSA value should be performed in patients in whom the identification of cancer would clearly alter BPH management. Twenty-eight percent of men with histologically proven BPH have a serum PSA value greater than 4.0 ng/mL, and PSA levels at baseline increase with age [10]. According to the results of 16-year longitudinal changes in serum PSA levels of the Olmsted County Study, the median serum PSA levels were determined as 0.7,0.9, 1.4, and 2.1 ng/mL for men in their 40s, 50s, 60s,and 70s, respectively. These results were similar to those obtained in previous age-specific reference ranges [11], as baseline PSA level increases with age (Table 16.3) [12].

Table 16.3 Distribution of 2-year pairwise absolute annualized differences in serum PSA level, by baseline age: Olmsted County Study of urinary symptoms and health status among men, 1990–2007

	Serum PSA level (ng/mL)				
Baseline age (y)	No. of participants	Median	25th percentile	75th percentile	95th percentile
All	2,315	0.10	–0.10	0.30	1.20
40–49	589	0.02	–0.10	0.20	0.68
50–59	917	0.08	–0.10	0.30	0.99
60–69	503	0.10	–0.10	0.47	1.30
≥70	306	0.16	–0.14	0.60	1.60

PSA prostate specific antigen
Source: Mayo Clin Proc. January 2012;87(1):34–40 doi:10.1016/j.mayocp.2011.09.002, http://www.mayoclinicproceedings.org

The benefits and risks of PSA testing should be discussed with the patient including the possibility of false-positive and false-negative results regarding cancer [9].

Frequency Volume Chart and Serum Creatinine

Frequency volume charts (FVC) are useful especially when the dominant symptom is nocturia. The time and voided volume are recorded during several 24-h periods and help to identify nocturnal polyuria or excessive fluid intake, which are common in the elderly male [9]. The routine serum creatinine measurement is not indicated in the initial evaluation of men with LUTS, even for elderly patients [6].

Therapy Decision

The clinician and the patient choose the treatment after they engage in a shared decision-making process following the initial evaluation [6]. If the patient has no polyuria and if medical treatment is considered, the physician can proceed with modifiable factors such as concomitant drugs, regulation of fluid intake (especially in the evening), lifestyle (increasing activity), and diet (avoiding excess of alcohol and highly seasoned or irritative foods) [13]. If pharmacological treatment is necessary, it is recommended the patient be monitored to assess treatment success and possible adverse events. The time from the initiation of therapy to treatment assessment varies according to the pharmacological agent prescribed. It is important to analyze the effects of the other drugs taken by the patients for other diseases and how they may react with those given for LUTS. If the treatment is successful and the patient is satisfied, yearly follow-ups should be scheduled and include a repeat of the initial evaluation. The follow-up strategy will allow the physician to detect any changes that have occurred and, more specifically, if symptoms have progressed or become more severe or if a complication has developed that requires surgery [7].

Detailed Management

If the initial evaluation demonstrates the patient has complicated LUTS, then the patient should be referred to a urologist for detailed management (Fig. 16.2). The urologist may use additional tests for detailed management of the elderly patient. If drug therapy is considered, decisions will be influenced by coexisting overactive bladder symptoms, prostate size, or serum PSA levels. The decision for the choice of therapy should be based on the patient's preferences. If storage symptoms predominate and if there is no indication of BOO from a flow study, an overactive bladder is probably due to idiopathic detrusor overactivity. The treatment options should be discussed with the patient: lifestyle intervention (fluid intake alteration), behavioral modification, or pharmacotherapy (anticholinergic drugs). The patient should be followed to assess the level of success or possible adverse events of the treatment regime [6].

Additional Diagnostic Tests

After the initial assessment the urologist should perform additional tests for the detailed management of elderly patients. Urinary flow rate, postvoid residual (PVR) urine volume, and pressure-flow urodynamic studies are appropriate tests for the evaluation of these men [10].

Uroflowmetry

Uroflowmetry can be one of the additional tests used for detailed management of elderly patients with LUTS. There is no direct correlation between the results of uroflowmetry and the cause of the symptom.

For example, an abnormally low flow rate may be caused by an obstruction (e.g., hyperplastic prostate, urethral stricture, meatal stenosis) or by detrusor hypocontractility. Neither subjectively assessed symptoms nor quantified symptom score analysis correlates strongly with uroflowmetry

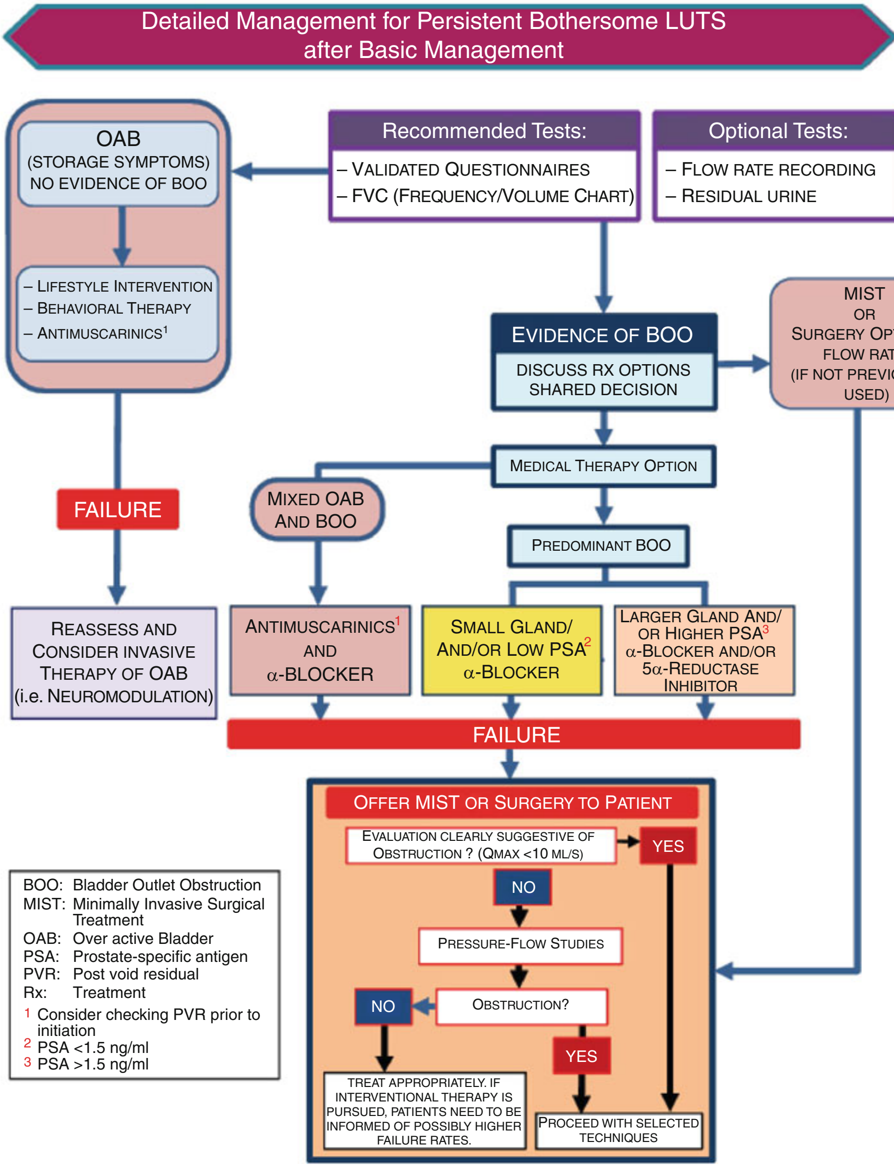


Fig. 16.2 Detailed management of persistent, bothersome lower urinary tract symptoms after basic management

measurements; each is an independent assessment. Patients with a peak flow rate (PFR:Qmax) greater than 15 mL/s may have somewhat poorer outcomes after surgery than those with a PFR less than 15 mL/s (although the majority of patients still improve). A PFR less than 15 mL/s does not differentiate between outflow obstruction and detrusor impairment. No minimal threshold of PFR reliably diagnoses detrusor failure or predicts a poor surgical outcome [10].

Post-void Residual Urine Volume

PVR urine volume measurements have significant intraindividual variability that limits its clinical usefulness, and it does not correlate well with other signs or symptoms of clinical BPH (McConnell et al., 1994). Traditionally, urologists have assumed that increasing amounts of PVR urine denote BPH progression and are thus an "indication" for surgery. Unfortunately, data are lacking to support the predictive value of PVR urine volume. PVR urine volume is best viewed as a "safety parameter" [10]. Men with significant PVR amounts should be monitored more closely if they elect nonsurgical therapy, particularly if antimuscarinic therapy is chosen (see below).

Pressure-Flow Studies

Pressure-flow studies should be performed to distinguish between the patients with a low PFR secondary to obstruction and those whose low PFR is caused by impaired detrusor contractility.

These studies should be performed when the distinction between the two will affect therapeutic decisions [10]. If the patient's initial evaluation and condition do not suggest obstruction (e.g., maximum flow rate of 10 mL/s), pressure-flow studies then become optional. This is true if an invasive treatment is considered (i.e., surgery) or if surgical treatment has failed. Treatment failure rates are higher in the absence of obstruction. If therapy is planned without evidence of obstruction, the patient needs to be informed of possibly experiencing higher procedure failure rates [6]. Patients with a history of neurologic diseases known to affect bladder or sphincteric functions may also benefit from urodynamic evaluation and especially if surgical therapy is considered [10].

Cystoscopy

Cystoscopy can be useful for elderly men with LUTS who have a history of microscopic or gross hematuria, urethral stricture disease (or risk factors such as history of urethritis or urethral injury), bladder cancer or suspicion of carcinoma in situ, or prior lower urinary tract surgery (especially prior TURP). Cystoscopy is not recommended to determine the need for treatment.

Upper Urinary Tract Imaging

Upper urinary tract imaging is not recommended in the routine evaluation of elderly men with LUTS. It can be performed when the patient with LUTS has one or more of the following: hematuria, UTI, renal insufficiency, history of urolithiasis, or history of urinary tract surgery [10].

Treatment Alternatives

The physician should inform and discuss all acceptable treatment modalities with the patient. The patient should be informed about the benefits, risks, and costs of each treatment alternative. The best treatment choice is reached by the physician and the patient at the end of this shared decision-making process with the active participation of the patient [7]. Treatment alternatives for men with BPH are listed in Table 16.4.

Table 16.4 Treatment alternatives for patients with BPH

Watchful waiting
Medical therapies
Alpha-blockers
– Tamsulosin
– Doxazosin
– Alfuzosin
– Terazosin
– Silodosin
5-Alpha-reductase inhibitors (5-ARIs)
– Dutasteride
– Finasteride
Combination therapy
– Alpha-blocker and 5-alpha-reductase inhibitor
Antimuscarinic agents
– Tolterodine, oxybutynin, fesoterodine, darifenacin, trospium, solifenacin
Phytotherapy
Minimally invasive therapies
– Prostate stents
– Transurethral needle ablation (TUNA)
– Transurethral microwave thermotherapy (TUMT)
Surgical therapies
– Transurethral resection of the prostate (TURP)
– Transurethral incision of the prostate (TUIP)
– Lasers
– Open prostatectomy
Other therapies
– Intraprostatic botulinum toxin injections

Watchful Waiting

Watchful waiting (active surveillance) is a management strategy in which the patient is monitored by the physician, but does not receive active intervention for BPH. This surveillance strategy is especially preferred for mildly symptomatic (AUA-SI score <8) elderly patients [7].

This is also an appropriate option for men with moderate-to-severe symptoms (AUA-SI score >8) who are not affected by these symptoms and who have no complications from LUTS and BOO (e.g., renal insufficiency, urinary retention, or recurrent infection). According to the watchful waiting strategy, the physician should reassess the patient annually by repeating the initial evaluation algorithm. During the surveillance period, the patient's symptoms may be reduced with simple measures such as avoiding decongestants or antihistamines and managing their fluid intake. A lifestyle recommendation such as decreasing caffeine and alcohol intake is important. Physicians should consider the elderly patient's cardiac and neurological situation and the drugs used for LUTS at every visit. The symptoms, prostate volume (as assessed by DRE and PSA—prostate volume proxy), and selective ancillary studies including PVR should be assessed, periodically. After this assessment, the physician can decide if the patient should continue watchful waiting or be transferred to another course of therapy [7].

Medical Therapies

Medical therapies extensively used for BPH include adrenergic blockers, 5-alpha reductase inhibitors, phosphodiesterase type 5 inhibitors (PDE5Is), antimuscarinic drugs, and various plant extracts.

Alpha Adrenergic Receptor Blockers (Alpha-Blockers) (α1-Adrenoceptor Antagonists)

Noradrenergic sympathetic nerves have been demonstrated to effect the contraction of prostatic smooth muscle [7]. The lower urinary tract, and specifically the bladder neck and prostate, is richly innervated with adrenergic receptor endings, most of which are α1a-receptors [9]. Contraction of the human prostate is mediated predominantly by these α1a-adrenoceptors [14].

Mechanism of Action: α1-Adrenoceptor Antagonists

α1a-blockers are thought to act by inhibiting the effect of endogenously released noradrenalin on prostate smooth muscle cells, thereby reducing prostate tone and bladder outlet obstruction. By blocking these receptors with receptor-blocking drugs, the smooth muscle tissue relaxes, allowing for improved urine flow and improved LUTS [9].

However, these drugs affect other α1-receptors located outside the prostate such as in the urinary bladder, spinal cord, blood vessels, non-prostatic smooth muscle cells, and in the central nervous system. Because of this interaction, there are numerous side effects noted.

Drugs and Efficacies

Alpha-1-blockers are often considered the first-line drug treatment of moderate-to-severe male LUTS. A 2003 AUA guideline statement indicating the data were insufficient to support a recommendation for the use of phenoxybenzamine and prazosin as treatment alternatives for LUTS has been maintained [7]. Following the early use of these two agents in LUTS treatment, the α1-blocker drugs that are currently available in use are terazosin (1, 2, 5, and 10 mg, requiring dose titration), doxazosin (1, 2, 4, and 8 mg, requiring dose titration), tamsulosin (0.4 mg, titration optional to twice a day dosing), alfuzosin (10 mg slow-release formulation), and silodosin (4 and 8 mg) [9].

Alpha-blockers produced a reduction of significant symptoms compared to placebo. Tests have shown there is no statistical or clinical difference between the efficacies of the alpha-blockers.

Alfuzosin, doxazosin, tamsulosin, and terazosin are appropriate and effective treatment alternatives for elderly patients with bothersome, moderate-to-severe LUTS secondary to BPH (AUA-SI score ≥8). Although there are differences in the adverse event profiles of these agents, the effectiveness and efficacy of the four alpha-blockers under consideration appear to be similar [7].

α1-blockers improve the IPSS score by approximately 4–6 points and increase the PFR by approximately 20–25 % [14]. Although these improvements take a few weeks to develop fully, statistically significant efficacy over placebo has been demonstrated within hours to days. These drugs do not reduce prostate size and may not prevent acute urinary retention according to the results of long-term studies such as Medical Therapy of Prostatic Symptoms (MTOPS) and Alfuzosin Long-Term Efficacy and Safety Study (ALTESS) [15]. Eventually, some patients will have to be surgically treated. Nevertheless, the efficacy of α1-blockers appears to be maintained over at least 4 years [14].

Tolerability, Safety, and Side Effects

All α1-blockers are available in formulations, which are suitable for once-daily administration. To minimize adverse events, it is recommended that dose titration is used to initiate treatment with doxazosin and terazosin; however, this is not necessary with alfuzosin and tamsulosin. Although doxazosin and terazosin require dose titration and blood pressure monitoring, they are inexpensive, are dosed once daily, and appear to be equally effective to tamsulosin and alfuzosin [7].

Rates for specific adverse events were low and similar between treatment and placebo groups. The most frequent side effects of α1-blockers are dizziness, asthenia, and (orthostatic) hypotension. Dizziness is the most common adverse event, with rates reported between 2 and 14 % in patients receiving alpha-blocker treatment [7].

Vasodilating effects are regularly observed with the use of doxazosin and terazosin and are much less common for alfuzosin and tamsulosin. In particular, elderly patients who are on vasoactive treatment regimes for cardiovascular diseases may be susceptible to α-blocker-induced vasodilatation. These drugs include antihypertensive drugs, such as α-adrenoceptor antagonists, diuretics, Ca2+−channel blockers, angiotensin-converting enzyme inhibitors, and angiotensin receptor antagonists, but also phosphodiesterase (PDE) inhibitors prescribed for erectile dysfunction or male LUTS [13, 14].

A systematic review concluded that α1-blockers do not adversely affect libido, have a small beneficial effect on erectile function, but sometimes cause abnormal ejaculation [14, 16].

With regard to tamsulosin, the approximate 10 % risk of ejaculatory disturbance cited in the 2003 AUA guideline appears to be lower in a more recent study [7]. Originally, the abnormal ejaculation was thought to be retrograde, but more recent data demonstrate it is due to relative anejaculation (absence of emission), often incorrectly labeled as retrograde ejaculation. Young age is a risk factor for this side affect. Although abnormal ejaculation has been observed more frequently with tamsulosin than with other α1-blockers, it is not associated with an overall reduction of overall sexual function [14, 16]. The more α1a-selective agents have apparently greater risk for abnormal ejaculation [14, 17].

In the elderly population, convenience of single dose versus dose titration, and with a desire to avoid cardiovascular adverse events, may be the deciding factors when choosing one α-blocker over another. The most problematic adverse events for elderly men are dizziness and orthostatic hypotension. A study on men with BPH older than 80 treated with terazosin and doxazosin reported no serious adverse events. Surprisingly, the incidence of adverse effects in several reviews was not age dependent. However, in a more current review, patients taking this class of drugs had a greater chance of falling due to dizziness caused by vasodilatation [10].

In the elderly population cataracts are a common ophthalmic disease, and the urologist should be aware about the intraoperative floppy iris syndrome (IFIS). IFIS is a triad of progressive intraoperative miosis despite preoperative dilation, billowing of a flaccid iris, and iris prolapse toward the incision site during phacoemulsification for cataracts [7, 18]. Operative complications in some cases included posterior capsule rupture with vitreous loss and postoperative intraocular pressure spikes, though visual acuity outcomes appeared preserved. Iris dilator smooth muscle inhibition by the preoperative use of tamsulosin or other alpha-blockers has been suggested as a potential mechanism [7, 11].

Although IFIS has been observed with all a1-blockers, most reports have been related to tamsulosin. Whether this reflects a greater risk with tamsulosin than with other α1-blockers, or rather its more widespread use, is not clear, particularly as the ratio between doses yielding ocular effects and those acting on the lower urinary tract is similar for all α1-blockers [12]. It therefore appears prudent not to initiate α1-blocker treatment prior to cataract surgery, while existing α1-blocker treatment should be stopped, though it is not clear how long before surgery takes place [14]. Men with LUTS secondary to BPH for whom alpha-blocker therapy is offered should be asked about planned cataract surgery. Men with planned cataract surgery should avoid the initiation of alpha-blockers until their cataract surgery is completed [6].

5-Alpha-reductase Inhibitors

Mechanism of Action

Dihydrotestosterone (DHT) is converted in the prostatic stroma cells from its precursor testosterone by the enzyme 5α-reductase, a nuclear-bound steroid enzyme [14, 19]. This enzyme has two isoforms:

- 5α-reductase type 1, with minor expression and activity in the prostate but predominant activity in extraprostatic tissues, such as skin and liver
- 5α-reductase type 2, with predominant expression and activity in the prostate

Finasteride inhibits only 5α-reductase type 2, whereas dutasteride inhibits both 5α-reductase types 1 and 2.

5α-reductase inhibitors act by reducing the androgenic effect in the prostate, which induces apoptosis of prostate epithelial cells [14, 20], leading to prostate size reduction of about 18–28 %. In addition, the compound reduces circulating PSA levels to about 50 % of the previous levels after 6–12 months of treatment [14, 21].

Drugs and Efficacies

There are two available drugs in this class: finasteride (5 mg) and dutasteride (0.5 mg). Continuous treatment with these drugs reduces the serum DHT concentration: finasteride 70 % reduction and dutasteride 95 % reduction. However, prostate DHT concentration is reduced to 85–90 % by combining both 5a-reductase inhibitors [9]. Both of them are metabolized by the liver and excreted in the feces. The elimination half-life varies between the drugs: dutasteride (3–5 weeks) and finasteride (less than 1 day). The level of symptom reduction by these agents depends on initial prostate size [14, 22–24]. Indirect comparison between individual studies supports that dutasteride and finasteride are equally effective in the treatment of LUTS [14, 21]. The CombAT study (Combination of Avodart and Tamsulosin), a long-term trial with dutasteride in symptomatic men with a prostate volume greater than 30 mL, showed the 5-ARIs reduce LUTS in these patients at least as much or even more effectively than tamsulosin [14, 16]. According to these studies it becomes clear that 5-ARIs may work better in patients with larger prostates and higher serum PSA values. 5-ARI prevents the long-term (>1year) risk of acute urinary retention or need for surgery [15], while a1-blockers delay but do not prevent the risk [14]. Treatment with 5a-reductase inhibitors is appropriate and effective for elderly men with moderate-to-severe LUTS who have enlarged prostates (>40 mL) or elevated PSA concentrations (>1.4–1.6 μg/L). Due to the slow onset of action, 5a-reductase inhibitors are more suitable for long-term treatment of these elderly patients [14]. Additionally, finasteride reduces the prostate-related hematuria by suppressing the prostatic vascular endothelial growth factor (VEGF). Prostate-related bleeding was reduced or completely stopped [25, 26]. So finasteride is an appropriate and effective treatment alternative in men with refractory hematuria due to prostatic bleeding. According to the updated AUA guideline, it is the expert opinion of the panel that dutasteride likely functions in a similar fashion [6]. Of interest, 5a-reductase inhibitors (finasteride) might reduce blood loss during transurethral prostate surgery, probably due to their effects on prostatic vascularization, but there is insufficient evidence to recommend using these drugs in the setting of TURP of an elderly patient [6].

Tolerability, Safety, and Side Effects

The most relevant adverse effects of 5a-reductase inhibitors are related to sexual function and include reduced libido and erectile dysfunction. To a lesser degree, ejaculation disorders, labeled as retrograde ejaculation, ejaculation failure, or decreased semen volume [17, 21], are found to be a side effect. Gynecomastia is reported in less than 1 % of patients [14].

Combination Therapy of Alpha1-Blockers and 5-Alpha-reductase Inhibitors

Combination therapy of α1-blockers and 5a-reductase inhibitors aims to combine the differential effects of both drug classes to create synergistic efficacy in symptom improvement and prevention of disease progression. The α1-blockers provide clinical effects within hours or days, whereas the 5a-reductase inhibitors need several months (at least) to develop significant clinical results. The combination of finasteride administered with alfuzosin, doxazosin, or terazosin, or combining dutasteride together with tamsulosin, has been tested in clinical trials. A 4-year data analysis from MTOPS and results from the CombAT have demonstrated combination treatment is superior to either monotherapy in regard to symptom reduction and PFR improvement. The combinations are superior to a1-blocker administered alone in reducing the risk of acute urinary retention and/or the need for surgery [27–29].

The CombAT study demonstrated combination treatment is superior to either monotherapy with regard to symptom improvement and PFR starting from month 9 and superior to a1-blocker with regard to the reduction in the risk of acute urinary retention and the need for surgery after month 8 [9, 14].

In both the CombAT and MTOPS trials, overall drug-related adverse events were significantly more frequent during combination treatment than during either monotherapy, since the side effects are additive of both the drug types. Combination therapy should therefore be used in elderly men who have moderate-to-severe LUTS with higher prostate volume and higher PSA concentration when long-term treatment (more than 12 months) is intended [14].

Antimuscarinic (Anticholinergic Agents)

Mechanism of Action

Muscarinic receptor antagonists inhibit muscarinic receptor stimulation and therefore reduce smooth muscle cell contractions of the bladder. Antimuscarinic effects might also be induced or modulated by the urothelium of the bladder and/or by the central nervous system [4, 5]. Five muscarinic receptor subtypes (M1–M5) have been described in humans, of which the M2 and M3 subtypes are predominantly expressed in the detrusor. Although approximately 80 % of these muscarinic receptors are M2 and 20 % M3 subtypes, only M3 seems to be involved in bladder contractions in healthy males [14, 30, 31].

Drugs and Efficacies

There are many drugs available in this category, but not all have been reported in male patients. The majority of studies have used tolterodine. Randomized controlled trials (RCTs) evaluated the use of tolterodine either as monotherapy or in combination with an alpha-blocker in men with LUTS related to BPH. These trials did not sufficiently demonstrate the efficacy or effectiveness of tolterodine [28–30]. The AUA guideline concluded the use of anticholinergic agents could benefit elderly men suffering from LUTS secondary to BPH without an elevated PVR urine volume and when LUTS are predominantly irritative. Additional studies have also been conducted with fesoterodine and oxybutynin. Other drugs in this class are darifenacin, trospium, and solifenacin [6].

Muscarinic receptor antagonists might be considered in elderly men with moderate-to-severe LUTS who have predominantly bladder storage symptoms. But caution is advised in men with bladder outlet obstruction. Before the initiation of these drugs, baseline PVR urine should be assessed. Anticholinergics should be used with caution in patients with a post-void residual greater than 250–300 mL [6].

Side Effects

Anticholinergic agents are generally well tolerated. The most common side effects include dry mouth (up to 24 %) [32], constipation (up to 4 %), micturition difficulties (up to 2 %), nasopharyngitis (up to 3 %), and dizziness (up to 5 %). Ejaculation disorders (ED) and significant morbidity and mortality were not reported with the use of tolterodine alone or in combination with tamsulosin [7]. There is no association found between oxybutynin and increased risk of falls among the elderly population [33]. The side effects of the antimuscarinic agents on the central nervous system (CNS) of older adults are limited to dizziness which is reported in patients medicated with oxybutynin (3 %), propiverine (3.2 %), and of tolterodine (1.8 %) compared with placebo (1.6 %) [34].

Phytotherapy

Phytotherapy includes the medical use of extracts of different plants. The most important compounds which are believed to be responsible to relieve symptoms of LUTS are phytosterols, ß-sitosterol, fatty acids, and lectins. However, most in vitro effects have not been confirmed in vivo, so mechanisms of action of these extracts remain unclear [14]. The most common plant extracts in use of LUTS are the saw palmetto plant (*Serenoa repens*) and stinging nettle (*Urtica dioica*). The other extracts are from *Secale cereale*, *Pygeum africanum*, *Hypoxis rooperi,* and *Cucurbita pepo*. Recent studies with more rigorous methods have generally failed to confirm a clinically important role for saw palmetto in the treatment of LUTS; the AUA and the European Association of Urology (EAU) guidelines for the management of male LUTS do not recommend the use of any of these supplements [7, 9, 35, 36].

Minimally Invasive Therapies

A wide range of different stent types has been developed and undergone clinical study to determine which are most efficient. In general, stents are subject to misplacement, migration, poor tolerability because of exacerbation of LUTS, and encrustation. The most common side effect following stent placement includes perineal pain or irritative voiding symptoms in most patients. Because of the side effects and high migration rate, prostatic stents have a limited role in the treatment of LUTS. Prostatic stents remain an alternative to transurethral catheterization for men who have recurrent urinary retention and elderly men who are at high risk for surgery [14].

Transurethral Needle Ablation (TUNA™) of the Prostate

The TUNA™ procedure works by inducing a coagulative necrosis within the transition zone of the prostate. As a result of scar maturation, there may be a reduction in transition zone volume and, therefore, a reduction of BPH. The device delivers low-level radiofrequency energy to the prostate via needles inserted transurethrally into the prostatic parenchyma. Needles are placed under direct vision using an attachment to the standard cystoscope. This technique can be performed as an outpatient procedure under local anesthesia, although intravenous sedation is sometimes required. Because of this reason, this procedure can be considered as a treatment choice for elderly patients who have higher risk for general anesthesia [14].

This technique has been shown to decrease the symptoms and improve the QoL and urinary flow rates, but is not as effective as TURP. A high long-term re-treatment rate for TUNA has been reported; up to 20 % of patients treated with TUNA™ need to be re-treated with TURP even in a short-term period such as 12 months [37]. A recent study described a failure rate of TUNA with a need of re-treatment of up to 50 % over a 20-month long-term follow-up period [14, 38].

TUNA is a safe treatment alternative with low perioperative complications such as bleeding. Postoperative urinary retention is seen in 13.3–41.6 % of patients and lasts for a mean of 1–3 days; within 1 week, 90–95 % of patients are catheter-free. Irritative voiding symptoms up to 4–6 weeks are common [39]. TUNA does not affect the erectile function and continence status. TUNA™ is an appropriate and effective treatment alternative to TURP for patients with moderate-to-severe LUTS who wish to avoid complications of TURP, but patients should be aware of significant re-treatment rates and less improvement in symptoms and quality of life. It should be an option for elderly patients who have a high risk of general anesthesia [14].

Transurethral Microwave Therapy

Microwave thermotherapy of the prostate works by emitting microwave radiation through an intraurethral antenna mounted on a urethral catheter to deliver heat into the prostate. Tissue is destroyed by being heated at temperatures above cytotoxic thresholds (>45 °C) by the mechanism of coagulation necrosis. The heat also causes apoptosis and denervation of α-receptors, thereby decreasing the smooth muscle tone of the prostatic urethra [14]. A systematic review of all available RCTs on TUMT reported that TUMT was somewhat less effective than TURP in reducing LUTS. The mean symptom score for men undergoing TUMT decreased by 65 % in 12 months compared to 77 % in men undergoing TURP. Greater improvement was achieved with TURP in PFR (119 %) than TUMT (70 %) [40]. A prospective, randomized, multicenter study after 5 years has obtained comparable clinical results with TUMT to those seen with TURP [41]. No statistically significant differences were found in PFR and IPSS between the two treatment groups at 5 years. In the TUMT group, 10 % needed additional treatment versus 4.3 % in the TURP arm. In addition, in many studies patients who remained in the study would likely to represent the best "responders" data [14].

Treatment is generally well tolerated. Most of the patients suffer from perineal discomfort and urinary urgency and require pain medication for the therapy. The catheterization time, incidence of dysuria/urgency, and urinary retention were significantly less with TURP, while the incidence of hospitalization, hematuria, clot retention, transfusions, transurethral resection (TUR) syndrome, urethral strictures, and impact on sexual function (erectile dysfunction, retrograde ejaculation) were significantly less for TUMT [14, 40]. TUMT can be performed as an outpatient procedure without the need of anesthesia. Cystoscopy is essential because it is important to identify the presence of an isolated enlarged middle lobe or an insufficient length of the prostatic urethra. Reported low morbidity and the absence of any need for anesthesia (spinal or general) make TUMT an excellent outpatient procedure option for elderly patients with moderate-to-severe LUTS who have comorbidities with high operative risk and are unsuitable for invasive treatment [14, 42].

Surgical Therapies

Surgical Procedures

Surgical therapy alternatives are the most invasive options for the treatment of elderly men with LUTS secondary to BPH. Surgical intervention is an appropriate treatment alternative for patients with moderate-to-severe LUTS and for patients who have developed AUR or other BPH-related complications. For elderly men who cannot tolerate or fail medical therapy, these surgical procedures are viable options. According to the AUA guidelines surgery is recommended for patients who have renal insufficiency secondary to BPH; who have recurrent UTIs, bladder stones, or gross hematuria due to BPH; and those who have LUTS refractory to other therapies. The presence of a bladder diverticulum is not an absolute indication for surgery unless associated with recurrent UTI or progressive bladder dysfunction. TURP remained the benchmark for surgical therapy. Alternative technologies such as laser-assisted TURP were reported to offer lower morbidities but were typically still performed in the operating room setting and require anesthesia. Open prostatectomy is still an option for those with the largest of prostates [7].

Transurethral Resection of the Prostate

The basic principle of TURP is the removal of tissue from the transition zone of the prostate endoscopically using special resectoscopes and cutting loops. This procedure reduces prostatic obstruction. TURP is still regarded as the gold standard for the treatment of LUTS secondary to BPH even in elderly patients with prostate volumes between 30 and 80 mL. The suggested threshold prostate size limits depend on the surgeon's experience, resection speed, and resectoscope sizes. In 1999, TURP represented 81 % of all surgeries for BPH in the USA, but by 2005, TURP represented only 39 % of surgical procedures for BPH, due to the combined effect of fewer prostatic operations and more minimally invasive procedures [14, 43]. Urinary tract infections (UTIs) should be treated prior to TURP. Prophylactic antibiotics should be used routinely before the operation for reducing bacteriuria, fever, sepsis, and the need for additional antibiotics after TURP [14, 44].

Durability

TURP provides durable clinical outcomes. A meta-analysis of 29 RCTs reported a mean LUTS improvement of 70.6 % after TURP. The need for re-treatment after TURP is 1–2 % per year. A review analyzing 29 RCTs found a re-treatment rate of 2.6 % after a mean follow-up of 16 months [14].

Complications

In the most recent study, perioperative mortality (during the first 30 days) was 0.1 %. The risk of transurethral resection (TUR) syndrome is less than 1.1 %. Risk factors associated with TUR syndrome are excessive bleeding with opening of venous sinuses, prolonged operation time, large prostates, and past or present nicotine abuse [45]. The incidence of blood transfusion following TURP reported as 8.4 %. Contemporary real-life data from 10,564 TURP procedures reported procedure-related bleeding requiring blood transfusion in 2.9 % of patients [14].

Long-Term Mortality Risk

Data from TURPs and open prostatectomies (OP) showed that the 8-year incidence of myocardial infarction was identical after TURP (4.8 %) and OP (4.9 %). Similarly, mortality rates at 90 days (0.7 vs. 0.9 %), 1 year (2.8 vs. 2.7 %), 5 years (12.7 vs. 11.8 %), and 8 years (20 vs. 20.9 %) were almost identical [14, 46].

Long-Term Complications of TURP

Urinary incontinence: The Veteran Affairs (VA) Cooperative Study reported that a 1 % risk of urinary incontinence is similar to the incidence in the watchful waiting group. The median risk of postoperative stress urinary incontinence is approximately 2.2 % after TURP [47].

Bladder neck contracture and urethral stricture: After TURP, the risks of urethral strictures and bladder neck stenoses are 3.8 and 4.7 %, respectively [48].

Sexual function: The impact of TURP on erectile function is not conclusive. In the analysis of 29 RCTs, the incidence of ED following TURP was reported as 6.5 % [48]. The Veteran Affairs (VA) Cooperative Study reported this increase seems to be caused by confounding factors (e.g., age) rather than being the direct result of TURP. Retrograde ejaculation results from resection/destruction of the bladder neck and is reported by 65.4 % of patients after TURP [48]. Irritative voiding symptoms, UTI, and hematuria are the other complications [14].

Bipolar Turp

Bipolar TURP (B-TURP) uses a specialized resectoscope loop, which incorporates both active and return electrodes. This technique permits electrosurgical tissue cutting in a conductive saline medium. After activation of the high-frequency current, the physiological saline around the loop is heated up to the boiling point, and the voltage between electrode and saline solution forms an arc. The tissue is heated indirectly by the heat of the ignition of the arc; this facilitates both resection and coagulation [14].

The overall occurrence of side effects was significantly lower with B-TURP compared to monopolar TURP (28.6 vs. 15.5 %) [23]. Because the bipolar resectoscope uses physiological saline irrigation solution, the risk of TUR syndrome is eliminated with B-TURP. The other advantages of B-TURP are reduced blood loss, decreased incidences of postoperative clot retention, and the need for blood transfusions. Both postoperative catheterization and hospitalization times were shorter with bipolar TURP compared to monopolar TURP [14]. This is due to reduced bleeding associated with improved coagulation abilities in the B-TURP technique [49].

TURP is an appropriate and effective primary alternative for surgical therapy in elderly men with moderate-to-severe LUTS. B-TURP offers an attractive alternative to monopolar TURP with similar efficacy but lower morbidity. The choice of a monopolar or bipolar approach should be based on the patient's anatomy, the surgeon's experience, and discussion of the potential risks and likely benefits.

Transurethral Incision of the Prostate

TUIP is an outpatient endoscopic technique used for the treatment of LUTS in prostate sizes <30 mL and without prostate middle lobes. During the TUIP procedure, one or two cuts are made into the prostatic parenchyma and capsule, thereby reducing urethral resistance. TUIP results in degrees of symptomatic improvement equivalent to those attained after TURP in patients with small prostates (<20–30 mL) and no prostate median lobe (96–99). The advantages of TUIP are reduced bleeding incidents, shorter operation time, avoidance of TUR syndrome, minimal and shorter postoperative bladder irrigation, low risk of retrograde ejaculation, and shorter times for catheterization and hospitalization. The disadvantages are a higher rate of symptom recurrence and the need for additional surgery [7].

Laser Therapies of the Prostate

Laser energy can be used to produce a variety of effects within prostate tissue including coagulation, necrosis, or vaporization and resection of the tissue. Recently, the holmium and variants of the laser are the most common laser technologies used to treat BPH [7]. Several types of new-generation lasers for prostate surgery have emerged during recent years. These are holmium:YAG, potassium titanyl phosphate:yttrium–aluminum–garnet (KTP:YAG), thulium:yttrium–aluminum–garnet (thulium:YAG), light blue optics:yttrium–aluminum–garnet (LBO:YAG), and the diode lasers. Energy can be transmitted through a bare, right angle, or interstitial fiber. Each laser has wavelength-specified energy–tissue interaction. Prostatic tissue destruction results from both thermal and nonthermal effects [14].

Transurethral laser enucleation [holmium laser resection of the prostate (HoLRP), holmium laser enucleation of the prostate (HoLEP) and transurethral side-firing laser ablation [holmium laser ablation of the prostate (HoLAP) and photoselective vaporization (PVP)] are appropriate and effective treatment alternatives in elderly men with moderate-to-severe LUTS. Laser approaches have been associated with shorter catheterization time and length of stay, with comparable improvements in LUTS. The laser techniques are appropriate options for elderly men with even very large prostates (>100 g) [7].

According to the National Institutes of Health (2012), the frequency of laser surgeries for BPH is increasing, while other therapies performed are decreasing in number [4]:

Transurethral Holmium Laser Techniques

The Holmium:Yttrium–Aluminum–Garnet Laser Technology

The Holmium:Yttrium–Aluminum–Garnet (Ho:YAG) laser (2,140 nm) is a pulsed, solid-state laser that is used for soft tissues and for the disintegration of urinary stones. The wavelength of the Ho:YAG laser is strongly absorbed by water. This means the area of tissue coagulation and the resulting tissue necrosis is limited to 3–4 mm, which is enough to obtain adequate homeostasis [50]. Peak power produces intense, nonthermal, localized, tissue destruction, resulting in precise and efficient cutting of prostatic tissue [14].

Transurethral Holmium Laser Ablation of the Prostate

In HoLAP technique the Ho:YAG laser uses a 550 μm side-firing laser fiber in a noncontact mode. This device delivers laser energy at a wavelength of 2,120 nm (infrared range), which is absorbed primarily by water and results in an optical penetration depth of 0.4 mm. The HoLAP procedure is intended to be comparable to TURP in that the prostatic lobes may be vaporized down to the surgical capsule resulting in a TURP-like effect [7].

Transurethral Holmium Laser Enucleation of the Prostate

Instrumentation for this technique includes a 550 μm, end-firing, quartz fiber and an 80 W Ho:YAG laser. A continuous-flow resectoscope is required with a working element, while physiological saline solution is for irrigation. Mimicking open prostatectomy, the prostatic lobes are completely enucleated separating the adenoma from the surgical capsule, from apex to base, after any median lobe has been freed from the bladder neck [14]. Then the prostate pieces are pushed into the bladder, before being fragmented and aspirated by a morcellator [51]. Long-term studies indicate that HoLEP results are durable, and most patients remained satisfied with this procedure. PFR at 12 months was significantly better with HoLEP [52]. In prostate volumes that are >100 mL, HoLEP proved to be as effective as open prostatectomy with equally low reoperation rates at 5-year follow-up [53]. There are no specific limitations to the procedure. Patients taking anticoagulant medication and those with urinary retention can be treated safely [14]. HoLEP has a significantly shorter catheterization time and hospital stay, reduced blood loss, and fewer blood transfusions, but had a longer operation time than TURP [50]. Thus, this procedure should be a treatment option for elderly patients with moderate-to-severe LUTS [14].

Photoselective Vaporization of the Prostate

This procedure uses a laser with a wavelength of 532 nm (in the green visible spectrum) which is absorbed by both the water irrigation and hemoglobin. This results in an optical penetration depth of 0.8 mm. The other acronyms for this procedure, KTP (potassium titanyl phosphate), "greenlight" laser vaporization, and LBO (lithium borate), identify the crystal used in the laser generator. Following the application of laser energy, the prostatic tissue is vaporized by a sudden increase in tissue temperature from 50 to 100 °C. This sudden increase in tissue temperature results with intracellular vacuoles (bubbles), followed by an increase in intracellular cell pressure. Once the cell pressure exceeds compatibility with cellular integrity, the vacuoles are released [14].

The operation is performed by using a 600 μm side-firing laser fiber in a noncontact mode with a 70° deflecting laser beam and a 30° deflecting laser cystoscope. Normal saline solution is used for irrigation. Under direct vision of a continuous-flow scope, vaporization is performed with a fiber-sweeping technique [14, 54].

Two prospective RCTs and three non-randomized trials have been published. Symptom scores improved consistently in all studies [7], QoL scores, and maximum urinary flow rates [7, 55]. The longest available follow-up of a RCT is only 12 months; this trial indicated that PVP was equivalent to TURP in symptom improvement [56]. Both groups showed a significant increase in PFR. In the TURP group, PFR increased from 8.7 to 17.9 mL/s (149 %) and in the PVP group from 8.5 to 20.6 mL/s (167 %). The IPSS decreased from 25.4 to 12.4 (50 %) in the TURP group and from 26 to 12 (50 %) in the PVP group [14].

PVP is a safe technique even in patients with oral anticoagulation, urinary retention, or prostate volumes >80 mL [56]. Compared to TURP, PVP has the advantages of reduced length of hospital stay, duration of catheterization, and adverse events. The duration of catheterization was significantly less in the PVP than the TURP, with a mean (range) of 13 (0–24) hours versus 44.7 (6–192) hours. Additionally, the length of hospital stay is significantly shorter with a mean (range) of 1.09 (1–2) versus 3.6 (3–9) days [57].

Emerging evidence suggests a possible role of transurethral enucleation and laser vaporization as options for men with very large prostates (>100 g). Laser therapies can be performed effectively for elderly men with the advantages of reduced length of hospital stay, duration of catheterization, and decreased adverse events [14].

Open Prostatectomy

In this oldest surgical technique used in the treatment of BPH, prostatic adenomas are enucleated via a suprapubic or retropubic incision in the lower abdominal area. The index finger is then inserted, either from the inside of the bladder (Freyer procedure) or through the anterior prostatic capsule (Millin procedure). This technique is performed on patients with prostate volumes greater than 80–100 mL and for patients with bladder diverticula or bladder stones [7]. HoLEP and PVP lead to similar outcomes compared to open prostatectomy in men with large glands (>70, 80, and 100 mL) at a significantly lower complication rate [53, 58, 59].

A known urinary tract infection should be treated before surgery [60]. The routine use of prophylactic antibiotics remains controversial [14].

Mortality following open prostatectomy is less than 0.25 % in contemporary series [15]. The estimated need for blood transfusion following surgery is about 7–14 % [53, 61]. Compared to TURP there is significant risk of blood loss, transfusion, and a longer hospital stay associated with open prostatectomy.

Long-term complications are incontinence with the risk up to 10 % [62] and bladder neck contracture and urethral stricture with the risk up to 6 % [14, 53].

Open prostatectomy is an appropriate and effective treatment alternative for men with moderate-to-severe LUTS. The choice of approach should be based on the patient's anatomy, the surgeon's experience, and discussion of the potential benefit and risks for complications. Intraoperative and long-term complications, larger loss of blood, and longer hospital stay are the disadvantages of this procedure, especially for elderly patients.

Conclusions

Benign prostatic hyperplasia is common among elderly men. Careful evaluation with history, physical examination, symptom survey instruments and adjunctive tests is useful to guide therapy. A wide variety of treatment modalities are available. Successful treatment can help to improve LUTS, quality of life, and other clinical outcomes for older men with BPH.

References

1. Population Division, DESA, United Nations. World population aging 1950–2050. Executive summary. Available at: http://www.un.org/esa/population/publications/worldageing19502050/Pdf/62executivesummary.english.pdf. Accessed 15 Feb 2010.
2. Surveillance Epidemiology and End Results (SEER). SEER data for 200–2004. Available at: http://www.cancer.gov. Accessed 15 Feb 2010.
3. Guzzo T, Drach G. Major urologic problems on geriatrics: assessment and management. Med Clin North Am. 2011;95:253–64.
4. Urologic Diseases in America 2012. National Institutes of Health. BPH/LUTS and bladder stones. p. 48, table 2-2.
5. Mazur D, Helfand B, McVary T. Influences of neuroregulatory factors on the development of lower urinary tract symptoms/benign prostatic hyperplasia and erectile dysfunction in aging men. Urol Clin North Am. 2012;39:77–88.
6. McVary KT, Roehrborn C, Avins A, et al. Update on AUA guideline on the management of benign prostatic hyperplasia. J Urol. 2011;185:1793–803.
7. McVary KT, Roehrborn C, Avins A, et al. AUA guideline on the management of benign pros- tatic hyperplasia, chapter 1. AUA Education and Research; 2010. http://www.auanet.org/common/pdf/education/clinical-guidance/Benign-Prostatic-Hyperplasia.pdf, retrieved date 12.2.13.
8. Prchon L, P'ntarelli V, Bezerra E, et al. Quality of life in elderly men with aging symptoms and lower urinary tract symptoms. Neurourol Urodyn. 2011;30:515–9.
9. Roehrborn C. Male lower urinary tract symptoms and benign prostatic hyperplasia. Med Clin North Am. 2011;95:87–100.
10. McNicholas, TA, Kirby RS, Lepor H. Chapter 92: Evaluation and Nonsurgical Management of Benign Prostatic Hyperplasia. In Wein A, Kavoussi L, Novick A, Partin A and Peters C: Campbell-Walsh Urology. 10th. Ed. 2011.
11. Abdel-Aziz S, Mamalis N. Intraoperative floppy iris syndrome. Curr Opin Ophthalmol. 2009;20:37.
12. Jacobsen S, Jacobson D, McGree M, et al. Sixteen year longitudinal changes in serum prostate-specific antigen levels: the Olmsted County Study. Mayo Clin Proc. 2012;87(1):34–40.
13. Marberger MJ. Long-term effects of finasteride in patients with benign prostatic hyperplasia: a double-blind, placebo-controlled, multicenter study. PROWESS Study Group. Urology. 1998;51(5):677–86.
14. Oelke M, Bachmann A, Descazeud A, et al. Guidelines on the management of male lower urinary tract symptoms (LUTS), including benign prostatic obstruction (BPO). European Association of Urology. 2012. http://www.uroweb.org
15. McConnell JD, Bruskewitz R, Walsh P, et al. The effect of finasteride on the risk of acute urinary retention and the need for surgical treatment among men with benign prostatic hyperplasia. N Engl J Med. 1998;338(9):557–63.
16. Roehrborn CG, Siami P, Barkin J, CombAT Study Group, et al. The effects of dutasteride, tamsulosin and combination therapy on lower urinary tract symptoms in men with benign prostatic hyperplasia and prostatic enlargement: 2-year results from the CombAT study. J Urol. 2008;179(2):616–21.
17. Roehrborn CG, Siami P, Barkin J, CombAT Study Group, et al. The effects of combination therapy with dutasteride and tamsulosin on clinical outcomes in men with symptomatic benign prostatic hyperplasia: 4-year results from the CombAT study. Eur Urol. 2010;57(1):123–31.
18. Chang D, Campbell J. Intraoperative floppy iris syndrome associated with tamsulosin. J Cataract Refract Surg. 2005;31:664.
19. Andriole G, Bruchovsky N, Chung LW, et al. Dihydrotestosterone and the prostate: the scientific rationale for 5a-reductase inhibitors in the treatment of benign prostatic hyperplasia. J Urol. 2004;172(4 Pt 1):1399–403.
20. Rittmaster RS, Norman RW, Thomas LN, et al. Evidence for atrophy and apoptosis in the prostates of men given finasteride. J Clin Endocrinol Metab. 1996;81(2):814–9.
21. Naslund MJ, Miner M. A review of the clinical efficacy and safety of 5á-reductase inhibitors for the enlarged prostate. Clin Ther. 2007;29(1):17–25.
22. Boyle P, Gould AL, Roehrborn CG. Prostate volume predicts outcome of treatment of benign prostatic hyperplasia with finasteride: meta-analysis of randomised clinical trials. Urology. 1996;48(3):398–405.
23. Roehrborn CG, Lukkarinen O, Mark S, et al. Long-term sustained improvement in symptoms of benign prostatic hyperplasia with the dual 5a-reductase inhibitor dutasteride: results of 4-year studies. BJU Int. 2005;96(4):572–7.
24. Gittelman M, Ramsdell J, Young J, et al. Dutasteride improves objective and subjective disease measures in

men with benign prostatic hyperplasia and modest or severe prostate enlargement. J Urol. 2006;176(3): 1045–50.
25. Roehrborn CG. BPH progression: concept and key learning from MTOPS, ALTESS, COMBAT, and ALF-ONE. BJU Int. 2008;101 Suppl 3:17–21.
26. Kirby RS, Vale J, Bryan J, et al. Long-term urodynamic effects of finasteride in benign prostatic hyperplasia: a pilot study. Eur Urol. 1993;24(1):20–6.
27. Lepor H, Williford WO, Barry MJ, et al. The efficacy of terazosin, finasteride, or both in benign prostatic hyperplasia. N Engl J Med. 1996;335(8):533–9.
28. Kirby R, Roehrborn CG, Boyle P, et al. Prospective European doxazosin and combination therapy study investigators. Efficacy and tolerability of doxazosin and finasteride, alone or in combination, in treatment of symptomatic benign prostatic hyperplasia: the prospective European doxazosin and combination therapy (PREDICT) trial. Urology. 2003;61(1):119–26.
29. Andersen JT, Ekman P, Wolf H, et al. Can finasteride reverse the progress of benign prostatic hyperplasia? A two-year placebo-controlled study. The Scandinavian BPH Study Group. Urology. 1995;46(5):631–7.
30. Chess-Williams R, Chapple CR, Yamanishi T, et al. The minor population of M3-receptors mediate contraction of human detrusor muscle in vitro. J Auton Pharmacol. 2001;21(5–6):243–8.
31. Matsui M, Motomura D, Karasawa H, et al. Multiple functional defects in peripheral autonomic organs in mice lacking muscarinic acetylcholine receptor gene for the M3 subtype. Proc Natl Acad Sci USA. 2000;97(17):9579–84.
32. Abrams P, Kaplan S, De Koning Gans H, et al. Safety and tolerability of tolterodine for the treatment of overactive bladder in men with bladder outlet obstruction. J Urol. 2006;175:999.
33. Gomes T, Juurlink D, Mamdani M. Comparative adherence to oxybutynin to tolterodine among older patients. Eur J Clin Pharmacol. 2012;68(1):97–9.
34. Paquettte A, Gou P, Tannenbaum C. Systematic review and meta-analysis: do clinical trials testing antimuscarinic agents for overactive bladder adequately measure central nervous systems adverse events ? J Am Geriatr Soc. 2011;59(7):1332–9.
35. Abrams P, Chapple C, Khoury S, et al. Evaluation and treatment of lower urinary tract symptoms in older men. J Urol. 2009;181(4):1779–87.
36. Madersbacher S, Alivizatos G, Nordling J, et al. EAU 2004 guidelines on assessment, therapy and follow-up of men with lower urinary tract symptoms suggestive of benign prostatic obstruction (BPH guidelines). Eur Urol. 2004;46(5):547–54.
37. Chapple CR, Issa MM, Woo H. Transurethral needle ablation (TUNA). A critical review of radiofrequency thermal therapy in the management of benign prostatic hyperplasia. Eur Urol. 1999;35(2):119–28.
38. Benoist N, Bigot P, Colombel P, et al. TUNA: clinical retrospective study addressing mid-term outcomes. Prog Urol. 2009;19(1):54–9.
39. Schatzl G, Madersbacher S, Lang T, et al. The early postoperative morbidity of transurethral resection of the prostate and of four minimally invasive treatment alternatives. J Urol. 1997;158(1):105–10.
40. Hoffman RM, Monga M, Elliot S, et al. Microwave thermotherapy for benign prostatic hyperplasia. Cochrane Database Syst Rev 2007;(4):CD004135.
41. Mattiasson A, Wagrell L, Schelin S, et al. Five-year follow-up of feedback microwave thermotherapy versus TURP for clinical BPH: a prospective randomised multicenter study. Urology. 2007;69(1): 91–6.
42. D'Ancona FC, van der Bij AK, Francisca EA, et al. The results of high energy transurethral microwave thermotherapy in patients categorized according to the American Society of Anaesthesiologists operative risk classification (ASA). Urology. 1999;53(2): 322–8.
43. Yu X, Elliott SP, Wilt TJ, et al. Practice patterns in benign prostatic hyperplasia surgical therapy: the dramatic increase in minimally invasive technologies. J Urol. 2008;180(1):241–5.
44. Bootsma A, Laguna Pes M, Geerlings S, et al. Antibiotic prophylaxis in urologic procedures systematic review. Eur Urol. 2008;54(6):1270–86.
45. Hahn RG. Smoking increases the risk of large scale fluid absorption during transurethral prostatic resection. J Urol. 2001;166(1):162–5.
46. Madersbacher S, Lackner J, Brossner C, et al. Reoperation, myocardial infarction and mortality after transurethral and open prostatectomy: a nationwide, long-term analysis of 23,123 cases. Eur Urol. 2005;47(4):499–504.
47. Lourenco T, Armstrong N, N'Dow J, et al. Systematic review and economic modelling of effectiveness and cost utility of surgical treatments for men with benign prostatic enlargement. Health Technol Assess. 2008;12(35):1–146.
48. Madersbacher S, Marberger M. Is transurethral resection of the prostate still justified? Br J Urol. 1999;83(3):227–37.
49. Issa MM. Technological advances in transurethral resection of the prostate: bipolar versus monopolar TURP. J Endourol. 2008;22(8):1587–95.
50. Gilling PJ, Cass CB, Malcolm AR, et al. Combination Holmium and Nd: YAG laser ablation of the prostate: initial clinical experience. J Endourol. 1995;9(2):151–3.
51. Fraundorfer MR, Gilling PJ. Holmium:YAG laser enucleation of the prostate combined with mechanical morcellation: preliminary results. Eur Urol. 1998;33(1): 69–72.
52. Lourenco T, Pickard R, Vale L, Benign Prostatic Enlargement team, et al. Alternative approaches to endoscopic ablation for benign enlargement of the prostate: systematic review of randomised controlled trials. BMJ. 2008;337:a449.
53. Kuntz RM, Lehrich K, Ahyai SA. Holmium laser enucleation of the prostate versus open prostatectomy for prostates greater than 100 grams: 5-year follow-up results of a randomised clinical trial. Eur Urol. 2008;53(1):160–6.

54. Heinrich E, Schiefelbein F, Schoen G. Technique and short-term outcome of green light laser (KTP,80W) vaporisation of the prostate. Eur Urol. 2007;52(6): 1632–7.
55. Malek R, Kuntzman R, Barrett D. Photoselective potassium-titanyl-phosphate laser vaporization of the benign obstructive prostate: observations on long-term outcomes. J Urol. 2005;174(4 Pt 1):1344–8.
56. Bouchier-Hayes DM, Anderson P, Van Appledorn S, et al. KTP laser versus transurethral resection: early results of a randomised trial. J Endourol. 2006;20(8): 580–5.
57. Bouchier-Hayes DM, Van Appledorn S, Bugeja P, et al. A randomised trial of photoselective vaporisation of the prostate using the 80-W potassium-titanyl-phosphate laser vs transurethral prostatectomy, with a 1-year follow-up. BJU Int. 2010;105(7):964–9.
58. Skolarikos A, Papachristou C, Athanasiadis G, et al. Eighteen-month results of a randomised prospective study comparing transurethral photoselective vaporisation with transvesical open enucleation for prostatic adenomas greater than 80 cc. J Endourol. 2008;22(10): 2333–40.
59. Naspro R, Suardi N, Salonia A, et al. Holmium laser enucleation of the prostate versus open prostatectomy for prostates >70 g: 24-month follow-up. Eur Urol. 2006;50(3):563–8.
60. ElMalik EM, Ibrahim AI, Gahli AM, et al. Risk factors in prostatectomy bleeding: preoperative urinary infection is the only reversible factor. Eur Urol. 2000;37(2):199–204.
61. Gratzke C, Schlenker B, Seitz M, et al. Complications and early postoperative outcome after open prostatectomy in patients with benign prostatic enlargement: results of a prospective multicenter study. J Urol. 2007;177(4):1419–22.
62. Tubaro A, Carter S, Hind A, et al. A prospective study of the safety and efficacy of suprapubic transvesical prostatectomy in patients with benign prostatic hyperplasia. J Urol. 2001;166(1):172.

Prostate Cancer in Older Adults

17

Christopher Warlick, Christopher Weight, and Badrinath Konety

The definition of the "geriatric" population is somewhat variable. For the purposes of this chapter, we will define it as those aged 70 years and older. Management of prostate cancer in this population can be particularly challenging due to two inherent yet seemingly contradictory truths. Age is a risk factor for the diagnosis of prostate cancer and also for the presence of higher risk disease. However, older men with prostate cancer are at higher risk of dying from competing causes than younger men with comparable disease. Therefore, it is imperative to recognize this reality and individualize care to each particular man with age and comorbidities in mind to try to minimize both overtreatment and undertreatment of geriatric patients with prostate cancer.

Epidemiology of Prostate Cancer

There will be roughly 238,000 men diagnosed with prostate cancer in 2013 representing 28 % of all new cancer diagnoses that year. Nearly 29,000 men will die from prostate cancer in the USA during that year, accounting for 10 % of all male cancer deaths in 2013 [1]. The likelihood of being diagnosed with prostate cancer rises over one's lifetime, with a risk of diagnosis of 1 in 7,964 for those under age 40 to 1 in 8 for those aged 70 and older [1]. According to the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) database, of those diagnosed with prostate cancer between 2005 and 2009, 68.2 % were men aged 65 and older and 22.7 % of cases were diagnosed in men aged 75 and older [2]. Men aged 65–74, 75–84, and over 85 years accounted for 19.8, 38.6, and 32 of prostate cancer deaths, respectively [2]. However, while the risk of death from prostate cancer increases with age, observational studies have shown that for men aged 70 years and older, death from competing causes is common. Elderly men diagnosed in the pre-prostate-specific antigen (PSA) era, when men presented with higher disease burdens than typically seen now in the PSA era, with well to moderately differentiated disease, and men on observation for prostate cancer die from other causes compared to prostate cancer at ratios of between 10:1 and 3:2 over a 20-year period [3]. Men aged 70–74 on observation even for poorly differentiated disease die from other causes compared to prostate cancer at a ratio of roughly 1:1 compared to a ratio of 1:10 for men with similar disease diagnosed between the ages of 55 and 59. This highlights the fact that while older patients are more likely to be diagnosed with prostate cancer, even those with aggressive disease are much less likely than their

C. Warlick, M.D., Ph.D. • C. Weight, M.D.
Department of Urology, University of Minnesota, 420 Delaware St SE Suite B534, Minneapolis, MN 55455, USA

B. Konety, M.D. (✉)
Department of Urology, University of Minnesota, 420 Delaware Street S.E. Mayo Mail Code 394, Minneapolis, MN 55455, USA
e-mail: brkonety@umn.edu

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_17,

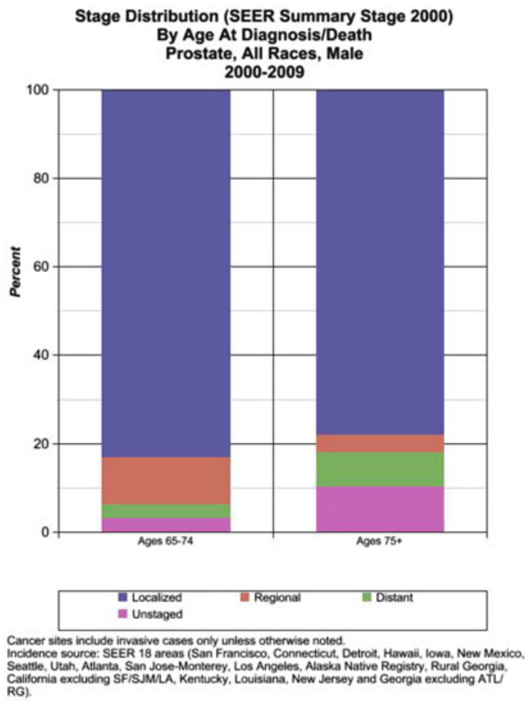


Fig. 17.1 Prostate cancer stage at diagnosis stratified by age

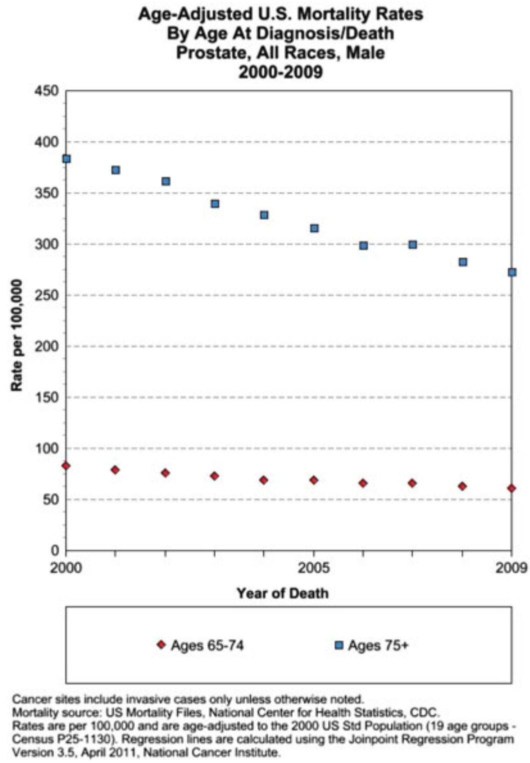


Fig. 17.2 Prostate cancer mortality rates over time stratified by age

younger counterparts to die from prostate cancer. Even those with low- to intermediate-risk disease are at higher risk of death from causes other than prostate cancer [3]. Additionally, it should be noted that these data come from the pre-PSA era when men presented with significantly more disease at the time of diagnosis than is seen currently. This effect in older men is likely to be amplified by the inclusion of screen-detected cancers which are associated with a significant lead time in diagnosis [4]. In addition to observational studies, a randomized controlled trial also conducted prior to the PSA era has shown that there was no survival advantage conferred by surgery compared to observation for men over 65 years of age [5]. In contrast, there was an observed survival advantage for surgery in younger men. Thus, even though older men diagnosed with high-risk disease die at a significant rate, since most men are diagnosed with low- to intermediate-risk disease (Fig. 17.1), the majority of men diagnosed with prostate cancer after age 70 are likely to die "with prostate cancer" and not "from prostate cancer." Additionally, as prostate cancer deaths in general have been on the decline for the past several years, they have been declining for older patients as well (Fig. 17.2). This is likely due to advances in the treatment of advanced prostate cancer which will be highlighted later in this chapter.

Prostate Cancer Screening

Currently, most prostate cancer is diagnosed due to an abnormal PSA level or abnormal digital rectal exam. Many of the abnormal PSA values are detected through routine screening or are obtained in the evaluation of lower urinary tract symptoms unlikely to be related to prostate cancer. Results from recent randomized trials of PSA screening have generated significant controversy surrounding the efficacy of routine PSA screening [6, 7]. The results of the Prostate Lung, Colorectal and Ovarian (PLCO) [6] Screening Study, a randomized trial of observation versus surgery in over 76, 000 men, failed to demonstrate a survival advantage in men undergoing PSA screening compared to men undergoing "usual care." However, limitations of the study may have confounded the findings. Over half of the men in the "usual care" arm ended up receiving at least one PSA test over the course of the study, while only 85 % of men in the screening arm actually underwent screening, thereby limiting the ability to compare the two groups and mitigating potentially small benefits which may have otherwise been detected.

The European Randomized Screening Study of Prostate Cancer (ERSPC) [7] also intended to answer the question of whether PSA screening prevents deaths from prostate cancer. This study, performed concurrently with the PLCO, included 182,000 men aged 50–74 years from several different European countries. Men were randomized to receive PSA screening on average once every 4 years. The screening compliance rate was 82 %. This study demonstrated a relative reduction in the risk of death from prostate cancer of approximately 20 % among the men who were screened. Interestingly, however, there also appeared to be a high risk of "overdiagnosis," defined as the detection of a cancer that would have remained clinically silent in the absence of screening. Initial analysis suggested that roughly 1,480 men needed to be invited to undergo screening, in order to prevent one death from prostate cancer.

Results from the PLCO and ERSPC trials among others have prompted much debate regarding the general utility of prostate cancer screening, culminating in a statement from the US Preventive Services Task Force (USPSTF) articulating their stance against the routine PSA screening for all men the way it is currently practiced in the USA [8]. This statement was an update of the committee's previous statement in 2008 which stated opposition to prostate cancer screening of men aged 75 years or older [9]. The committee cited concerns regarding overdiagnosis and subsequent overtreatment among the reasons for their statement. Absent from their analysis, however, was any significant discussion about the use of screening among high-risk populations such as African-Americans, or those with a family history of prostate cancer.

While much debate remains surrounding the wisdom of stopping all PSA screening, concerns about overdiagnosis and overtreatment among older men are indeed substantiated by increasing amounts of data. PSA screening results in the detection of prostate cancer between 6 and 10 years earlier than in the absence of screening [10]. Therefore, depending on the age and comorbidities of older men, it becomes unclear whether the prostate cancer would have been discovered during the man's life, in the absence of screening. Detection of such a cancer would be considered overdetection. Unfortunately, many older men in the USA continue to be screened although they are unlikely to benefit from detection of a screen-detected cancer. Data from a study by Walters et al. [11] showed that in a Veterans Administration population, 64 % of men aged 70–74 years and 36 % of men aged greater than 85 years underwent PSA screening. Statistically, however, less than 60 % and less than 10 % of men in these two groups, respectively, would be expected to live longer than 10 years and therefore long enough to benefit from screening. Furthermore, when this population of men was stratified by comorbidity status, there appeared to be no difference in the rate of PSA testing among men with the least versus most number of comorbidities [11]. These older men with the worst health status are extremely unlikely to benefit from screening for prostate cancer, and yet were subjected to testing. The main danger to these men from such testing is the discovery and subsequent treatment with inherent risk of treatment-related morbidity for a cancer that otherwise by itself would have resulted in no morbidity, and certainly not mortality during the man's lifetime had it remained undetected.

Prostate Cancer Treatment Decisions

Once diagnosed with prostate cancer, many men face difficult treatment decisions depending on the stage and disease characteristics at diagnosis.

These decisions can be particularly agonizing among older men who must balance competing risks including the rational and irrational fear of the morbidity and mortality from prostate cancer, and concern of side effects from prostate cancer therapy with subsequent possible decreases in quality of life. All of this also occurs within the context of an uncertain though relatively limited life expectancy.

All forms of prostate cancer therapy carry risks of side effects that can diminish one's quality of life in terms of both genitourinary function and overall [12, 13]. Uncertainty often surrounds the information about life expectancy and disease severity that would be required to make a completely informed decision at the time men must choose their treatment. Often there is no "right" or "wrong" answer about how to manage one's prostate cancer. For some men, the goal may be to maximize length of life, regardless of the quality. For others, it may be to maximize quality of life even if that results in a potentially shorter life span. The primary objective should be to engage in shared decision making between the physician and patient to determine a course of treatment most consistent with the patient and his family's goals. This requires factoring into account an objective assessment of the risks posed by the severity of the patient's prostate cancer, an objective assessment of his life expectancy based upon age and comorbidities, and an estimate of the risk for potential side effects associated with the various treatment options.

Therapeutic options for prostate cancer are divided into two main categories depending on the stage of disease. For patients with metastatic disease, first-line treatment includes hormone deprivation therapy which involves lowering the body's testosterone level. Testosterone stimulates the growth of prostate cancer cells, and removal of this stimulus results in the death of hormone-sensitive prostate cancer cells. While hormone deprivation controls prostate cancer, typically for a period of years, it does not cure prostate cancer. If a man lives long enough, eventually the prostate cancer cells learn to grow even in an environment of low testosterone, which defines the entrance into the castration-resistant state. At this point in the natural history of the disease, secondary hormonal manipulation and/or other modalities of therapy are required to control the disease. Hormone therapy will be discussed in greater detail later in this chapter.

For patients who have presumed localized prostate cancer, many options exist for those who wish to undergo definitive therapy. These options include surgery, either with open or robot-assisted laparoscopic approaches; radiation therapy including external beam, proton, or brachytherapy; cryotherapy; and high-intensity focused ultrasound (HIFU). HIFU is currently under clinical trial in the USA and is not yet approved by the US Food and Drug Administration (FDA). We will exclude proton beam, cryotherapy, and HIFU from discussion in this chapter as the numbers of men undergoing these therapies are relatively small. As an alternative to definitive therapy, observation with either active surveillance or watchful waiting remains a viable and likely underutilized management option, particularly for older patients.

Surgery

Surgery remains a proven treatment option with excellent long-term cure rates for men with organ-confined disease [14]. Advances in surgical techniques beginning in the early 1980s [15–17] and continuing through the evolution of robot-assisted laparoscopic approaches [18] have significantly improved the morbidity of the procedure. However, surgery still carries with it several significant risks. Perioperative risks may be substantial, particularly for geriatric patients. Many older men may harbor occult cardiac or vascular disease which increases the risk of perioperative complications such as heart attack or stroke which can result in significant morbidity or death. However, surgery has been shown to be safe, even in well-selected septuagenarians and octogenarians [19, 20].

In addition to perioperative complications, older patients are at increased risk of the major side effects following prostate cancer surgery including stress urinary incontinence [2] and erectile dysfunction [21]. One study reported incontinence rates of 33 % at 6 months in men older than age 71 years undergoing laparoscopic radical prostatectomy compared to 9 % of men aged 59 years and younger [21]. Similarly, others have reported continence rates at 1 year of between 66 and 59 % for men ages 65 and 75 years, respectively [22]. It is important to remember that as many as 30 % of men in this age group may suffer from some degree of incontinence at baseline [12].

Besides incontinence, erectile dysfunction is another major potential side effect following radical prostatectomy. Many factors influence the likelihood of men being able to have erections sufficient for intercourse following surgery including age, preexisting erectile function, comorbidities, and nerve-sparing status during surgery [22, 23]. Many older men suffer from various predictors of poor erectile function independent of their prostate cancer. Roughly 43 % of men aged 75–84 years report some degree of erectile dysfunction at baseline with over 28 % of men reporting their erectile dysfunction as a "big problem [12]." However, it is also true that if a man has existing erectile dysfunction rendering him impotent, then surgery is unlikely to change his quality of life in terms of sexual function. It is probable that men with marginal preoperative erectile function and little physiologic reserve are the most likely to lose enough function from surgical intervention that they will notice the greatest decrement to quality of life. Recent potency outcomes in older men have been reported to be 66 and 46 % for men aged 65 and 75 years, respectively [22]. Therefore, for older men considering surgery, some degree of erectile dysfunction is a significant possibility. Some men who wish to remain sexually active following radical prostatectomy may benefit from oral phosphodiesterase-5 (PDE5) inhibitors such as sildenafil and tadalafil. However, use of these medications may be problematic in elderly men with other preexisting conditions such as coronary artery disease and congestive heart failure which are medical contraindications. Alternatives to PDE5 inhibitors include penile injection of alprostadil, use of a vacuum erection device, or placement of a penile prosthesis. Unfortunately, many older men may find these more "invasive" interventions too cumbersome to use due to decreased manual dexterity, poor visual acuity, and limited partner interest.

Radiation Therapy

Many forms of radiation therapy for prostate cancer exist including external beam radiation, brachytherapy, and proton beam therapy. Detailed decisions regarding the type of radiation that is most appropriate hinge on a variety of personal, clinical, and disease characteristics and are beyond the scope of this chapter. The side effect profiles for the varying types of radiation, however, are similar enough that they can be discussed together. There are differences in outcomes depending on the dose of radiation and the delivery methods utilized. Radiation techniques are continuously evolving with improved outcomes being reported in more recent studies compared to historical outcomes [24, 25]. In terms of urinary function, radiation therapy can cause worsening of preexisting irritative voiding symptoms or de novo onset of symptoms including urgency, frequency, or urge incontinence. A recent study reported the rate of significant late genitourinary toxicity from three different modern radiation therapy modalities to be between 21 and 28 % [24]. Since the prostate also rests on the rectum, men may experience irritative defecation symptoms including urgency and frequency of stooling or chronically loose stools. Patients may also experience hematuria or hematochezia secondary to radiation therapy. Gastrointestinal complications have recently been reported to be between 2 and 20 % [24]. In addition, urethral strictures can occur after radiation which can result in significant subsequent morbidity requiring additional operations [26, 27]. The development of irritative voiding symptoms following radiation therapy is particularly relevant in the discussion regarding geriatric patients. Many older men already suffer from some degree of these types of symptoms at baseline due to urinary obstruction secondary to concomitant benign prostatic hyperplasia. Men with such lower urinary tract symptoms (LUTS) should be counseled that radiation therapy could make their symptoms worse. Indeed, severe LUTS should be considered a relative contraindication to radiation therapy. Men with obstruction leading to their irritative voiding symptoms should consider undergoing a prophylactic transurethral resection of the prostate (TURP) prior to radiation to minimize risk of development of worsening irritative symptoms or possible obstruction following radiation.

Erectile dysfunction is also a side effect of radiation therapy. However, it tends to be a late complication of therapy with the delayed effect often not evident for over a year or more. Rates of potency following radiation therapy have been reported to be approximately 50 % at 3 years following brachytherapy [28] and 36 % of patients after external beam radiation [29]. It should be noted that concomitant androgen deprivation therapy, often given to patients in conjunction with radiation therapy for patients with intermediate- to high-risk disease, will further negatively impact erectile function and libido.

Observation

Observation for prostate cancer can be performed in two distinct ways, including active surveillance and watchful waiting. While these two terms are often used interchangeably, they are fundamentally different. Active surveillance is the close monitoring of men with suspected low-risk, low-volume prostate cancer, who are young enough and healthy enough to require cure, but it is unclear if the disease that they are harboring is severe enough to warrant this. Thus, the best candidates for active surveillance are some fraction of men with low-risk prostate cancer with the most favorable disease characteristics, who will be compliant with the surveillance protocol and who do not suffer anxiety from the presence of untreated prostate cancer. Men are monitored very closely with frequent PSA measurements and digital rectal examinations and repeat prostate biopsies to ensure the disease is not progressing. If men demonstrate evidence of disease progression on repeat biopsy and/or by significant PSA changes, intervention is undertaken with *curative* intent typically in the form of surgery or radiation. In contrast, watchful waiting is the observation of men presumed too old or too sick to require cure of their prostate cancer regardless of the disease characteristics. These men have a limited life span or the strong desire to avoid definitive therapy and the possible side effects. These men are monitored less intensely, typically only with repeat digital rectal examinations and PSA measurements, though not as frequently as for men on active surveillance. Importantly, intervention is reserved until the men demonstrate evidence of clinical disease progression as determined by the onset of symptoms attributable to prostate cancer or the development of radiographic evidence of metastatic disease. The intervention at that time is *palliative* in the form of hormone deprivation therapy, which controls prostate cancer, although it does not cure prostate cancer. The advantage of observational approaches to managing prostate cancer is that one may avoid the potential side effects of definitive therapy, particularly when there is an unclear survival advantage. The major risks, however, include that the disease could progress to an incurable state during the period of observation or that one could suffer morbidity or even potential mortality from disease progression that could have been avoided with some form of definitive therapy. While no uniformity exists in terms of defining exactly who is a safe candidate for observation, how to best follow patients in terms of PSA measurement or repeat biopsy intervals, or what the ideal triggers are for intervention, the results from cohorts reported in the literature are very encouraging [30–32]. Klotz et al. [31] recently published an update of their active surveillance cohort where selected men were over 18 times more likely to die from other causes than they are from prostate cancer. They also analyzed the six largest published active surveillance cohorts in the literature. They reported that in aggregate, approximately 2,168 patients have been followed on active surveillance with a median follow-up of 43 months. Among these cohorts are over 200 men who have been followed for more than 10 years. The prostate cancer-specific survival for all men in these cohorts is 99.7 %, suggesting that this approach appears to be safe for appropriately selected men [31]. Because most men were older than 65, longer-term follow-up will be required to determine the safety of this approach for younger men and to define optimized surveillance protocols and triggers for intervention. The key is to minimize the morbidity of observation protocols such as repeat biopsies and minimize the risk of losing the window of curability prior to intervention in active surveillance patients or the development of symptomatic metastases or death in watchful waiting patients.

Risk Stratification and Life Expectancy

The recognition that prostate cancer therapy can be morbid combined with the unclear survival advantage conferred upon many older men by definitive therapy has increased the concern about overdiagnosis and overtreatment. This is particularly true for older patients who may have a limited life expectancy. Data from observational studies have shown that older men generally die more often from other causes than from prostate cancer [3]. In fact, for men over age 65, only men who have Gleason scores of seven or higher have death rates from prostate cancer greater than 25–30 % at 20 years while on observation. Nearly 100 % of the remaining men will die from other causes over the same time period. In addition, observations from a Swedish cohort demonstrated no survival advantage to men over age 65 years undergoing surgery compared to those on observation [5]. Furthermore, recent data from the Prostate Cancer Intervention Versus Observation Trial (PIVOT) [33] which randomized men in the PSA era to undergo surgery or observation demonstrated that there was no survival advantage conferred upon men with low- or intermediate-risk disease (PSA ≤ 20, clinical stage ≤ T2b, and Gleason sum score ≤ 7) compared to observation over the first 10–12 years from diagnosis. Therefore, for men with these disease parameters who are of average health and over 70 years of age, it is unclear if definitive therapy will confer any survival advantage. However, for men in the high-risk group (PSA ≥ 20, clinical stage ≥ T3, and Gleason sum score ≥ 8), the risk of death from prostate cancer was reduced by approximately 60 % with surgery compared to observation. Interestingly, the advantage of surgery did not appear for approximately 7–8 years, suggesting that for men with a significantly limited life expectancy, observation may remain appropriate even for select men with high-risk prostate cancer [33].

Because older men are at highest risk of overtreatment if diagnosed with prostate cancer, it must first be decided whether to pursue observation or definitive therapy. To determine which path seems most appropriate, both the severity of the cancer and the patient's life expectancy need to be considered. Of these variables, life expectancy proves to be the most difficult to assess. The fundamental challenge in assessing life expectancy is that models are based on populations of patients and therefore do not apply directly to individuals. Furthermore, many social factors significantly influence life expectancy and are difficult to measure. Thus, while there are plenty of sources to determine the average life expectancy for individuals of a given age, there is no reliable method for predicting life expectancy for a given individual.

Heart disease remains the number one cause of death in the USA for all ages and for those aged 85 years and over, accounting for approximately 25 % of all male deaths [34]. Therefore, assessment of the likelihood of cardiac morbidity is one way to begin to stratify health status. Several tools are available to assist in this including modifications of the Framingham risk calculator [35] which predicts the likelihood of development of cardiovascular disease events. In addition, well-known general comorbidity scales such as the Charlson Comorbidity Index can also help to risk stratify men's health and aid in their decisions of whether to undergo definitive therapy [36].

Table 17.1 Commonly used hormonal agents in men with prostate cancer

	Drug name (trade names)	Route of administration	Dosages (mg)	Duration (days)
LHRH agonists	Leuprolide acetate (Lupron Depot, Eligard[a])	Intramuscular injection	7.5 22.5 30 45	28 84 112 180
	Leuprolide acetate (Viadur)	Subcutaneous implant	65	365
	Goserelin acetate (Zoladex)	Subcutaneous implant	3.6 10.8	28 84
	Triptorelin acetate (Trelstar, Trelstar LA)	Intramuscular injection	3.75 11.25	28 84
	Histrelin acetate (Vantas)	Subcutaneous implant	50	365
LHRH antagonists	Abarelix (Plenaxis)	Intramuscular injection	100	28
	Degarelix acetate (Firmagon)	Subcutaneous injection	80[b]	28
Antiandrogens	Bicalutamide (Casodex)	Oral	50 qd	1
	Flutamide (Eulexin, Flutamin)	Oral	250 tid	1
	Nilutamide (Nilandron)	Oral	150 qd[c]	1

[a]Subcutaneous injection as same dosage levels
[b]Initial dose of 240 mg followed by monthly 80 mg injections
[c]Initial dose of 300 mg for 1 month then 150 mg daily thereafter

Tools specific to prostate cancer patients have also been published that determine competing risk mortality for patients undergoing radical prostatectomy and radiation therapy [37–39]. These include nomograms for calculation of likelihood of prostate cancer-specific death versus other cause mortality in individual patients undergoing radical prostatectomy or radiation therapy [37, 39]. Many of these tools can be helpful in educating patients about what their objective risks are of dying from prostate cancer as opposed to other causes. It is very likely that inaccurate perceptions about the true risks of dying from prostate cancer push many patients and physicians toward definitive therapy without realizing that for many older men, there will be minimal to no survival benefit.

Hormone Deprivation for Prostate Cancer

Hormone deprivation for the treatment of prostate cancer was first described over 80 years ago by Charles Huggins [40] and to this day remains one of the principal, most effective, and frequently used treatments for men with advanced prostate cancer. However, despite its nearly uniform initial effectiveness against even the most advanced cancers, the regression of cancer is not durable. Even as Dr. Huggins was accepting the 1966 Noble Prize in Physiology and Medicine for his work with hormones and prostate cancer, he and others recognized that hormone deprivation does not cure prostate cancer noting, "There are many failures of endocrine therapy to control the disease." [41]

In recent years, hormones have largely been reserved for men with metastatic prostate cancer, but they have also been studied in both localized and locally advanced diseases and have been found to be useful in certain settings. A list of commonly used hormonal therapies for prostate cancer is shown in Table 17.1. We will first discuss their indications for use in the case of metastatic prostate cancer and then discuss their role in localized or locally advanced disease. Finally, we will discuss the common side effects and symptom management.

Hormones in Metastatic Prostate Cancer

Androgen deprivation is the first-line treatment for metastatic prostate cancer. This can be achieved through three primary mechanisms including removal of the organs responsible for androgen production, inhibition of production of androgens, or blockade of the end organ effects of androgens.

Orchiectomy

Hormone deprivation for the treatment of metastatic prostate cancer was historically obtained by surgical castration with removal of the testicles. Since the testicles produce 90 % of this hormone, orchiectomy leads to a precipitous drop in serum testosterone levels. Within 24 h [3], testosterone levels are less than 50 ng/dL (<1.74 nmol/L) which is considered a castrate level [42, 43]. Indeed many older surgeons from the pre-PSA era remember performing an orchiectomy in a man with painful bone metastases and the patient waking from anesthesia already feeling much better. A simple orchiectomy through the scrotum is the chosen operation and can even be done under local anesthetic. Recovery is minimal and the effect is durable. This method of surgical androgen deprivation is by far the most cost-effective option and has seen a recent resurgence in the treatment of men with metastatic prostate cancer [44].

The adrenal glands are also responsible for the production of approximately 10 % of circulating testosterone. Surgical or medical ablation of the adrenal glands has been attempted, but this generally necessitates cortisol replacement. Because the side effects are greater than the benefits, this method has been largely abandoned.

Androgen Synthesis Inhibition

Inhibition of androgen synthesis by manipulating the hormonal signals stimulating its production has supplanted surgical castration as the most commonly used method of androgen deprivation [45]. A brief review of this hormonal axis will aid in understanding how these agents work in achieving castrate levels of testosterone. Testosterone production in the testicles is heavily influenced by a hormone produced in the pituitary gland called luteinizing hormone (LH). LH production is in turn heavily influenced by a hormone produced in the hypothalamus called gonadotropin-releasing hormone (GnRH). Therefore, increases in GnRH in the hypothalamus will stimulate the pituitary to release serum LH, which in turn will stimulate the testicles to produce more testosterone [46]. In an unmanipulated system, the rise in testosterone and inhibin from the testicles exerts a negative feedback signal to both the hypothalamus and pituitary gland, and GnRH and LH levels fall. Once the testosterone begins to degrade, the negative feedback is abrogated, and GnRH is released from the hypothalamus to stimulate LH production in the pituitary, and the cycle is repeated. This feedback mechanism keeps testosterone levels relatively stable.

Luteinizing hormone-releasing hormone (LHRH) is a synthetic analog of GnRH. When administered as a bolus, it initially leads to a surge in serum LH levels and testosterone levels. Subsequently, due to downregulation of the GnRH receptor in the pituitary gland, serum LH and thereby testosterone levels plummet to castrate levels [47]. The efficacy of LHRH agonists in the treatment of prostate cancer has been compared to surgical castration in many thousands of patients in over 20 different trials and has been found to be equivalent [48].

There are now various preparations of LHRH agonists including 1-, 3-, 4-, 6-, and 12-month depots or implants (Table 17.1). The names of the various hormones are leuprolide acetate depot (Lupron), goserelin acetate (Zoladex), and triptorelin pamoate (Trelstar). There are also some long-acting (1-year) implants including leuprolide acetate (Viadur) and histrelin acetate implant (Vantas).

These LHRH agonists have become the mainstay of androgen deprivation in the treatment of metastatic prostate cancer because they are easy to administer, are generally well tolerated, do not require surgery, avoid the associated stigma of an empty scrotum, and allow for intermittent or temporary hormone therapy. The primary drawback is cost. Annual Medicare expenditures for medical castration peaked at 1.23 billion in 2003 [44]. There is also the need for constant follow-up and medication administration.

Another detail that is imperative to remember in the administration of these LHRH agonists is the associated testosterone flare. This surge in both LH and testosterone occurs with every LHRH agonist and can result in serum LH and testosterone levels as high as 10 times the normal levels [49]. This flare can last for as many as 10–20 days and can be potentially dangerous or even life threatening to a small proportion of men (4–10 %) with a metastasis near a vital structure [50]. Fortunately, this threat can be easily avoided with the concomitant administration of an antiandrogen (see below) for the first 3–4 weeks of LHRH agonist treatment [51].

There is also a family of medications that work as LHRH antagonists. Examples include abarelix, cetrorelix (not FDA approved for prostate cancer), and degarelix. They reduce serum testosterone levels to a similar degree as the LHRH agonists and do not have the associated testosterone flare. Unfortunately, they usually must be administered monthly and have been associated with severe allergic reactions even when previously tolerated. These two factors have limited the enthusiasm for this family of medications [52], and abarelix is no longer available for new patients.

Antiandrogens

This class of medications works at the level of the androgen receptor. They exert an anticancer effect by blocking the binding of testosterone to its receptor and thereby preventing downstream effects such as transcriptional activity. Antiandrogens have an advantage over other hormonal manipulations in that they are administered orally and their mechanism offers activity on the cancer without inducing a state of hypogonadism.

The antiandrogens including flutamide, bicalutamide, and nilutamide have been studied both as monotherapy and as a part of combined androgen blockade when used in conjunction with LHRH agonists. When used as monotherapy in patients with metastatic cancer, the results are generally inferior to surgical or medical castration, although as many as 40 % [53] will have objective response rates [54, 55]. More recently, some studies have found that a high dose of bicalutamide (150 mg daily) may be equivalent to castration in cancer control and superior in some measures of quality of life [56]. Nevertheless, these medications are most commonly used to block the flare associated with LHRH agonist administration, as part of total androgen blockade, or as second-line therapy after the failure of castration.

Antiandrogens are associated with a well-described withdrawal phenomenon. When patients are on both an LHRH agonist and an antiandrogen, stopping the antiandrogen will result in a significant drop of up to 50 % in the serum PSA level within 4–6 weeks in approximately 15–30 % of patients [57]. Unfortunately, this PSA drop is often of short duration, typically 2–3 months, and may not be associated with any measurable tumor response or advantage in overall survival [46].

Hormones for Patients Without Metastatic Disease

Hormonal agents are not often used in the treatment of nonmetastatic prostate cancer. Part of this is due to the adverse side effects of treatment and part due to the lack of efficacy. However, there are some examples in the case of locally advanced disease where hormones are indicated.

Hormone Deprivation with Radical Prostatectomy

Non-randomized observational data has suggested neoadjuvant hormone deprivation prior to radical prostatectomy could be beneficial. Therefore, several randomized trials were conducted comparing 3 months of neoadjuvant androgen deprivation plus radical prostatectomy to radical prostatectomy alone. Although all four studies of this type identified a significant reduction in positive surgical margins, not one demonstrated an advantage in biochemical progression-free survival and therefore this treatment is not indicated [58–61].

Hormone Deprivation with Radiation Therapy

Contrary to the disappointing results observed with hormone deprivation and surgery, many randomized clinical trials have demonstrated a survival advantage with hormones plus radiation compared to radiation alone. The benefit is most pronounced in men with locally advanced or high-risk cancer [62]. Most studies indicate that 2–3 years of hormones combined with external beam radiation compared to radiation alone confers an overall, cancer-specific, and progression-free survival advantage [46].

Side Effects of Hormone Deprivation Therapy

The side effects of hormone deprivation therapy are usually less severe than traditional chemotherapy. Hair loss, chronic nausea, and hematopoietic suppression are uncommon. However, hormonal therapy can significantly affect the quality of life of men undergoing treatment. Side effects can be ameliorated somewhat by effective management.

Surgical Side Effects of Orchiectomy

The perioperative side effects of orchiectomy are quite low. Complications such as infection, bruising, and pain are uncommon. The main long-term consequences are negative psychological effects related to alterations in body image. It is also irreversible and therefore does not allow for intermittent therapy [63]. Most recognized complications of castration listed below occur with either surgical or medical castration.

Osteoporosis

Hypogonadism has long been associated with osteoporosis. This is complicated by the fact that men who develop prostate cancer are already older and up to 50 % already have osteopenia prior to initiation of androgen ablation [64]. It has been estimated that androgen ablation increases the risk of bone fracture by as much as sixfold per year [65]. Therefore, it is imperative that the bone health of men on androgen ablation is closely monitored with bone mineral density tests. Vitamin D and calcium need to be administered along with androgen deprivation therapy to mitigate some of these bone effects. The rate of bone loss can be ameliorated by the use of bisphosphonates such as pamidronate, alendronate, or zoledronic acid [66] or denosumab [67]. Bone loss may not be as great in men on antiandrogens compared to LHRH agonists [68].

Sexual Side Effects

Androgen ablation is associated with loss of libido and erectile dysfunction in most men, although 20 % are able to maintain some sexual function [69]. Because antiandrogens maintain or even increase the serum testosterone levels, this effect is not as pronounced [56]. There appears to be no effective treatment for this condition.

Hot Flashes

Flushing of the torso and upper body as a response to androgen ablation is very common and is one of the most common side effects occurring in nearly 80 % of men [70]. They are not life threatening and tend to decrease over time. If they are bothersome, they can be treated with megestrol acetate, 20 mg BID. Diethylstilbestrol (DES) is also effective at reducing hot flashes but has severe side effects such as painful gynecomastia and thromboembolic events. Clonidine and the selective serotonin reuptake inhibitors (SSRIs) have also been effective in limiting hot flashes in some studies [46].

Metabolic Syndrome/Cardiovascular Effects

Castration results in a complicated syndrome of fatigue, muscle loss, decreased energy, insulin resistance, lipid alterations, and obesity.

It has also been associated with increased cardiovascular disease [71]. These metabolic effects are an important focus of ongoing research related to hormonal therapy for prostate cancer.

Cognitive Dysfunction

Many small studies have identified declines in cognitive functioning in the areas of verbal fluency, complex tasks, and spatial reasoning in association with hormonal therapy. The scientific quality of these studies is variable and control is often nonexistent or inadequate. However, many patients anecdotally describe a decline in this domain [72].

Gynecomastia

Painful swelling of the breasts is a common side effect of antiandrogens. This is particularly problematic with high-dose bicalutamide, occurring in up to 60–70 % of men. It can occur with androgen ablation, but is much less common. Once it occurs, it can only be treated by surgery. Prophylactic radiation to the breasts with low-dose radiation (10 Gy) is effective in preventing or reducing this complication [46].

Liver Toxicity

Antiandrogens can lead to liver dysfunction ranging from mild elevations in liver function tests to fulminant liver failure. Because of this, liver function tests need to be monitored in patients who are taking antiandrogens and stopped if liver dysfunction is noted [73].

Non-hormone Therapies for Advanced Prostate Cancer

As mentioned previously, although most men will observe a clinically significant response to hormone deprivation, the majority with metastatic prostate cancer will progress within 36 months on continuous androgen deprivation [74]. This has led to the development of a new class of medications in the setting of hormone refractory prostate cancer. There are currently five options in the hormone refractory setting that have demonstrated improvements in overall survival. These include docetaxel, cabazitaxel, abiraterone, sipuleucel-T, and enzalutamide. It should be noted that although the disease progresses while on hormonal therapy and it is termed “hormone refractory prostate cancer,” the hormone deprivation therapy is often continued in addition to these agents for its beneficial therapeutic effect.

Chemotherapy

Although many agents have been employed in the treatment of hormone refractory prostate cancer, docetaxel (Taxotere) is the most commonly used first-line cytotoxic agent. This is because docetaxel plus prednisone was shown to be superior to mitoxantrone and prednisone alone in a phase III clinical trial [75]. Cabazitaxel (Jevtana) has been FDA approved for docetaxel failures because it demonstrated increased overall survival compared to mitoxantrone [76].

Abiraterone

Abiraterone (Zytiga) is a novel agent that functionally blocks androgen synthesis by inhibiting cytochrome p17. This enzyme is necessary for the androgen synthesis pathway in the adrenal gland, which can produce 5–10 % of androgens independent of the hypothalamic pituitary axis. Abiraterone has demonstrated improved overall survival in docetaxel failures [77]. It must be administered with prednisone because inhibition of the adrenal enzymes can also decrease synthesis of mineralocorticoids. Abiraterone has been approved for use in men with advanced prostate cancer prior to and after failing chemotherapy.

Sipuleucel-T

Sipuleucel-T (Provenge) is a novel immunotherapy wherein white blood cells from patients with cancer are apheresed and "taught" how to fight the prostate cancer and then reinfused into the patient. In a phase III trial in men with asymptomatic or minimally symptomatic metastatic castrate-resistant prostate cancer, improved overall survival was noted in patients getting sipuleucel-T compared to placebo [78].

Enzalutamide

Enzalutamide (Xtandi) is a next-generation androgen receptor antagonist. It has an advantage over traditional androgen receptor blockers such as flutamide and bicalutamide in that it is a more effective blocker and it does not exhibit any paradoxical receptor agonist activity. This agent was recently FDA approved after demonstrating improvements in overall survival in chemotherapy failures [79]. A unique side effect observed in the early trials of this drug was the occurrence of seizures. This must be considered when prescribing this medication to patients, particularly in those with a prior history of seizures.

Bone Health

Metastatic prostate cancer has a strong predilection for the bones with 90 % of metastases to bone versus 10 % to visceral organs [46]. Because of this, preserving bone health has been a primary focus of advanced prostate cancer treatment. The two primary therapies currently available include bisphosphonates such as zoledronate (Zometa) and rank ligand inhibitors such as denosumab (Xgeva) [80].

End of Life Care

If patients with prostate cancer progress through these treatments, as with other types of advanced cancer, the focus shifts from cancer control to symptom management. This can be achieved through a combination of pain control methods including opioids, steroids, nerve blocks, and focal radiation for symptomatic lesions. Palliative medicine specialists and medical oncologists are often most well suited to manage men in this stage of their cancer.

Summary

Prostate cancer is common in elderly men. Although some men will develop metastatic disease and die from prostate cancer, the majority of men diagnosed with this condition will die of competing causes from other comorbid conditions. Because of this, routine screening for prostate cancer in elderly men is not recommended. However, in select cases, diagnostic evaluation is indicated to provide a basis for decision making regarding clinical care. A variety of treatments are available for elderly men diagnosed with prostate cancer ranging from watchful waiting and active surveillance to surgery, radiotherapy, and hormonal manipulation. The choice of therapies should be made individually for each patient taking into consideration his clinical cancer parameters, overall health, estimated remaining life expectancy, quality of life, and goals of therapy.

References

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. CA Cancer J Clin. 2013;63:11–30.
2. Howlader NNA, Krapcho M, Neyman N, Aminou R, Altekruse SF, Kosary CL, Ruhl J, Tatalovich Z, Cho H, Mariotto A, Eisner MP, Lewis DR, Chen HS, Feuer EJ, Cronin KA, editors. SEER cancer statistics review, 1975–2009 (vintage 2009 populations). Bethesda, MD: National Cancer Institute; 2012.
3. Albertsen PC, Hanley JA, Fine J. 20-year outcomes following conservative management of clinically localized prostate cancer. JAMA. 2005;293:2095–101.
4. Etzioni R, Penson DF, Legler JM, di Tommaso D, Boer R, Gann PH, Feuer EJ. Overdiagnosis due to prostate-specific antigen screening: lessons from U.S. prostate cancer incidence trends. J Natl Cancer Inst. 2002;94:981–90.
5. Bill-Axelson A, Holmberg L, Ruutu M, Garmo H, Stark JR, Busch C, Nordling S, Haggman M, Andersson SO, Bratell S, et al. Radical prostatectomy versus watchful waiting in early prostate cancer. N Engl J Med. 2011;364:1708–17.

6. Andriole GL, Grubb III RL, Buys SS, Chia D, Church TR, Fouad MN, Gelmann EP, Kvale PA, Reding DJ, Weissfeld JL, et al. Mortality results from a randomized prostate-cancer screening trial. N Engl J Med. 2009;360:1310–9.
7. Schroder FH, Hugosson J, Roobol MJ, Tammela TLJ, Ciatto S, Nelen V, Kwiatkowski M, Lujan M, Lilja H, Zappa M, et al. Screening and prostate-cancer mortality in a randomized European study. N Engl J Med. 2009;360:1320–8.
8. Moyer VA, Force USPST. Screening for prostate cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2012;157:120–34.
9. Force USPST. Screening for prostate cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2008;149:185–91.
10. Draisma G, Boer R, Otto SJ, van der Cruijsen IW, Damhuis RA, Schroder FH, de Koning HJ. Lead times and overdetection due to prostate-specific antigen screening: estimates from the European Randomized Study of Screening for Prostate Cancer. J Natl Cancer Inst. 2003;95:868–78.
11. Walter LC, Bertenthal D, Lindquist K, Konety BR. PSA screening among elderly men with limited life expectancies. JAMA. 2006;296:2336–42.
12. Hoffman RM, Barry MJ, Stanford JL, Hamilton AS, Hunt WC, Collins MM. Health outcomes in older men with localized prostate cancer: results from the Prostate Cancer Outcomes Study. Am J Med. 2006;119:418–25.
13. Singh J, Trabulsi EJ, Gomella LG. The quality-of-life impact of prostate cancer treatments. Curr Urol Rep. 2010;11:139–46.
14. Porter CR, Kodama K, Gibbons RP, Correa Jr R, Chun FK, Perrotte P, Karakiewicz PI. 25-year prostate cancer control and survival outcomes: a 40-year radical prostatectomy single institution series. J Urol. 2006;176:569–74.
15. Walsh PC, Donker PJ. Impotence following radical prostatectomy: insight into etiology and prevention. J Urol. 1982;128:492–7.
16. Walsh PC, Lepor H, Eggleston JC. Radical prostatectomy with preservation of sexual function: anatomical and pathological considerations. Prostate. 1983; 4:473–85.
17. Lepor H, Gregerman M, Crosby R, Mostofi FK, Walsh PC. Precise localization of the autonomic nerves from the pelvic plexus to the corpora cavernosa: a detailed anatomical study of the adult male pelvis. J Urol. 1985;133:207–12.
18. Ou YC, Yang CK, Wang J, Hung SW, Cheng CL, Tewari AK, Patel VR. The trifecta outcome in 300 consecutive cases of robotic-assisted laparoscopic radical prostatectomy according to D'Amico risk criteria. Eur J Surg Oncol. 2013;39:107–13.
19. Thompson RH, Slezak JM, Webster WS, Lieber MM. Radical prostatectomy for octogenarians: how old is too old? Urology. 2006;68:1042–5.
20. Pierorazio PM, Humphreys E, Walsh PC, Partin AW, Han M. Radical prostatectomy in older men: survival outcomes in septuagenarians and octogenarians. BJU Int. 2010;106:791–5.
21. Poulakis V, Witzsch U, de Vries R, Dillenburg W, Becht E. Laparoscopic radical prostatectomy in men older than 70 years of age with localized prostate cancer: comparison of morbidity, reconvalescence, and short-term clinical outcomes between younger and older men. Eur Urol. 2007;51:1341–8. discussion 1349.
22. Shikanov S, Desai V, Razmaria A, Zagaja GP, Shalhav AL. Robotic radical prostatectomy for elderly patients: probability of achieving continence and potency 1 year after surgery. J Urol. 2010; 183:1803–7.
23. Ficarra V, Novara G, Ahlering TE, Costello A, Eastham JA, Graefen M, Guazzoni G, Menon M, Mottrie A, Patel VR, et al. Systematic review and meta-analysis of studies reporting potency rates after robot-assisted radical prostatectomy. Eur Urol. 2012;62:418–30.
24. Mohammed N, Kestin L, Ghilezan M, Krauss D, Vicini F, Brabbins D, Gustafson G, Ye H, Martinez A. Comparison of acute and late toxicities for three modern high-dose radiation treatment techniques for localized prostate cancer. Int J Radiat Oncol Biol Phys. 2012;82:204–12.
25. Budaus L, Bolla M, Bossi A, Cozzarini C, Crook J, Widmark A, Wiegel T. Functional outcomes and complications following radiation therapy for prostate cancer: a critical analysis of the literature. Eur Urol. 2012;61:112–27.
26. Glass AS, McAninch JW, Zaid UB, Cinman NM, Breyer BN. Urethroplasty after radiation therapy for prostate cancer. Urology. 2012;79:1402–5.
27. Meeks JJ, Brandes SB, Morey AF, Thom M, Mehdiratta N, Valadez C, Granieri MA, Gonzalez CM. Urethroplasty for radiotherapy induced bulbomembranous strictures: a multi-institutional experience. J Urol. 2011;185:1761–5.
28. Merrick GS, Butler WM, Wallner KE, Galbreath RW, Anderson RL, Kurko BS, Lief JH, Allen ZA. Erectile function after prostate brachytherapy. Int J Radiat Oncol Biol Phys. 2005;62:437–47.
29. van der Wielen GJ, van Putten WL, Incrocci L. Sexual function after three-dimensional conformal radiotherapy for prostate cancer: results from a dose-escalation trial. Int J Radiat Oncol Biol Phys. 2007;68:479–84.
30. Tosoian JJ, Trock BJ, Landis P, Feng Z, Epstein JI, Partin AW, Walsh PC, Carter HB. Active surveillance program for prostate cancer: an update of the Johns Hopkins experience. J Clin Oncol. 2011;29:2185–90.
31. Klotz L, Zhang L, Lam A, Nam R, Mamedov A, Loblaw A. Clinical results of long-term follow-up of a large, active surveillance cohort with localized prostate cancer. J Clin Oncol. 2010;28:126–31.
32. Bul M, van den Bergh RC, Zhu X, Rannikko A, Vasarainen H, Bangma CH, Schroder FH, Roobol MJ. Outcomes of initially expectantly managed patients with low or intermediate risk screen-detected localized prostate cancer. BJU Int. 2012;110:1672–7.

33. Wilt TJ, Brawer MK, Jones KM, Barry MJ, Aronson WJ, Fox S, Gingrich JR, Wei JT, Gilhooly P, Grob BM, et al. Radical prostatectomy versus observation for localized prostate cancer. N Engl J Med. 2012;367:203–13.
34. Heron M. Deaths: leading causes for 2009: national vital statistics report. Hyattsville, MD: Division of Vital Statistics National Center For Health Statistics; 2012.
35. D'Agostino Sr RB, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, Kannel WB. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. Circulation. 2008;117:743–53.
36. Daskivich TJ, Chamie K, Kwan L, Labo J, Dash A, Greenfield S, Litwin MS. Comorbidity and competing risks for mortality in men with prostate cancer. Cancer. 2011;117:4642–50.
37. Abdollah F, Sun M, Schmitges J, Tian Z, Jeldres C, Briganti A, Shariat SF, Perrotte P, Montorsi F, Karakiewicz PI. Cancer-specific and other-cause mortality after radical prostatectomy versus observation in patients with prostate cancer: competing-risks analysis of a large North American population-based cohort. Eur Urol. 2011;60:920–30.
38. Abdollah F, Sun M, Schmitges J, Thuret R, Tian Z, Shariat SF, Briganti A, Jeldres C, Perrotte P, Montorsi F, et al. Competing-risks mortality after radiotherapy vs. observation for localized prostate cancer: a population-based study. Int J Radiat Oncol Biol Phys. 2012;84:95–103.
39. Walz J, Gallina A, Saad F, Montorsi F, Perrotte P, Shariat SF, Jeldres C, Graefen M, Benard F, McCormack M, et al. A nomogram predicting 10-year life expectancy in candidates for radical prostatectomy or radiotherapy for prostate cancer. J Clin Oncol. 2007;25:3576–81.
40. Huggins C, Stevens RE, Hodges CV. Studies on prostatic cancer: II the effects of castration on advanced carcinoma of the prostate gland. Arch Surg. 1941;43:209–23.
41. Huggins C. Endocrine-induced regression of cancers: Nobel lectures: physiology or medicine 1963–1970. Amsterdam: Elsevier; 1972. p. 235–47.
42. Maatman TJ, Gupta MK, Montie JE. Effectiveness of castration versus intravenous estrogen therapy in producing rapid endocrine control of metastatic cancer of the prostate. J Urol. 1985;133:620–1.
43. Heidenreich A. Current approach to androgen deprivation therapy in patients with advanced prostate cancer. Eur Urol Suppl. 2010;9:776–8.
44. Weight CJ, Klein EA, Jones JS. Androgen deprivation falls as orchiectomy rates rise after changes in reimbursement in the U.S. Medicare population. Cancer. 2008;112:2195–201.
45. Elliott SP, Jarosek SL, Wilt TJ, Virnig BA. Reduction in physician reimbursement and use of hormone therapy in prostate cancer. J Natl Cancer Inst. 2010; 102:1826–34.
46. Nelson JB. Hormone therapy for prostate cancer. In: Wein AJ, editor. Campbell-Walsh urology, vol. 3. Philadelphia, PA: Saunders Elsevier; 2012. p. 2934–53.
47. Schally AV. Luteinizing hormone-releasing hormone analogs: their impact on the control of tumorigenesis. Peptides. 1999;20:1247–62.
48. Seidenfeld J, Samson DJ, Hasselblad V, Aronson N, Albertsen PC, Bennett CL, Wilt TJ. Single-therapy androgen suppression in men with advanced prostate cancer: a systematic review and meta-analysis. Ann Intern Med. 2000;132:566–77.
49. Weckermann D, Harzmann R. Hormone therapy in prostate cancer: LHRH antagonists versus LHRH analogues. Eur Urol. 2004;46:279–83. discussion 283–4.
50. Bubley GJ. Is the flare phenomenon clinically significant? Urology. 2001;58:5–9.
51. Labrie F, Dupont A, Belanger A. Simultaneous administration of pure antiandrogens, a combination necessary for the use of luteinizing hormone-releasing hormone agonists in the treatment of prostate cancer. Proc Natl Acad Sci USA. 1984;81:3861–3.
52. Mottet N, Bellmunt J, Bolla M, Joniau S, Mason M, Matveev V, Schmid HP, Van Der Kwast T, Wiegel T, Zattoni F, et al. EAU guidelines on prostate cancer. Part II: treatment of advanced, relapsing, and castration-resistant prostate cancer. Eur Urol. 2011;59:572–83.
53. Decensi AU, Boccardo F, Guarneri D, Positano N, Paoletti MC, Costantini M, Martorana G, Giuliani L. Monotherapy with nilutamide, a pure nonsteroidal antiandrogen, in untreated patients with metastatic carcinoma of the prostate. J Urol. 1991;146:377–81.
54. Chang A, Yeap B, Davis T, Blum R, Hahn R, Khanna O, Fisher H, Rosenthal J, Witte R, Schinella R, et al. Double-blind, randomized study of primary hormonal treatment of stage D2 prostate carcinoma: flutamide versus diethylstilbestrol. J Clin Oncol. 1996;14:2250–7.
55. Kaisary AV, Tyrrell CJ, Beacock C, Lunglmayr G, Debruyne F. A randomised comparison of monotherapy with Casodex 50 mg daily and castration in the treatment of metastatic prostate carcinoma. Casodex study group. Eur Urol. 1995;28:215–22.
56. Iversen P. Bicalutamide monotherapy for early stage prostate cancer: an update. J Urol. 2003;170:S48–52. discussion S52-4.
57. Small EJ, Srinivas S. The antiandrogen withdrawal syndrome. Experience in a large cohort of unselected patients with advanced prostate cancer. Cancer. 1995;76:1428–34.
58. Soloway MS, Pareek K, Sharifi R, Wajsman Z, McLeod D, Wood Jr DP, Puras-Baez A. Neoadjuvant androgen ablation before radical prostatectomy in cT2bNxMo prostate cancer: 5-year results. J Urol. 2002;167:112–6.
59. Schulman CC, Debruyne FM, Forster G, Selvaggi FP, Zlotta AR, Witjes WP. 4-Year follow-up results of a

European prospective randomized study on neoadjuvant hormonal therapy prior to radical prostatectomy in T2-3N0M0 prostate cancer. European Study Group on Neoadjuvant Treatment of Prostate Cancer. Eur Urol. 2000;38:706–13.
60. Klotz L, Gleave M, Goldenberg SL. Neoadjuvant hormone therapy: the Canadian trials. Mol Urol. 2000;4:233–7. discussion 239.
61. Aus G, Abrahamsson PA, Ahlgren G, Hugosson J, Lundberg S, Schain M, Schelin S, Pedersen K. Three-month neoadjuvant hormonal therapy before radical prostatectomy: a 7-year follow-up of a randomized controlled trial. BJU Int. 2002;90:561–6.
62. Kollmeier MA, Zelefsky MJ. What is the role of androgen deprivation therapy in the treatment of locally advanced prostate cancer? Nat Clin Pract Urol. 2008;5:584–5.
63. Hammerer P, Madersbacher S. Landmarks in hormonal therapy for prostate cancer. BJU Int. 2012;110 Suppl 1:23–9.
64. Conde FA, Sarna L, Oka RK, Vredevoe DL, Rettig MB, Aronson WJ. Age, body mass index, and serum prostate-specific antigen correlate with bone loss in men with prostate cancer not receiving androgen deprivation therapy. Urology. 2004;64:335–40.
65. Daniell HW. Osteoporosis after orchiectomy for prostate cancer. J Urol. 1997;157:439–44.
66. Michaelson MD, Kaufman DS, Lee H, McGovern FJ, Kantoff PW, Fallon MA, Finkelstein JS, Smith MR. Randomized controlled trial of annual zoledronic acid to prevent gonadotropin-releasing hormone agonist-induced bone loss in men with prostate cancer. J Clin Oncol. 2007;25:1038–42.
67. Smith MR, Egerdie B, Toriz NH, Feldman R, Tammela TLJ, Saad F, Heracek J, Szwedowski M, Ke C, Kupic A, et al. Denosumab in men receiving androgen-deprivation therapy for prostate cancer. N Engl J Med. 2009;361:745–55.
68. Smith MR, Fallon MA, Goode MJ. Cross-sectional study of bone turnover during bicalutamide monotherapy for prostate cancer. Urology. 2003;61:127–31.
69. Potosky AL, Knopf K, Clegg LX, Albertsen PC, Stanford JL, Hamilton AS, Gilliland FD, Eley JW, Stephenson RA, Hoffman RM. Quality-of-life outcomes after primary androgen deprivation therapy: results from the Prostate Cancer Outcomes Study. J Clin Oncol. 2001;19:3750–7.
70. Moyad MA. Complementary/alternative therapies for reducing hot flashes in prostate cancer patients: reevaluating the existing indirect data from studies of breast cancer and postmenopausal women. Urology. 2002;59:20–33.
71. Isbarn H, Boccon-Gibod L, Carroll PR, Montorsi F, Schulman C, Smith MR, Sternberg CN, Studer UE. Androgen deprivation therapy for the treatment of prostate cancer: consider both benefits and risks. Eur Urol. 2009;55:62–75.
72. Jamadar RJ, Winters MJ, Maki PM. Cognitive changes associated with ADT: a review of the literature. Asian J Androl. 2012;14:232–8.
73. Dawson LA, Chow E, Morton G. Fulminant hepatic failure associated with bicalutamide. Urology. 1997;49:283–4.
74. Eisenberger MA, Blumenstein BA, Crawford ED, Miller G, McLeod DG, Loehrer PJ, Wilding G, Sears K, Culkin DJ, Thompson Jr IM, et al. Bilateral orchiectomy with or without flutamide for metastatic prostate cancer. N Engl J Med. 1998;339:1036–42.
75. Tannock IF, de Wit R, Berry WR, Horti J, Pluzanska A, Chi KN, Oudard S, Theodore C, James ND, Turesson I, et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. N Engl J Med. 2004;351:1502–12.
76. de Bono JS, Oudard S, Ozguroglu M. Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial. Lancet. 2010;376:1147–54.
77. de Bono JS, Logothetis CJ, Molina A. Improved survival from metastatic prostate cancer with abiraterone acetate. N Engl J Med. 2011;364:1995–2005.
78. Kantoff PW, Higano CS, Shore ND, Berger ER, Small EJ, Penson DF, Redfern CH, Ferrari AC, Dreicer R, Sims RB, et al. Sipuleucel-T immunotherapy for castration-resistant prostate cancer. N Engl J Med. 2010;363:411–22.
79. Scher HI, Fizazi K, Saad F, Taplin ME, Sternberg CN, Miller K, de Wit R, Mulders P, Chi KN, Shore ND, et al. Increased survival with enzalutamide in prostate cancer after chemotherapy. N Engl J Med. 2012;367:1187–97.
80. Fizazi K, Carducci M, Smith M. Denosumab versus zoledronic acid for treatment of bone metastases in men with castration-resistant prostate cancer: a randomized double-blind study. Lancet. 2011;377:813–22.

18 Bladder Cancer

Daniel J. Lee, Shahrokh Shariat, and Jeffrey M. Holzbeierlein

Introduction

Bladder cancer represents an important cause of morbidity and mortality worldwide. An estimated 386,300 new cases of bladder cancer and 150,200 deaths occurred in 2008 worldwide [1]. In 2011, it was the second most common genitourinary cancer in the USA, with 69,250 new cases and 14,990 deaths [2]. Currently, the prevalence of bladder cancer is estimated at more than 1,000,000 American and European men and women. Urothelial carcinoma of the bladder (UCB) represents the most common bladder cancer histology in Western countries with more than 90 % of cases. At initial diagnosis, about 70 % of patients present with non-muscle-invasive UCB. These cancers are usually managed with endoscopic resection and selective use of intravesical therapy. The recurrence rate for these tumors ranges between 50 and 70 %, while approximately 5–30 % progress to muscle invasion over a 5-year period [3–6]. Disease recurrence may be seen locally, in the urethra, or in the upper urinary tract even after several years, necessitating lifelong surveillance [6, 7]. Approximately 30 % of patients have muscle-invasive UCB at initial diagnosis, from which 30 to 50 % experience disease recurrence within 5 years and eventual death despite aggressive treatment [8–13].

Age is accepted as one of the greatest risk factors, independent of smoking, for developing UCB, primarily due to the long latency periods associated with exposure to agents which contribute to bladder cancer (Table 18.1) [14–16]. While UCB can occur at any age, it is generally a disease of older adults with the median age at diagnosis being above 70 years [17]. Because of the close relationship between age and disease incidence, UCB will become an enormous challenge with the growth of our aging population. Men and women aged 65 years and older currently represent approximately 12 % (36.8 million) of the US population, a number expected to double by the year 2030 to over 70 million; globally the percentage will rise from 7 to 12 % [18–26]. Approximately half of all US citizens currently alive can expect to reach the ninth decade of life [27]. These statistics will result in significant challenges to the medical care system, individual providers, and more importantly, the patients themselves.

D.J. Lee, M.D.
Department of Urology, University of Iowa Hospitals, 200 Hawkins Dr, Iowa City, IA 52242, USA

S. Shariat, M.D.
Department of Urology, Weill Cornell Medical College, 525 East 68th Street, Starr Pavilion, 9th Floor, Room 900, New York, NY 10065, USA

J.M. Holzbeierlein, M.D. (✉)
Department of Urology, The University of Kansas Hopsital, 3901 Rainbow Blvd, Mail Stop 3016, Kansas City, KS 66160, USA
e-mail: jholzbeierlein@kumc.edu

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_18,

Table 18.1 Risk factors for bladder cancer

Smoking
Prior history of radiation
Aromatic amines/hydrocarbons
Cyclophosphamide
Caucasian
Male
Schistosomiasis-squamous cell carcinoma primarily

Unfortunately, evidence-based practice guidelines regarding the short- and long-term management of UCB in older adults are nonexistent. The aim of this chapter is to discuss the effect of age on the incidence, prognosis, and therapy for UCB, focusing on salient management strategies. The goal was to include information based on the highest level of evidence available.

Definition of Elderly in the Bladder Cancer Literature

Frequently, people aged ≥65 years old are considered elderly [15, 28–30]. Generally in the healthcare setting, this population is subdivided into young old (65–74 years), old (75–84 years), and oldest old (≥85 years) [14–16]. In the setting of radical cystectomy, the majority of authors used a limit of 75 or 80 years of age to define elderly patients. Explanations for choosing certain age-related stratification cutoffs, however, are usually not given in the related literature. It is conceivable that in some cases, the aim of collecting a sample size sufficient for analysis influenced the cutoff choice rather than biological or clinical reasons. For advanced bladder cancer, there is no generally accepted age limit like the traditional 10-year life expectancy rule usually considered a requirement to justify curative treatment for other cancers [31]. In large part this is due to the high potential for lethality of bladder cancer. Moreover, life expectancy and performance status are determined not by chronological age alone but also by comorbidities which influence "physiological" age.

Preoperative Considerations

Physiologic Changes with Aging

Elderly patients represent a heterogeneous population with varying degrees of comorbidities and functional impairments. Even for the most active and healthy elderly patients, there are physiologic changes that affect every organ system. These may become more clinically apparent with the additional stressors of a major illness and surgical intervention. Beginning at the age of 30, almost all the organ systems show a progressive physiologic decline in function [32–34], although there is considerable individual variability on the rate and degree of decline. Over 60 % of individuals aged 65–79 years report some disability, with more than 76 % of individuals over 80 years reporting some disabling condition [35]. Thorough characterization of the normal physiologic changes with aging can help guide potential preventive measures and can significantly reduce the risks associated with the medical and surgical care of elderly patients [36].

The leading cause for postoperative complications and death for all patients, but especially for older adults, is cardiovascular in nature [37]. Aging is accompanied with a 1 % decrease in cardiac output per year, decreased response to catecholamines with stress, and decreased maximal heart rate [34, 38–40]. There is a greater reliance on ventricular filling and increases in stroke volume to achieve increases in cardiac output [41]. The left ventricle also becomes less compliant with age, impairing diastolic relaxation and making the ventricle less tolerant of any shifts in intravascular volume [37, 41]. Any loss of intravascular volume from blood loss or dehydration could produce a marked decrease in systolic blood pressure and could impair coronary artery perfusion, especially with the vasodilatory effects of many of the general anesthetic agent. This could exacerbate any existing coronary artery disease or prior myocardial ischemia. Conversely, any large increase in intravascular volume could result in pulmonary congestion or exacerbate any existing congestive heart failure. Maintaining proper fluid balance, limiting myocardial oxygen demand, and identifying and optimizing any modifiable cardiac disease are imperative to help limit any treatment-related complications.

Pulmonary complications account for almost half of all postoperative complications and 20 % of preventable postoperative deaths [42]. Approximately 35 mL of the FEV1 is lost each year after the age of 35, and by the age of 70, the maximal breathing capacity is 50 % of the capacity at the age of 30 [43]. There is a decreased response to hypoxemia and hypercapnia and an increased ventilation/perfusion mismatch with increasing age [32–34, 44]. Aging is also associated with decreased airway sensitivity and clearance and increased closure of small airways during respiration which can lead to increased atelectasis and shunting postoperatively [41]. These physiologic changes are also exacerbated by previous smoking history, prior environmental exposure to various substances, and preexisting pulmonary disease, all of which are commonly found in patients being treated for bladder cancer. A baseline chest radiograph, thorough past medical history screening, screening spirometry, and baseline arterial blood gas levels can help identify any modifiable risk factors, identify hypoxemia, and help plan postoperative management in the patient at risk. Early mobilization and perioperative use of bronchodilators and incentive spirometry can have a significant influence in decreasing the rates of postoperative complications [45].

Renal size and function decrease with age. Changes in renal function with age are due to increasing glomerulosclerosis with a decrease in renal size by 25–30 % over time and decreased number of functional glomeruli, which is often exacerbated by a decrease in cardiac output [38, 46, 47]. Glomerular filtration decreases by 1 mL/min per year after age 40 [46, 47]. Elderly patients with decreased renal function are therefore more susceptible to fluid shifts, electrolyte abnormalities, nephrotoxic drugs, and potentially any drug that is renally excreted. Acute renal failure can dramatically increase the morbidity and mortality of elderly patients by up to 50 % [38]. Serum creatinine is not an ideal indicator of renal function in older adults [48], so it is essential to have an accurate measure of the preoperative renal function [49]. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation appears to be a more generalizable and accurate equation for estimating GFR in comparison with the Modification of Diet in Renal Disease (MDRD) equation. Additional studies in subgroups such as older adults, in the general population where individuals are not selected for being at high risk of chronic kidney disease, and across different race/ethnic populations are needed in order to further generalize these findings. In the meantime, there is accumulating evidence to support the recommendation that the CKD-EPI equation should replace the MDRD equation [50]. In addition, careful management of fluid balance, avoidance of nephrotoxic agents, and early recognition of any renal compromise are essential for elderly patients.

The immune system also shows signs of deterioration with age, with T-cell function significantly decreasing with increasing age [44, 51–54]. Impaired immune system function increases the risk of postoperative complications but may also play an important role in the development and progression of cancer. Aging has been associated with a decrease in thymic mass with a decrease in antigen-processing and effector lymphocytes, decreased production of thymic hormones, and a decrease in antibody response, which may contribute to the increased prevalence and biological aggressiveness of some cancers with aging [51–54].

Aging also influences the endocrine system with decreases in insulin-like growth factor, growth hormones, and sex steroids and increases in levels of insulin, norepinephrine, vasopressin, and atrial natriuretic peptides with increasing age [32–34, 55]. Increased visceral fat mass, along with a decreased lean body mass, is associated with decreased levels of testosterone and increased levels of proinflammatory markers such as C-reactive protein and IL-6, which have been linked to accelerated decreases in muscle mass and strength [56]. These changes are also closely related to the changes in body composition with age. Decreased muscle strength with age ultimately affects the functional capacity and mobility and can exacerbate any acute illness or stress if the strength falls below clinical thresholds, especially if the patient is, for example, unable to cough sufficiently or unable to ambulate [56]. In fact, muscle strength has been shown to be an independent predictor of mortality [57].

Nutritional status also changes significantly with aging and can be adversely affected by physiologic, psychosocial, and economic challenges that accompany aging. Anywhere from 9 to 15 % of patients 65 years and older were found to be malnourished in an outpatient setting, which increases to 12–50 % in the acute inpatient hospital setting and 25–60 % in the chronic institutional settings [38, 58]. Nutritional deficiency is a known risk factor for complications such as infection, poor wound healing, and multiorgan system dysfunction and directly influences mortality and overall survival [38, 58, 59]. Specifically, in radical cystectomy patients, poor nutrition has been associated with complications and an increased overall mortality [60]. Chronically undernourished or malnourished patients may not have enough nutritional reserve to sustain the hypermetabolic state induced by illness and surgery, causing protein energy malnutrition (PEM). The physiologic consequences of PEM include hepatic dysfunction, sarcopenia, and decreased mucosal proliferation [58]. Nutritional status has a significant impact on surgical outcomes and functional recovery, emphasizing the need for accurate preoperative assessment tools. Serum albumin levels correlate with PEM and postoperative complications in general surgery patients and those with UCB [58, 60]. Current recommendations suggest that 7–10 days of nutritional repletion be given prior to surgery if patients have serum albumin levels <2.5 g/dL or >10 % weight loss [48].

The mini nutritional assessment (MNA) is a validated nutritional assessment tool that can be valuable for the preoperative assessment of elderly patients [61–63]. The MNA assesses the body mass index, food intake and weight loss, mobility, and the presence of potential stressors, dementia, or depression, which can then be used to identify those who are malnourished or undernourished and help target interventions to improve the functional postoperative recovery in these patients.

Neurons stop reproducing after birth with a slow decrease in their number throughout life [56]. Noticeable brain atrophy occurs after 60 years at varying rates in different regions of the brain, which may contribute to the age-related declines in cognition and motor function [64]. In addition, the motor neurons in the spinal cord decrease at a rate of about 1 % each year after 30 years of age, which contributes to the decrease in fine motor control, coordination, and dexterity [56].

Directly related to the neurophysiologic changes with aging are the changes in cognition and functional status in older adults. Cognitive deficits have been found in as many as 25–50 % of patients in elderly patients with cancer [65]. Cognitive impairment, including delirium and confusion, occurs frequently in the postoperative period, with postoperative delirium rates ranging from 5 to 45 % in elderly patients undergoing major surgery [66]. The etiology of postoperative cognitive impairment can be multifactorial, including exacerbation of preexisting deficits, prior alcohol abuse, postoperative infections, hypoxia, hypotension, cerebrovascular event, drugs, or anesthetic effects. Whatever the cause, cognitive impairment can result in increased morbidity, delayed functional recovery, and prolonged hospitalizations. Cognitive impairment can remain even in the long term. In one study, up to 42 % of patients showed signs of significant cognitive decline 5 years after cardiac surgery, which was associated with diminished postoperative quality of life and functional status [67]. Knowledge of the patient's baseline cognitive function is crucial in order to accurately evaluate the postoperative course and plan for any necessary postoperative rehabilitation services.

Functional Status Changes and Assessment

Functional status in older adults is a measure of each individual's ability to perform activities of daily living, which include feeding, dressing, bathing, and toileting. This can be strongly influenced by any of the physiologic changes mentioned previously. An individual's functional status and the state of each organ system have been shown to be significant predictors of survival [68]. Small changes in functional status can have a significant impact on the quality of life after treatment. Several studies of elderly patients in the surgical intensive care unit have shown there are significant reductions in health-related quality of life indicators when compared to younger patients. This may translate into loss of independence to complete tasks of daily living with longer hospitalizations [69–71]. Those found to have invasive UCB who cannot perform normal activity without difficulty (scored as a Karnofsky performance score of less than 80) are almost twice as likely to die and have a 9-month survival disadvantage compared to those with higher performance scores, even after adjusting for other comorbidities and pathological factors [72].

Functional assessments, such as the hand grip strength test, timed up and go test, and functional reach test, are key prior to any surgery or other intervention treatment because they are independently predictive of time to recovery of activities of daily living after major surgery [38, 73]. These tests also provide an accurate evaluation of the patient's muscle mass, nutritional status, gait, balance, coordination, and mobility. Assessment of these components is valuable in predicting biological reserve, rehabilitation needs, and potential complications [38, 48, 73].

Aging and the Frailty Phenotype

Although the changes that occur with each system were described separately, these changes develop in a complex interactive and interconnected system. Each of these changes independently and in aggregate contributes to the overall well-being and performance status of an individual. These changes may also contribute to cancer development and be further compromised by any subsequent treatment, which further stress normal function and physiologic reserves.

When patients have multiple changes or problems in multiple systems affected by aging, they may develop extreme degrees of susceptibility and loss of resilience, which is generally characterized as being "frail." Approximately 10–25 % of individuals over 65 years are considered to be frail [74–76]. Frailty has been described as a physiologic syndrome, "a state of age-related physiologic vulnerability resulting from impaired homeostatic reserve and reduced capacity of the organism to withstand stress." [76, 77] This definition is generally characterized by weight loss, fatigue, impaired grip strength, diminished physical activity, and impaired gait; however, no standard definition has been developed [56]. The consequences of frailty have been well demonstrated in prospective studies in older adults and are usually categorized into five main issues. These include ineffective or incomplete homeostatic response to stress, comorbidities, polypharmacy, physical disability, and the geriatric syndromes.

At an early stage, mildly frail individuals may appear normal in the absence of any stress; however, they will exhibit reduced ability to withstand challenges, such as surgical procedures, chemotherapy, extended hospitalizations, or illnesses such as cancer. Frailty can predispose elderly individuals to the development of malignancy, and the presence and progression of malignancy can increase the vulnerability of different organ systems. The cancer treatments that may be required can further stress individuals as they age [32–34]. It is in this context that further investigations need to be performed to characterize the interactions among functional status, frailty, and cancer treatment so that older cancer patients can make informed choices regarding their treatment options.

The percentage of individuals affected by chronic medical conditions increases with age. By 65 years of age, more than 50 % of individuals will have two or more chronic diseases [78]. Comorbidities represent a coexisting medical problem that is a competing source of morbidity or mortality in the setting of a developing malignancy. The presence of comorbidity represents an additional stressor on the normal physiologic deterioration of the organ systems with aging. Comorbidities can affect the function of multiple organs and impact the efficacy and extent of treatments offered to patients. This can increase vulnerability to the risks, side effects, and potential complications of treatment, which in turn may influence the overall risk of morbidity and mortality. Patients with three or more comorbidities were found to have a fourfold increased mortality risk compared to those without any comorbidities [79]. Patients who have multiple medical conditions are often taking multiple medications, introducing another risk factor termed "polypharmacy." Age-related physiologic changes to various organ systems, such as decreases in lean body mass and in renal clearance, influence the pharmacokinetics and pharmacodynamics of various drugs and must be taken into account with any elderly individual.

Given the changes in physical and cognitive functions with aging, predicting risk factors for disability is extremely important. Frailty is closely related with disability; however, disability will often occur late in the development of frailty when the physiologic reserve is exhausted [56]. In the early stages of frailty, the impact of aging on the organ systems and cognitive and functional status can occur without significant impact on the activities of daily living (ADLs). However, by the time disability is clinically evident in elderly individuals, the cause is usually multifactorial, and multiple disrupted aging processes are usually involved. The decrease in muscle tone, poor nutrition, high levels of proinflammatory markers, and neurocognitive deficits can all contribute to disability. Early assessment of the level of disability and functional status is therefore essential for elderly individuals undergoing cancer treatment. Several validated tools have been used to measure and assess the functional status in elderly patients [80–88]. These tools can be used to identify those patients who are at significant risk of disability, which may result in loss of independence and subsequent need for placement in a skilled nursing facility.

Psychosocial factors are also subject to many changes with aging and need to be evaluated carefully. Elderly patients are less likely to perceive control over their own health with aging and will frequently adjust their expectations on their current state of health or ability to recover from illness [89, 90]. Older adults are significantly more likely to be discharged from the hospital to an extended care facility. Of patients who undergo radical cystectomy, more than 20 % of those older than 70 years of age and almost 40 % of those 80 and older will be discharged to an extended care facility [91]. Each patient's social situation must be evaluated in order to determine the availability of support in terms for long-term care and assistance with daily function, transportation, and living arrangements. Ideally these discussions and evaluations should begin prior to starting treatment for bladder cancer. These could drastically influence an individual's treatment plans. Specific issues can affect the social network and family dynamics, warranting careful consideration in the decision-making process.

Aging and the Risk of Urothelial Carcinoma of the Bladder

Age represents a strong and independent risk factor for predicting presence of UCB [17]. Demographic studies have shown that individuals aged 65 and older have an approximate 11-fold increase in the incidence of UCB in general and a 15-fold increase in UCB mortality in particular when compared to individuals under the age of 65 [17].

Analysis of the California Cancer Registry revealed that the peak incidence of UCB occurs at 85 years [92]. This occurs 10 years after the peak incidence of both lung and bronchial cancers, malignancies that share similar carcinogenic risk factors with bladder cancer including tobacco and industrial exposures. It has been hypothesized that this difference in peak incidence is because the lungs are the first organs directly exposed to these carcinogens. In contrast, the bladder is the last organ exposed to these carcinogens which have been diluted in the urine. Thus, the bladder may require a longer exposure to develop cellular mutations by carcinogens. Long dwell time of urine in the bladder may increase this exposure risk. Moreover, with advancing age, pulmonary function diminishes which increases the cumulative amount of systemically absorbed carcinogens. This results in higher concentrations of carcinogens filtered by the kidneys and eventually reaching the bladder.

Several additional theories have been proposed to explain the interaction between carcinogenesis and the aging process. First, the cumulative environmental exposure to carcinogens such as cigarette smoking and environmental carcinogens increases with time. Second, aging allows time for the development and accumulation of cellular events that can lead to neoplastic transformation. The existence of a lag time between these exposures, the subsequent cellular events, and the clinical expression of malignancy may account for the delayed appearance of bladder cancer in an older population. Third, aging may be accompanied by a decreased ability to fully empty the bladder, potentially prolonging the exposure time for carcinogens excreted in the urine. This can be exacerbated by behavioral modifications such as patients drinking less as they get older in an attempt to mitigate bothersome voiding symptoms. Finally, the ability to detoxify potential carcinogens may be reduced in older adults as a result of physiologic or pathological organ system deterioration.

In recent years, there has been a small but steadily growing recognition that the link between aging and cancer is more complex than the simple passage of time to which the age dependence of cancer has traditionally been ascribed. Research on changes in the growth regulatory function of genes and proteins with advancing age has led to a better understanding of the biological relationships between cancer development and aging which has introduced new possibilities for intervention [93, 94]. Certain genes may be activated, while others may be suppressed with advancing age. This can lead to an increase in oncogene activity, resulting in the genesis of a malignant cancer cell. Conversely, there may be a decrease in tumor-suppressor gene activity, with the consequent inability to suppress or clear an organ from transformed neoplastic cells [3, 95]. Furthermore, an aged cell may have a decreased capacity for repair of mutations in its DNA [95]. In UCB, various oncogenes and tumor-suppressor genes have been associated with cancer development, progression, and metastasis [5, 94, 96]. The protein products of these genes are differentially altered in individual UCBs, perhaps explaining some of the variability in the biological and clinical behavior of UCB among patients [94–98].

Prognosis of Bladder Cancer in Older Adults

Multiple studies have examined the biological and clinical behavior of UCB in younger versus older patients with a general trend to increased mortality from UCB in older adults. The ratio of cancer-specific mortality to incidence for men and women in the USA aged 65–69 years is 14 % and 18 %, respectively, whereas for men and women aged 80–84, it is 30 % and 37 %, respectively (SEER, 1973–1997) [17]. This higher mortality in older adults has several possible explanations. In patients under the age of 40, UCB tends to be well differentiated and therefore more indolent [99–101]. Other explanations include more advanced stage at diagnosis due to social and biological reasons. Older adults may be offered less aggressive and less effective therapies including avoidance or delay of radical cystectomy, avoidance of or inadequate lymphadenectomy, and/or avoidance of neoadjuvant chemotherapy.

Treatment of Non-Muscle-Invasive Bladder Cancer

The current staging system for bladder cancer is shown in Table 18.2. Treatments for non-muscle-invasive UCB (clinical T1 and lower) are generally well tolerated by older adults and are typically the same as those used in younger patients. Transurethral resection (TUR) procedures are generally short, with no major fluid shifts or strain on other organ systems. Anesthesia required for this procedure is generally well tol-

Table 18.2 TNM staging

T stage	N stage	M stage
Tx—primary tumor cannot be assessed	Nx—nodes cannot be assessed	Mx—not assessed
T0—no evidence of tumor	N0—no lymph node mets	M0—no distant mets
Ta—noninvasive papillary	N1—single lymph node in true pelvis	M1—distant mets
Tis—carcinoma in situ	N2—multiple nodes in true pelvis	
T1—tumor invades subepithelium	N3—node in common iliac chain	
T2—tumor invades muscularis propria		
pT2a—tumor invades superficial muscularis propria (inner half)		
pT2b—tumor invades deep muscularis propria (outer half)		
T3—tumor invades perivesical fat		
pT3a—microscopic invasion		
pT3b—gross invasion		
T4—tumor invasion of contiguous organs including prostatic stroma, seminal vesicles, uterus, vagina, pelvic side wall, abdominal wall		
pt4a—tumor invades prostatic stroma, uterus, vagina		
pT4b—tumor invades pelvic wall, abdominal wall		

erated. These procedures can often be performed under spinal anesthesia which limits pulmonary and cognitive side effects. Moreover, the sequelae, side effects, and complications of endoscopic resection, with or without intravesical instillation of chemotherapeutic or immunotherapeutic agents, are usually well tolerated, even when repeat treatments are necessary. Serious consideration should be given to the instillation of mitomycin C at the time of TURBT in order to reduce the risk of recurrence. This may be particularly important in older patients in whom it is paramount to reduce the number of procedures requiring an anesthetic. In certain elderly patients, comorbid conditions or side effects may prohibit surgical treatment. Fortunately, most non-muscle-invasive UCB are low grade and exhibit a nonaggressive behavior, and do not pose a threat to the patient's overall survival [6, 102]. In addition, some of these tumors can be treated with a simple cauterization in the clinic during surveillance cystoscopy excluding the need for anesthesia. This may be an important consideration in order to prevent the complications associated with the growth of these tumors such as bleeding and bladder outlet obstruction. Even when this is not possible, most low-grade noninvasive UCBs rarely progress or result in death [12, 103].

Patients with high-grade non-muscle-invasive tumors have a higher risk of disease progression and are usually given intravesical therapy after TUR. Intravesical Bacillus Calmette-Guerin (BCG) is widely accepted as the most effective therapy for patients with high-risk non-muscle-invasive UCB [104]. The instillation of intravesical BCG has been shown to reduce or delay time to recurrence and progression, decreasing the need for immediate radical cystectomy [104–106]. However, several studies have shown a lower response rate to intravesical BCG in older adults compared to their younger counterparts. Herr et al. reported a 10 % absolute difference in freedom from disease at 5 years after intravesical treatment with BCG for patients over 70 years of age (27 %) versus younger patients (37 %) [107]. Similarly, Joudi et al. reported a 22 % lower absolute disease-free rate after intravesical BCG plus interferon in patients aged 80 or older versus those aged 60–70 [108]. In a study of 491 patients treated with TUR, either with or without intravesical BCG therapy for primary non-muscle-invasive UCB, Kohjimoto et al. found that older age, analyzed as a categorical variable by decade, was a significant predictor of tumor recurrence and progression [109].

The decreased efficacy of TUR with BCG may be explained by a more aggressive variant of disease, impaired host defense, less aggressive treatment, or greater resistance to treatment. As discussed previously, the immune system decreases in strength with advancing age. The lower success rates of intravesical BCG together with the higher complication rates [110] suggest that patients older than 80 years should be considered for risk-stratified treatment. For example, low-risk patients could be candidates for repeated TUR and alternative intravesical regimens, while high-risk patients could be considered for early radical cystectomy [6, 102].

For patients who, due to comorbid conditions, are deemed not to be good candidates for cystectomy, other intravesical treatments after BCG failure can be considered. These include BCG plus interferon or valrubicin which is approved for BCG refractory carcinoma in situ in patients who are not fit for cystectomy.

Treatment of Muscle-Invasive Bladder Cancer

Radical Cystectomy

When muscle-invasive UCB is diagnosed in older adults, treatment decision making becomes more complicated. The standard treatment for muscle-invasive UCB is radical cystectomy, bilateral lymphadenectomy, and urinary diversion [8, 9] with or without perioperative systemic chemotherapy [111–117]. However, this treatment creates substantial stress on most organ systems, particularly for older adults in whom physiologic reserve is limited. This leads to a greater number of potential side effects and complications as well as decreased response to therapy. Comorbid conditions further compromise the ability to deliver full-dose treatments in geriatric patients.

Geriatric patients are less likely to be treated with extirpative surgery compared to their younger counterparts [118, 119]. An analysis of patients from the SEER database revealed that only 55 % of eligible radical cystectomy candidates aged 55–59 years actually underwent surgery [118]. The rate further decreased with advancing patient age with only about 25 % of patients aged 70–79 years appropriately treated with radical cystectomy. These findings were confirmed by Gore et al., who reported that only 21 % of 3,262 Medicare beneficiaries aged 66 years or older diagnosed with muscle-invasive bladder cancer underwent radical cystectomy [120]. The authors found that older age at diagnosis was strongly associated with decreased odds of undergoing radical cystectomy (≥80 vs. 66–69 years old, OR = 0.10, 95 % CI = 0.07–0.14). They further reported that overall survival was significantly better for patients who underwent radical cystectomy compared with those who underwent alternative treatments such as chemotherapy and/or radiation therapy (HR of death = 1.5, 95 % CI = 1.3–1.8) or no active treatment (HR of death = 1.9, 95 % CI = 1.6–2.3). Thus, radical cystectomy is all too often withheld or delayed in elderly patients who potentially would benefit from such treatment [121]. Reasons for this are multifactorial and can only be hypothesized. They include a delay in diagnosis, the overuse of nonsurgical alternatives for an inappropriately long period of time, the relative inexperience of many surgeons leading them to avoid performing radical cystectomy, or a perceived or real belief that many patients simply will not tolerate surgery because of age and/or underlying comorbidity.

Age may have a significant impact on survival after RC. The ratio of cancer-specific mortality to incidence for men and women aged 65–69 years is 14 % and 18 %, respectively, which increases to 30 % and 37 %, respectively, for those aged 80–84 years [122]. The overall mortality rate in elderly patients who undergo RC for UCB is around 0–11 % [28], with 90-day mortality rates of approximately 3.9 % [29]. In a study of 314 patients treated with RC, age was not associated with an increased 90-day mortality rate or an increase in postoperative complications [123]. However, in two other larger studies, increasing age was independently associated with inhospital mortality [124] and postoperative complication risk [125] after RC. Differences in the study designs, populations, definitions, and patient selection may have contributed to the different conclusions of these studies. However, the combined data suggest that chronological age alone may not be sufficient to predict complications or survival in elderly patients with UCB who are treated with RC and that chronological age should not preclude surgical therapy.

While younger and healthier patients are typically better able to withstand the medical stress of surgery and sufficiently capable of adapting to their new urinary tract reconstructions, prognosis for patients with invasive bladder cancer is more highly correlated with the extent of the cancer than with patient age [126–129]. Moreover, RC has previously demonstrated survival benefits even among older adults [119, 128]. Thus, although age and comorbidity can be examined as factors for medical candidacy for RC, the majority of invasive UCB patients without contraindication to prolonged anesthesia should undergo potentially curative radical surgery.

Complications After Radical Cystectomy and Urinary Diversion

Radical cystectomy with bilateral lymphadenectomy and the associated urinary diversion each challenge the patient not only in their initial recovery but also over the long term. While morbidity after radical cystectomy and urinary diversion has declined due to significant improvements in perioperative care, [8, 130, 131] it remains at 40–60 %, even at major referral centers with substantial experience [9, 10, 28, 132, 133].

A recent review of 20 studies in elderly patients (study sample sizes: 12–842) reported ileus rates of 2–32 %, infectious complications (mainly pyelonephritis) in 5–39 % patients, and urinary diversion-related complications in up to 33 % [28]. The definitions of mortality and complications as well as the length of study period (30, 60, and 90 days) were heterogeneous between these studies. One problem when reviewing various studies is that even very frequent and typical complications such as pyelonephritis were not recorded in all reviewed studies. This suggests that the definition of a complication in this setting partially depended on the personal views of the authors rather than on general criteria. However, most studies support that older adults have a higher rate of perioperative complication than their younger counterparts. For example, a study of 2,538 radical cystectomy patients from the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) found that increasing age was independently associated with an increased risk of any postoperative complication (odds ratio, 1.3; CI, 1.2–1.5) [125]. In a well-done study of 117 octogenarians treated with radical cystectomy at Memorial Sloan-Kettering Cancer Center (MSKCC), Donat et al. found a trend toward increased overall complication rate in elderly compared to young patients (72 % vs. 64 %, $p=0.08$) using a standardized grading system for complications. However, the authors found no difference in the rate of major complications (17 % vs. 13 %, $p=0.3$) [134]. After adjusting for the effect of preoperative characteristics, the risk of any complication was roughly flat across all ages. The risk of experiencing a major complication increased almost linearly with respect to age from 30 to 65 years and plateaued at approximately age 65. The authors concluded that the rate of major complications in older adults was similar to that observed in younger patients and was not a sufficient reason to avoid radical cystectomy in properly selected octogenarians. In addition, this study suggests that the most obvious cut point to dichotomize the risk of high-grade complications would be approximately age 65 years. However, it is clear that radical cystectomy cannot and should not be restricted based on age alone and offered only to patients younger than 65 years. One caveat to the findings is that these were nonrandomized studies with an inherent selection bias. Thus, one can assume that some patients both young and old, but more likely older, were excluded from radical cystectomy based on the presence of severe comorbidities.

Fewer data are available regarding the impact of age on perioperative mortality. The reported mortality rates in elderly patients undergoing radical cystectomy range between 0 % and 11 % [28]. Generally, a low mortality rate has been reported even when specifically evaluating patients both older than 75 years of age and with significant comorbidities as measured using the American Society of Anesthesiologists physical status classification [135]. Several series report a mortality rate of zero, but often these studies were weakened by very small sample sizes and short follow-up, often limited to the immediate perioperative period. Expanding the definition of perioperative mortality to a 90-day period and including deaths occurring after discharge from the hospital may yield higher mortality rates [134]. This is necessary to reflect the true health-related quality-of-life effect of radical cystectomy. Three series used such an approach for elderly radical cystectomy patients and reported 90-day mortality rates of 5.5 % in patients aged ≥65 years [136], 7.5 % in patients aged ≥75 years [137], and 7–11 % in patients aged ≥80 years [134, 138]. This appears to be particularly true for those patients who are discharged to a skilled nursing facility rather than to home.

In contrast, some studies have reported significantly increased perioperative mortality in elderly patients treated with radical cystectomy [29, 124, 134, 139–141]. The Healthcare Cost and Utilization Project involving 13,964 patients who underwent radical cystectomy showed that increasing age was independently associated with inhospital mortality after surgery (odds ratio, 1.05; CI, 1.03–1.07) [124]. Using data from 5,510 patients treated with partial or radical cystectomy within four SEER registries between 1984 and 2004, age was independently associated with 90-day mortality [29]. Furthermore, in the abovementioned series from MSKCC, the 90-day mortality rate was approximately three times higher in octogenarians compared with younger patients (6.8 % vs. 2.2 %) [134]. Only one patient died of disease progression during that time, and all others died of a surgically related complication, urosepsis, infection, or an acute thromboembolic and/or cardiac event.

Quality of Life After Radical Cystectomy and Urinary Diversion

Quality of life after radical cystectomy and urinary diversion is an important consideration. Alterations in body image and urinary, sexual, and social function after radical cystectomy and urinary diversion are still not completely defined. Some data suggest an inverse relationship between age and continence recovery after orthotopic neobladder substitution [28]. There seems to be a similar relationship concerning recovery of erectile function in men. Three studies suggest an association of age with increased blood loss and transfusion rates [142–144]. One explanation could be that age and its associated concomitant cardiovascular morbidity and/or anticoagulant use trigger blood transfusion at an earlier time point compared to younger and healthier patients.

Elderly patients are typically offered an ileal conduit for urinary diversion, while an orthotopic neobladder is usually reserved for younger and healthier patients [9, 10, 145]. A detailed review of the literature revealed that continent diversion, mostly with ileal neobladder, was done in only 30 % of elderly patients [28]. If ileal neobladder is chosen for older adults, it appears that continence rates are somewhat lower than in younger patients. Decreased long-term reservoir capacity, higher rate of nocturia, and worse continence status were noted in older patients [146]. In another study, continence status at 5-year follow-up approached 100 % in patients younger than 50 years versus 90 % for those older than 60 years [147]. Experienced centers, however, report high continence rates in properly selected patients over 65 years of age. Rates of 90 % daytime and about 80 % nighttime continence have been reported, when continence was defined as complete dryness or loss of no more than a few drops once or twice a month [148]. In contrast, a recently published three-center study of patients aged

≥75 years receiving ileal orthotopic neobladder revealed less favorable figures, with daytime and 25 % nighttime continence and 30 % of patients requiring clean intermittent catheterization due to chronic retention [149]. Possible explanations for the decrease in function in older adults compared to their younger counterparts include worsening external urethral sphincter function [147] and decreased urethral sensitivity with advancing age [150]. Erectile dysfunction is a common sequelae after radical cystectomy often independent of the type of diversion. Similar to urinary continence, age and preoperative erectile function are the best predictors of recovery of erectile function after radical cystectomy [148].

As previously stated, most elderly patients undergoing radical cystectomy are advised to have an ileal conduit urinary diversion. However, it is still important to recognize the significant potential implications of this diversion. An assessment of manual dexterity in order to change urostomy bags is critical and may determine future patient independence. For those who are discharged to a skilled nursing facility, it is imperative that the facility staff have experience with urostomy management to prevent complications and declines in quality of life associated with poor stomal management. Finally, stomal care including peristomal skin maintenance is particularly important in geriatric patients whose skin is often more sensitive to effects of exposure to urine. A physician who is knowledgeable in stomal management or who has an active stomal therapist or nurse is critical to helping elderly patients successfully adjust to their new urostomy.

Age and Systemic Chemotherapy

A variety of chemotherapy regimens are used to treat bladder cancer (Table 18.3). Perioperative use of systemic chemotherapy also adds to the complexity and risk for older individuals. Up to 60 % of patients who undergo radical cystectomy for muscle-invasive UCB are likely to have occult metastases that will be clinically evident in the majority of patients within 2 years of surgery [8, 9, 111–117]. Unless there is a palliative intent in performing radical cystectomy, surgery will by definition not be curative in those who already harbor micrometastases. Although neoadjuvant chemotherapy has been suggested to improve cancer-specific survival in patients with muscle-invasive UCB [111–117], it can have deleterious effects on various organ systems. These potential side effects can delay surgery; some older patients may not fully recover. In addition, any preexisting compromise to organ systems due to either comorbid conditions or age-related physiologic deterioration, such as impaired renal function, can lead to suboptimal chemotherapy regimens, thereby limiting the potential benefits offered by chemotherapy. Ongoing treatment for comorbid conditions such as diabetes, pulmonary disease, and heart disease can also result in various drug interactions when chemotherapy is introduced. Chronic diseases, such as renal or liver disease, may alter the pharmacokinetics and pharmacodynamics of chemotherapeutic agents. These changes, as well as alterations in drug absorption, distribution, metabolism, and excretion, may result in greater exposure to toxicities among older patients [151, 152]. These risks have led to elderly UCB patients being less likely than younger patients to receive optimal types and doses of systemic chemotherapy [128, 153, 154].

Unfortunately, geriatric patients with bladder cancer have generally been excluded from clinical trials. This has particularly limited the evaluation of pharmacokinetic parameters of chemotherapy and biological therapy in this age group. Most publications describing chemotherapy in older patients are retrospective subset analyses in which older patients make up a small fraction of patients [155]. Because of the overall lack of information, particularly for patients over 80 years of age, clinicians will continue to have the task of extrapolating data to fit individual patients.

Cisplatin-based chemotherapy is the most effective systemic chemotherapy for UCB. However, it is associated with various toxicities including nephrotoxicity, ototoxicity, and neurotoxicity. It can also create a number of vascular toxicities including cardiovascular, cerebrovascular, thrombotic microangiopathy, and Raynaud's

Table 18.3 Chemotherapy regimens for advanced bladder cancer

Agent(s)	Response rates (%)	Side effects
MVAC (methotrexate, vinblastine, adriamycin, cisplatin)	39–65	Myelosuppression, neurotoxicity, cardiotoxicity, renal toxicity, alopecia, ototoxicity, Raynaud's, GI toxicity
GC (gemcitabine, cisplatin)	30–60	Myelosuppression, neurotoxicity, renal toxicity, ototoxicity, GI toxicity
Taxol/carboplatin	10–30	Myelosuppression, alopecia neurotoxicity
Gemcitabine monotherapy	46	Myelosuppression, GI toxicity
Gemcitabine/carboplatin	24	Myelosuppression, GI side effects

phenomenon (Table 18.3) [156]. The probability of these toxicities is increased by an age-related decline in renal function leading to a longer half-life of the toxic metabolites of chemotherapeutic regimens. Indeed, Dash et al. found that impaired renal function made >40 % of patients aged >70 years ineligible for cisplatin-based chemotherapy [157]. Retrospective analysis of clinical trials, however, has not reported an undue incidence of age-related nephrotoxicity and hearing loss [158]. Thus cisplatin is a viable option in properly selected elderly patients. Hydration, which helps mitigate the side effects of platinum-based chemotherapeutics, must be monitored carefully to prevent fluid overload which could lead to congestive heart failure or pulmonary edema. Concomitant use of other potentially nephrotoxic drugs should be strictly avoided. Split-dose therapy may improve the tolerability of cisplatin-containing regimens. Carboplatin, which is also completely eliminated through the kidneys, has less renal-function-dependent toxicity than cisplatin, but unfortunately has been shown to be less effective than cisplatin. Despite this, because of the low incidence of non-hematologic toxicity, it is often used in the palliative setting or in cases where the issue of cisplatin toxicity is of concern.

Non-platinum-based chemotherapy regimens have become an attractive alternative for elderly patients with advanced UCB, despite their apparently inferior efficacy. Castagneto et al. assessed the efficacy of gemcitabine mono-chemotherapy in 23 unselected older adults with advanced UCB (median age 76 years; range 71–87) [159]. At the end of the therapy, the Comprehensive Geriatric Assessment parameters improved in four cases (17 %), remained unchanged in 17 cases (74 %), and worsened in two cases (9 %). The overall response rate was 45.5 % (95 % CI 24.3–65.7), median overall survival was 8 months, and median time to progression was 5 months. Treatment was generally well tolerated, with one patient having grade 3 gastrointestinal toxicity and three having grade 4 neutropenia. The authors concluded that gemcitabine mono-chemotherapy was safe and effective and did not worsen the functional status of elderly patients.

In another study, Bamias et al. evaluated the safety and efficacy of first-line combination gemcitabine and carboplatin in 34 patients aged >70 years with advanced UCB who were not candidates for cisplatin-based chemotherapy (ECOG performance status ≥2, creatinine clearance <50 mL/min, or comorbidities precluding cisplatin administration) [160]. Response rate was 24 % (95 % CI: 11–41), median progression-free survival was 4.4 months (95 % CI: 1.03–7.75), and median overall survival was 9.8 months (95 % CI: 4.7–14.9). Patients who were independent in their activities of daily living (ADLs) or instrumental activities of daily living (IADLs) and with no comorbidities or those with IADL dependency or one-to-two comorbidities did better than elderly patients with ADL dependency or more than two comorbidities. To date, no perioperative non-platinum-containing chemotherapy regimens have demonstrated a survival advantage. With no Level 1 evidence supporting the use of non-platinum therapy, these treatments should not be used outside of a protocol setting.

Careful assessment of how comorbid conditions, changes in organ function, and physiologic reserve may lead to suboptimal treatment dosing among older patients warrants further research. Among older cancer patients, decreased physical function and disability are associated with losses of functional reserve, which, in the presence of chemotherapy, increases the likelihood that these patients will experience toxic side effects [75, 152]. Additional studies are needed to define tolerance and response to treatment among older patients with various levels of disability, to describe how these treatments impact patients' functional reserves, and to define the ability to recover reasonable levels of functioning after the end of treatment. Finally, the interplay between adequate treatment, organ function, and dose delays, reductions, and stoppages needs to be assessed carefully. Such information can help estimate life expectancy and treatment tolerance and ultimately establish a common classification of physical function that may be useful in planning care for older individuals.

More investigations of non-cisplatin chemotherapy regimens are necessary in both the perioperative and metastatic setting for elderly patients. In addition, further evaluation of non-cisplatin and cisplatin-based multimodal therapy is necessary before widespread use of current bladder preservation protocols can be recommended. A recent phase III randomized trial compared synchronous chemoradiotherapy (CRT) to radiotherapy (RT) alone in muscle-invasive bladder cancer. Results indicated that CRT using 5FU and mitomycin C was well tolerated and significantly improved loco-regional disease-free survival compared to RT alone, with good bladder function and no increase in late toxicity [161]. In this context, geriatric assessment tools need to be integrated in both research and clinical management of older adults to allow assessment of longitudinal changes in functional status and improve prediction of outcomes. Finally, more clinical trials evaluating the utility and efficacy of novel agents in older adults with advanced UCB are necessary.

Future Perspective: Potential Advances in the Care of UCB in Older Adults

The decision to undergo treatment for cancer is a trade-off between loss of function and independence on one hand and extension of life on the other. This trade-off is complicated by a host of concomitant issues including comorbid medical conditions, functional declines and "frailty," family dynamics, and social and psychological issues. With an aging population and increased life expectancy, we need to devote greater attention to the development and treatment of UCB in older adults. Healthcare professionals must deal with concurrent health problems of geriatric patients, as cancer frequently occurs in the presence of one or more other chronic diseases. These comorbid conditions can increase the risk of complications and mortality from treatment interventions. This information must be carefully integrated when making decisions regarding treatment and multispecialty perioperative care. Radical cystectomy has previously demonstrated survival benefits even among older adults [119, 128]. Thus, although age and comorbidity should determine medical candidacy for this surgery, the majority of invasive bladder cancer patients without contraindication to prolonged anesthesia should undergo potentially curative radical surgery. Unfortunately, radical cystectomy is all too often withheld or delayed in elderly patients who could potentially benefit from such treatment.

Radical cystectomy for muscle-invasive UCB in older adults remains an important treatment option but continues to be underused in the community. Without randomized trials, it is not possible to judge the potential degree of benefit of bladder-preserving approaches for elderly patients compared with radical cystectomy. One should keep in mind that no less aggressive treatment is currently available that can control the potentially devastating symptoms of untreated, progressing bladder cancer.

Despite a higher prevalence of comorbidities in older adults, radical cystectomy can provide similar disease control and survival outcomes compared to younger patients. The risks of major perioperative morbidity are comparable to those in younger patients at high-volume centers. The critical factor for success of treatment for muscle-invasive UCB in geriatrics is patient selection. Additional research into the selection of elderly patients for aggressive surgical and/or medical treatment is necessary to identify which patients will benefit from it. Elderly patients, when treated adequately, tolerate and respond well to cancer therapies [162]. The treatment and management decisions for older cancer patients should be guided by management of comorbid conditions, organ function, frailty, and cognitive status. It is important to understand how variations in each of these indicators accompany and successively change in older patient cohorts. While perioperative morbidity and mortality are increased in elderly patients, chronological age should not be viewed as a barrier to treatment [128]. A multidisciplinary approach to bladder cancer that integrates geriatricians, urologists, nutritionists, physical therapists, and social workers could allow for optimized care and outcomes. For example, elderly patients could be screened using validated assessment tools and could potentially be risk stratified for treatment options based on functional status. Frail patients could undergo intervention in specialized clinics to optimize their health.

It is imperative that healthcare practitioners and researchers from disparate disciplines collectively focus their efforts toward gaining a better understanding of what the consequences of UCB and its treatments are for older adults. This will help to appropriately meet the multifaceted medical and psychosocial needs of this growing population.

References

1. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin. 2011;61:69–90.
2. Siegel R, Ward E, Brawley O, Jemal A. Cancer statistics, 2011: the impact of eliminating socioeconomic and racial disparities on premature cancer deaths. CA Cancer J Clin. 2011;61:212–36.
3. Shariat SF, Tokunaga H, Zhou J, et al. p53, p21, pRB, and p16 expression predict clinical outcome in cystectomy with bladder cancer. J Clin Oncol. 2004;22:1014–24.
4. Shariat SF, Casella R, Wians Jr FH, et al. Risk stratification for bladder tumor recurrence, stage and grade by urinary nuclear matrix protein 22 and cytology. Eur Urol. 2004;45:304–13. author reply 13.
5. Lotan Y, Shariat SF. Impact of risk factors on the performance of the nuclear matrix protein 22 point-of-care test for bladder cancer detection. BJU Int. 2008;101:1362–7.
6. Bochner BH. Optimal timing of radical cystectomy for patients with T1 bladder cancer. Urol Oncol. 2009;27:329–31.
7. Dalbagni G, Vora K, Kaag M, et al. Clinical outcome in a contemporary series of restaged patients with clinical T1 bladder cancer. Eur Urol. 2009; 56:903–10.
8. Shariat SF, Karakiewicz PI, Palapattu GS, et al. Outcomes of radical cystectomy for transitional cell carcinoma of the bladder: a contemporary series from the bladder cancer research consortium. J Urol. 2006;176:2414–22. discussion 22.
9. Stein JP, Lieskovsky G, Cote R, et al. Radical cystectomy in the treatment of invasive bladder cancer: long-term results in 1,054 patients. J Clin Oncol. 2001;19:666–75.
10. Madersbacher S, Hochreiter W, Burkhard F, et al. Radical cystectomy for bladder cancer today–a homogeneous series without neoadjuvant therapy. J Clin Oncol. 2003;21:690–6.
11. Bochner BH, Kattan MW, Vora KC. Postoperative nomogram predicting risk of recurrence after radical cystectomy for bladder cancer. J Clin Oncol. 2006;24:3967–72.
12. Karakiewicz PI, Shariat SF, Palapattu GS, et al. Nomogram for predicting disease recurrence after radical cystectomy for transitional cell carcinoma of the bladder. J Urol. 2006;176:1354–61. discussion 61–2.
13. Shariat SF, Karakiewicz PI, Palapattu GS, et al. Nomograms provide improved accuracy for predicting survival after radical cystectomy. Clin Cancer Res. 2006;12:6663–76.
14. Chromecki TF, Mauermann J, Cha EK, et al. Multicenter validation of the prognostic value of patient age in patients treated with radical cystectomy. World J Urol. 2012;30(6):753–9.
15. Shariat SF, Milowsky M, Droller MJ. Bladder cancer in the elderly. Urol Oncol. 2009;27:653–67.
16. Shariat SF, Sfakianos JP, Droller MJ, Karakiewicz PI, Meryn S, Bochner BH. The effect of age and gender on bladder cancer: a critical review of the literature. BJU Int. 2010;105:300–8.
17. Messing EM. Urothelial tumors of the bladder. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA, editors. Campbell-walsh urology, vol.

Chapter 75. 9th ed. Philadelphia, PA: Saunders-Elsevier; 2008. p. 2407–46.
18. American Cancer Society. Cancer facts and figures 2008. Atlanta: American Cancer Society; 2008.
19. Kent MM, Mather M. What drives US population growth? Population Bull. 2002;57:1–40.
20. Kinsella K, Velkoff VA. An aging world: 2005 US Census Bureau, series P95/005-1. Washington, DC: US Government Printing Office; 2005.
21. UBoCw. http://www.census.gov. Accessed 10 Nov 2008.
22. Yancik R, Ries LA. Cancer in older persons: an international issue in an aging world. Semin Oncol. 2004;31:128–36.
23. Havlik RJ, Yancik R, Long S, Ries L, Edwards B. The National Institute on Aging and the National Cancer Institute SEER collaborative study on comorbidity and early diagnosis of cancer in the elderly. Cancer. 1994;74:2101–6.
24. Yancik R, Ries LA. Aging and cancer in America. Demographic and epidemiologic perspectives. Hematol Oncol Clin North Am. 2000;14:17–23.
25. Edwards BK, Howe HL, Ries LA, et al. Annual report to the nation on the status of cancer, 1973–1999, featuring implications of age and aging on U.S. cancer burden. Cancer. 2002;94:2766–92.
26. Hewitt M, Rowland JH, Yancik R. Cancer survivors in the United States: age, health, and disability. J Gerontol A Biol Sci Med Sci. 2003;58:82–91.
27. Jaklitsch MT, Bueno R, Swanson SJ, Mentzer SJ, Lukanich JM, Sugarbaker DJ. New surgical options for elderly lung cancer patients. Chest. 1999;116:480S–5.
28. Froehner M, Brausi MA, Herr HW, Muto G, Studer UE. Complications following radical cystectomy for bladder cancer in the elderly. Eur Urol. 2009;56:443–54.
29. Isbarn H, Jeldres C, Zini L, et al. A population based assessment of perioperative mortality after cystectomy for bladder cancer. J Urol. 2009;182:70–7.
30. Shariat SF, Godoy G, Lotan Y, et al. Advanced patient age is associated with inferior cancer-specific survival after radical nephroureterectomy. BJU Int. 2009;105(12):1672–7.
31. Whitmore Jr WF, Marshall VF. Radical total cystectomy for cancer of the bladder: 230 consecutive cases five years later. J Urol. 1962;87:853–68.
32. Sawhney R, Sehl M, Naeim A. Physiologic aspects of aging: impact on cancer management and decision making, part I. Cancer J. 2005;11:449–60.
33. Sehl M, Sawhney R, Naeim A. Physiologic aspects of aging: impact on cancer management and decision making, part II. Cancer J. 2005;11:461–73.
34. Hurria AMH, Cohen HJ, editors. Cancer and aging (Chapter 75). Hamilton: BC Decker; 2003.
35. http://www.cdc.gov/nchs/agingact.thm. 2008. Accessed 14 Dec 2008.
36. Hazen SE, Larsen PD, Martin JL. General anesthesia and elderly surgical patients. AORN J. 1997;65(815–9):21–2.
37. Malani PN, Vaitkevicius P, Orringer MB. Perioperative evaluation, and management. Chapter 35. In: Halter JB, Ouslander J, Tinetti ME, Studenski S, High KP, Asthana S editors. http://www.accessmedicine.com/content.aspx?aID=5114524. Accessed 25 Oct 2009.
38. Hardin RE. ZMCSCitEIBF. In: Andersen DK, Billiar TR, Dunn DL, Hunter JG, Matthews JB, Pollock RE, editors. Schwartz's principles of surgery. 9th ed. New York, NY: McGraw-Hill; 2011. http://www.accessmedicine.com/content.aspx?aID=5028914. Accessed 24 Oct 2011.
39. Pedelty L, Gorelick PB. Management of hypertension and cerebrovascular disease in the elderly. Am J Med. 2008;121:S23–31.
40. Baruch L. Hypertension and the elderly: more than just blood pressure control. J Clin Hypertens (Greenwich). 2004;6:249–55.
41. Watters JM. Surgery in the elderly. Can J Surg. 2002;45:104–8.
42. Ergina PL, Gold SL, Meakins JL. Perioperative care of the elderly patient. World J Surg. 1993;17:192–8.
43. Loran DB, Zwischenberger JB. Thoracic surgery in the elderly. J Am Coll Surg. 2004;199:773–84.
44. Sharma G, Goodwin J. Effect of aging on respiratory system physiology and immunology. Clin Interv Aging. 2006;1:253–60.
45. Lawrence VA, Cornell JE, Smetana GW. Strategies to reduce postoperative pulmonary complications after noncardiothoracic surgery: systematic review for the American College of Physicians. Ann Intern Med. 2006;144:596–608.
46. Muhlberg W, Platt D. Age-dependent changes of the kidneys: pharmacological implications. Gerontology. 1999;45:243–53.
47. Turnheim K. When drug therapy gets old: pharmacokinetics and pharmacodynamics in the elderly. Exp Gerontol. 2003;38:843–53.
48. Pasetto LM, Lise M, Monfardini S. Preoperative assessment of elderly cancer patients. Crit Rev Oncol Hematol. 2007;64:10–8.
49. Stevens LA, Li S, Kurella Tamura M, et al. Comparison of the CKD epidemiology collaboration (CKD-EPI) and modification of diet in renal disease (MDRD) study equations: risk factors for and complications of CKD and mortality in the kidney early evaluation program (KEEP). Am J Kidney Dis. 2011;57:S9–16.
50. Madero M, Sarnak MJ. Creatinine-based formulae for estimating glomerular filtration rate: is it time to change to Chronic Kidney Disease Epidemiology Collaboration Equation? Curr Opin Nephrol Hypertens. 2011;20:622–30.
51. Weinberger B, Herndler-Brandstetter D, Schwanninger A, Weiskopf D, Grubeck-Loebenstein B. Biology of immune responses to vaccines in elderly persons. Clin Infect Dis. 2008;46:1078–84.
52. Fulop T, Larbi A, Hirokawa K, et al. Immunosupportive therapies in aging. Clin Interv Aging. 2007;2:33–54.

53. Kumar R, Burns EA. Age-related decline in immunity: implications for vaccine responsiveness. Expert Rev Vaccines. 2008;7:467–79.
54. Wu D, Meydani SN. Age-associated changes in immune and inflammatory responses: impact of vitamin E intervention. J Leukoc Biol. 2008;84:900–14.
55. Nass R, Johannsson G, Christiansen JS, Kopchick JJ, Thorner MO. The aging population–is there a role for endocrine interventions? Growth Horm IGF Res. 2009;19:89–100.
56. Ferrucci L. SSCCPoAILD. In: Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, editors. Harrison's principles of internal medicine. 18th ed. New York, NY: McGraw-Hill; 2011. http://www.accessmedicine.com/content.aspx?aID=9099513. Accessed 25 Oct 2011.
57. Rantanen T, Masaki K, Foley D, Izmirlian G, White L, Guralnik JM. Grip strength changes over 27 yr in Japanese-American men. J Appl Physiol. 1998; 85:2047–53.
58. Rosenthal RA. Nutritional concerns in the older surgical patient. J Am Coll Surg. 2004;199:785–91.
59. Mainous MR, Deitch EA. Nutrition and infection. Surg Clin North Am. 1994;74:659–76.
60. Gregg JR, Cookson MS, Phillips S, et al. Effect of preoperative nutritional deficiency on mortality after radical cystectomy for bladder cancer. J Urol. 2011;185:90–6.
61. Vellas B, Villars H, Abellan G, et al. Overview of the MNA–Its history and challenges. J Nutr Health Aging. 2006;10:456–63. discussion 63–5.
62. Rubenstein LZ, Harker JO, Salva A, Guigoz Y, Vellas B. Screening for undernutrition in geriatric practice: developing the short-form mini-nutritional assessment (MNA-SF). J Gerontol A Biol Sci Med Sci. 2001;56:M366–72.
63. Guigoz Y. The mini nutritional assessment (MNA) review of the literature–what does it tell us? J Nutr Health Aging. 2006;10:466–85. discussion 85–7.
64. Raz N, Rodrigue KM, Haacke EM. Brain aging and its modifiers: insights from in vivo neuromorphometry and susceptibility weighted imaging. Ann N Y Acad Sci. 2007;1097:84–93.
65. Extermann M, Hurria A. Comprehensive geriatric assessment for older patients with cancer. J Clin Oncol. 2007;25:1824–31.
66. Finlayson E. BJCSOIHJ. In: Ouslander JG, Tinetti ME, Studenski S, High KP, Asthana S, editors. Hazzard's geriatric medicine and gerontology. 6th ed. New York, NY: McGraw-Hill; 2011. http://www.accessmedicine.com/content.aspx?aID=5114872. Accessed 26 Oct 2011.
67. Newman MF, Kirchner JL, Phillips-Bute B, et al. Longitudinal assessment of neurocognitive function after coronary-artery bypass surgery. N Engl J Med. 2001;344:395–402.
68. Reuben DB, Rubenstein LV, Hirsch SH, Hays RD. Value of functional status as a predictor of mortality: results of a prospective study. Am J Med. 1992; 93:663–9.
69. Hennessy D, Juzwishin K, Yergens D, Noseworthy T, Doig C. Outcomes of elderly survivors of intensive care: a review of the literature. Chest. 2005; 127:1764–74.
70. Montuclard L, Garrouste-Orgeas M, Timsit JF, Misset B, De Jonghe B, Carlet J. Outcome, functional autonomy, and quality of life of elderly patients with a long-term intensive care unit stay. Crit Care Med. 2000;28:3389–95.
71. Vazquez Mata G, Rivera Fernandez R, Gonzalez Carmona A, et al. Factors related to quality of life 12 months after discharge from an intensive care unit. Crit Care Med. 1992;20:1257–62.
72. Weizer AZ, Joshi D, Daignault S, et al. Performance status is a predictor of overall survival of elderly patients with muscle invasive bladder cancer. J Urol. 2007;177:1287–93.
73. Williams SLJP, Pofahl WE. Preoperative management of the older patient-A surgeon's perspective: part 1. Clin Geriatr Med. 2006;14:24.
74. Want J, Kamas G, Nguyen TN. Disease management in the frail and elderly population: integration of physicians in the intervention. Dis Manag. 2008;11:23–8.
75. Balducci L. Aging, frailty, and chemotherapy. Cancer Control. 2007;14:7–12.
76. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56:M146–56.
77. Walston J, Fried LP. Frailty and the older man. Med Clin North Am. 1999;83:1173–94.
78. Wolff JL, Starfield B, Anderson G. Prevalence, expenditures, and complications of multiple chronic conditions in the elderly. Arch Intern Med. 2002;162:2269–76.
79. Satariano WA, Ragland DR. The effect of comorbidity on 3-year survival of women with primary breast cancer. Ann Intern Med. 1994;120:104–10.
80. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. The index of ADL: a standardized measure of biological and psychosocial function. JAMA. 1963;185:914–9.
81. Lawton MP. Scales to measure competence in everyday activities. Psychopharmacol Bull. 1988; 24:609–14.
82. Mahoney FI, Barthel DW. Functional evaluation: the Barthel Index. Md State Med J. 1965;14:61–5.
83. Keith RA, Granger CV, Hamilton BB, Sherwin FS. The Functional Independence Measure: a new tool for rehabilitation. Adv Clin Rehabil. 1987;1:6–18.
84. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol. 1994;49:M85–94.
85. Berg KO, Wood-Dauphinee SL, Williams JI, Maki B. Measuring balance in the elderly: validation of an instrument. Can J Public Health. 1992;83 Suppl 2:S7–11.
86. Studenski S. Bradypedia: is gait speed ready for clinical use? J Nutr Health Aging. 2009;13:878–80.

87. Guyatt GH, Sullivan MJ, Thompson PJ, et al. The 6-minute walk: a new measure of exercise capacity in patients with chronic heart failure. Can Med Assoc J. 1985;132:919–23.
88. Newman AB, Simonsick EM, Naydeck BL, et al. Association of long-distance corridor walk performance with mortality, cardiovascular disease, mobility limitation, and disability. JAMA. 2006;295: 2018–26.
89. Brandtstadter J, Renner G. Tenacious goal pursuit and flexible goal adjustment: explication and age-related analysis of assimilative and accommodative strategies of coping. Psychol Aging. 1990;5:58–67.
90. Lockenhoff CE, Carstensen LL. Socioemotional selectivity theory, aging, and health: the increasingly delicate balance between regulating emotions and making tough choices. J Pers. 2004;72:1395–424.
91. Halter JB, Ouslander J, Tinetti ME, Studenski S, High KP, Asthana S. Hazzard's Geriatric Medicine and Gerontology, 6th Ed. New York, NY: McGraw-Hill; 2009. http://www.accessmedicine.com
92. Schultzel M, Saltzstein SL, Downs TM, Shimasaki S, Sanders C, Sadler GR. Late age (85 years or older) peak incidence of bladder cancer. J Urol. 2008;179:1302–5. discussion 5–6.
93. Campisi J. Aging and cancer cell biology, 2008. Aging Cell. 2008;7:281–4.
94. Shariat SF, Lotan Y, Karakiewicz PI, et al. p53 predictive value for pT1-2 N0 disease at radical cystectomy. J Urol. 2009;182:907–13.
95. Shariat SF, Karam JA, Lerner SP. Molecular markers in bladder cancer. Curr Opin Urol. 2008;18:1–8.
96. Wu XR. Urothelial tumorigenesis: a tale of divergent pathways. Nat Rev Cancer. 2005;5:713–25.
97. Shariat SF, Matsumoto K, Kim J, et al. Correlation of cyclooxygenase-2 expression with molecular markers, pathological features and clinical outcome of transitional cell carcinoma of the bladder. J Urol. 2003;170:985–9.
98. Shariat SF, Weizer AZ, Green A, et al. Prognostic value of P53 nuclear accumulation and histopathologic features in T1 transitional cell carcinoma of the urinary bladder. Urology. 2000;56:735–40.
99. Benson Jr RC, Tomera KM, Kelalis PP. Transitional cell carcinoma of the bladder in children and adolescents. J Urol. 1983;130:54–5.
100. Fitzpatrick JM, Reda M. Bladder carcinoma in patients 40 years old or less. J Urol. 1986;135:53–4.
101. Linn JF, Sesterhenn I, Mostofi FK, Schoenberg M. The molecular characteristics of bladder cancer in young patients. J Urol. 1998;159:1493–6.
102. Shariat SF. Selecting patients for immediate cystectomy. Rev Urol. 2007;9:239–41.
103. Shariat SF, Pahlavan S, Baseman AG, et al. E-cadherin expression predicts clinical outcome in carcinoma in situ of the urinary bladder. Urology. 2001;57:60–5.
104. Chade DC, Shariat SF, Dalbagni G. Intravesical therapy for urothelial carcinoma of the urinary bladder: a critical review. Int Braz J Urol. 2009;35:640–50. discussion 51.
105. Sylvester RJ, van der Meijden AP. Intravesical bacillus Calmette-Guerin reduces the risk of progression in patients with superficial bladder cancer: a meta-analysis of the published results of randomized clinical trials. J Urol. 2002;168:1964–70.
106. Hall MC, Chang SS, Dalbagni G, et al. Guideline for the management of nonmuscle invasive bladder cancer (stages Ta, T1, and Tis): 2007 update. J Urol. 2007;178:2314–30.
107. Herr HW, Dotan Z, Donat SM, Bajorin DF. Defining optimal therapy for muscle invasive bladder cancer. J Urol. 2007;177:437–43.
108. Joudi FN, Dahmoush L, Spector DM, Konety BR. Complete response of bony metastatic bladder urothelial cancer to neoadjuvant chemotherapy and cystectomy. Urol Oncol. 2006;24:403–6.
109. Kohjimoto Y, Iba A, Shintani Y, Inagaki T, Uekado Y, Hara I. Impact of patient age on outcome following bladder-preserving treatment for non-muscle-invasive bladder cancer. World J Urol. 2010;28(4): 425–30.
110. Heiner JG, Terris MK. Effect of advanced age on the development of complications from intravesical bacillus Calmette-Guerin therapy. Urol Oncol. 2008;26:137–40.
111. Grossman HB, Natale RB, Tangen CM, et al. Neoadjuvant chemotherapy plus cystectomy compared with cystectomy alone for locally advanced bladder cancer. N Engl J Med. 2003;349:859–66.
112. von der Maase H, Sengelov L, Roberts JT, et al. Long-term survival results of a randomized trial comparing gemcitabine plus cisplatin, with methotrexate, vinblastine, doxorubicin, plus cisplatin in patients with bladder cancer. J Clin Oncol. 2005;23:4602–8.
113. Advanced Bladder Cancer (ABC) Meta-analysis Collaboration. Neoadjuvant chemotherapy in invasive bladder cancer: update of a systematic review and meta-analysis of individual patient data Advanced Bladder Cancer (ABC) Meta-analysis Collaboration. Eur Urol. 2005;48:202–5. discussion 5–6.
114. Advanced Bladder Cancer (ABC) Meta-analysis Collaboration. Adjuvant chemotherapy in invasive bladder cancer: a systematic review and meta-analysis of individual patient data Advanced Bladder Cancer (ABC) Meta-analysis Collaboration. Eur Urol. 2005;48:189–99. discussion 99–201.
115. Pectasides D, Pectasides M, Nikolaou M. Adjuvant and neoadjuvant chemotherapy in muscle invasive bladder cancer: literature review. Eur Urol. 2005;48:60–7. discussion 7–8.
116. Schultz PK, Herr HW, Zhang ZF, et al. Neoadjuvant chemotherapy for invasive bladder cancer: prognostic factors for survival of patients treated with M-VAC with 5-year follow-up. J Clin Oncol. 1994;12:1394–401.
117. Sonpavde G, Petrylak DP. Perioperative chemotherapy for bladder cancer. Crit Rev Oncol Hematol. 2006;57:133–44.

118. Prout Jr GR, Wesley MN, Yancik R, Ries LA, Havlik RJ, Edwards BK. Age and comorbidity impact surgical therapy in older bladder carcinoma patients: a population-based study. Cancer. 2005;104:1638–47.
119. Hollenbeck BK, Miller DC, Taub D, et al. Aggressive treatment for bladder cancer is associated with improved overall survival among patients 80 years old or older. Urology. 2004;64:292–7.
120. Gore JL, Litwin MS, Lai J, et al. Use of radical cystectomy for patients with invasive bladder cancer. J Natl Cancer Inst. 2010;102(11):802–11.
121. Lodde M, Palermo S, Comploj E, et al. Four years experience in bladder preserving management for muscle invasive bladder cancer. Eur Urol. 2005;47:773–8. discussion 8–9.
122. Messing EM, editor. Urothelial tumors of the bladder. Philadelphia, PA: Saunders-Elsevier; 2008.
123. Fairey A, Chetner M, Metcalfe J, et al. Associations among age, comorbidity and clinical outcomes after radical cystectomy: results from the Alberta Urology Institute radical cystectomy database. J Urol. 2008;180:128–34. discussion 34.
124. Konety BR, Dhawan V, Allareddy V, Joslyn SA. Impact of hospital and surgeon volume on in-hospital mortality from radical cystectomy: data from the Health Care Utilization Project. J Urol. 2005;173:1695–700.
125. Hollenbeck BK, Miller DC, Taub D, et al. Identifying risk factors for potentially avoidable complications following radical cystectomy. J Urol. 2005;174:1231–7. discussion 1237.
126. Konety BR, Joslyn SA. Factors influencing aggressive therapy for bladder cancer: an analysis of data from the SEER program. J Urol. 2003;170:1765–71.
127. Clark PE, Stein JP, Groshen SG, et al. Radical cystectomy in the elderly: comparison of clinical outcomes between younger and older patients. Cancer. 2005;104:36–43.
128. Nielsen ME, Shariat SF, Karakiewicz PI, et al. Advanced age is associated with poorer bladder cancer-specific survival in patients treated with radical cystectomy. Eur Urol. 2007;51:699–706. discussion −8.
129. Prout GR, Marshall VF. The prognosis with untreated bladder tumors. Cancer. 1956;9:551–8.
130. Rosario DJ, Becker M, Anderson JB. The changing pattern of mortality and morbidity from radical cystectomy. BJU Int. 2000;85:427–30.
131. Shabsigh A, Korets R, Vora KC, et al. Defining early morbidity of radical cystectomy for patients with bladder cancer using a standardized reporting methodology. Eur Urol. 2009;55:164–74.
132. Shabsigh A, Korets R, Vora KC, et al. Defining early morbidity of radical cystectomy for patients with bladder cancer using a standardized reporting methodology. Eur Urol. 2008;55(1):164–74.
133. Donat SM, Shabsigh A, Savage C, et al. Potential impact of postoperative early complications on the timing of adjuvant chemotherapy in patients undergoing radical cystectomy: a high-volume tertiary cancer center experience. Eur Urol. 2009; 55:177–85.
134. Donat SM, Siegrist T, Cronin A, Savage C, Milowsky MI, Herr HW. Radical cystectomy in octogenarians-does morbidity outweigh the potential survival benefits? J Urol. 2010;183(6):2171–7.
135. Farnham SB, Cookson MS, Alberts G, Smith Jr JA, Chang SS. Benefit of radical cystectomy in the elderly patient with significant co-morbidities. Urol Oncol. 2004;22:178–81.
136. Bostrom PJ, Kossi J, Laato M, Nurmi M. Risk factors for mortality and morbidity related to radical cystectomy. BJU Int. 2009;103:191–6.
137. Zebic N, Weinknecht S, Kroepfl D. Radical cystectomy in patients aged > or = 75 years: an updated review of patients treated with curative and palliative intent. BJU Int. 2005;95:1211–4.
138. Mendiola FP, Zorn KC, Gofrit ON, et al. Cystectomy in the ninth decade: operative results and long-term survival outcomes. Can J Urol. 2007;14:3628–34.
139. Knap MM, Lundbeck F, Overgaard J. Early and late treatment-related morbidity following radical cystectomy. Scand J Urol Nephrol. 2004;38:153–60.
140. Elting LS, Pettaway C, Bekele BN, et al. Correlation between annual volume of cystectomy, professional staffing, and outcomes: a statewide, population-based study. Cancer. 2005;104:975–84.
141. Yamanaka K, Miyake H, Hara I, Inoue TA, Fujisawa M. Significance of radical cystectomy for bladder cancer in patients over 80 years old. Int Urol Nephrol. 2007;39:209–14.
142. Chang SS, Jacobs B, Wells N, Smith Jr JA, Cookson MS. Increased body mass index predicts increased blood loss during radical cystectomy. J Urol. 2004;171:1077–9.
143. Lowrance WT, Rumohr JA, Chang SS, Clark PE, Smith Jr JA, Cookson MS. Contemporary open radical cystectomy: analysis of perioperative outcomes. J Urol. 2008;179:1313–8. discussion 8.
144. Cardenas-Turanzas M, Cooksley C, Kamat AM, Pettaway CA, Elting LS. Gender and age differences in blood utilization and length of stay in radical cystectomy: a population-based study. Int Urol Nephrol. 2008;40:893–9.
145. Stroumbakis N, Herr HW, Cookson MS, Fair WR. Radical cystectomy in the octogenarian. J Urol. 1997;158:2113–7.
146. Madersbacher S, Mohrle K, Burkhard F, Studer UE. Long-term voiding pattern of patients with ileal orthotopic bladder substitutes. J Urol. 2002; 167:2052–7.
147. Hautmann RE, Miller K, Steiner U, Wenderoth U. The ileal neobladder: 6 years of experience with more than 200 patients. J Urol. 1993;150:40–5.
148. Kessler TM, Burkhard FC, Perimenis P, et al. Attempted nerve sparing surgery and age have a significant effect on urinary continence and erectile

function after radical cystoprostatectomy and ileal orthotopic bladder substitution. J Urol. 2004; 172:1323–7.

149. Sogni F, Brausi M, Frea B, et al. Morbidity and quality of life in elderly patients receiving ileal conduit or orthotopic neobladder after radical cystectomy for invasive bladder cancer. Urology. 2008;71:919–23.
150. Hugonnet CL, Danuser H, Springer JP, Studer UE. Decreased sensitivity in the membranous urethra after orthotopic ileal bladder substitute. J Urol. 1999;161:418–21.
151. Cohen HJ. The cancer aging interface: a research agenda. J Clin Oncol. 2007;25:1945–8.
152. Lichtman SM, Wildiers H, Chatelut E, et al. International Society of Geriatric Oncology Chemotherapy Taskforce: evaluation of chemotherapy in older patients–an analysis of the medical literature. J Clin Oncol. 2007;25:1832–43.
153. Surbone A, Kagawa-Singer M, Terret C, Baider L. The illness trajectory of elderly cancer patients across cultures: SIOG position paper. Ann Oncol. 2007;18:633–8.
154. Terret C, Zulian G, Droz JP. Statements on the interdependence between the oncologist and the geriatrician in geriatric oncology. Crit Rev Oncol Hematol. 2004;52:127–33.
155. Lichtman SM, Boparai MK. Anticancer drug therapy in the older cancer patient: pharmacology and polypharmacy. Curr Treat Options Oncol. 2008;9: 191–203.
156. Li SH, Chen WH, Tang Y, et al. Incidence of ischemic stroke post-chemotherapy: a retrospective review of 10,963 patients. Clin Neurol Neurosurg. 2006;108:150–6.
157. Dash A, Pettus 4th JA, Herr HW, et al. A role for neoadjuvant gemcitabine plus cisplatin in muscle-invasive urothelial carcinoma of the bladder: a retrospective experience. Cancer. 2008;113:2471–7.
158. Langer CJ, Manola J, Bernardo P, et al. Cisplatin-based therapy for elderly patients with advanced non-small-cell lung cancer: implications of Eastern Cooperative Oncology Group 5592, a randomized trial. J Natl Cancer Inst. 2002;94:173–81.
159. Castagneto B, Zai S, Marenco D, et al. Single-agent gemcitabine in previously untreated elderly patients with advanced bladder carcinoma: response to treatment and correlation with the comprehensive geriatric assessment. Oncology. 2004;67:27–32.
160. Bamias A, Lainakis G, Kastritis E, et al. Biweekly carboplatin/gemcitabine in patients with advanced urothelial cancer who are unfit for cisplatin-based chemotherapy: report of efficacy, quality of life and geriatric assessment. Oncology. 2007;73:290–7.
161. James D, Hussain S, Hall E, et al. Results of a phase III randomized trial of synchronous chemoradiotherapy (CRT) compared to radiotherapy (RT) alone in muscle-invasive bladder cancer (MIBC). J Clin Oncol. 2010;28:15s (suppl; abstr 4517).
162. Kemeny MM. Surgery in older patients. Semin Oncol. 2004;31:175–84.

Kidney Cancer

19

Robert Abouassaly and Steven C. Campbell

Introduction

The increased use of abdominal imaging has contributed to a rise in the incidence of kidney tumors. Notably the greatest increase has been in small renal masses among older adults. This has led to a treatment dilemma given the unclear impact of these small tumors on life expectancy, particularly in patients with advanced age or multiple comorbidities. This has contributed to the development of minimally invasive treatment approaches as well as the use of active surveillance for this disease. This chapter provides a concise review of the epidemiology, etiology, diagnosis, and treatment of kidney cancer, with particular focus on elderly patients.

Epidemiology

Kidney cancer is the sixth and eighth most common malignancy in the USA in men and women, respectively, with an annual incidence of approximately 60,000 new cases and 13,000 deaths per year [1]. The worldwide incidence is estimated to be 209,000 cases and 102,000 deaths per year [2]. Renal cell carcinoma (RCC) accounts for 2–3 % of all malignancies and approximately 85 % of all kidney tumors [3]. RCC demonstrates a male/female ratio of 3/2 and typically presents in the sixth and seventh decade of life [4]. RCC can be viewed as two disease states: advanced disease which is highly lethal and small renal masses (SRMs) which tend to have an indolent course. Although RCC has been traditionally viewed as the most lethal urologic malignancy, with 35 % of patients dying from the disease at 5 years [4], currently more than 70 % of individuals present with localized disease, and those with tumors <4 cm (stage T1a) [5] have an excellent prognosis [6].

In the last three decades, there has been a 2–3 % yearly increase in the incidence of RCC in North America, primarily due to a rapid increase in early-stage disease [6]. Increases in RCC incidence have occurred in all age groups; [6] however, the greatest increase in the incidence of RCC has been observed in the seventh and eighth decades of life [7]. The observed increased incidence has been mostly attributed to the incidental detection of small tumors with the more prevalent use of noninvasive abdominal imaging such as ultrasound and computed tomography. There has also been an observed steadily increasing death rate from RCC since the 1980s [6], suggesting that a change in tumor biology may also have occurred during the past several decades.

R. Abouassaly, M.D., M.Sc., F.R.C.S.C. (✉)
Urologic Institute, University Hospitals Case Medical Center, 11100 Euclid Avenue, Mailstop LKS 5046, Office 4565, Cleveland, OH 44106, USA
e-mail: robert.abouassaly@uhhospitals.org

S.C. Campbell, M.D., Ph.D.
Urology, Cleveland Clinic, Room Q10-120, 9500 Euclid Avenue, Cleveland, OH 44022, USA
e-mail: campbes3@ccf.org

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_19,

This may be related to environmental factors such as diet, tobacco use, and exposure to other carcinogens or an increased prevalence of obesity and hypertension, both well-established risk factors for RCC.

Etiology

Tobacco use is the most consistently established risk factor for RCC and has been estimated to account for approximately 20 % of tumors [3]. Obesity has now also emerged as an important risk factor for RCC; a recent meta-analysis estimated the relative risk to be 1.24 and 1.34 for men and women, respectively, for each 5 kg/m^2 increase in body mass index (BMI) [8]. It is estimated that 30 % of RCC cases may be attributed to obesity. Family history has also been found to be associated with an increased risk for RCC, with a meta-analysis estimating the risk to be 2.2-fold increased in patients with affected first-degree relatives [9]. Other potential iatrogenic causes include radiation therapy and antihypertensive medications; however, the relative risks are low [10, 11]. Finally, approximately 2–3 % of RCCs are familial, including several well-described autosomal dominant syndromes (e.g., von Hippel-Lindau syndrome); however, these typically affect younger adults [12].

As is the case with many malignancies, increasing age is a risk factor for RCC. The median age at treatment is 60 years, and more than three-quarters of those diagnosed are over the age of 50 years [13]. Additionally, the likelihood of undergoing abdominal imaging increases with age, and therefore so does the probability of being diagnosed with incidental SRMs. The increased number of SRMs being diagnosed in patients with advanced age has had a significant influence on the approach to treatment in these potentially high-risk patients.

Diagnosis

RCC demonstrates a male predominance, with an overall male/female ratio of 3/2. However, this ratio has been observed to increase with age, such that the ratio is 1.3/1, 2.0/1, and 3.3/1 in patients 40 years or younger, 41–59 years, and 60 years or older, respectively [14]. Typically patients present in the sixth and seventh decades of life [4], and fewer than half of patients are symptomatic at diagnosis [15, 16]. When present, local signs and symptoms include hematuria, abdominal/flank pain, or an abdominal mass. Systemic symptoms can result from either a paraneoplastic syndrome (present in about 20 % of patients) or metastatic disease and most commonly include hypertension, polycythemia, hypercalcemia, or wasting syndromes [17]. The "classic triad," often referred to as the "too late triad," of hematuria, flank pain, and abdominal mass is uncommon at presentation and is an indicator of advanced disease [15]. One study found that the incidence of symptoms increases with age, with over two-thirds of patients over the age of 60 years presenting with symptoms, compared with 28 % of patients under the age of 40 years [14].

With respect to imaging, computed tomography (CT) is the modality of choice for detection and diagnosis of renal cortical tumors. In addition to characterizing the lesion of interest, modern contrast-enhanced CT morphologically assesses the contralateral kidney as well as detects adrenal, hepatic, venous, or regional lymph node involvement [18]. Approximately 10–20 % of lesions suspicious for RCC on CT prove to be benign (e.g., oncocytomas or fat-poor angiomyolipomas) after excision. The incidence of benign pathology increases with decreasing tumor size and increasing age [19, 20]. Interestingly, the effect of age appears to differ by gender. A preoperative nomogram for solid-enhancing renal tumors found that the probability of benign histology increases with age in men but decreases in women (Fig. 19.1) [21]. Other studies have demonstrated similar gender effects; Eggener et al. reported that 36 % of SRMs in women 18–45 years old were benign compared with 9.5 % of SRMs in young men [22], and Snyder et al. found that the relative risk of benign pathology in women was 1.8 compared with that in men [23]. With the exception of angiomyolipoma, CT cannot reliably distinguish between benign and malignant lesions. Magnetic resonance imaging and ultrasonography are typically used adjunc-

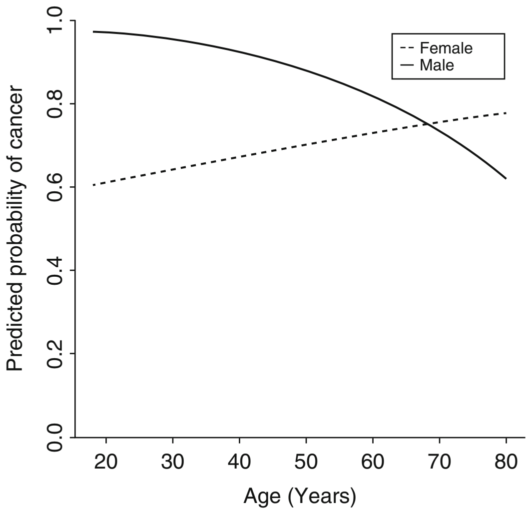


Fig. 19.1 Predicted probability that a small renal mass amenable to partial nephrectomy is cancer in a nonsmoker with an incidentally detected 3 cm solid renal tumor. Note that likelihood of cancer increases with advanced age in females and decreases with advanced age in males. Figure originally published in the *Journal of Urology* by Lane et al. 2007 [21]

tively or in patients with contraindications to the administration of intravenous (IV) contrast.

All patients with renal masses suspicious for RCC should undergo metastatic evaluation including liver function tests and chest radiography [24]. Radionuclide bone scans are reserved for patients with elevated alkaline phosphatase, bone pain, or decline in performance status [25]. Routine imaging of the brain is not indicated, given that patients harboring disease in this site are usually symptomatic.

Traditionally, the role of percutaneous renal mass biopsy in the diagnosis of RCC has been limited. Early published reports raised concerns about a high false-negative rate and potential complications associated with renal mass biopsy [26]. However, in recent years, due to refinements in technique, the safety and diagnostic accuracy have significantly improved [27]. This has led many to revisit the role of renal mass biopsy for localized renal tumors. In the near future, renal mass biopsy may be incorporated into algorithms to aid in risk stratification and treatment decision making for patients at high surgical risk, such as those with advanced age or significant comorbidity [28].

Pathologic Characteristics

RCC is subdivided, based on morphological appearance, into clear cell (70–80 %), papillary (10–15 %), chromophobe (3–5 %), collecting duct (1 %), and unclassified (1 %) subtypes [29]. Clear cell RCC often presents with higher grade and stage than papillary and chromophobe subtypes and as a result has a worse disease-specific survival [30]. Sarcomatoid features can exist in all histological subtypes, and this finding is associated with poor prognosis [31].

Several studies have shown age to influence the distribution of histological subtypes; however, findings have not been entirely consistent [20, 32–35]. Although most studies suggest that the proportion of tumors with clear cell histology increases with age (70–82 % for patients ≤40 years old vs. 82–94 % for older patients) [32–34], others have either found the opposite [20] or no effect [35]. Such conflicting results can be potentially explained by the fact that these studies relied on data from either single or multiple institution case series, which are susceptible to significant selection bias. Indolent-appearing masses in elderly patients may be more likely observed or ablated, thus altering the histological subtype distribution of those treated surgically. A more consistent finding across these studies is that the proportion of tumors with chromophobe histology decreases with increasing age [20, 32–35].

Prognostic Indicators

Stage

The most commonly used staging system is the 2010 TNM system (Table 19.1) [36]. T1 and T2 tumors are confined to the kidney and are divided as being ≤or>7 cm in greatest dimension, respectively. T1 tumors are further subdivided into T1a (≤4 cm) and T1b (>4 cm but ≤7 cm). This subdivision has important implications in terms of treatment options. Typically only T1a tumors are considered for elective partial nephrectomy,

Table 19.1 TNM staging system for renal cell carcinoma (2010 American Joint Committee on Cancer (AJCC) 7th Edition)

Primary tumor (T)	
Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor 7 cm or less in greatest dimension, limited to the kidney
T1a	Tumor 4 cm or less in greatest dimension, limited to the kidney
T1b	Tumor more than 4 cm but not more than 7 cm in greatest dimension, limited to the kidney
T2	Tumor more than 7 cm in greatest dimension, limited to the kidney
T2a	Tumor more than 7 cm but not more than 10 cm in greatest dimension, limited to the kidney
T2b	Tumor more than 10 cm in greatest dimension, limited to the kidney
T3	Tumor extends into the major vein or perinephric tissues but not into the ipsilateral adrenal gland and not beyond Gerota's fascia
T3a	Tumor grossly extends into the renal vein or its segmental (muscle-containing) branches, or tumor invades perirenal and/or renal sinus fat but not beyond Gerota's fascia
T3b	Tumor grossly extends into the vena cava below the diaphragm
T3c	Tumor grossly extends into the vena cava above the diaphragm or invades the wall of the vena cava
T4	Tumor invades beyond Gerota's fascia (including contiguous extension into the ipsilateral adrenal gland)
Regional lymph nodes (N)	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastases
N1	Metastasis in regional lymph node(s)
Distant metastasis (M)	
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

ablative therapy, or active surveillance [37–39]. However, many centers are now managing T1b tumors in a similar manner.

The effect of age on tumor stage at the time of treatment is, once again, not consistent across studies. Some studies suggest that tumors in elderly patients are more often locally advanced (i.e., T3 or greater in 42–46 % of patients ≥60 years compared with 22–31 % of patients ≤40 years old) [34, 40], whereas other studies have failed to identify an association between age and stage [32, 33, 35]. Similarly, although most studies show similar incidence of lymph node involvement with age [32, 34], a few studies have found higher lymph node involvement in younger patients [14, 40]. Again, these conflicting results may be explained by selection bias, as older patients with enlarged lymph nodes on imaging are less likely to undergo surgical treatment compared with younger patients. With respect to distant metastasis, the incidence appears to be consistent across age groups [32, 34, 40].

Grade

The Fuhrman grading system is the most widely used system. Increasing nuclear size and irregularity as well as nucleolar prominence are used to categorize tumors into four nuclear grades. Higher Fuhrman grade is associated with more advanced disease [41], and grade is an independent predictor of survival in RCC [42].

Some studies suggest that the proportion of patients with high-grade tumors (i.e., Fuhrman grade 3 or 4) increases with age [34, 35], others found the opposite [14], and still others failed to detect a significant association between tumor grade and age [32, 33, 40]. One study that developed a nomogram to predict whether renal tumors were indolent or potentially aggressive based on histological subtype and nuclear grade found that age was independently associated with aggressiveness, with the predicted likelihood of a potentially aggressive renal cancer increasing with advanced age [21].

Others

Increasing tumor size is strongly correlated with worse outcome after treatment [43, 44], prevalence of metastasis at diagnosis [45–47], and mortality [47]. Some studies have shown that tumor size at the time of surgical treatment increases with age, such that the proportion of tumors ≥6 cm increases from 49 % in patients ≤40 years old compared with 64 % of patients

≥80 years old [34] and that the mean tumor size increases from 2.65 cm in patients ≤40 years old to 2.89 cm in patients >60 years old [35]. This may reflect the fact that SRMs in elderly patients are more likely to be treated by active surveillance, thus increasing the size of tumors treated surgically in this age group.

Finally, the presence of symptoms related to the renal mass and a poor performance status correlate with worse prognosis for patients with RCC [48]. Although the presence of symptoms is similar among age groups [32, 33, 35], as one would expect, ECOG (Eastern Cooperative Oncology Group) performance status tends to be worse with age [34, 35].

Treatment of Localized Disease

The management of localized renal masses in older adults is complicated by a variety of important considerations including comorbidities and reduced functional reserve, shortened life expectancy, and an increased prevalence of chronic renal insufficiency. The biological aggressiveness of the tumor must also be taken into account, particularly for SRMs, of which 20 % are benign and only 20 % exhibit a potentially aggressive phenotype (Fig. 19.2).

Radical Nephrectomy

With RCC being radiation and chemotherapy resistant, surgery is the cornerstone of treatment. Open radical nephrectomy (RN), as described by Robson over 40 years ago, was previously considered the gold standard for treating clinically localized RCC [49]. This includes removal of the entire kidney, perinephric fat, regional lymph nodes, and ipsilateral adrenal gland. Although this offers excellent disease control, it has a substantial impact on renal function [50]. Over the last two decades, the introduction of minimally invasive or laparoscopic RN has led to fewer indications for open RN. The laparoscopic approach offers reduced perioperative morbidity and a more rapid convalescence compared to the open approach while maintaining equivalent cancer control [51, 52]. However, open and laparoscopic RN both have deleterious impact on renal function, and this is a major consideration in the elderly patient population.

The efficacy and safety of RN in elderly patients has been studied in a number of case series in the published literature. Many of these have concluded that RN appears to have morbidity and oncologic outcomes comparable to surgery in younger patients [53–55]. They found that age alone did not increase perioperative

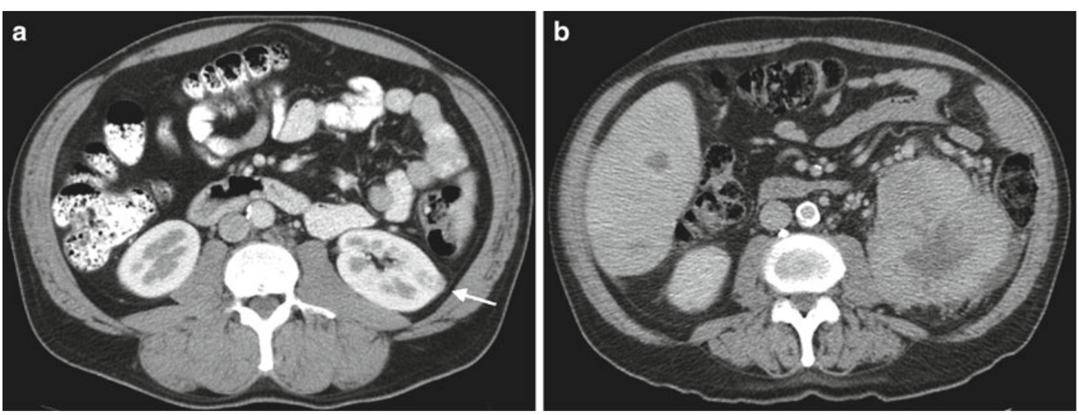


Fig. 19.2 Computed tomographic images of an SRM that has 20 % or greater likelihood of being benign, typically slow growth rate, and low metastatic potential (**a**) and a locally advanced renal mass with increased likelihood of high-grade malignancy and substantial metastatic potential (**b**), illustrating the difference in biological aggressiveness of renal tumors

Table 19.2 The effect of age on morbidity rates after nephrectomy by complication type for radical and partial nephrectomy

	Age category (%)				
Complication type	<50	50–59	60–69	70–79	≥80
Radical nephrectomy					
Overall	28.7	29.4	34.0	39.6	44.5
Cardiac	1.06	2.5	5.1	8.7	14.1
Respiratory	7.8	7.7	9.2	12.2	14.5
Vascular	6.8	9.3	10.7	12.3	14.2
Wound/bleeding	6.2	7.6	7.9	8.7	9.5
Genitourinary	7.3	5.9	6.7	7.8	10.9
Miscellaneous medical	5.4	7.0	9.3	11.6	12.8
Miscellaneous surgical	4.4	5.4	6.2	7.3	6.8
Nephrectomy specific	5.6	5.2	4.8	4.3	4.8
Partial nephrectomy					
Overall	28.4	30.5	35.2	42.3	52.8
Cardiac	0.7	1.9	4.8	8.9	15.8
Respiratory	6.1	6.5	8.1	8.8	14.2
Vascular	7.1	6.1	9.9	11.5	17.3
Wound/bleeding	4.6	4.5	7.2	8.3	14.2
Genitourinary	11.7	12.5	11.4	13.4	14.2
Miscellaneous medical	4.5	6.6	8.5	13.6	15.0
Miscellaneous surgical	3.2	2.9	4.2	5.0	11.0
Nephrectomy specific	7.4	6.1	8.7	6.8	10.2

Adapted from Abouassaly R et al. J Urol 186: 811, 2011 [60]

complications independent of comorbidity. With respect to laparoscopic nephrectomy in patients with advanced age, this approach has been shown to offer similar oncologic outcomes to their younger counterparts [56]. In elderly patients, compared with the open approach, laparoscopic RN has been shown to offer a quicker resumption of oral intake, decreased narcotic requirements, shorter hospital stay, and faster convalescence [57]. Although overall surgical morbidity is similar to that of younger patients, laparoscopy in older adults may result in a slightly longer hospital stay [58].

When the effect of age on the morbidity of RN is examined on a population level, a small but statistically significant increased complication rate is observed with increasing age (OR for 10-year increase in age 1.17, 95 % CI 1.04–1.32), even after adjusting for potential confounders such as comorbidity [59]. Similarly, a Canadian study found that the odds of experiencing an inhospital complication was 74 % higher in patients ≥80 years old compared with patients <50 years old [60]. They also found that although most complication types increased with age, the most dramatic increases were observed for medical complications (Table 19.2). For example, after RN cardiac complications developed in only 1.1 % of patients younger than 50 years compared with 14.1 % of those 80 years or older.

Partial Nephrectomy

Recently published data demonstrating an association between chronic kidney disease (CKD) and cardiovascular morbidity and mortality has highlighted the need for renal function preservation [61–64]. Partial nephrectomy (PN) is a treatment alternative in selected patients with RCC. Although this technique requires more technical expertise than RN, PN is now widely used. It involves occlusion of the renal vasculature, excision of the tumor with a rim of normal renal parenchyma, and reconstruction of the urinary collecting system and cortex. Traditionally, PN

Table 19.3 Comparison of complications and mortality for RN and PN in the published literature

	Randomized controlled trial [68]		Single institution report [69]		Surveillance, Epidemiology and End Result (SEER) data [101]		Department of Veterans Affairs administrative data [102]	
Observation period	1992–2003		1995–2002		1988–2004		1991–1998	
Procedure	RN	PN	RN	PN	RN	PN	RN	PN
Sample size	273	268	688	361	22,259	2,276	1,373	512
Overall complication rate (%)	12.9	22.8	3	9	N/A	N/A	15	16.2
30-day mortality (%)	0	0	0	0	0.9	0.4	2.0	1.6

N/A not available

was reserved for patients at high risk for renal failure following RN including those with a solitary kidney, bilateral tumors, and preexisting CKD [65]. Acceptable rates of disease control in this population encouraged more widespread use. There now exists substantial evidence to use PN for tumors less than 4 cm (stage T1a) where technically feasible, particularly in those with other risk factors for CKD such as diabetes mellitus or hypertension [66]. For patients with T1a tumors, the 5-year disease-specific survival rate is over 90 % for both PN and RN [44], and 10-year disease-specific survival rates for PN of 88–97 % have been reported [66, 67]. PN is, however, associated with a slightly higher complication rate than RN [68–70]. Nevertheless, the majority of these complications are classified as minor, and no difference in mortality or long-term morbidity has been observed [71, 72]. Recently published clinical guidelines from the American Urological Association (AUA) for the management of SRMs suggest that PN be considered a standard of care and that RN should be reserved for those in whom PN is not technically feasible [73]. Although publications supporting the use of PN are increasing in number, they rely on retrospective data making comparisons between RN and PN susceptible to selection bias, despite mathematical adjustment for measured confounders. In fact, a European randomized trial found that for tumors less than 5 cm in size, PN did not demonstrate an advantage with respect to overall survival (OS) (10-year OS rates of 81.1 % for RN and 75.7 % for PN) [74]. However, in the latter study the effect of intervention on quality of life was not addressed.

As mentioned above, studies comparing the morbidity after RN and PN have consistently shown higher complication rates after PN (Table 19.3). However, many also showed that the unadjusted inhospital mortality is higher for RN, likely because of higher comorbidity and age in this treatment group. Again, the data indicate that the morbidity associated with PN increases with age [59, 60]. Although some have shown that this increased morbidity was similar for PN and RN [59], others have suggested that the increase in complications and mortality is more dramatic for PN (Fig. 19.3). Nonetheless, most believe that given the potential advantages of renal function preservation, the benefits of PN outweigh the risks in the treatment of renal tumors in elderly patients [59].

Ablative Therapies

Contemporary technology has provided an alternative to tumor excision in the form of thermal ablation. Currently available tissue ablative techniques include radiofrequency ablation (RFA) and cryoablation. Ablation is performed either percutaneously under image guidance (usually CT) or under direct vision via the laparoscopic approach. Although these modalities show promise in terms of morbidity and intermediate-term oncologic efficacy [75], long-term follow-up is not yet available. Furthermore, the surrogate outcome measures used to evaluate treatment success, such as loss of contrast enhancement on imaging, have recently come into question [76]. Salvage of ablation failures is another ongoing

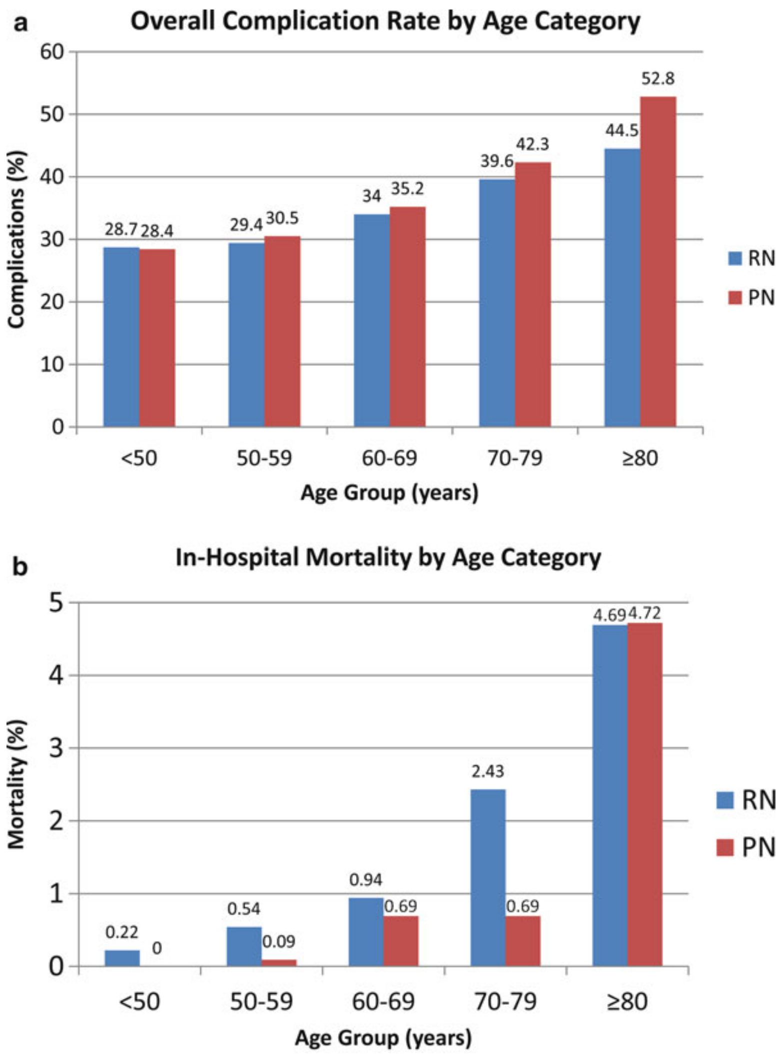


Fig. 19.3 (**a**) Overall complication rate by age category. (**b**) Inhospital mortality by age category

concern, because this can be problematic due to treatment-associated fibrosis that can complicate surgical excision.

A meta-analysis comparing tumor ablation with PN has demonstrated significantly increased local progression rates for cryoablation (relative risk (RR) = 7.45) and RFA (RR = 18.23) [77]. However, no statistical differences were detected in the incidence of metastatic progression regardless of whether lesions were excised or ablated. At the present time, ablative therapies are probably best reserved for patients with limited life expectancy (such as the very elderly) or significant medical comorbidity or those who either refuse or are not considered surgical candidates. In this setting, thermal ablation offers a way to offer proactive treatment with less risk than surgical excision.

Active Surveillance

The seemingly low rate of disease progression of SRMs indicates that delayed treatment or the complete absence of treatment may be a reasonable management option for many elderly patients. The significant number of renal masses diagnosed only at autopsy suggests that many patients die *with* disease rather than *of* disease [78]. The approach of following renal masses with serial imaging and only intervening with evidence of disease progression has been termed active surveillance (AS). Similar to ablative therapies, this is usually reserved for older patients or those at high risk for surgical intervention [79]. A limitation of this approach is the lack of a validated trigger for active treatment. However, a period of surveillance of SRMs of up to several years seems to be associated with a low risk of progression to incurable disease while maintaining most therapeutic options [80].

One study specifically examined treatment outcomes in clinical T1 renal tumors in elderly patients (≥75 years of age) and compared RN, nephron-sparing interventions (PN, cryoablation, and RFA), and AS [81]. The authors found that surgical management of clinically localized renal cortical tumors was not associated with increased survival. Most of the deaths in these patients were due to cardiovascular causes rather than from cancer progression. They suggested that current paradigms lead to overtreatment of localized renal tumors and that AS should be strongly considered in patients with limited life expectancy.

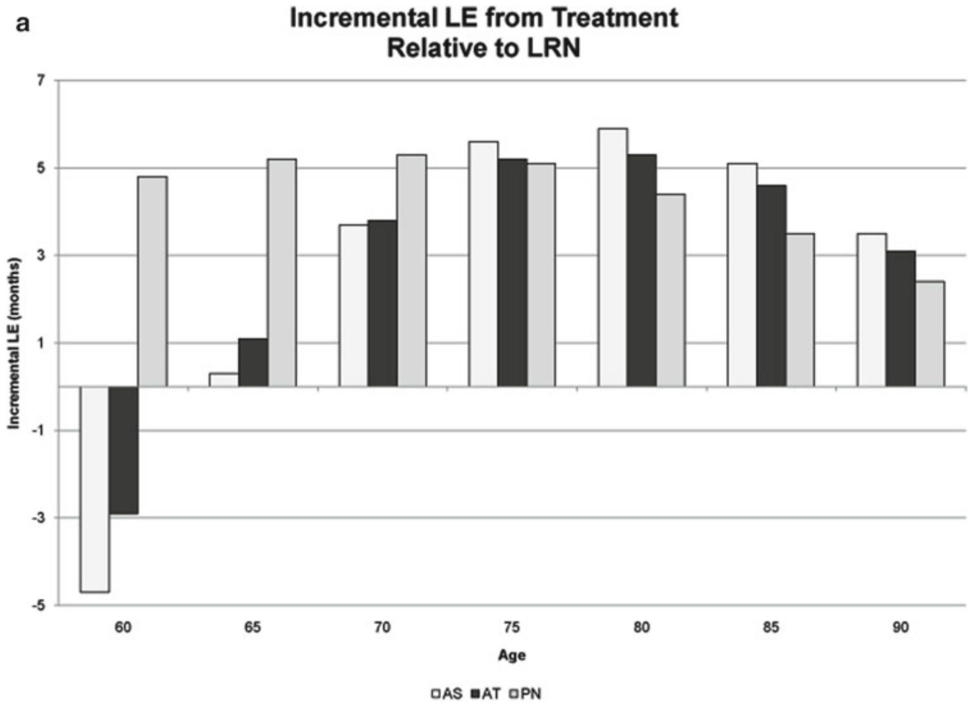
Age and Treatment Choice

Using available published data and taking into account the uncertainty associated with outcomes, one study compared treatment options using a Markov decision-analytic model to determine the optimal treatment modality for patients with SRMs [82]. They found that for a 60-year-old patient with an incidentally detected SRM, PN offers higher life expectancy than RN, ablative therapy, or AS. In older patients, however, AS appears to offer the best life expectancy and quality-adjusted life expectancy, with ablative therapies close behind, suggesting that one should favor less invasive management approaches with the goal of renal function preservation in patients with advanced age [82] (Fig. 19.4).

Treatment of Metastatic Disease

Approximately one-third of patients with RCC have metastatic disease at the time of initial presentation, and of those with apparent localized disease, 30–40 % will subsequently develop distant metastases [83]. Removal of the affected kidney in the setting of metastatic RCC (cytoreductive nephrectomy) plays an integral role in the management of this condition. Two randomized trials demonstrated a survival benefit for cytoreductive nephrectomy and immunotherapy (interferon alpha) over immunotherapy alone [84, 85]. In a combined analysis of these trials, median overall survival was 13.6 months for nephrectomy plus interferon compared with 7.8 months for interferon alone (hazard ratio 0.69, 95 % CI 0.55–0.87) [86]. Unfortunately, in these studies no data were presented specifically examining outcomes in the older patient group. One article comparing the results of cytoreductive nephrectomy in elderly patients (median age 78 years) to younger patients (median age 57 years) found that the perioperative mortality was significantly higher in elderly patients (20.8 % vs. 1.1 %) [87]. Overall survival also appeared to be worse in older adults (median 16.6 months vs. 13.7 months in younger patients), but this did not reach statistical significance. Exact chronological age cutoffs for consideration of cytoreductive nephrectomy remain controversial, and physiologic age is the more important consideration.

Until relatively recently, few options existed for patients requiring systemic therapy for metastatic RCC. Immunotherapy in the form of interferon alpha and interleukin-2 were the only agents with any measureable response, usually at the expense of significant toxicity. Currently, the use of targeted therapy such as tyrosine kinase inhibitors like sunitinib or sorafenib or other agents that target the VEGF or MTOR pathways has revolutionized the treatment of metastatic RCC. Many of these agents lead to improved progression-free survival [88, 89] and overall survival [90]. With respect to outcomes of these agents in elderly patients, data from TARGET



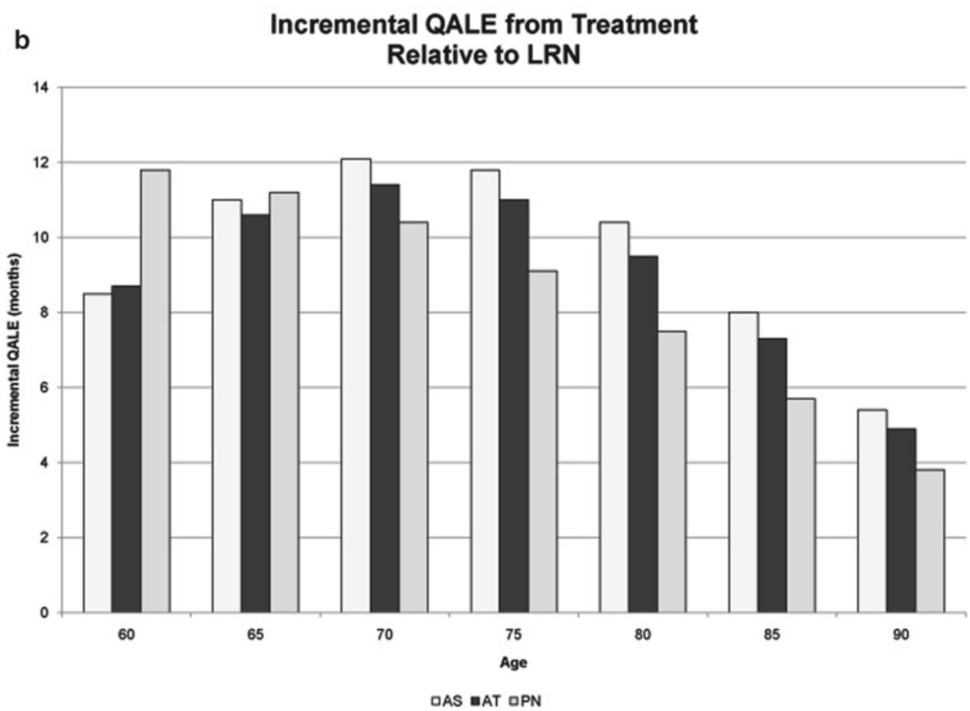


Fig. 19.4 (**a**) Incremental life expectancy (LE) and (**b**) quality-adjusted life expectancy (QALE) gains by age at presentation for AS, ablative therapy, and PN compared to LRN [82]

(Treatment Approach in Renal Cancer Global Evaluation Trial) showed that in a subset analysis of patients with metastatic RCC treated with sorafenib, outcomes in older compared with younger patients (≥70 years vs. <70 years) were similar with respect to oncologic outcomes, adverse events, and improvement in quality of life [91]. However, rates of treatment discontinuation (21.4 % vs. 8.1 %, $p = 0.0015$) and the incidence of grade 3–5 cardiovascular events (5 % vs. 0 %, $p = 0.0020$) differed in favor of younger patients. Data for other targeted agents (i.e., sunitinib and everolimus) in elderly groups are also becoming available and have yielded similar conclusions [92, 93].

Additionally, a number of prognostic models have been developed to integrate clinical and pathologic information into a schema that better predicts survival or prognosis than staging alone [94, 95]. The incorporation of age as a variable in these prognostic models has failed to increase their predictive accuracy, suggesting that age does not appear to be independently associated with outcome in patients with advanced renal cell carcinoma.

Effect of Age on Disease Outcomes

Patients with early-stage RCC usually have a favorable prognosis, with disease-specific survival rate over 90 % for stage T1 disease [67]. Disease recurrence is rare and estimated to occur in only a few percent of treated patients [96]. One study examining disease recurrence in 710 patients with pathologic T1 RCC treated with radical nephrectomy found that age at diagnosis was independently related to disease recurrence on multivariable analysis [97]. They found that patients over 65 years of age had nearly 9 times the risk of having a recurrence compared with patents 65 years and younger. Others have presented similar results, with 10-year recurrence-free survival rates of 100 % for patients ≤40 years old, 95.7 % for patients 41–60 years old, and 79.0 % for patients >60 years old [35]. Median time to recurrence was also found to differ in another study, 32.4 months for patients ≤40 years old compared with 23.5 months for patients 58–61 years old (hazard ratio (HR) 2.23, 95 % CI 1.45–4.79) [40].

Age has also been found to be associated with disease-specific survival in many studies, with younger patients demonstrating improved survival compared with older patients [32, 40, 98]. For pathologically localized disease (i.e., pT1–pT2), one study estimated 5-year CSS of 99.0 % for patients ≤45 years old compared with 95.4 % for patients >45 years old [33]. For all disease stages, another study estimated cancer-specific survival (CSS) rates at 5 and 10 years for patients 18–40 years old were 75.3 % and 69.6 %, respectively, compared with 71.9 % and 62.3 %, respectively, for patients 60–70 years old [32]. They found that younger patients had a higher incidence of low-stage and cystic tumors and postulated that this may have contributed to the improved CSS in these patients.

When survival is examined on a population level, similar findings emerge. One study examining outcomes for localized RCC using data from the Surveillance, Epidemiology, and End Results (SEER) database found that age was not a significant predictor of CSS for patients with small (less than 4 cm) or large (greater than 7 cm) tumors [99]. However, a statistically significant trend toward lower survival with increasing age was demonstrated in patients with medium-size tumors (4–7 cm). A more recent study using data from SEER examined the effect of age on CSS using competing-risks regression models [100]. They found that age categories 50–59, 60–69, 70–79, and ≥80 years portend a 1.4-, 1.5-, 1.6-, and 1.9-fold higher risk of cancer-specific mortality than age category <50 years, respectively. They also observed that the effect of age on cancer-specific mortality was most pronounced for stage 1, low-grade RCC, and was nearly absent in patients with stage 2–4 RCC. Several potential explanations for these findings have been proposed. These include differences in tumor biology, immune status, intensity of medical evaluation or treatment, and access to care with age. At the current time, however, these explanations are purely speculative, and further study is needed to confirm and determine potential causes for the observed worse survival in older patients with RCC.

Summary

The incidence of serendipitously detected SRMs is rising, particularly in elderly patients who often have comorbid disease processes, preexisting CKD, and reduced life expectancy. Prognostic factors such as tumor histology, grade, and stage may differ with age, although studies are inconsistent and likely influenced by selection biases. Minimally invasive techniques such as laparoscopy and percutaneous tumor ablation are increasingly being used, and active surveillance with delayed intervention is gaining acceptance, particularly in those with significant comorbidity or advanced age. There is increasing evidence that older patients with localized RCC have an increased risk of disease recurrence and cancer-specific mortality after treatment, although the reasons for this are not clear and further study will be required. Although the treatment of metastatic RCC has been revolutionized with the introduction of recently approved targeted therapies, these may not be as well tolerated in older patients. Further research into the impact of age on tumor biology and patient evaluation and management should be prioritized moving forward.

References

1. American Cancer Society. Cancer Facts and Figures 2011. American Cancer Society (2011). Accessed 17 Aug 2011.
2. Gupta K, Miller JD, Li JZ, Russell MW, Charbonneau C. Epidemiologic and socioeconomic burden of metastatic renal cell carcinoma (mRCC): a literature review. Cancer Treat Rev. 2008;34(3):193–205.
3. Lipworth L, Tarone RE, McLaughlin JK. The epidemiology of renal cell carcinoma. J Urol. 2006;176(6 Pt 1):2353–8.
4. Pantuck AJ, Zisman A, Belldegrun AS. The changing natural history of renal cell carcinoma. J Urol. 2001;166(5):1611–23.
5. Nguyen CT, Campbell SC. Staging of renal cell carcinoma: past, present, and future. Clin Genitourin Cancer. 2006;5(3):190–7.
6. Chow WH, Devesa SS, Warren JL, Fraumeni Jr JF. Rising incidence of renal cell cancer in the United States. JAMA. 1999;281(17):1628–31.
7. Katz DL, Zheng T, Holford TR, Flannery J. Time trends in the incidence of renal carcinoma: analysis of Connecticut tumor registry data, 1935–1989. Int J Cancer. 1994;58(1):57–63.
8. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet. 2008;371(9612):569–78.
9. Clague J, Lin J, Cassidy A, et al. Family history and risk of renal cell carcinoma: results from a case-control study and systematic meta-analysis. Cancer Epidemiol Biomarkers Prev. 2009;18(3):801–7.
10. Romanenko A, Morell-Quadreny L, Nepomnyaschy V, Vozianov A, Llombart-Bosch A. Pathology and proliferative activity of renal-cell carcinomas (RCCS) and renal oncocytomas in patients with different radiation exposure after the Chernobyl accident in Ukraine. Int J Cancer. 2000;87(6):880–3.
11. Dhote R, Thiounn N, Debre B, Vidal-Trecan G. Risk factors for adult renal cell carcinoma. Urol Clin North Am. 2004;31(2):237–47.
12. Rini BI, Campbell SC, Escudier B. Renal cell carcinoma. Lancet. 2009;373(9669):1119–32.
13. Abouassaly R. Predictors of partial nephrectomy utilization and inequities of care in the treatment of renal cell carcinoma in Canada. [M.Sc. Thesis]. Toronto, Canada: University of Toronto; 2010.
14. Jun C, Zhishun X, Xianzhou J, Qiang F, Jin W. Association between age and clinical characteristics of renal cell carcinoma in adult patients. Int J Urol. 2006;13(5):515–9.
15. Jayson M, Sanders H. Increased incidence of serendipitously discovered renal cell carcinoma. Urology. 1998;51(2):203–5.
16. Luciani LG, Cestari R, Tallarigo C. Incidental renal cell carcinoma-age and stage characterization and clinical implications: study of 1092 patients (1982–1997). Urology. 2000;56(1):58–62.
17. Gold PJ, Fefer A, Thompson JA. Paraneoplastic manifestations of renal cell carcinoma. Semin Urol Oncol. 1996;14(4):216–22.
18. Bach AM, Zhang J. Contemporary radiologic imaging of renal cortical tumors. Urol Clin North Am. 2008;35(4):593–604.
19. Rothman J, Egleston B, Wong YN, Iffrig K, Lebovitch S, Uzzo RG. Histopathological characteristics of localized renal cell carcinoma correlate with tumor size: a SEER analysis. J Urol. 2009;181(1):29–33. discussion 33–4.
20. Skolarus TA, Serrano MF, Berger DA, et al. The distribution of histological subtypes of renal tumors by decade of life using the 2004 WHO classification. J Urol. 2008;179(2):439–43.
21. Lane BR, Babineau D, Kattan MW, et al. A preoperative prognostic nomogram for solid enhancing renal tumors 7 cm or less amenable to partial nephrectomy. J Urol. 2007;178(2):429–34.
22. Eggener SE, Rubenstein JN, Smith ND, et al. Renal tumors in young adults. J Urol. 2004;171(1):106–10.

23. Snyder ME, Bach A, Kattan MW, Raj GV, Reuter VE, Russo P. Incidence of benign lesions for clinically localized renal masses smaller than 7 cm in radiological diameter: influence of sex. J Urol. 2006;176(6 Pt 1):2391–5.
24. Novick AC, Campbell SC, et al. Guideline for management of the clinical stage 1 renal mass. Linthicum, MD: American Urological Association Education and Research; 2009.
25. Seaman E, Goluboff ET, Ross S, Sawczuk IS. Association of radionuclide bone scan and serum alkaline phosphatase in patients with metastatic renal cell carcinoma. Urology. 1996;48(5):692–5.
26. Herts BR, Baker ME. The current role of percutaneous biopsy in the evaluation of renal masses. Semin Urol Oncol. 1995;13(4):254–61.
27. Schmidbauer J, Remzi M, Memarsadeghi M, et al. Diagnostic accuracy of computed tomography-guided percutaneous biopsy of renal masses. Eur Urol. 2008;53(5):1003–11.
28. Lane BR, Samplaski MK, Herts BR, Zhou M, Novick AC, Campbell SC. Renal mass biopsy–a renaissance? J Urol. 2008;179(1):20–7.
29. Storkel S, Eble JN, Adlakha K, et al. Classification of renal cell carcinoma: workgroup No. 1. Union Internationale Contre le Cancer (UICC) and the American Joint Committee on Cancer (AJCC). Cancer. 1997;80(5):987–9.
30. Teloken PE, Thompson RH, Tickoo SK, et al. Prognostic impact of histological subtype on surgically treated localized renal cell carcinoma. J Urol. 2009;182(5):2132–6.
31. de Peralta-Venturina M, Moch H, Amin M, et al. Sarcomatoid differentiation in renal cell carcinoma: a study of 101 cases. Am J Surg Pathol. 2001; 25(3):275–84.
32. Gillett MD, Cheville JC, Karnes RJ, et al. Comparison of presentation and outcome for patients 18 to 40 and 60 to 70 years old with solid renal masses. J Urol. 2005;173(6):1893–6.
33. Komai Y, Fujii Y, Iimura Y, et al. Young age as favorable prognostic factor for cancer-specific survival in localized renal cell carcinoma. Urology. 2011; 77(4):842–7.
34. Verhoest G, Veillard D, Guille F, et al. Relationship between age at diagnosis and clinicopathologic features of renal cell carcinoma. Eur Urol. 2007;51(5):1298–304.
35. Jeong IG, Yoo CH, Song K, et al. Age at diagnosis is an independent predictor of small renal cell carcinoma recurrence-free survival. J Urol. 2009;182(2): 445–50.
36. Nguyen CT, Lane BR, Kaouk JH, et al. Surgical salvage of renal cell carcinoma recurrence after thermal ablative therapy. J Urol. 2008;180(1):104–9.
37. Ficarra V, Schips L, Guille F, et al. Multiinstitutional European validation of the 2002 TNM staging system in conventional and papillary localized renal cell carcinoma. Cancer. 2005;104(5):968–74.
38. Frank I, Blute ML, Leibovich BC, Cheville JC, Lohse CM, Zincke H. Independent validation of the 2002 American Joint Committee on Cancer primary tumor classification for renal cell carcinoma using a large, single institution cohort. J Urol. 2005;173(6): 1889–92.
39. Salama ME, Guru K, Stricker H, et al. pT1 substaging in renal cell carcinoma: validation of the 2002 TNM staging modification of malignant renal epithelial tumors. J Urol. 2005;173(5):1492–5.
40. Sanchez-Ortiz RF, Rosser CJ, Madsen LT, Swanson DA, Wood CG. Young age is an independent prognostic factor for survival of sporadic renal cell carcinoma. J Urol. 2004;171(6 Pt 1):2160–5.
41. Bretheau D, Lechevallier E, de Fromont M, Sault MC, Rampal M, Coulange C. Prognostic value of nuclear grade of renal cell carcinoma. Cancer. 1995;76(12):2543–9.
42. Moch H, Gasser T, Amin MB, Torhorst J, Sauter G, Mihatsch MJ. Prognostic utility of the recently recommended histologic classification and revised TNM staging system of renal cell carcinoma: a Swiss experience with 588 tumors. Cancer. 2000;89(3):604–14.
43. Crispen PL, Boorjian SA, Lohse CM, et al. Outcomes following partial nephrectomy by tumor size. J Urol. 2008;180(5):1912–7.
44. Hafez KS, Fergany AF, Novick AC. Nephron sparing surgery for localized renal cell carcinoma: impact of tumor size on patient survival, tumor recurrence and TNM staging. J Urol. 1999;162(6):1930–3.
45. Thompson RH, Kurta JM, Kaag M, et al. Tumor size is associated with malignant potential in renal cell carcinoma cases. J Urol. 2009;181(5):2033–6.
46. Lughezzani G, Jeldres C, Isbarn H, et al. Tumor size is a determinant of the rate of stage T1 renal cell cancer synchronous metastasis. J Urol. 2009; 182(4):1287–93.
47. Nguyen MM, Gill IS. Effect of renal cancer size on the prevalence of metastasis at diagnosis and mortality. J Urol. 2009;181(3):1020–7.
48. Lee CT, Katz J, Fearn PA, Russo P. Mode of presentation of renal cell carcinoma provides prognostic information. Urol Oncol. 2002;7(4):135–40.
49. Robson CJ, Churchill BM, Anderson W. The results of radical nephrectomy for renal cell carcinoma. J Urol. 1969;101(3):297–301.
50. Huang WC, Levey AS, Serio AM, et al. Chronic kidney disease after nephrectomy in patients with renal cortical tumours: a retrospective cohort study. Lancet Oncol. 2006;7(9):735–40.
51. Berger A, Brandina R, Atalla MA, et al. Laparoscopic radical nephrectomy for renal cell carcinoma: oncological outcomes at 10 years or more. J Urol. 2009;182(5):2172–6.
52. Hollingsworth JM, Miller DC, Dunn RL, Montgomery JS, Wolf Jr JS. Cost trends for oncological renal surgery: support for a laparoscopic standard of care. J Urol. 2006;176(3):1097–101.

53. Berdjis N, Hakenberg OW, Novotny V, Froehner M, Wirth MP. Treating renal cell cancer in the elderly. BJU Int. 2006;97(4):703–5.
54. Staehler M, Haseke N, Stadler T, et al. Renal surgery in the elderly: morbidity in patients aged >75 years in a contemporary series. BJU Int. 2008;102(6): 684–7.
55. Roos FC, Hampel C, Thuroff JW. Renal cancer surgery in the elderly. Curr Opin Urol. 2009;19(5):459–64.
56. Harano M, Eto M, Yokomizo A, Tatsugami K, Hamaguchi M, Naito S. The efficacy of laparoscopic radical nephrectomy for renal cell cancer in the elderly: an oncological outcome analysis. Int J Urol. 2008;15(7):577–81.
57. Hsu TH, Gill IS, Fazeli-Matin S, et al. Radical nephrectomy and nephroureterectomy in the octogenarian and nonagenarian: comparison of laparoscopic and open approaches. Urology. 1999;53(6): 1121–5.
58. Lai FC, Kau EL, Ng CS, Fuchs GJ. Laparoscopic nephrectomy outcomes of elderly patients in the 21st century. J Endourol. 2007;21(11):1309–13.
59. Lowrance WT, Yee DS, Savage C, et al. Complications after radical and partial nephrectomy as a function of age. J Urol. 2010;183(5):1725–30.
60. Abouassaly R, Alibhai SM, Tomlinson GA, Urbach DR, Finelli A. The effect of age on the morbidity of kidney surgery. J Urol. 2011;186(3):811–6.
61. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med. 2004;351(13):1296–305.
62. Ford I, Bezlyak V, Stott DJ, et al. Reduced glomerular filtration rate and its association with clinical outcomes in older patients at risk of vascular events: secondary analysis. PLoS Med. 2009;6(1):76–82.
63. Rifkin DE, Shlipak MG, Katz RDP, et al. Rapid kidney function decline and mortality risk in older adults. Arch Intern Med. 2008;168(20):2212–8.
64. Shlipak MG, Katz R, Sarnak MJ, et al. Cystatin C and prognosis for cardiovascular and kidney outcomes in elderly persons without chronic kidney disease. Ann Intern Med. 2006;145(4):237–46.
65. Novick AC, Derweesh I. Open partial nephrectomy for renal tumours: current status. BJU Int. 2005;95 Suppl 2:35–40.
66. Herr HW. Partial nephrectomy for unilateral renal carcinoma and a normal contralateral kidney: 10-year followup. J Urol. 1999;161(1):33–4.
67. Fergany AF, Hafez KS, Novick AC. Long-term results of nephron sparing surgery for localized renal cell carcinoma: 10-year followup. J Urol. 2000;163(2):442–5.
68. Van Poppel H, Da Pozzo L, Albrecht W, Matveev V, Bono A, Borkowski A, Marechal JM, Klotz L, Skinner E, Keane T, Claessens I, Sylvester R, European Organization for Research and Treatment of Cancer (EORTC), National Cancer Institute of Canada Clinical Trials Group (NCIC CTG), Southwest Oncology Group (SWOG), Eastern Cooperative Oncology Group (ECOG). A prospective randomized EORTC intergroup phase 3 study comparing the complications of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. Eur Urol. 2007;51(6): 1606–15.
69. Stephenson AJ, Hakimi AA, Snyder ME, Russo P. Complications of radical and partial nephrectomy in a large contemporary cohort. J Urol. 2004;171(1): 130–4.
70. Lau WK, Blute ML, Weaver AL, Torres VE, Zincke H. Matched comparison of radical nephrectomy vs nephron-sparing surgery in patients with unilateral renal cell carcinoma and a normal contralateral kidney. Mayo Clin Proc. 2000;75(12):1236–42.
71. Campbell SC, Novick AC, Streem SB, Klein EA. Management of renal cell carcinoma with coexistent renal artery disease. J Urol. 1993;150(3):808–13.
72. Thompson RH, Leibovich BC, Lohse CM, Zincke H, Blute ML. Complications of contemporary open nephron sparing surgery: a single institution experience. J Urol. 2005;174(3):855–8.
73. Campbell SC, Novick AC, Belldegrun A, et al. Guideline for management of the clinical T1 renal mass. J Urol. 2009;182(4):1271–9.
74. Van Poppel H, Da Pozzo L, Albrecht W, et al. A prospective, randomised EORTC intergroup phase 3 study comparing the oncologic outcome of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. Eur Urol. 2011;59(4):543–52.
75. Stein RJ, Kaouk JH. Renal cryotherapy: a detailed review including a 5-year follow-up. BJU Int. 2007;99(5 Pt B):1265–70.
76. Weight CJ, Kaouk JH, Hegarty NJ, et al. Correlation of radiographic imaging and histopathology following cryoablation and radio frequency ablation for renal tumors. J Urol. 2008;179(4):1277–81.
77. Kunkle DA, Egleston BL, Uzzo RG. Excise, ablate or observe: the small renal mass dilemma–a meta-analysis and review. J Urol. 2008;179(4):1227–33.
78. Mindrup SR, Pierre JS, Dahmoush L, Konety BR. The prevalence of renal cell carcinoma diagnosed at autopsy. BJU Int. 2005;95(1):31–3.
79. Abouassaly R, Lane BR, Novick AC. Active surveillance of renal masses in elderly patients. J Urol. 2008;180(2):505–8.
80. Chawla SN, Crispen PL, Hanlon AL, Greenberg RE, Chen DY, Uzzo RG. The natural history of observed enhancing renal masses: meta-analysis and review of the world literature. J Urol. 2006; 175(2):425–31.
81. Lane BR, Abouassaly R, Gao T, et al. Active treatment of localized renal tumors may not impact overall survival in patients aged 75 years or older. Cancer. 2010;116(13):3119–26.
82. Abouassaly R, Yang S, Finelli A, Kulkarni GS, Alibhai SM. What is the best treatment strategy for incidentally detected small renal masses? A decision analysis. BJU Int. 2011;108(8 Pt 2):E223–31.

83. Bukowski RM. Natural history and therapy of metastatic renal cell carcinoma: the role of interleukin-2. Cancer. 1997;80(7):1198–220.
84. Flanigan RC, Salmon SE, Blumenstein BA, et al. Nephrectomy followed by interferon alfa-2b compared with interferon alfa-2b alone for metastatic renal-cell cancer. N Engl J Med. 2001;345(23): 1655–9.
85. Mickisch GH, Garin A, van Poppel H, de Prijck L, Sylvester R, European Organisation for Research and Treatment of Cancer (EORTC) Genitourinary Group. Radical nephrectomy plus interferon-alfa-based immunotherapy compared with interferon alfa alone in metastatic renal-cell carcinoma: a randomised trial. Lancet. 2001;358(9286): 966–70.
86. Flanigan RC, Mickisch G, Sylvester R, Tangen C, Van Poppel H, Crawford ED. Cytoreductive nephrectomy in patients with metastatic renal cancer: a combined analysis. J Urol. 2004;171(3):1071–6.
87. Kader AK, Tamboli P, Luongo T, et al. Cytoreductive nephrectomy in the elderly patient: the M.D. Anderson Cancer Center experience. J Urol. 2007;177(3):855–60.
88. Motzer RJ, Hutson TE, Tomczak P, et al. Sunitinib versus interferon alfa in metastatic renal-cell carcinoma. N Engl J Med. 2007;356(2):115–24.
89. Escudier B, Eisen T, Stadler WM, et al. Sorafenib in advanced clear-cell renal-cell carcinoma. N Engl J Med. 2007;356(2):125–34.
90. Motzer RJ, Hutson TE, Tomczak P, et al. Overall survival and updated results for sunitinib compared with interferon alfa in patients with metastatic renal cell carcinoma. J Clin Oncol. 2009;27(22): 3584–90.
91. Eisen T, Oudard S, Szczylik C, et al. Sorafenib for older patients with renal cell carcinoma: subset analysis from a randomized trial. J Natl Cancer Inst. 2008;100(20):1454–63.
92. Porta C, Calvo E, Climent MA, et al. Efficacy and safety of everolimus in elderly patients with metastatic renal cell carcinoma: an exploratory analysis of the outcomes of elderly patients in the RECORD-1 trial. Eur Urol. 2012;61(4):826–33.
93. Hutson TE, Bukowski RM, Rini BI, et al. A pooled analysis of the efficacy and safety of sunitinib in elderly patients with metastatic renal cell carcinoma. J Clin Oncol. 2011;29:4604. suppl; abstrt.
94. Zisman A, Pantuck AJ, Dorey F, et al. Improved prognostication of renal cell carcinoma using an integrated staging system. J Clin Oncol. 2001;19(6):1649–57.
95. Heng DY, Xie W, Regan MM, et al. Prognostic factors for overall survival in patients with metastatic renal cell carcinoma treated with vascular endothelial growth factor-targeted agents: results from a large, multicenter study. J Clin Oncol. 2009; 27(34):5794–9.
96. Eggener SE, Yossepowitch O, Pettus JA, Snyder ME, Motzer RJ, Russo P. Renal cell carcinoma recurrence after nephrectomy for localized disease: predicting survival from time of recurrence. J Clin Oncol. 2006;24(19):3101–6.
97. Muramaki M, Miyake H, Sakai I, et al. Age at diagnosis as a powerful predictor for disease recurrence after radical nephrectomy in Japanese patients with pT1 renal cell carcinoma. Int J Urol. 2011; 18(2):121–5.
98. Denzinger S, Otto W, Burger M, et al. Sporadic renal cell carcinoma in young and elderly patients: are there different clinicopathological features and disease specific survival rates? World J Surg Oncol. 2007;5:16.
99. Scoll BJ, Wong YN, Egleston BL, Kunkle DA, Saad IR, Uzzo RG. Age, tumor size and relative survival of patients with localized renal cell carcinoma: a surveillance, epidemiology and end results analysis. J Urol. 2009;181(2):506–11.
100. Sun M, Abdollah F, Bianchi M, et al. A stage-for-stage and grade-for-grade analysis of cancer-specific mortality rates in renal cell carcinoma according to age: a competing-risks regression analysis. Eur Urol. 2011;60(6):1152–9.
101. Cloutier V, Capitanio U, Zini L, et al. Thirty-day mortality after nephrectomy: clinical implications for informed consent. Eur Urol. 2008;56(6): 998–1003.
102. Corman JM, Penson DF, Hur K, et al. Comparison of complications after radical and partial nephrectomy: results from the National Veterans Administration Surgical Quality Improvement Program. BJU Int. 2000;86(7):782–9.

20 Penis, Testis, Urethra, and Other Genitourinary Malignancies

Joshua Griffin and Moben Mirza

Introduction

There are other urologic malignancies that can be seen in the geriatric population. Of those discussed in this chapter, penile cancers are likely the most common that will be encountered in this age group, and early diagnosis and treatment are essential in order to optimize outcomes. Testicular neoplasms, also discussed herein, are not as common but do occur and are usually associated with a good prognosis, although secondary malignancies at this site require different treatment algorithms compared to germ cell tumors. Urethral cancers of both the male and female are exceedingly rare and associated with a poor prognosis unless diagnosed at an early stage. Evaluation and management for these cancers is not different in other age groups; however, comorbid diseases may complicate treatment and outcomes. Lastly, within this group long-term complications of radiation therapy are increasingly seen affecting other organ systems as well as health-related quality of life.

J. Griffin, M.D.
Department of Urology, University of Kansas Medical Center, Kansas City, KS, USA

M. Mirza, M.D. (✉)
Department of Urology, University of Kansas Hospitals and Clinics, Kansas City, KS, USA
e-mail: mmirza@kumc.edu

Testicular Neoplasms

Epidemiology

There is a worldwide geographic variation for rates of testicular cancer. The highest reported incidence is in the European countries and the lowest in African and Asian countries. In the USA, the age-adjusted incidence in 2008 was 5.5 cases 100,000 population. The National Cancer Institute estimated that approximately 8,000 new cases of testicular cancer were diagnosed in 2011, accounting for 350 deaths [1]. Based on Surveillance, Epidemiology and End Results (SEER) data from 13 cancer registries in the USA, the incidence peaks in the fourth decade and steeply declines thereafter (Fig. 20.1). White men have greater than a threefold increased incidence of testicular cancer compared to black men [2].

Risk Factors

There are several known factors which may contribute to the development of testicular cancer including cryptorchidism, gonadal dysgenesis, family history, and prior history of testicular germ cell cancer. Other risk factors include male infertility and prenatal exposures. These risk factors are important when obtaining a history in all patients including elderly men.

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_20,

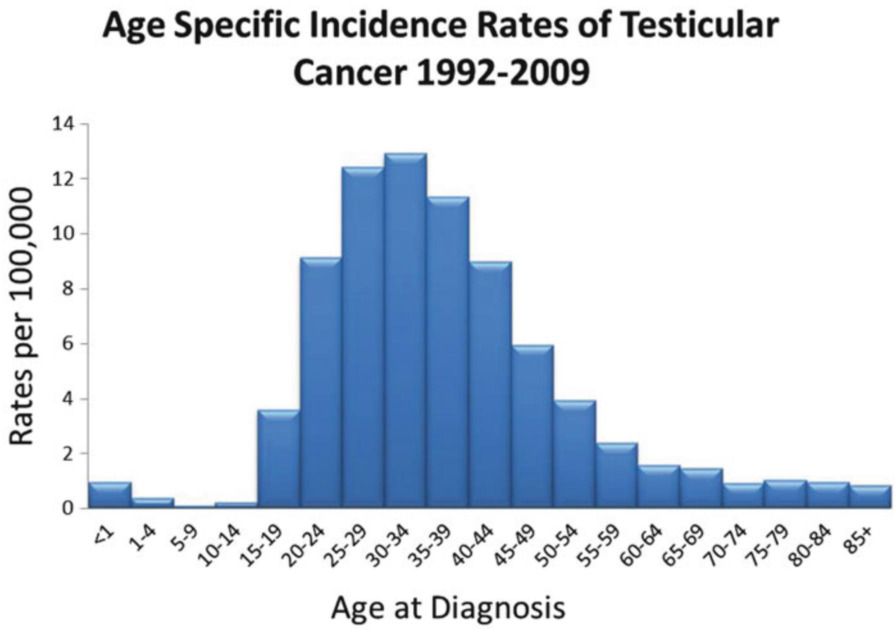


Fig. 20.1 Incidence rates of testicular cancer by age in the USA (From SEER, Surveillance, Epidemiology, and End Results (SEER) Program Fast Stats: An interactive tool for access to SEER cancer statistics. Surveillance Research Program, National Cancer Institute. http://seer.cancer.gov/faststats (Accessed on 9-28-2012))

Cryptorchidism is the most common genital anomaly in boys. Factors that contribute to the development of testicular cancer in the undescended testicle are poorly understood, but mechanisms involving genetic and environmental factors have both been proposed. A meta-analysis of over 20 publications that evaluated the association between undescended testicle and testicular cancer found an overall relative risk of 4.8 (95 % CI 5.0–5.7) [3]. Furthermore, another study has demonstrated that a history of undescended testicle increases the risk of a contralateral germ cell tumor (GCT), although to a lesser degree (RR 1.74) [4]. It has previously been thought that orchiopexy has no effect on future development of GCT. However, Pettersson and colleagues reported on a long-term cohort of over 16,000 males treated with orchiopexy and found that those who underwent treatment before 13 years of age had a significantly reduced relative risk of testicular cancer compared to those who were older (2.23 vs. 5.40) [5]. These data suggest that orchiopexy may reduce risk of development of testicular cancer if done before puberty, although likely not to that of the general population.

A previous history of testicular cancer is the most important risk factor. Males with a prior history of testicular GCT have a 25-fold increased relative risk of developing a metachronous testicular tumor, with a significantly higher cumulative risk if age is less than 30 years. The median time to development of a metachronous tumor was 5 years in the Norwegian experience [6].

Family history has been shown to increase risk of testicular cancer, with the strongest association seen between male siblings. The relative risk of developing GCT for an affected brother and father ranges from 8 to 10 and 4 to 6, respectively [7]. Despite this known association, there is little known in respect to a specific inheritance pattern or genetic markers, and much research work is needed in this area.

Other risk factors include a history of intratubular germ cell neoplasia, disorders of sexual development including Klinefelter disease and gonadal dysgenesis, and trisomy 21 (Down syndrome). While prenatal risk factors such as smoking and estrogen exposure have been evaluated, there has been no conclusive evidence to show an association between these and testicular cancer.

Testicular Neoplasms: Histologic Classifications

GCTs comprise approximately 90 % of all testicular tumors with non-germ cell tumors being less common. GCTs are further categorized into seminoma or nonseminoma histologic subtypes. Seminoma is the most common morphologic pattern, while nonseminomatous germ cell tumors (NSGCT) may consist of teratoma, yolk sac tumor, embryonal cell carcinoma, and choriocarcinoma. In reality, the majority of NSGCTs are comprised of a combination of these morphologic patterns and are referred to as mixed germ cell tumors.

Non-germ cell malignancies include sex cord stromal tumors, Leydig cell, Sertoli cell, granulosa cell tumors, and gonadoblastoma. They can also include secondary neoplasms such as lymphomas, metastases, and leukemic infiltrations, all of which are important considerations in the elderly patient. Adenocarcinoma of the rete testes is another rare lesion found in the testicle. Lastly, tumors of the testicular adnexa including adenomatoid tumor, cystadenoma, sarcoma, and mesothelioma can be classified in this group.

Histopathologic types of testicular neoplasms have important implications in determining prognosis and treatment. For instance, retroperitoneal nodal metastases from seminoma are known to be highly radiosensitive, but nonseminomatous tumors are usually resistant to this modality. Teratomas, commonly seen in various degrees in mixed NSGCT, are typically resistant to both chemotherapy and radiation, and thus, surgical therapy is a cornerstone in management. Non-germ cell tumors, which could include metastatic, lymphomatous, or leukemoid lesions, are important to consider in the elderly population and will be discussed later.

Evaluation of the Testicular Mass

Presentation

Testicular masses usually present as a painless swollen hemiscrotum, although in some cases patients will experience pain. Pulmonary symptoms including cough, hemoptysis, and dyspnea can occur in the setting of metastatic disease. If bulky retroperitoneal lymphadenopathy is present, patients may complain of back pain, gastrointestinal symptoms, neurologic deficits, or lower extremity edema as a result of compression on the vena cava. On rare occasions, gynecomastia can be found as a result of elevated human chorionic gonadotropin (HCG).

History and Physical Examination

Prior history of cryptorchidism, previous scrotal surgery, infertility, and family history should be inquired as well as previous history of testicular cancers. Especially in older men, a thorough past medical history should be performed. A history of night sweats, weight loss, or fevers could suggest a possible systemic disease process such as lymphoma or leukemia, as these findings are not typically seen in early stage testicular cancer. A thorough physical examination is of the utmost importance. The scrotum should be carefully examined in a bimanual fashion with attention paid first to the normal testicle. A normal testicle is smooth, mobile, and not fixed to the overlying skin. The epididymis can be palpated posteriorly as a separate structure from the testis itself. Suspicious findings include firm nodules, nonmobile, or diffusely enlarged testicle. It is not uncommon for a surrounding hydrocele to be present which makes an examination more challenging. Large hydroceles in particular can render a physical exam of the scrotum almost useless, and it is in this situation that scrotal ultrasound is particularly helpful. In addition to the scrotal exam, attention should be directed toward the abdomen where a palpable mass may suggest bulky lymph node metastasis. The supraclavicular nodes are another area where lymphadenopathy can be found. Lastly, a chest examination looking for breast enlargement or tenderness and auscultation of the lungs can sometimes reveal evidence of distant disease.

Diagnostic Evaluation

Scrotal ultrasonography gives reliable imaging and is a useful adjunct to the physical examination. Testicular masses often appear heterogeneous or

Table 20.1 Testicular cancer staging system of the American Joint Committee on Cancer, 7th Edition[a] [8]

Primary tumor (T)	Definition
pTX	Primary tumor cannot be assessed
pT0	No evidence of primary tumor (e.g., histologic scar in testis)
pTis	Intratubular germ cell neoplasia (carcinoma in situ)
pT1	Tumor limited to the testis and epididymis without vascular/lymphatic invasion; tumor may invade into the tunica albuginea but not the tunica vaginalis
pT2	Tumor limited to the testis and epididymis with vascular/lymphatic invasion or tumor extending through the tunica albuginea with involvement of the tunica vaginalis
pT3	Tumor invades the spermatic cord with or without vascular/lymphatic invasion
pT4	Tumor invades the scrotum with or without vascular/lymphatic invasion
Regional lymph nodes (N)	
Clinical	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis with a lymph node mass ≤2 cm in greatest dimension or multiple lymph nodes, none >2 cm in greatest dimension
N2	Metastasis with a lymph node mass >2 cm but not >5 cm in greatest dimension or multiple lymph nodes, any one mass >2 cm but not >5 cm in greatest dimension
N3	Metastasis with a lymph node mass >5 cm in greatest dimension
Pathologic (pN)	
pNx	Regional lymph nodes cannot be assessed
pN0	No regional lymph node metastasis
pN1	Metastasis with a lymph node mass ≤2 cm in greatest dimension and ≤5 nodes positive, none >2 cm in greatest dimension
pN2	Metastasis with a lymph node mass >2 cm but not >5 cm in greatest dimension; or >5 nodes positive, none >5 cm; or evidence of extranodal extension of tumor
pN3	Metastasis with a lymph node mass >5 cm in greatest dimension
Distant metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis
M1a	Nonregional nodal or pulmonary metastasis
M1b	Distant metastasis other than to nonregional lymph nodes and lung

[a]Adapted from 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 New York, Inc [8]

hypoechoic and have increased blood flow on Doppler images. Scrotal ultrasound also helps rule out other causes of testicular pain and swelling such as epididymitis, testicular torsion, spermatocele, hydrocele, or hematoma.

Tumor Markers

There are three tumor markers found in germ cell testicular cancers, which have important implications in terms of staging and treatment. Alpha-fetoprotein (AFP), beta human chorionic gonadotropin (HCG), and lactic acid dehydrogenase (LDH) levels should be drawn in patients with a confirmed mass prior to performing radical inguinal orchiectomy. These markers will be explained in more detail later.

Staging of Testicular Cancer

Adequate clinical staging of testicular cancer consists primarily of pathologic findings at radical orchiectomy, imaging studies, and serum tumor markers. The American Joint Committee on Cancer (AJCC) updated the staging for germ cell tumors in 1997 with the addition of serum tumor marker levels which applies to both seminomas and NSGCT [8] (Table 20.1). In general, stage I disease is confined to the testes while stage II involves metastatic spread to regional lymph nodes including those in the retroperitoneum. Stage III encompasses nonregional lymph node or distant metastasis, along with the degree of serum tumor marker elevation (not shown).

Role of Imaging and Tumor Markers in Clinical Staging

Computed tomography (CT) of the abdomen and pelvis is invaluable for clinical staging of GCTs, which have a predictable route of spread to the retroperitoneal lymph nodes. Therefore, CT of the abdomen should be obtained in all patients with a confirmed GCT. If CT is contraindicated, then magnetic resonance imaging (MRI) is an alternative. Despite the usefulness of CT imaging, it does have limitations, and some patients may have clinically and radiographically normal nodes but actually harbor metastatic disease [9].

Pulmonary and mediastinal disease can be evaluated with a chest X-ray, but in cases of known metastatic disease or persistent tumor marker elevation, CT scan examination of the chest should be performed. Brain imaging is generally not necessary, but should be considered when there are neurological findings or HCG is markedly elevated in the setting of choriocarcinoma. Choriocarcinoma has the propensity to metastasize through hematologic routes [10].

Serum Tumor Markers

Serum tumor markers play an important role in cancer staging, treatment choice, and follow-up. Both AFP and β-HCG are required early in life for normal fetal development but drop precipitously during the first year and then remain at low levels indefinitely. Certain GCTs will secrete these glycoproteins which can be easily detected in blood tests. Failure of these markers to normalize after orchiectomy suggests persistent extra-testicular disease.

Alpha-Fetoprotein

Alpha-fetoprotein (AFP) is a glycoprotein that is normally produced and secreted by the liver, gastrointestinal tract, and fetal yolk sac. With a half-life of 5–7 days, it declines during the first year of life and under normal conditions is less than 15 ng/mL in men [11]. AFP can be secreted in embryonal carcinoma, teratoma, and yolk sac tumors but is never produced by choriocarcinoma or seminoma. Therefore, a pure seminoma will never have abnormal levels of AFP. In the setting of elevated AFP, when the histologic diagnosis is seminoma, the cancer should be managed as a mixed germ cell tumor.

Beta Human Chorionic Gonadotropin

Beta human chorionic gonadotropin (HCG) is another glycoprotein that is in normal circulation during fetal growth but in adults is normally less than 1.5 IU/mL. HCG is the most commonly elevated serum tumor marker in testicular cancer. It plays an important role in regulating the corpus luteum and stimulating progesterone in early development. After placental development, HCG is secreted by syncytiotrophoblastic cells, which are also present in both choriocarcinomas and embryonal cell tumors of the testes. In addition, a minority of seminomas (approximately 15 %) may secrete HCG. Other causes of abnormally elevated HCG include malignancies of the gastrointestinal or biliary tract, breast, and kidney, as well as marijuana use.

Hypogonadism is common in the geriatric population and presents a special case for HCG. HCG shares a common alpha subunit with luteinizing hormone (LH), which plays an important role in testosterone production. Patients with elevated LH from hypogonadism can have a falsely elevated HCG on assay. HCG that normalizes after testosterone administration supports a diagnosis of hypogonadism rather than a malignant process.

Lactate Dehydrogenase

Lactate dehydrogenase (LDH) is an enzyme produced in the muscle tissue and is pathologically elevated in several disease processes. LDH elevation in germ cell tumors has been closely

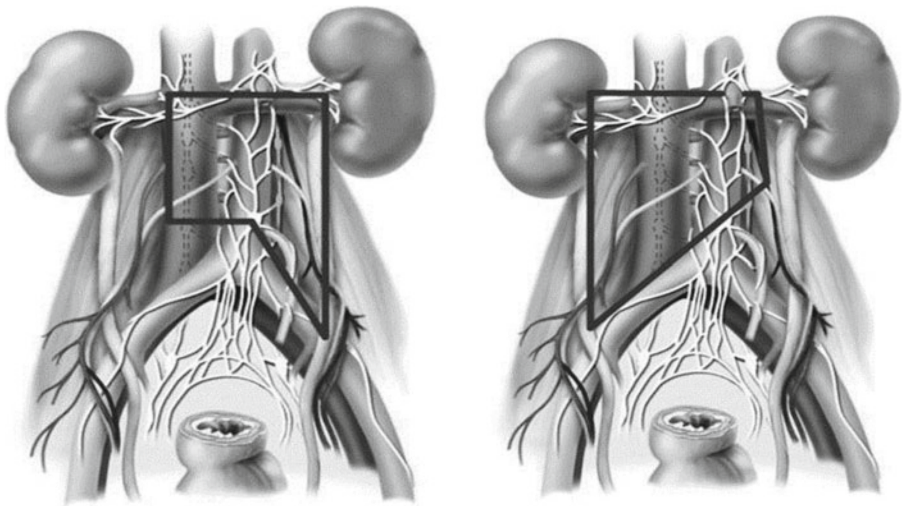


Fig. 20.2 Modified templates for retroperitoneal lymph node dissection. Left template (*shown left*) and right template (*shown right*) (*Reprinted with permission* [12])

correlated with bulk of disease and thus is also used as an adjunct in both staging and prognosis. Patients with suspected germ cell tumors of the testis should have serum tumor markers drawn prior to undergoing orchiectomy. Levels of markers before and after treatment have important implications on management and prognosis.

Treatment of Germ Cell Tumors

GCTs have enjoyed great success in terms of treatment and long-term survival, with 5 year survival of > 90 % even in those with metastatic disease. This is mainly due to the development of platinum-based chemotherapeutic agents to which most GCTs are sensitive. The treatment pathways for germ cell tumors nonetheless can be quite complicated and are beyond the scope of this chapter. Chemotherapy and retroperitoneal lymph node dissection each have important roles in the treatment of both pure and mixed NSGCTs. The predictable pattern of nodal spread has allowed for modified templates for retroperitoneal lymph node dissection in a low-stage disease, as shown in Fig. 20.2 [12]. For seminomas, essentially no patients have a poor prognosis, and surveillance, single-agent chemotherapy, and radiation to the retroperitoneum have all been used with great success.

Germ Cell Tumors in Older Adults

As mentioned previously, testicular GCTs are most commonly diagnosed in men between 18 and 35 years of age. An exception to this includes pure seminoma, which tends to occur more commonly in the fourth and fifth decades of life. A review of 50 men with germ cell tumor older than 60 years of age found seminoma to be the most common histologic type (82 %). The median tumor size was also larger compared to younger men (6 cm, range 2–11 cm) and of higher stage, with rete testes invasion and vascular invasion [13].

A variant of seminoma, spermatocytic seminoma, is a rare subtype that has a benign course and rarely metastasizes. A retrospective review of over 700 patients from Canada identified 13 cases of spermatocytic seminoma. Interestingly, the mean patient age was 62 years. Five patients received para-aortic radiation with the remainder on surveillance. At a median follow-up of almost 9 years, there were no relapses in this small group [14]. Radical inguinal orchiectomy alone is curative in this histologic subtype, and no further treatment is necessary.

NSGCT in elderly men is less common but does occur. Platinum-based chemotherapy and retroperitoneal lymph node dissection (RPLND) have roles in NSGCT depending on the stage.

While the chemotherapy regimen typically uses either three cycles of BEP (bleomycin, etoposide, and cisplatin) or four cycles of EP (etoposide and cisplatin), little is known on the tolerability and toxicity in this older age group. Previous clinical trials have typically excluded those of older age or with significant comorbidities. Bleomycin in particular is associated with significant pulmonary toxicity, and its use in this age group would very likely be detrimental. Furthermore, while RPLND is well tolerated in the young healthy patient, this operation in the older patient may indeed be associated with higher complication rates and inferior outcomes. In a population-based analysis of perioperative mortality after RPLND for mixed NSGCT, it was shown that mortality increased as age increased. In patients over 40 years, the perioperative mortality rate was 2.7 %, compared to 0 % for patients less than 30 years of age [15]. While data on surgical outcomes after RPLND in the geriatric population is mostly limited to single institution case reports, the ultimate effect of age on treatment of metastatic germ cell tumors has not been evaluated in a prospective fashion.

Non-germ Cell Tumors in Older Adults

Sex cord stromal tumors (SCST) consist of Leydig cell tumors, Sertoli cell tumors, and granulosa cell tumors. These are rare in general and together account for approximately less than 5 % of primary testicular tumors. These tumors are exceedingly rare in elderly men. Treatment consists of radical orchiectomy and in some cases RPLND and/or chemotherapy, although there is no general consensus. Both Sertoli cell and Leydig cell tumors may be hormonally active, and presenting symptoms include gynecomastia, erectile dysfunction, and decreased libido.

Mesothelioma of the testes is another rare non-germ cell tumor that arises from the tunica vaginalis. With approximately 100 cases reported to date, it represents 0.3–5 % of malignant mesotheliomas. This is a highly aggressive tumor and typically presents in middle aged or elderly men, with a mean age of presentation at 53.5 years. Patients most commonly present with a hydrocele, and an ultrasound may reveal a thickened tunical layer. It has been associated with asbestos exposure similar to its pleural-based counterpart. Other proposed risk factors include history of trauma, radiation, potassium bromate, chronic hydrocele, and previous hernia repair [16]. Treatment is primarily by radical orchiectomy with systemic chemotherapy in the setting of metastatic disease. Nonetheless, median survival for malignant mesothelioma of the tunical vaginalis is less than 2 years with extent of disease at time of diagnosis the most significant prognostic indicator [17, 18]. Since malignant mesothelioma of the tunica is most commonly encountered in older patients, it is important to keep this diagnosis in mind, especially in those with a prior history of asbestos exposure.

Lymphomas, Leukemic Infiltration, and Other Hematologic Malignancies of the Testis

Hematologic and lymphatic malignancies involving the testis deserve special attention in elderly men, as they are more common in this population. Primary testicular lymphoma (PTL) accounts for about 1 % of lymphomas. In a retrospective review from 1972 to 2002, Darby et al. identified 30 patients with PTL [19]. The median age at diagnosis was 74 years, and 60 % of patients were greater than 70 years old. The most common histologic pattern is diffuse large B-cell type, which has a propensity to metastasize to extranodal sites and carries a poor prognosis. Single institution case series have reported median overall survivals ranging from 11 months to 96 months [20]. This discrepancy is likely due to differences in patient age and stage at presentation among these different series.

PTL cannot be distinguished radiographically or by physical examination from germ cell tumors; therefore, radical orchiectomy remains a cornerstone for both treatment and staging. Spread to the contralateral testicle and central nervous system is not uncommon, and other sites of involvement can include lung, pleura, skin, and Waldeyer's ring [20]. Systemic treatment as well as prophylactic intrathecal chemotherapy can improve long-term remission rates, as reported by Vural, who achieved an 8 % relapse rate and 88 % progression-free survival at 10 years in a small series [21]. Still, others have recommended that full treatment with CHOP (cyclophosphamide, vincristine, doxorubicin, and prednisone) with intrathecal chemotherapy and adjuvant scrotal radiation should be administered. At present, there are no prospective controlled trials evaluating the ideal treatment regimen for PTL; therefore, management of this malignancy remains highly variable.

Other hematologic malignancies which can be found in the testes include multiple myeloma and leukemia. Multiple myeloma is characterized as a neoplastic process involving overproduction of monoclonal proteins from plasma cells. It typically manifests as skeletal "blastic" lesions that lead to bone destruction. Testicular plasmacytoma has been found in 0.6–2.7 % of patients with multiple myeloma, and in rare instances, this may be the only site of disease. The median age in one literature review was 56 years [22].

It has been proposed that the testes are an immune privileged site for chemotherapy, and patients previously treated for leukemia can often relapse in this area. Most of the literature regarding these processes are limited to small case reports and usually involve acute lymphoblastic leukemia, which is most commonly seen in children and adolescents.

Conclusion

Testicular masses are uncommon in elderly men. Pure seminoma, in particular the spermatocytic type, is the most common GCT in this population. Fortunately, radical orchiectomy alone is all that is usually required for definitive treatment. In the older patient presenting with a testicular mass, primary testicular lymphoma should be high on the differential diagnosis list. Scrotal ultrasound and serum tumor markers should always be obtained in the evaluation with prompt referral for surgical excision. Data are sparse in regard to optimal management of both mixed germ cell tumors and non-germ cell tumors in this population due to both the low incidence in elderly men and lack of inclusion of these patients in clinical trials.

Penile Cancer

Penile cancer is associated with significant morbidity and mortality and, although rare, is predominantly diagnosed in elderly men. The peak incidence occurs in men who are in their 70s. If detected at an early stage, surgical therapy offers the best curative treatment with approximately 90 % overall 5 years survival. While patients may experience genital disfigurement and impaired quality of life from penectomy, recent advances in organ-sparing surgery have resulted in improved functional outcomes.

Epidemiology

The incidence of squamous cell carcinoma of the penis varies among different populations, with the highest reported rates in African and South American countries at up to 10 %. In the Western world, penile cancer accounts for less than 1 % of all malignancies. An estimated 1,500 new cases and 300 deaths due to penile cancer are projected to occur in 2012 [23]. A review of SEER data from 1998 to 2003 revealed that the age-adjusted incidence of penile cancer increased with age. In men over 80 years old, the incidence of penile cancer was 5.73/100,000 compared to 0.14/100,000 in patients younger than 50 years. The median age of presentation was 68 years but tended to be younger in the African America population. Incidence rates between blacks and whites were similar; however, Hispanics were noted to have much higher incidence rates [24].

Clinical Presentation and Findings

Most patients present with a painless lesion located on the glans, coronal sulcus, or inner foreskin. Tumors on the penile shaft are common.

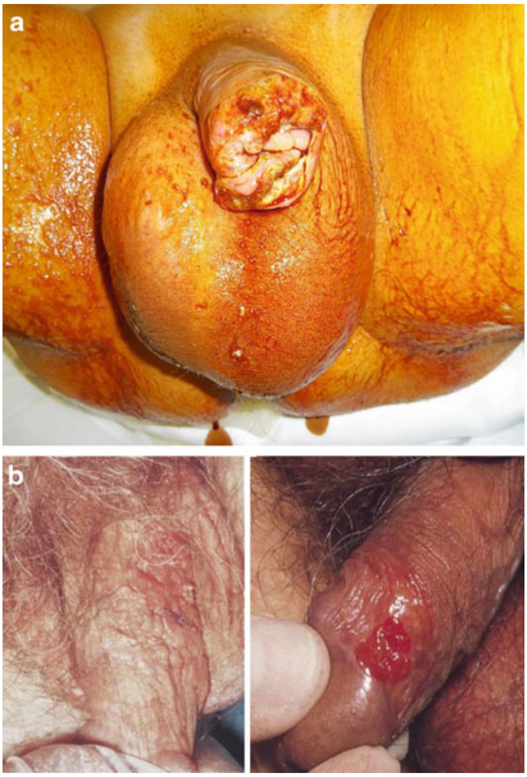


Fig. 20.3 (**a**) Fungating distal penile cancer in an uncircumcised 72-year-old male (*Courtesy of Dr. Hadley Wyre, Assistant Professor Kansas University Medical Center*). (**b**) Carcinoma in situ of the penis. Involvement of the penile shaft, Bowen's disease (*on left*) and glans, and erythroplasia of Queyrat (*on right*) (*Reprinted with permission* [25])

Fig. 20.4 Patient EMPD presenting with pruritus and an erythematous, dry, and raised lesion of the scrotum (*Reprinted with permission* [26])

The lesions vary from a subtle induration to a fungating or ulcerated mass (Figs. 20.3 and 20.4). Patients are almost always uncircumcised as circumcision at birth has shown to virtually eliminate the risk of penile cancer. Furthermore, associated phimosis (nonretractile foreskin) is a common finding and can hinder an adequate physical examination. Those patients presenting with locally advanced disease may also complain of lower urinary tract symptoms, hematuria, or a groin mass, which in some cases can ulcerate through the skin. Constitutional symptoms such as weight loss and cachexia may be present in the setting of metastatic disease. Paraneoplastic syndromes causing hypercalcemia and leukocytosis have been reported [27].

Patient reluctance to seek medical attention can lead to delayed presentations of up to one year or more in some cases. Some patients undergo extended courses of topical treatments or antibiotics which may further delay diagnostic evaluation [28]. Physician referral patterns may also delay evaluation and treatment by a urologist, resulting in locally advanced disease at time of management [29]. Therefore, it is important to examine the genitalia as part of any annual history and physical of men in the primary care setting, with urgent referral to the urologist.

Histopathology and Risk Factors

Over 90 % of penile malignancies are squamous cell carcinoma (SCC); however, other histologic types include basal cell carcinoma, melanoma, Kaposi's sarcoma (especially in men with HIV/AIDS), and adenocarcinoma. For SCC, over 95 % are of the classic keratinizing or "usual" type. In addition, there are a number of subtypes that have been described, which in some cases may have prognostic importance [30]. For example, patients diagnosed with SCC at age 70 or greater are more likely to have verrucous and pseudohyperplastic carcinomas, both of which are typically low grade and have a good prognosis [31]. Precancerous lesions also occur and include lichen sclerosis, a chronic inflammatory condition of the glans and foreskin, and penile intraepithelial neoplasia (PIN). PIN includes dysplastic processes such as Bowen's disease (carcinoma in situ of the penile shaft); erythroplasia of Queyrat (carcinoma in situ of the glans penis), as shown in Fig. 20.4; and the Buschke–Lowenstein tumor (giant condyloma), all of which may progress to invasive penile cancer at varying frequencies. The details of this discussion are beyond the scope of this chapter. The authors recommend Vogelzang's Comprehensive Textbook of Genitourinary Oncology for a detailed discussion of these histologic subtypes and premalignant conditions [31].

There are several well-established risk factors for penile cancer. The most common is phimosis, a condition in which the foreskin is unable to be retracted behind the glans. While circumcision at birth has shown to essentially eliminate the development of penile cancer, it is generally thought that poor hygiene habits and long-term exposure to smegma in the preputial skin lead to chronic inflammation and carcinogenesis. This hypothesis is supported by the relatively low frequency of penile cancers arising on the penile shaft. Certain human papillomaviruses (HPV), especially types 16 and 18, are found in a high percentage of penile cancers, with reports ranging from 25 % to 76 % of cases [32]. While the exact etiology is not known, Daling et al. found in a case–control study that smoking was associated with a 4.5-fold increased risk in development of invasive SCC [33]. Other risk factors include psoralen and ultraviolet A (PUVA), a photo-chemotherapy treatment for psoriasis.

Evaluation, Diagnosis, and Initial Management

Evaluation begins with a thorough history and physical examination. Specific questions regarding any known risk factors should be addressed. Lesion size, morphology (warty, flat, or ulcerated), location, and possible extension into the corporal tissue or urethra should be assessed. For proximal lesions, the perineum should be palpated and any fixation to the pubic bone should also be determined. In addition to the penile examination, the inguinal lymph nodes should be carefully palpated in efforts to determine if there is evidence of lymphadenopathy. If there are palpable lymph nodes, notation should be made regarding mobility, size, and evidence of ulceration. As will be discussed later, inguinal nodal involvement has a significant effect on surgical management and prognosis.

Diagnosis is established through biopsy and microscopic examination. For small superficial lesions, a punch biopsy may be sufficient; however, excisional biopsy may be more accurate in determining depth of invasion and histologic grade [34]. Not all cases require biopsy and surgery in separate settings. Patients with large fungating or ulcerated masses in the setting of inguinal lymphadenopathy can have confirmatory frozen sections obtained at the time of total or partial penectomy in efforts to prevent further delay in treatment.

Clinical staging of the penile lesion is best performed by physical examination, but inaccurate staging can be present in approximately 25 % of cases [35]. Imaging techniques, including penile ultrasound and magnetic resonance imaging (MRI), have been proposed in efforts to improve accuracy in regard to depth of invasion. While MRI performed with induction of an artificial erection has been shown to improve detection of corporal body invasion for indeterminate cases, there is no level 1 evidence to recommend its use in routine practice [36].

Physical examination is also sufficient for the inguinal lymph node evaluation as neither CT nor MRI has been shown to be helpful when there is no palpable adenopathy. However, in obese patients the groin examination may not be accurate, and CT imaging can be helpful to evaluate for clinically enlarged nodes. In those with abnormal groin examinations, additional staging with CT and/or MRI of the abdomen and pelvis is especially helpful to detect presence of enlarged pelvic lymph nodes and metastatic disease.

Staging of Penile Cancer

Tumor staging is determined by depth of invasion after resection of the tumor. Tis and Ta are both noninvasive while T1–T4 extend beyond the epithelial layer to varying degrees. The most current edition of TNM staging has been modified to reflect the prognostic importance of both clinical and pathologic nodal staging (Table 20.2) [37].

Table 20.2 Penile cancer staging system of the American Joint Committee on Cancer, 7th Edition[a]

Primary tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
Ta	Noninvasive verrucous carcinoma
T1a	Tumor invades subepithelial connective tissue without lymph vascular invasion and is not poorly differentiated (i.e., grades 3–4)
T1b	Tumor invades subepithelial connective tissue with lymph vascular invasion or is poorly differentiated
T2	Tumor invades corpus spongiosum or cavernosum
T3	Tumor invades urethra
T4	Tumor invades other adjacent structures
Regional lymph nodes (N)	
Clinical stage definition (*based on palpation or imaging*)	
cNX	Regional lymph nodes cannot be assessed
cN0	No palpable or visibly enlarged inguinal lymph nodes
cN1	Palpable mobile unilateral inguinal lymph node
cN2	Palpable mobile multiple or bilateral inguinal lymph nodes
cN3	Palpable fixed inguinal nodal mass or pelvic lymphadenopathy unilateral or bilateral
Pathologic stage definition	
pNX	Regional lymph nodes cannot be assessed
pN0	No regional lymph node metastasis
pN1	Metastasis in a single inguinal lymph node
pN2	Metastases in multiple or bilateral inguinal lymph nodes
pN3	Extranodal extension of lymph node metastasis or pelvic lymph node(s) unilateral or bilateral
Distant metastasis	
M0	No distant metastasis
M1	Distant metastasis

[a]Adapted from 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 New York, Inc [37]

Treatment of Penile Cancer

Surgery

The mainstay of treatment for penile cancer is surgical excision of the tumor. In select cases of small low-stage tumors confined to the prepuce (Cis, Ta, T1), circumcision alone may be adequate. For larger, higher stage lesions (T2 or greater) located distally on the glans or coronal margin, partial penectomy is required. Historically, it was thought that a 2-cm margin was necessary in order to prevent local recurrence, but results of Agrawal's experience demonstrate that smaller margins of 1 cm result in equivalent outcomes in terms of survival and local recurrence [38]. With this in mind, many patients can be left with enough functional length to stand while voiding and in some cases have sexual function. Contemporary local recurrence rates with partial penectomy are variable, ranging from 6 % to 20 %, but do not appear to adversely affect survival [39, 40]. Despite preservation of penile length with partial penectomy, only a minority of patients report satisfactory sexual intercourse.

More proximal, deeply invasive tumors located on the shaft or base of the penis and even some distal tumors with extension to the shaft or base of the penis require total penectomy. In this procedure the urethra is dissected off the corporal bodies and brought through the perineum where a urethrostomy is performed.

Penile sparing surgery has gained popularity over the last decade. Multiple techniques have been described, including local excision, glansectomy with skin grafting, Mohs microsurgery, and laser ablation. There is no question that these approaches offer superior results in terms of preservation of function. Nonetheless, important considerations for these therapies include tumor size, stage, location, and patient compliance. At present, most penile cancers treated with these strategies include carcinoma in situ and T1 stage lesions.

Laser therapy in particular has been associated with excellent cosmetic and functional results using either carbon dioxide (CO_2) or neodymium–yttrium–aluminum–garnet (Nd:YAG) energy. The depth of penetration is 0.01 mm and 3–6 mm for CO_2 and Nd:YAG, respectively. Circumcision should be performed simultaneously in these cases. Schlenker et al. recently reported long-term outcomes of patients treated with Nd:YAG laser therapy [41]. While the majority of the 54 patients had CIS (72.2 %), the recurrence rate for the entire cohort was over 40 % at a mean of 53 months. Although there was no adverse effect on survival, this highlights the need for long-term follow-up of patients treated with this modality. A separate experience reported on 56 patients with pathologic stage T1 treated with CO_2 and reported a 20 % recurrence rate at 66 months, with 2 patients experiencing inguinal metastasis [42]. In many cases of local recurrence, retreatment with laser ablation is sufficient and partial penectomy is rarely required.

Mohs microsurgery is a highly specialized technique that involves sequential excision of tumor margins in thin layers with simultaneous frozen section pathologic analysis and mapping of remaining tumor. Long-term control rates of over 90 % have been reported, although this surgery, like laser ablation, is usually preserved for small, low-stage lesions (Cis and T1) [43].

Radiation

Radiation therapy in the form of brachytherapy or external beam radiation has been utilized in select cases. The ideal candidate for this therapy would have a lesion less than 4 cm in diameter and tumor stage T1 or T2. Penile interstitial brachytherapy has been used in several European countries as well as Canada but has not gained wide popularity in the USA. This technique involves placement of needles through the tumor under anesthesia, which are then loaded with radioactive seeds (usually Iridium-192). The radioactivity has a short half-life and is emitted at a high dose over 4–5 days which requires inpatient hospitalization during treatment. Significant local toxicity can occur, including urethral stricture, meatal stenosis, skin necrosis, and urethrocutaneous fistula. Most reports are limited to single institution case series with local control rates and a 5-year cancer-specific survival ranging from 70 % to 85 % and 60 % to 90 %, respectively [44].

Role of Chemotherapy

Given the low incidence of penile cancer, well-designed prospective trials utilizing chemotherapy have been slow to develop. Small prospective trials have been performed using various platinum-based combinations with response rates of 50 % at best. At present, the role of systemic chemotherapy for penile cancer is limited to those who have metastatic disease or bulky lymph nodes.

Management of Inguinal and Pelvic Lymph Nodes

Penile cancer has a predictable route of spread to the regional inguinal lymph nodes as the first landing site, followed by pelvic lymph nodes. Hemotogenous spread to distant sites in the setting of no inguinal or pelvic nodal disease is essentially nonexistent. Patients may present with palpable inguinal adenopathy or develop this later after local treatment. Inguinal lymph node dissection (ILND) is both diagnostic and potentially curative in some patients; however, this procedure is associated with significant morbidity. There continues to be debate regarding which clinically node-negative patients gain the most benefit from this procedure. The argument for performing a prophylactic inguinal lymph node dissection in higher risk clinically node-negative patients is that approximately 20 % actually contain metastatic disease. Furthermore, retrospective reviews have shown a significant survival advantage in patients who had early ILND compared to those who underwent the procedure after developing palpable disease [45]. The argument against performing ILND on all patients with penile cancer is that over 80 % of patients will not have node-positive disease, especially those with lower stage tumors, and would thus lead to overtreatment. Given the significant complications that can arise from this procedure, this should not be taken lightly.

The algorithm for management for ILND can be somewhat complicated and is beyond the scope of this chapter. In general, however, those with more advanced tumors T2–T4, or poorly differentiated T1, should undergo ILND. In patients with CIS, Ta, or T1, ILND can be deferred. It is not uncommon for chronic inflammation to be present in this anatomic region, and this can lead to clinically palpable lymph nodes. In these cases, a short course of antibiotics may be administered with a repeat examination to determine resolution. This practice should only be performed in low-risk patients, as those with high-risk features should undergo primary ILND. Pelvic lymph node dissection is usually performed after the finding of positive inguinal lymph nodes but is sometimes performed concurrently. Patients with positive pelvic lymph nodes have extremely poor prognosis with a 5-year survival less than 25 %.

Surgical Technique and Complications

The procedure involves removal of all the subcutaneous lymphatic tissue bounded by the inguinal ligament superiorly, the sartorius muscle laterally, the adductor longus muscle medially, and the base of the femoral triangle inferiorly. In doing so, the lymphatic drainage of the ipsilateral lower extremity may be impaired, leading to chronic lymphedema. Other potential complications include wound infection, skin flap necrosis, hematoma, lymphocele, or seroma formation.

Sentinel Lymph Node Biopsy (SLNB)

In principle, the sentinel node is the first landing site from a tumor to its regional lymphatics. In efforts to avoid the risks and morbidity from ILND in those without palpable lymphadenopathy, some centers have proposed this technique whereby this node is identified and biopsied. At the time of surgery, if the sentinel node is positive, a full ILND is performed, and if negative it would be avoided. SLNB has been used in other cancers such as breast and melanoma with good diagnostic accuracy. The procedure is commonly performed with the aid of lymphoscintigraphy and a gamma probe to assist with localization of the sentinel node. In some high-volume centers with a vast experience in the SLNB technique, sensitivity rates have approached 80 %. While this procedure holds promise, it has not become standard of care in the USA.

Oncologic Outcomes

The best predictor for long-term survival is the status of the inguinal lymph nodes. For patients who have negative lymph nodes and undergo resection of the primary tumor, 5-year survival rates are approximately 90 %. For those with positive inguinal lymph nodes who undergo complete resection, 5-year cancer-specific survival approaches 60 %. As mentioned previously, pelvic nodal metastasis is considered distant disease (stage IV), and the prognosis is extremely poor.

Conclusion

The geriatric group has the highest incidence of penile cancer. The clinician should include evaluation of the penis as part of a thorough history and physical, as early diagnosis of penile cancer leads to optimal oncologic and functional outcomes. Phimosis is common in the uncircumcised patient and should be considered a risk factor for penile cancer in the geriatric patient. Fortunately, most histologic types in elderly men are well differentiated with low malignant potential. When feasible, organ-sparing surgery should be offered to these patients in efforts to preserve urinary and sexual function, but never at the cost of incomplete excision. While sentinel lymph node biopsy techniques are still developing, they may in the future have a bigger role in penile cancer staging and thus circumvent the problems arising from ILND. Although the complications of ILND are significant, this procedure should be performed in those with high-risk features in order to provide the best chance for cure.

Urethral Cancer

Primary urethral cancers are exceedingly rare and involve less than 1 % of all genitourinary malignancies. Due to the low incidence of this malignancy, standardization of treatment is lacking as there have been no prospective studies comparing efficacy of multiple treatment modalities. In this section, we will provide an overview of both male and female urethral cancers in regard to epidemiology, histopathology, evaluation, and treatment. Lastly, outcomes will be reviewed based on what data is present in the literature.

Epidemiology, Risk Factors, and Etiology

It has previously been thought that primary urethral cancers are 2–3-fold higher in women with squamous cell carcinoma being the predominant histologic pattern [46]. However, an analysis of SEER database by Swartz et al. identified approximately 1,500 cases in the USA between 1973 and 2002 and found just the opposite (1,075 men and 540 women). Furthermore, urothelial cell carcinoma comprised over 50 % of cases [47]. A possible explanation of these findings is that the database was unable to exclude patients who had a synchronous urothelial cell cancer of the bladder which could skew the observed demographic and histologic patterns.

Age at presentation is highly variable, but patients most commonly present between middle and elderly age groups. Swartz et al. demonstrated that the US incidence rate was highest in those between 75 and 84 years (9.5/million) [47]. Using the data from SEER, Rabbani found that the median age at diagnosis for male urethral cancers between 1988 and 2006 was 73 years (range 64–80), suggesting that this is primarily a disease of elderly men [48]. Again, since the dominant histologic type for this group was urothelial cell carcinoma, this may not give an accurate depiction for isolated urethral cancers.

While the pathogenesis of urethral cancers is not fully understood, there are some known risk factors unique to both sexes. In men, urethral cancers have been associated with chronic inflammation, trauma, stricture disease, sexually transmitted diseases, and possibly long-standing urethral catheterization. Chronic inflammation is a proposed risk factor in women as well. One study has shown an association between female urethral cancer and human papillomavirus (HPV) types 16 and 18 for transitional and squamous cell carcinomas [49]. Urethral diverticulum arising from the female urethra is also a known risk factor for tumorigenesis, in particular clear cell carcinoma.

Anatomy

The female urethra is approximately 3–4 cm in length. Proximally it is lined by transitional epithelium and distally by squamous epithelium. The urethra runs in close proximity to the anterior vaginal wall and is surrounded by an inner longitudinal muscle layer and outer circular muscle layer. There are glands and ducts that surround the urethra, and these are likely the source of diverticula as well as adenocarcinomas. The relatively short length and proximity to the anterior vaginal wall makes local treatment challenging for both organ preservation and cancer control. The male urethra, being much longer, is divided into the prostatic, membranous, and penile segments. Transitional epithelium courses through the prostatic urethra then becomes pseudostratified columnar epithelium in the membranous and penile segments. The distal penile urethra along with the meatus contains stratified squamous epithelium. Depending on the location of the urethral cancer, one can see how the histologic type may vary. Lymphatic drainage for the distal urethra in both males and females is to the inguinal lymph nodes, while more proximal tumors drain to the pelvic lymphatic tissue.

Presentation and Evaluation

In women, urethral cancers typically present with dysuria, frequency, irritative voiding symptoms, and occasionally gross hematuria. For distal tumors or diverticula, a palpable mass may be present on physical examination. Late findings can include urinary retention from obstruction, ulceration into the vaginal wall, or vesicovaginal fistula. Men usually have a more insidious presentation, and symptoms may be nonspecific. Obstructive voiding symptoms are the most common followed by a perineal mass. Other presenting signs may be periurethral abscess, new onset stricture, hematuria, or fistula formation.

Evaluation begins with a thorough history and physical examination, with particular attention to the genitourinary system. In females, a pelvic examination should be performed with palpation of the anterior vaginal wall and close inspection of the urethral meatus. Examination of the inguinal lymph nodes may reveal enlarged nodes in both males and females. In men, palpation of the perineum and penile urethra may reveal a fixed or indurated mass. Cystourethroscopy allows direct visualization as well as lesion-directed biopsy and is a mainstay in the evaluation and diagnosis of urethral tumors. In some instances, particularly in men, a urethral lesion may be detected incidentally at the time of cystoscopy for evaluation of urethral stricture, bladder outlet obstruction, or hematuria.

Staging consists of pathologic findings after excision of primary tumor along with imaging using the AJCC TNM system as shown in Table 20.3 [50]. Radiographic imaging provides further anatomic detail of the urethra and can also demonstrate involvement of adjacent organs and metastatic disease. While CT is useful, the quality of soft tissue resolution with MRI is generally superior, and this is typically the imaging study of choice. Anterior urethral cancers are usually not as advanced as more proximal lesions, likely due to the late presentation of proximal disease.

Table 20.3 Urethral cancer staging system of the American Joint Committee on Cancer, 7th Edition[a]

Primary tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Ta	Noninvasive papillary, polypoid, or verrucous carcinoma
Tis	Carcinoma in situ
T1	Tumor invades subepithelial connection tissue
T2	Tumor invades any of the following: corpus spongiosum, prostate, periurethral muscle
T3	Tumor invades any of the following: corpus cavernosum, beyond prostatic capsule, anterior vagina, bladder neck
T4	Tumor invades adjacent organs
Regional lymph nodes (N)	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node involvement
N1	Metastasis in a single lymph node 2 cm or less in greatest dimension
N2	Metastasis in a single node more than 2 cm in greatest dimension or in multiple nodes
Distant metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis

[a]Adapted from 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 New York, Inc [50]

Treatment

To date there is no general consensus on the best treatment of urethral carcinomas, which may include surgery, radiation, chemotherapy, or a combination of all of these options. The literature mostly consists of single institution case series, with no prospective controlled comparison between different modalities. Surgical therapy ranges from local excision to removal of the entire urethra and bladder. Radiation therapy in combination with chemotherapy has also been utilized in some settings with good results. Some advocate that urethral squamous cell carcinomas in particular are analogous to other malignancies of this type such as head and neck, penile, and anal cancers and thus can be effectively treated with combined chemotherapy and radiation.

For small distal tumors, local excision, laser ablation, or partial penectomy and urethrectomy in men have all been reported. Consideration should be given to histologic grade with these conservative treatments as high grade cancers have a greater propensity to recur or progress. The proximity to the external sphincter is of particular importance because excision in this area can render the patient incontinent, especially in females who have a shorter urethra. More proximal lesions are typically not amenable to excision alone and are usually more advanced at presentation. Thus, total penectomy or radical cystectomy with urethrectomy is usually recommended. Depending on the extent of tumor, the vagina can be spared or reconstructed in women who wish to maintain sexual function. Urinary diversion with ileal conduit and continent diversion with a catheterizable stoma are both options and are based on patient preference. Pelvic lymphadenectomy is generally performed in proximal tumors that require radical surgery and inguinal lymph node dissection in the setting of palpable lymphadenopathy in the groins. Due to the morbidity of an inguinal lymph node dissection, these are not typically performed in the setting of non-palpable disease.

Radiation has been used in localized as well as advanced disease for tumor shrinkage prior to surgical excision. Radiation can be delivered by either external beam or brachytherapy. While radiation is an attractive modality in that it offers a possibility of organ preservation, it is associated with treatment toxicity including vaginal necrosis, fistula formation, and local edema. Recently, there has been more interest in combining radiation with chemotherapy, similar to other squamous cell carcinomas of the head and neck and anus. Agents commonly used include cisplatin, 5-FU, and mitomycin C. While the number of patients treated is small, and published studies are limited mostly to small case series, there have been reports of durable responses in selected individuals.

Prognosis and Outcomes of Treatment

Stage at presentation is the most important prognostic indicator. Distally located tumors in both men and women generally have a better prognosis due to earlier presentation. Nonetheless, recurrence rates are high and require close follow-up. At present, it is unclear if a particular histologic subtype is associated with worse outcomes, although some experts suggest that adenocarcinoma may have the worse prognosis.

The largest series reported on female urethral carcinoma was reported in a retrospective review of 53 patients treated at the Mayo Clinic [51]. Surgical treatment included transurethral resection, partial urethrectomy, radical urethrectomy with bladder preservation, or total pelvic exenteration. Radiation therapy and/or systemic chemotherapy were also utilized in some of these patients. Recurrence-free survival and cancer-specific survival at 10 years for the entire cohort were 45 ± 8 % and 60 ± 8 %, respectively. Recurrence rates were notably highest in those who underwent partial urethrectomy (22 %). Pathologic stage was most predictive of both recurrence and survival. The importance of complete resection was highlighted by the fact that those who recurred had a cancer mortality rate of 70 % at 5 years [51].

In men with urethral cancer, an analysis of SEER data revealed that overall survival for 2,000 patients at 5 and 10 years was 46 % (95 % CI: 43.9–48.6) and 29 % (CI 95 %: 26.6–32.0 %). Cancer-specific survival for this group was 68 % at 5 years. Predictors of death from cancer included age, higher grade and T stage, metastasis, and no surgical intervention. Surgery was reported to have a better outcome compared to radiation for tumor stages T2–T4 [48]. Caution should be advised in drawing conclusions in these retrospective studies due to the inherent selection bias and lack of randomization to treatment.

Urethral Cancers in Older Adults

Urethral cancers, although uncommon, are encountered in geriatric patients. The physician must be alert to symptoms suggestive of this disease, many of which are common urologic complaints seen in both elderly men and women. Whether it is a male with new onset of lower urinary tract symptoms or a female who presents with a painful mass in the vagina, a thorough examination with prompt referral to a urologist can lead to an earlier diagnosis and possibly improved outcomes. It is important to remember that females with a history of urethral diverticula are especially at risk.

Summary

Urethral carcinomas are rare but are occasionally seen in the elderly patient population. Distal lesions are most commonly squamous cell types, while more proximal lesions are more typically transitional cell or adenocarcinomas. Due to the often advanced stage and late presentation of proximal tumors, aggressive extirpative surgery is usually required. Distal lesions in select cases can be managed with organ-sparing treatment. The role of radiation and chemotherapy, whether used together or in addition to surgery, is still being defined. Due to the low incidence of this disease, clinical trials are difficult to construct and therefore make diagnosis and treatment a challenge.

Fig. 20.5 EMPD affecting the vulvar skin. (*Reprinted with permission* [52])

Other Genitourinary Malignancies in Older Adults

Gynecologic Cancers

In elderly females, primary gynecologic cancers arising from the uterus, cervix, ovaries, and vagina can occur. While these are most commonly detected by the gynecologist due to vaginal bleeding, local extension of these neoplasms can lead to urinary manifestations. Symptoms can include lower urinary tract voiding problems, gross hematuria, recurrent urinary tract infections, hydronephrosis, or vesicovaginal fistula. In most cases, ureteral obstruction is asymptomatic given the slow progressive nature of this process. Treatment depends on the primary organ involved and is beyond the scope of this chapter.

Both external beam radiation and interstitial brachytherapy play an important role in cervical, uterine, and vulvar cancers; thus, patients may be seen years after cure with treatment-related complications. Radiation cystitis, ureteral strictures, various fistulae, and secondary malignancies can all potentially develop as a result of pelvic radiation oftentimes presenting years after treatment. In addition, it is not uncommon for these patients to have a reduced bladder capacity after radiation, resulting in bothersome urinary symptoms. In patients with a prior history of radiation, it is imperative that any new onset urinary symptoms be promptly addressed along with referral to both a gynecologist and a urologist. Initial evaluation involves ruling out recurrent malignant disease.

Extramammary Paget's Disease

Extramammary Paget's disease (EMPD) is a rare adenocarcinoma arising from the apocrine glands that can be encountered in both elderly men and women. EMPD can present over a wide age range from 50 to 80 years [26]. It is most commonly diagnosed in white males and typically involves the scrotum, penis, and/or perineum (Fig. 20.4) [52]. In females, the vulva is typically affected, as shown in Fig. 20.5 [53]. It gives the appearance of a well-demarcated erythematous patch or a white plaque. Given the nonspecific appearance, diagnosis is often delayed, and patients might be treated for other conditions such as contact dermatitis, eczema, or psoriasis [52]. Histologic diagnosis is established after biopsy, which demonstrates abundant Paget cells in the epidermal layer. Definitive treatment most commonly involves wide local excision, although there have been reports of using Mohs microsurgery. Prognosis is poor for invasive tumors, and inguinal lymph node dissection may have a role in this setting. A thorough workup for metastatic disease should be performed as occult internal malignancy, most commonly, has been detected in all presentations of this condition [26, 54, 55].

Summary

Malignancies of the testis, penis, urethra, and other associated genitourinary structures are uncommon in older adults. However, these can occur and need to be accurately diagnosed using history, physical examination, imaging studies, and in some cases biopsy. Treatment includes a range of surgical and medical therapies depending on the specific condition. There is a paucity of data on clinical outcomes from treatment in the older adult population due to the scarcity of cases and the typical exclusion of older adults with comorbidities from clinical trials. Patients should be offered therapy for their cancers in the context of their overall health and clinical condition. Age by itself should not be the determining factor regarding treatment decisions. In most cases, early diagnosis can help improve overall outcomes.

References

1. National Cancer Institute. Testicular Cancer. Available at: http://www.cancer.gov/cancertopics/types/testicular
2. National Cancer Institute. SEER Database SEER Stat Fact Sheets: Testes Available at: http://seer.cancer.gov/statfacts/html/testis.html
3. Dieckmann KP, Pichlmeier U. Clinical epidemiology of testicular germ cell tumors. World J Urol. 2004;22:2–14.
4. Akre O, Pettersson A, Richiardi L. Risk of contralateral testicular cancer among men with unilaterally undescended testis: a meta analysis. Intl J Cancer. 2009;124(3):687–9.
5. Pettersson A, Richiardi L, Nordenskjold A, Kaijser M, Akre O. Age at surgery for undescended testis and risk of testicular cancer. N Engl J Med. 2007;356:1835–41.
6. Wanderas EH, Fossa SD, Tretli S. Risk of second germ cell cancer after treatment of a primary germ cell tumor in 2201 Norwegian male patients. Eur J Can. 1997;33:244–52.
7. Greene MH, Kratz CP, Mai PL. Familial testicular germ cell tumors in adults: 2010 summary of genetic risk factors and clinical phenotype. Endocr Relat Cancer. 2010;17(2):109–21.
8. Testis (2010) In: Edge SE, Byrd DR, Compton CC, et al., (eds). AJCC cancer staging manual. 7th ed. Springer, New York, NY pp 469–473
9. Fernandez EB, Moul JW, Foley JP, Colon E, McLeod DG. Retroperitoneal imaging with third and fourth generation computed axial tomography in clinical stage I nonseminomatous germ cell tumors. Urology. 1994;44:548–52.
10. Stephenson AJ, Gilligan TD. Neoplasms of the testis. In: Kavoussi LR, Novick AC, Partin AW, Peters CA, Wein A, editors. Campbell-Walsh urology. 10th ed. Philadelphia: Saunders; 2011. p. 848. Ch 31.
11. Salem M, Gilligan T. Serum tumor markers and their utilization in the management of germ-cell tumors in adult males. Exper Rev Anticancer Ther. 2011;11:1–4.
12. Yoon G, Stein J, Skinner D. Retroperitoneal lymph node dissection in the treatment of low-stage nonseminomatous germ cell tumors of the testicle: an update. Urol Oncol. 2005;23(3):168–77.
13. Berney DM, Warren AY, Verma M, et al. Malignant germ cell tumors in the elderly: a histopathological review of 50 cases in men aged 60 years or older. Mod Pathol. 2008;21:54–9.
14. Chung PW, Bayley AJ, Sweet J, et al. Spermatocytic seminoma: a review. Eur Urol. 2004;45:495–8.
15. Capitanio U, Jeldres C, Perrotte P, et al. Population-based study of perioperative mortality after retroperitoneal lymphadenectomy for nonseminomatous testicular germ cell tumors. Urology. 2009;74:373–7.
16. Chekol S, Chen-Chin S. Malignant mesothelioma of the tunica vaginalis testis: diagnostic studies and differential diagnosis. Arch Pathol Lab Med. 2012;136:113–7.
17. Ikegami Y, Kawai N, Tozawa K, Hayashi Y, Kohri K. Malignant mesothelioma of the tunica vaginalis testis related to recent asbestos. Int J Urol. 2008;15:560–1.
18. Abe K, Kato N, Miko K, et al. Malignant mesothelioma of testicular tunica vaginalis. Int J Urol. 2002;9(10):602–3.
19. Darby S, Hancock B. Localised non-Hodgkin lymphoma of the testis: The Sheffield Lymphoma Group Experience. Int J Oncol. 2005;26:1093–9.
20. Kemmerling R, Stintzing S, Mühlmann J, Dietze O, Neureiter D. Primary testicular lymphoma: a strictly homogenous hematological disease? Onc Reports. 2010;23:1261–7.
21. Vural F, Cagirgan S, Saydam G, Hekimgil M, Soyer NA, Tombuloglu M. Primary testicular lymphoma. J Natl Med Assoc. 2007;99:1277–82.

22. Anghel G, Petti N, Remotti D, Ruscio C, Blandino F, Majolino I. Testicular plasmacytoma: report of a case and review of the literature. Am J Hem. 2002;71:98–104.
23. American Cancer Society: Cancer Facts and Figures 2012. Available at: http://www.cancer.org/Cancer/PenileCancer/DetailedGuide/penile-cancer-key-statistics
24. Hernandez BY, Barnholtz-Sloan J, German RR, et al. Burden of invasive squamous cell carcinoma of the penis in the United States, 1998–2003. Cancer. 2008;113:2883–91.
25. Bunker CB. Skin conditions of the male genitalia. Medicine. 2010;38(6):294–9.
26. Zollo JD, Zeitouni NC. The Roswell Park Cancer Institute experience with extramammary Paget's disease. Br J Dermatol. 2000;142:59–65.
27. Doraiswamy V, Biboa J, Obafemi A, Goldschmid M. Leukocytosis and hypercalcemia: a rare combination of paraneoplastic features in squamous cell penile cancer. South Med J. 2010;103:474–6.
28. Buddington WT, Kickham CJ, Smith WE. An assessment of malignant disease of the penis. J Urol. 1963;89:442–9.
29. Lucky MA, Rogers B, Parr NJ. Referrals into a dedicated British penile cancer centre and sources of possible delay. Sex Transm Infect. 2009;85:527–30.
30. Bleeker MC, Heideman DA, Snijders PJ, Horenblas S, Dillner J, Meijer CJ. Penile cancer: epidemiology, pathogenesis and prevention. World J Urol. 2009;27:141–50.
31. Chaux A, Cubilla A. Diagnosis, epidemiology, and pathology of penile cancer. In: Scardino P, Linehan W, Zelefsky M, Vogelzang N, editors. Comprehensive textbook of genitourinary oncology. Philadelphia, PA: Lippincott Williams & Wilkins; 2011. p. 805–8.
32. Miralles-Guri C, Bruni L, Cubilla AL, Castellsague X, Bosch FX, De Sanjose S. Human papilloma virus prevalence and type distribution in penile carcinoma. J Clin Pathol. 2009;62:870–8.
33. Daling JR, Madeleine MM, Johnson LG, et al. Penile cancer: importance of circumcision, human papillomavirus and smoking in in situ and invasive disease. Int J Cancer. 2005;116:606–16.
34. Velazquez EF, Barreto JE, Rodriguez I, Piris A, Cubilla AL. Limitations in the interpretation of biopsies in patients with penile squamous cell carcinoma. Int J Surg Pathol. 2004;12:139–46.
35. Horenblas S, Van Tinteren H, Delemarre JF, Moonen LM, Lustig V, Kröger R. Squamous cell carcinoma of the penis: accuracy of tumor, nodes and metastases classification system and role of lymphangiography, computerized tomography scan, and fine needle aspiration cytology. J Urol. 1991;146:1279–83.
36. Solsona E, Algaba F, Horenblas S, Pizzocaro G, Windahi T. EAU guidelines on penile cancer. Eur Urol. 2004;46:1–8.
37. Penis (2010) In: Edge SB, Byrd DR, Compton CC, et al (eds) AJCC cancer staging manual. 7th ed. Springer, New York, NY pp 447–455
38. Agrawal A, Pai D, Ananthakrishnan N, Smile SR, Ratnakar C. The histological extent of the local spread of carcinoma of the penis and its therapeutic implications. BJU Int. 2000;85:299–301.
39. Horenblas S, van Tinteren H, Delemarre JF, Boon TA, Moonen LM, Lustig V. Squamous cell carcinoma of the penis II: treatment of the primary tumor. J Urol. 1992;147:1533–8.
40. Souillac I, Avances C, Camparo P, et al. Penile cancer in 2010: update from the oncology committee of the French Association of Urology: External Genital Organs Group (CCAFU-OGE). Prog Urol. 2011;21:909–16.
41. Schlenker B, Tilki D, Seitz M, et al. Organ-preserving neodymium-yttrium-aluminum-garnet laser therapy for penile carcinoma: a long-term follow-up. BJU Int. 2010;106:786–90.
42. Colecchia M, Nicolai N, Secchi P, et al. pT1 penile squamous cell carcinoma: a clinicopathologic study of 56 cases treated by CO_2 laser therapy. Anal Quant Cytol Histol. 2009;31:153–60.
43. Mohs FE, Snow SN, Larson PO. Mohs micrographic surgery for penile tumors. Urol Clin North Am. 1992;19:291–304.
44. Crook J. Radiation therapy for penile cancer. In: Scardino P, Linehan W, Zelefsky M, Vogelzang N, editors. Comprehensive textbook of genitourinary oncology. Philadelphia, PA: Lippincott Williams & Wilkins; 2011. p. 823–9. Chapter 48.
45. McDougall WS, Kirchner FK, Edwards RH, Killion LT. Treatment of carcinoma of the penis. The case for primary lymphadenectomy. J Urol. 1986;136:38–41.
46. Lynch D. Urethral cancer. AUA Update Ser. 2006; 25:109–16.
47. Swartz M, Porter M, Lin D, Weiss N. Urology incidence of primary urethral carcinoma in the United States. Urology. 2006;68:1164–8.
48. Rabbani F. Prognostic factors in male urethral cancer. Cancer. 2011;117:2426–34.
49. Wiener J, Walther P. A high association of oncogenic human papilloma viruses with carcinomas of the female urethra: polymerase chain reaction-based analysis of multiple histological types. J Urol. 1994;151:49–53.
50. Urethra (2010) In: Edge SB, Byrd DR, Compton CC, et al (eds.) American Joint Committee on Cancer Staging Manual, 7th, Springer, New York p 507
51. Dimarco DS, Dimarco CS, Zincke H, et al. Surgical treatment for local control of female urethral carcinoma. Urol Oncol. 2004;22:404–9.
52. Zhang N, Gong K, Zhang X, et al. Extramammary Paget's disease of the scrotum – report of 25 cases and literature review. Urol Oncol. 2010;28:28–33.
53. Chattopadhyay M, Sterling J. Skin diseases affecting the vulva. Obstetr Gynaecol Reprod Med. 2011;21(6):169–75.
54. Chan JYW, Li GKH, Chung JHP, Chow VLY. Extramammary Paget's disease: 20 years of experience in Chinese population. Int J Surg Oncol. 2012; article ID: 416418.
55. Fanning J, Lambert HC, Hale TM. Paget's disease of the vulva: prevalence of associated vulvar adenocarcinoma, invasive Paget's disease, and recurrence after surgical excision. Am J Obstet Gynecol. 1999;180 (1 Pt 1):24–7.

21 Renal Failure, Dialysis, and Transplantation in Older Adults

John M. Barry

Introduction

The purpose of this chapter is to provide the urologist who does not do kidney transplants with an overview of end-stage renal disease (ESRD) treatment in elderly patients with an emphasis on renal transplantation.

Epidemiology of Renal Failure

The incidence of ESRD in the USA is approximately 360 per million population per year, and it increases with age [1]. It is about 1,300 per million population for those 65–74 years of age and 1,700 per million population for those 75 and older. One-half of ESRD patients in the USA are over 65 years old, and their most common treatment for ESRD is in-center hemodialysis. The four main causes of ESRD, in descending order, are diabetes mellitus, glomerulonephritis, hypertension, and cystic kidney diseases. Patients treated with renal replacement therapy have decreased life expectancies when compared with the general population, usually because of death from cardiovascular disease, and better patient survival and quality of life are reported for kidney transplant recipients when dialysis and transplantation are compared as treatment modalities for ESRD. Based on annual death data, it is possible to construct a relative mortality rate table to estimate survival probabilities based on treatment modality (Table 21.1) [1–3].

About 1 in 6 patients wait-listed for a deceased donor kidney transplant in the USA is 65 or older [1]. Patients in this age group receive 18 % of deceased donor kidney transplants, the same as the proportion listed; however, only 11 % of living donor kidney transplant recipients are 65 or older. The median waiting times for deceased donor kidney transplants are similar for all adult age groups. Most of the 16,000 kidneys transplanted in the USA each year are from deceased donors, and 9 % of deceased organ donors are 65 years of age or older [1]. Elderly kidney transplant recipients have significantly lower patient and kidney transplant survival rates when compared to those of younger recipients, and they are more likely to die with a functioning kidney transplant than their younger counterparts. For this reason, an age-matched deceased donor kidney allocation plan, the Eurotransplant Senior Program (ESP), was begun in 1999 wherein kidneys from deceased donors aged older than 65 years were allocated to recipients 65 years of age and older [4]. A common practice in the United States is to offer expanded criteria donor (ECD) deceased donor kidneys, defined as those from any donor over the age of 60 or from any donor over the age of 50 with two of the following three characteristics: history of hypertension, final serum creatinine

J.M. Barry, M.D. (✉)
Department of Urology, Oregon Health and Science University, 3303 SW Bond Avenue, Portland, OR 97239, USA
e-mail: barryj@ohsu.edu

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_21,

>1.5 mg/dL, and cerebrovascular accident as cause of death, to transplant candidates over the age of 60 [5]. These kidneys are offered only to transplant candidates who agree to receive ECD kidneys at the time of listing. The result of this policy is that patients 65 and older receive 36 % of ECD kidney transplants [1]. Table 21.2 documents that, in spite of the severe shortage of transplantable kidneys, elderly transplant candidates are not disadvantaged by the current system [1].

The challenging task is to select the elderly ESRD patient who will benefit the most from renal transplantation.

Table 21.1 Survival estimates for renal replacement therapy

Therapy	Relative survival
Comparator, general population	1.0
Living donor kidney transplantation	0.7
Deceased donor kidney transplantation	0.6
Wait-listed for deceased donor kidney transplantation	0.5
Dialysis	0.25

Interpretation of data from US Renal Data System, USRDS 2010 Annual Data Report. Bethesda, MD: the National Institutes of Health, National Institute of Diabetes, Digestive, and Kidney Diseases 2010
Wolfe RA, Ashby VB,. Milford EL, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation and recipients of a first cadaver kidney transplant. N Engl J Med 1999; 348:1625–1730
Ojo AO, Hanson JA, Meier-Kriesche H, et al. Survival of marginal cadaveric donor kidneys compared with other recipients and wait-listed transplant candidates. J Am Soc Nephrol. 2001;12:589–597

Recipient Selection and Preparation

Not all patients with chronic kidney disease approaching ESRD are suitable candidates for renal replacement therapy, and medical management without dialysis or transplantation is an option that can be offered to some patients and their caregivers [6–8]. For example, a patient with two or more of the following criteria—age 75 or older, Charlson comorbidity score of 8 or more (Table 21.3) [9, 10], Karnofsky score of 40 (disabled, requires special care and assistance) or less, and serum albumin <2.5 mg/dL—may not have quality of life improvement or significantly increased longevity with renal transplantation or dialysis when compared with palliative care.

A renal transplant candidate consultation is done well in advance of renal transplantation for the detection and treatment of comorbidities and the prevention of significant morbidity, mortality, and premature graft loss [11, 12]. This basically consists of a complete history and physical examination with updating of healthcare maintenance items such as immunizations and cancer screening. This process removes the adoption of arbitrary age limits for renal transplant candidates. Generally accepted exclusion criteria for transplantation, regardless of age, are psychosocial or financial problems that would prevent compliance with a post-transplant treatment regimen, high probability of operative mortality, active invasive infection, active malignancy, and unsuitable anatomy for technical success.

Table 21.2 Wait-listed adult kidney transplant candidates and adult kidney transplant recipients: example from current era

Wait-listed on December 31, 2009			Transplanted in 2009 All		Deceased donor		Living donor	
Age (years)	*N*	%	*N*	%	*N*	%	*N*	%
18–64	64,892	82	13,305	83	8,006	81	5,299	88
65+	*14,469*	18	*2,659*	17	*1,906*	19	*753*	12
	79,361		15,964		9,912		6,052	

Data from US Renal Data System, USRDS 2110 Annual Report. Bethesda, MD: the National Institutes of Health, National Institute of Diabetes, Digestive, and Kidney Diseases 2010

Table 21.3 Charlson comorbidity index scoring system

Score	Condition
1 point each for	Myocardial infarction (history, not ECG changes only)
	Congestive heart failure
	Peripheral vascular disease (includes aortic aneurysm ≥6 cm)
	Cerebrovascular disease: CVA with mild or no residual or TIA
	Dementia
	Chronic pulmonary disease
	Connective tissue disease
	Mild liver disease (without portal hypertension, includes chronic hepatitis)
	Diabetes without end-organ damage (excludes diet controlled alone)
2 points each for	Hemiplegia
	Moderate-to-severe renal disease
	Diabetes with end-organ damage (retinopathy, neuropathy, nephropathy, or brittle diabetes)
	Tumor without metastases (exclude if >5 years from diagnosis)
	Leukemia (acute or chronic)
	Lymphoma
3 points for	Moderate-to-severe liver disease
6 points each for	Metastatic solid tumors
	AIDS (not just HIV positive)

For each decade >40 years of age, add 1 point

ECG electrocardiogram, *CVA* cerebrovascular accident, *TIA* transient ischemic attack, *AIDS* acquired immunodeficiency syndrome, *HIV* human immunodeficiency virus

Modified from Estimated prognosis for dialysis patients. http://www.nephron.org/cgi-bin/rpa_sdm.cgi. Accessed January 9, 2012 and Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation J Chron Dis. 1987;40:373–383

Psychosocial or Financial Problems

Psychosocial and financial screenings are performed to identify and correct problems that could result in noncompliance, for example, the lack of funds to pay for maintenance immunosuppression, mental dysfunction that would prevent a patient from following a post-transplant treatment plan, or an inadequate family or social support system.

High Probability of Operative Mortality

ESRD results in premature vascular disease, especially when combined with the factors of heredity, smoking, hypertension, diabetes mellitus, and hyperlipidemia. Findings of ischemia on stress cardiac imaging are usually evaluated with coronary arteriography, and significant lesions are managed with medication with or without angioplasty. The use of human recombinant erythropoietin allows the partial correction of ESRD anemia and contributes to the prevention of end-organ ischemia or infarction.

Patients with a history of peptic ulcer disease or dyspepsia should undergo endoscopy with treatment of inflammation or ulcers. Healing is usually documented by endoscopy prior to listing for transplantation.

Infection

The current Centers for Disease Control and Prevention immunization recommendations are followed [13]. These include vaccinations against hepatitis A and B, herpes zoster, influenza, pneumococcus, tetanus and diphtheria, and varicella if the transplant candidate has never had chicken pox. Meningococcal vaccination is advised for asplenic patients.

The most common sites of existing infection in the potential renal transplant recipient are the chest and urinary tract. Screening tests for pulmonary infectious diseases are chest X-ray and tuberculosis tests. Patients with inactive tuberculosis usually receive 9 months of prophylactic isoniazid. This need not delay transplantation, and the treatment course is simply continued after transplantation.

Urinary tract infection (UTI) must be resolved or controlled prior to transplantation. Patients with a history of symptomatic, recent, recurrent UTIs usually have monthly surveillance urinalyses with cultures. Treatment is based on culture and sensitivity results. If renal infection, stones, or ureteral obstruction is a real or potential source of recurrent or chronic bacteriuria, nephrectomy is performed, usually 6–8 weeks prior to transplantation.

Patients with a history of inflammatory bowel disease are evaluated with lower GI studies, and prophylactic segmental colectomy is recommended for patients with recurrent diverticulitis [14]. Cholelithiasis with cholecystitis is treated by pre-transplant cholecystectomy. Asymptomatic cholelithiasis without gall bladder thickening is usually monitored, and pre-transplant cholecystectomy is not required.

As in patients undergoing chemotherapy for cancers, dental infections must be resolved before immunosuppression in transplanted patients. Dental examination and treatment should be completed prior to active listing for transplantation.

Cytomegalovirus (CMV) antibody levels are determined because post-transplant CMV infection can result in significant morbidity and mortality in geriatric transplant patients. For this reason some transplant programs do not transplant kidneys from CMV seropositive donors into elderly recipients who are CMV seronegative. If hepatitis B or C viral antibody levels indicate active hepatitis, these patients are excluded from transplantation until cleared by hepatology consultation because of the risk of hepatitis exacerbation with immunosuppression. Recipients who are human immunodeficiency virus (HIV) positive may qualify for transplantation if CD4-lymphocyte counts are satisfactory [15]. Many centers obtain herpes simplex viral (HSV) titers. If the titers are elevated or the patient has a history of herpesvirus infection, antiviral prophylaxis is commonly instituted for 3–4 months after transplantation.

Active Malignancy

Patients with treated solid-organ cancer must have a low probability of recurrence by nomogram after transplantation. For example, waiting time is usually not necessary after removal of a T1a or a Fuhrman grade 1 or 2 T1b renal cell carcinoma or after curative treatment of a T1 or T2 low-to-intermediate-grade prostate cancer. Patients undergoing active treatment of malignancy will usually be treated with dialysis rather than renal transplantation.

Unsuitable Anatomy for Technical Success

The transplant candidate with a history suspicious for a genitourinary abnormality requires the same workup as a non-transplant candidate. The potential recipient must have an adequate urinary reservoir that empties or can be emptied by intermittent catheterization or an unobstructed urinary conduit [16]. An ultrasound of the post-void bladder or continent bladder substitute will screen for urinary retention, and contrast studies of continent reservoirs or urinary conduits are commonly done to check for stones, reflux, or obstruction. Significant stricture disease and benign prostatic obstruction (BPO) must be treated, or a management plan must be in place prior to transplantation. When medical management of BPO fails, invasive procedures are warranted. Following prostatectomy or transurethral incision of the prostate, it is reasonable to keep the denuded prostatic fossa open until reepithelialization occurs to prevent prostatic stricture. This usually takes 6–8 weeks. When native urine volume is inadequate, bladder cycling via intermittent catheterization or placement of a suprapubic cystostomy tube at the time of bladder outlet surgery will allow the patient to fill the bladder with sterile water and void. Bladder cycling is reasonable in a kidney transplant candidate who has had extensive lower urinary tract surgery to determine if the patient will be dry and the bladder will be a low-pressure reservoir between voids. The poorly compliant bladder that develops from nonuse in the oligoanuric patient will usually function normally by 6 weeks after successful kidney transplantation.

Ultrasonography to detect hydronephrosis, stones, or tumors is a minimum evaluation of the upper urinary tract. Renal tumors occur with increased frequency in patients who have the acquired cystic disease of chronic renal failure [17], and preliminary nephrectomy is usually done for solid tumors; however, T1a and Fuhrman grade 1 or 2 T1b renal cell carcinomas can probably be treated with nephrectomy at the time of transplantation. When polycystic kidneys extend below the level of the iliac crests and could interfere with placement of a kidney transplant or are associated with infection, stones, hemorrhage, pain, or early satiety, nephrectomy is commonly performed at least 6 weeks before or at the time of transplantation [18]. The surgical technique for native nephrectomy will depend on the risks to the patient for infection or tumor spread, proposed additional surgeries under the same anesthetic, the skill set of the surgical team, and the availability of specialized equipment.

Symptoms and signs of peripheral vascular disease are sought to be certain that arterial revascularization of the kidney graft is possible and that an ipsilateral lower extremity or buttock steal syndrome will not result from transplantation. Doppler flow studies of pelvic vessels and the splenic artery are helpful in patients with severe peripheral vascular disease or those who have undergone abdominal or pelvic vascular reconstructive procedures to select an appropriate arterial target. Foot ulcers must be healed to prevent infection with immunosuppression. This is particularly important in patients with underlying diabetes who may be at higher risk for lower extremity vascular disease and foot ulcers.

Recipient Evaluation Immediately Before Transplantation

At the time of admission for renal transplantation, a rapid clinical evaluation is performed to detect intercurrent illness that could prevent a successful operative procedure and immunosuppression. If necessary, a microlymphocytotoxicity crossmatch can be obtained if there has been a recent blood transfusion or infection. Many programs do a thrombophilia panel to detect a hypercoagulable state and plan for anticoagulation beginning in the preoperative area or the operating room. Immunosuppression is usually started during the deceased donor kidney transplant procedure. With elective living renal donor kidney transplantation, immunosuppression with a purine antagonist, such as azathioprine or mycophenolate mofetil, is commonly initiated a week before transplantation.

Recipient Operation

Technique

The technique has become standardized over the past 50 years.

A prophylactic antibiotic, usually a cephalosporin, is administered just before surgery and continued until the results of intraoperative cultures indicate a change or discontinuance. Because of antibiotic concentrations in renal cysts [19], a fluoroquinolone is recommended if polycystic kidneys are to be manipulated and removed at the time of renal transplantation.

After induction of anesthesia, a triple-lumen central venous pressure (CVP) line is placed to draw blood samples and for IV fluid administration and CVP monitoring. The genitalia and abdominal skin are prepared, and a self-retaining balloon catheter is placed in the bladder and hooked to a three-way system so that bladder irrigation with an antibiotic solution and bladder volume control for subsequent urinary tract reconstruction can be done (Fig. 21.1) [20]. During the operation, CVP is maintained between 5 and 10 cm H_2O to provide adequate volume for perfusion yet prevent congestive heart failure.

Usually, the kidney graft is placed extraperitoneally in the contralateral iliac fossa through a Rutherford Morison or modified Gibson incision so that the renal pelvis and ureter are the most medial of the hilar structures in case subsequent surgery is necessary on the collecting system of the kidney graft (Fig. 21.2). In men, the spermatic cord is preserved. In women, the round ligament is divided between ligatures. The peritoneal envelope is retracted medially. The iliac arteries are palpated, and a suitable site for the arterial anastomosis is selected. Because of arteriosclerosis in the elderly recipient, an end-to-end renal artery to internal iliac artery anastomosis is usually avoided. When it is done, internal iliac

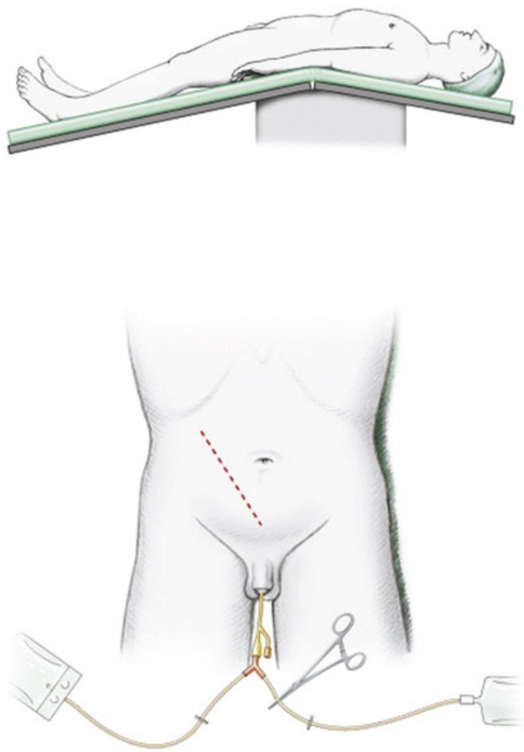


Fig. 21.1 Kidney transplant incision (*dotted line*) and Y-connector bladder setup to allow the bladder to be filled with antibiotic irrigation and drained. Reproduced with permission from Barry JM. Renal transplant recipient surgery. BJU Int 2007; 99:701–717

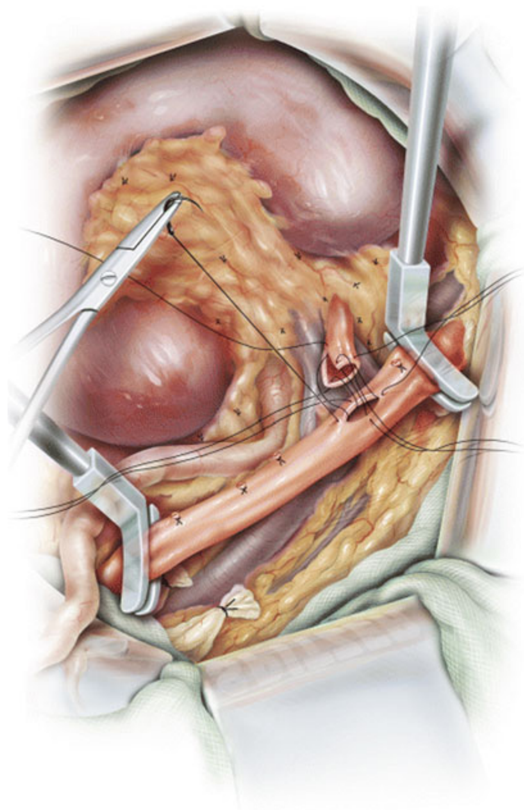


Fig. 21.2 *Left* kidney transplant into the *right* iliac fossa. The spatulated renal artery is set to be anastomosed to the external iliac artery. The spermatic cord is preserved and retracted medially. Reproduced with permission from Barry JM. Renal transplant recipient surgery. BJU Int 2007; 99:701–717

endarterectomy may be necessary. The most common type of arterial anastomosis in geriatric patients is renal artery or aortic patch to the side of the external iliac artery (Fig. 21.3). Rarely, it is necessary to anastomose the renal artery to the common iliac artery, the aorta, an aortoiliac graft, or the splenic artery. Care is taken when applying vascular clamps so as not to fracture intra-arterial plaque. An aortic punch is commonly used to create a smooth, round hole in a rigid, atherosclerotic artery or a graft. Sewing from inside out on atherosclerotic vessels will prevent separation of the diseased intima from the media and reduce the risk of vascular dissection on release of the vascular clamps. The renal vein is usually anastomosed to the side of the external or common iliac vein and rarely to the left renal vein after native nephrectomy. Complete mobilization of the external and common iliac veins by dividing the posterior tributary veins between ligatures will allow the venous anastomosis to fit comfortably onto the vein and within the bow of a redundant external iliac artery. If dual renal transplantation of marginal kidneys is planned, one can be placed in each iliac fossa, or they can be stacked one on top of the other in the same iliac fossa [21]. Mannitol, an osmotic diuretic and free radical scavenger, is given intravenously during and immediately after renal revascularization.

Urinary tract reconstruction is usually by extravesical ureteroneocystostomy (Figs. 21.3 and 21.4). Double-pigtail ureteral stents are commonly placed. If the bladder is small because of nonuse and does not adequately distend when filled with antibiotic irrigation, stented uretero-ureterostomy is a good alternative to ureteroneocystostomy. A single suction drain is commonly placed in the surgical bed and brought out through

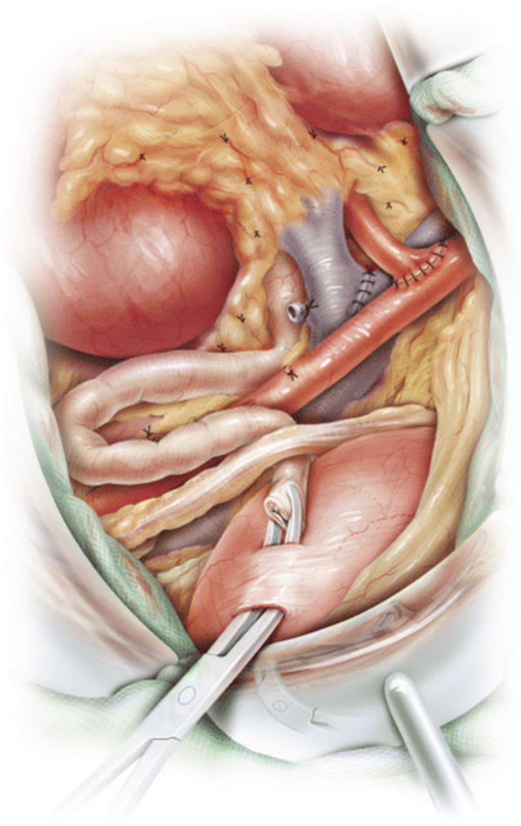


Fig. 21.3 Completed arterial and venous anastomoses with passage of the ureter under the spermatic cord. A submucosal tunnel has been developed to prevent reflux. Reproduced with permission from Barry JM. Renal transplant recipient surgery. BJU Int 2007; 99:701–717

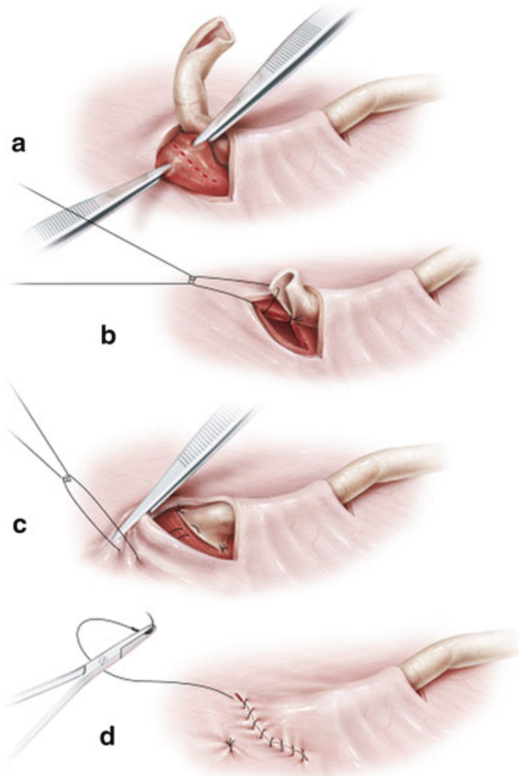


Fig. 21.4 Completion of ureteroneocystostomy. If a double-pigtail ureteral stent is used, it is placed between steps b and c. Reproduced with permission from Barry JM. Renal transplant recipient surgery. BJU Int 2007; 99:701–717

the abdominal wall. Care is taken to avoid placing the drain on either the vascular or ureteral anastomotic sites.

Postoperative Care

Intravenous fluid of 0.45 % saline is given at a rate equal to the urinary output. Insensible loss is replaced with 0.45 % saline in 5 % dextrose solution. Delayed graft function is managed by raising the CVP to 10 cm H_2O and administering intravenous furosemide. Serum electrolytes and hematocrit are monitored every 4–8 h until the values become stable. When the serum potassium is in the mid-normal range, potassium is added to the IV solution. Hyperkalemia or fluid overload is usually managed by dialysis. High serum levels of potassium can be counteracted by intravenous calcium chloride, and the level of serum potassium can be temporarily lowered by intravenous sodium bicarbonate and/or glucose and insulin. Bowel continuity usually returns within 3 days. Abdominal distention on physical examination is monitored with serial abdominal radiographs to detect pseudo-obstruction of the colon and prevent cecal perforation and sepsis.

When delayed graft function occurs, ultrasonogram and radioisotope renogram are obtained to determine kidney graft blood flow and function and to screen for ureteral obstruction or fluid collections. A urine culture is obtained 24 h before Foley catheter removal, and antibiotics are started or changed on the basis of organism identity or sensitivity testing. A single dose of tamsulosin may prevent urinary retention in elderly men when the urinary bladder catheter is removed. If external skin sutures or staples were used, they are removed 7–14 days postoperatively. If a ureteral stent was used and not secured to the bladder catheter, it is removed 4–12 weeks after the transplant procedure in the outpatient clinic. A prophylactic urinary antibiotic such as trimethoprim–sulfamethoxazole (TMP/SMX) is commonly administered for 3 months. Minor sulfa allergy can be managed by desensitization during transplant hospitalization. Major sulfa allergy is managed by substitution with single, daily dose of nitrofurantoin macrocystals. If TMP/SMX cannot be used, a substitute for postoperative *Pneumocystis jiroveci* pneumonia prevention, such as pentamidine, is used.

Renal Allograft Rejection

There is evidence that elderly recipients do not mount as strong an immune response to grafted tissue as younger recipients [22]. Kidney transplant rejection is prevented or minimized by histocompatibility between donor and recipient and immunosuppression [23, 24]. ABO blood group compatibility and a negative donor–recipient cytotoxic lymphocyte crossmatch are necessary. Antibody induction therapy is usually based on immunologic risk factors, and a simple scoring system has been used in our program since 1994 (Table 21.4) [23]. Maintenance immunosuppression is with a purine antagonist such as azathioprine or mycophenolate mofetil, a calcineurin inhibitor such as tacrolimus or cyclosporine, and decreasing doses of a glucocorticoid such as prednisone. Rejection crises are usually diagnosed by needle biopsy and treated with increased doses of a glucocorticoid. Glucocorticoid-resistant rejection is usually treated with lymphocyte-depleting antibody. Antibody-mediated rejection is managed with plasmapheresis and increased glucocorticoid. Prophylactic anti-infective therapy for bacteria, yeast, and viral infections is described in Table 21.5 [23].

The most frequent complication from azathioprine or mycophenolate mofetil is leukopenia, and peripheral blood leukocyte counts are monitored with decreasing frequency. The most common complication of calcineurin inhibitors is nephrotoxicity, and blood levels of these drugs are monitored with decreasing frequency after transplantation. Danazol, ketoconazole, erythromycin, nicardipine, diltiazem, and methyltestosterone have been reported to increase blood levels of calcineurin inhibitors. Rifampin, phenytoin, phenobarbital, intravenous TMP/SMX, and carbamazepine have been reported to decrease blood levels of calcineurin inhibitors because they increase hepatic metabolism of this class of drugs by inducing the cytochrome P-450 system. Nephrotoxic drugs, such as aminoglycosides and amphotericin B, and potassium-sparing diuretics should be used with caution in patients receiving tacrolimus or cyclosporine. Targets of maintenance immunosuppressant toxicities are listed in Table 21.6.

Table 21.4 Antibody induction in elderly kidney transplant recipients

Points	Risk factors
1 each for	Prior kidney transplant with early immunologic loss, all HLA antigen mismatched, delayed graft function, African–American ethnicity
2 each for	Panel reactive antibody >50 %, positive flow crossmatch, ABO blood group A2 into O or B, A2B into B
Subtract 1 for	Age over 60

For ≥2 points, use lymphocyte-depleting antibody; for 1 point, use anti-interleukin 2 receptor antibody; for no points or human leukocyte antibody identical sibling donor+, use no antibody induction

From Oregon Health and Science University Renal Transplant Program

Complications of Renal Transplantation

Management recommendations for post-transplant complications are summarized in Table 21.7.

Surgical

Acute postoperative hemorrhage within the urinary tract that cannot be controlled with catheter irrigation is managed by endoscopic fulguration or, rarely, open surgical correction. Hemorrhage within the extraperitoneal operative site is managed by graft exploration, identification of the

Table 21.5 Postoperative infection prophylaxis

Problem	Usual drug prophylaxis	Alternate(s)
Urinary retention	Tamsulosin at catheter removal	Any alpha blocker
Urinary infection	Trimethoprim-sulfamethoxazole X 3 months	Nitrofurantoin
Pneumocystis jiroveci	Trimethoprim-sulfamethoxazole X 3 months	Pentamidine inhalant
Oral candidiasis	Clotrimazole lozenges X 1–3 months	Nystatin troches
Vaginal candidiasis	Clotrimazole vaginal inserts	Nystatin inserts
HSV	Acyclovir X 3 months	Ganciclovir, valacyclovir, famciclovir
CMV	Ganciclovir X 4 months	Valacyclovir, acyclovir

CMV cytomegalovirus, *HSV* herpes simplex virus
Modified from Barry JM, Conlin MJ, Renal transplantation. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA, eds. Campbell-Walsh Urology, 10th edition. Philadelphia, PA: Elsevier; 2012:1248

Table 21.6 Major toxicity targets for maintenance immunosuppressants

	Glucocorticoid	Calcineurin inhibitor	Purine antagonist	mTOR inhibitor
Wound healing	X			X
Kidney		X		
Central nervous system	X	X		
Gastrointestinal system		X	X	
Hematopoietic system			X	X
Endocrine system	X	X		X
Lipid system	X			X

Glucocorticoid, methylprednisolone or prednisone; calcineurin inhibitor, cyclosporine or tacrolimus; purine antagonist, azathioprine or mycophenolate mofetil; mTOR inhibitor, sirolimus or everolimus

Table 21.7 Management of urologic problems after kidney transplantation

Problem	Recommendation(s)
Febrile urinary tract infection	Image native and transplanted kidney(s) Cystogram for reflux
Hematuria	Workup native and transplanted kidney(s)
Hydronephrosis	Radioisotope renogram with furosemide washout
Hydronephrosis due to obstruction	Percutaneous nephrostomy to monitor renal function and delineate cause
Stones	Treat as you usually would; do metabolic workup
Fluid collection with obstruction, fever, or pain	Aspirate for diagnosis and treatment
Fluid collection, asymptomatic	Leave it alone
Lymphocele	Aspirate 2–3 times; repair if it recurs
Penile prosthesis candidate	No perivesical reservoir
Prostate nodule or ↑ PSA	Calculate expected remaining lifetime before workup
Bladder outlet obstruction	Workup and treat as for non-transplant patient
Superficial bladder cancer	Avoid BCG

PSA prostate-specific antigen, *BCG* bacillus calmette-guerin

bleeding site, and vascular suturing or ligation. When late hematuria cannot be attributed to medical renal disease, urologic evaluation must include the retained native kidneys and ureters as well as the transplanted kidney or kidneys. Graft rupture is a rare occurrence that is due to severe, acute rejection or renal vein thrombosis. Allograft salvage is rare, and allograft nephrectomy is frequently necessary. Significant renal artery stenosis is unusual. When it occurs in the later postoperative period, severe hypertension that is poorly controlled with medications is followed by a decrease in renal function. Diagnosis is by renal arteriogram, and treatment is usually by transluminal angioplasty and stent placement.

Ureteral obstruction or urinary extravasation in the early postoperative period is detected by ultrasound and confirmed by contrast radiography or radioisotope renography. Minimally invasive techniques have been successful in managing these problems; however, open surgical revision is sometimes required.

Renal calculi are managed by extracorporeal shock wave lithotripsy, percutaneous nephrostolithotomy, or both. Ureteroscopic management can be problematic because of the tortuous distal transplant ureter. The procedure is easier if a refluxing ureteroneocystostomy, native uretero-ureterostomy, or native ureteropyelostomy was performed.

Lymphocele occurs weeks to months following transplantation. The usual presentation is decreased renal function with an ipsilateral cystic mass on ultrasonography accompanied by ipsilateral leg swelling. Treatment is by aspiration, aspiration with sclerosis or opening it into the peritoneal cavity.

Urinary leakage can be differentiated from lymphocele by creatinine determination of the aspirate. Urinoma has a high creatinine level when compared with serum, whereas lymphocele has a level similar to that of serum. If urine leakage is due to distal ureteral necrosis, operative repair is usually necessary.

Wound infection is largely prevented by the prophylactic measures previously outlined. When it occurs, treatment is with drainage and antibiotics. For severe infections, the purine antagonist is withheld, the glucocorticoid dose is reduced, and the calcineurin inhibitor is usually continued.

Medical

One of the risk factors for deep vein thrombosis and pulmonary embolism is advanced age. Anticoagulation protocols are commonly used to prevent thromboembolic complications, both arterial and venous. In addition to prophylaxis with anticoagulant medications, mechanical prophylaxis with lower extremity stockings or sequential compression devices can also be provided.

Post-transplant hypertension is common. Causes for this are intrinsic renal disease, graft rejection, transplant renal artery stenosis, and calcineurin inhibitor toxicity. Myocardial infarction and stroke continue to be the leading causes of death in this patient population despite aggressive preoperative assessment and treatment. Glucocorticoid immunosuppression increases cardiovascular risk because of hyperlipidemia, and post-transplant hyperlipidemia is treated with dietary changes and antilipid medications.

The second leading cause of death in renal transplant patients is infection [1]. Although pneumonia can be due to common bacterial organisms, *Legionella*, *Nocardia*, mycobacteria, viruses, parasites, and fungi can all be etiologic agents. Patients need to be carefully monitored for possible pneumonia, and symptoms need to be addressed quickly. Sputum cultures can be helpful to diagnose the underlying infectious organism and help guide antibiotic therapy. Imaging with chest X-ray or chest CT may be necessary to monitor resolution or progression.

UTI following renal transplantation is common. The risk factors of age and immunosuppression are always present. Modifiable risk factors including indwelling urinary catheter and urinary retention are commonly present. Diabetes mellitus is also a common risk factor, and improved glucose control can help reduce UTI rates. Episodes of graft dysfunction accompanied by fever can be due to either acute rejection or allograft pyelonephritis. These two conditions must be differentiated from one another because increased immunosuppression during a bout of untreated pyelonephritis can result in fatal sepsis. UTIs that occur months after transplantation are usually benign and respond readily to standard antimicrobial therapy.

New onset of diabetes occurs in a significant proportion of elderly renal transplant recipients. This is due to the diabetogenic effects of glucocorticoids or calcineurin inhibitors or both. Patients treated with oral hypoglycemics before transplantation usually require insulin therapy, and patients who required insulin prior to transplantation may require twice the insulin dosage afterwards. Persistent hyperparathyroidism following renal transplantation may necessitate subtotal parathyroidectomy and forearm implantation of parathyroid tissue.

When compared with the general population, transplant recipients have increased standardized incidence ratios (SIR) of infection-related cancers. These include the lymphoproliferative disorders, Kaposi's sarcoma, and carcinomas of the oropharynx, stomach, anus, cervix, penis, vulva, and vagina [25]. The SIRs for kidney and bladder cancers are 4.65 and 1.52, respectively. The SIR of prostate cancer is not increased. Elderly transplant recipients must be carefully monitored for signs or symptoms of these types of malignancies. Early diagnosis and treatment is important.

The Elderly Living Renal Donor

Clinical practice guidelines have been developed for the screening of living kidney donors to minimize harm to these individuals. There is general agreement that nephrologists should assess the medical suitability, surgeons should assess surgical risk, and mental health professionals should assess mental health and the relationship of the transplant candidate to potential donors [26]. Although elderly donors are a potential source of kidneys for transplantation, the rate of acceptable grafts is higher in younger donors. There is an approximately 15 % decrease in renal mass between the ages of 40 and 60, and the glomerular filtration rate begins to decline by the end of the third decade [27]. Generally accepted criteria for exclusion of a renal donor include the following: renal function below normal for age; proteinuria >300 mg/day; microalbuminuria >30 mg/day; body mass index >35 kg/m^2; blood pressure >140/90 with or without treatment; diabetes mellitus; nephrolithiasis if multiple stones, bilateral stone disease, or high recurrence probability because of metabolic condition or anatomic abnormality; malignancy with risk of transmission or future need for nephrotoxic therapy; infection with risk of transmission resulting in recipient morbidity or death; coercion; mental illness; and lack of social support and coping mechanisms. Sometimes a kidney biopsy is necessary before donation to exclude significant disease in the aging kidney. Kidney transplants from living donors more than 55 years old into recipients more than 60 years old had better patient and graft survivals when compared with SCD and ECD deceased donors transplanted into the same-aged recipients [28].

Conclusions

Renal transplantation can be successfully performed in elderly ESRD patients who are carefully selected and who have major risk factors treated prior to transplantation. The use of ECD and age-matched deceased donor kidneys in elderly recipients may balance equity and justice in the distribution of deceased donor organs. The major surgical problems are due to arteriosclerosis and urinary tract abnormalities. Post-transplant infectious complications can be reduced by immunizations, donor assessment, prophylactic anti-infective agents, and carefully selected and monitored immunosuppression. Elderly living kidney donation can be done when generally accepted criteria for donor safety and renal quality are applied.

Acknowledgment Thank you to Megan Taylor, Administrative Coordinator for the Department of Urology, for 30 years of helping me write articles and book chapters and for helping me meet publication deadlines.

References

1. U.S. Renal Data System, USRDS. Annual data report: atlas of chronic kidney diseases and end-stage renal disease in the United States. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2010.
2. Wolfe RA, Ashby VB, Milford EL, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation and recipients of a first cadaver kidney transplant. N Engl J Med. 1999;341:1725–30.

3. Ojo AO, Hanson JA, Meier-Kriesche H, et al. Survival of marginal cadaveric donor kidneys compared with other recipients and wait-listed transplant candidates. J Am Soc Nephrol. 2001;12:589–97.
4. Frei U, Noeldeke J, Machold-Fabrizii V, et al. Prospective age-matching in elderly kidney transplant recipients – a 5-year analysis of the Eurotransplant Senior Program. Am J Transplant. 2008;8:50–7.
5. Grams ME, Womer KL, Ugarte RM, et al. Listing for expanded criteria donor kidneys in older adults and those with predicted benefit. Am J Transplant. 2010;10:802–9.
6. Clinical practice guideline on shared decision-making in the appropriate initiation and withdrawal from dialysis. http://www.aacn.org/WD/Practice/Docs/CP_Guideline. Accessed 11 Sept 2011.
7. Beddhu S, Bruns FJ, Saul M, et al. A simple morbidity scale predicts clinical outcomes and costs in dialysis patients. Am J Med. 2000;108:609–13.
8. Karnofsky DA, Burcherval JH. The clinical evaluation of chemotherapeutic agents in cancer. In: MacLeod CM, editor. Evaluation of chemotherapeutic agents in cancer. New York, NY: Columbia University Press; 1949. p. 191–205.
9. Estimated prognosis for dialysis patients. http://www.nephron.org/cgi-bin/rpa_sdm.cgi. Accessed 9 Jan 2012.
10. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40:373–83.
11. Bunnapradist S, Danovich GM. Evaluation of adult kidney transplant candidates. Am J Kindey Dis. 2007;50:890–8.
12. Kasiske BL, Cangro CB, Hariharan S, et al. The evaluation of renal transplant candidates: clinical practice guidelines. Am J Transplant. 2001;1 Suppl 2:3–95.
13. Recommended immunizations schedules for children, teens, and adults. http://www.immunize.org/catg.d/p2011.pdf. Accessed 3 Jan 2012.
14. Salem L, Anaya D, Veenstra D, Sullivan S, Flum D. Timing of colectomy for diverticulitis: a modeled decision analysis. J Am Coll Surg. 2004;199:904–12.
15. Yoon SC, Hurst FP, Jindal RM, George SA, Neff RT, Agodoa LY, Kimmel PL, Abbott KC. Trends in renal transplantation in patients with human immunodeficiency virus infection: an analysis of the United States renal data system. Transplantation. 2011;91:864–8.
16. Barry JM. Kidney transplantation into patients with abnormal bladders. Transplantation. 2004;77:1120–3.
17. Kuroda N, Ohe C, Mikami S, Hes O, et al. Review of acquired cystic disease-associated renal cell carcinoma with focus on pathobiological aspects. Histol Histopathol. 2011;26:1215–8.
18. Wagner MD, Prather JC, Barry JM. Selective, concurrent bilateral nephrectomies at renal transplantation for autosomal dominant polycystic kidney disease. J Urol. 2007;177:2250–4.
19. Bennett WM, Elzinga L, Pulliam JP, Rashad AL, Barry JM. Cystic fluid antibiotic concentrations in autosomal-dominant polycystic kidney disease. Am J Kidney Dis. 1985;6:400–4.
20. Barry JM. Renal transplant recipient surgery. BJU Int. 2007;99:701–17.
21. Ekser B, Furian L, Broggiato A, et al. Technical aspects of unilateral dual kidney transplantation from expanded criteria donors: experience of 100 patients. Am J Transplant. 2010;10:2000–7.
22. Tullis SG, Tran H, Guleria I, et al. The combination of donor and recipient age is critical in determining host immunoresponsiveness and renal transplant outcome. Ann Surg. 2010;252:662–74.
23. Barry JM, Conlin MJ. Renal transplantation. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA, editors. Campbell-Walsh urology. 10th ed. Philadelphia, PA: Elsevier; 2012. p. 1226–53.
24. Halloran PF. Immunosuppressive drugs for kidney transplantation. N Engl J Med. 2004;351:2715–29.
25. Engels EA, Pfeiffer RM, Fraumeni Jr JF, et al. Spectrum of cancer risk among US solid organ transplant recipients. JAMA. 2011;306:1891–901.
26. Tong A, Chapman JR, Wong G, de Bruijn J, Craig JC. Screening and follow-up of living donors: a systematic review of clinical practice guidelines. Transplantation. 2011;92:962–72.
27. Zowanda ET. The aging kidney. In: Massry SG, Glassock RJ, editors. Textbook of nephrology. 2nd ed. Baltimore, MD: Williams and Wilkins; 1990. p. 996.
28. Gill J, Bunnapradist S, Danvovitch GM, et al. Outcomes of kidney transplantation from older living donors to older recipients. Am J Kidney Dis. 2008;52(3):541–52.

Stones and Endourology in Older Adults

22

David A. Duchene and Margaret S. Pearle

Introduction

Urolithiasis is a common medical condition that may affect patients of all age groups. It has been estimated that 13 % of men and 7 % of women in the USA will be diagnosed with a kidney stone during their lifetime [1]. The prevalence of kidney stones is also increasing. Combining an overall increase in the prevalence of kidney stones and an increasing life-expectancy, we can expect to see an additional number of older individuals with kidney stones. The geriatric patient with urolithiasis may present differently than their younger counterparts, have more medical comorbidities, and need different preoperative, intraoperative, and postoperative care. This chapter is designed to explore the prevalence of urolithiasis in the elderly population, discuss differences in clinical presentation, and outline treatment options and outcomes in the endourological management of older adults.

D.A. Duchene, M.D. (✉)
University of Kansas Medical Center, Kansas City, KS, USA
e-mail: dduchene@kumc.edu

M.S. Pearle, M.D., Ph.D.
UT Southwestern Medical Center, Dallas, TX, USA
e-mail: Margaret.Pearle@UTSouthwestern.edu

Incidence and Prevalence of Urolithiasis in Older Adults

Although older individuals have potential risk factors such as swallowing difficulties, decreased fluid intake due to immobility or fear of incontinence, and comorbid medical conditions including diabetes, hypertension, renal insufficiency, or urinary tract infections, that may predispose to kidney stone disease, the data on the effect of age and urolithiasis are inconsistent. Payne et al. demonstrated that urolithiasis was more likely to develop in elderly patients [2], but other older studies did not demonstrate a difference in older aged individuals [3, 4]. A more recent study by Gentle et al. showed that geriatric stone formers comprised approximately 12 % of stone patients and that the incidence of urinary stone disease was similar between geriatric and younger patients [5]. The incidence of geriatric urinary stone disease appeared to be between 0.1 and 2 % in that study. The incidence of stone disease in Rochester, MN, in 2000 was approximately 0.1 % in individuals 70 years or greater [6].

Only three countries in a recent global review of urolithiasis had sufficiently accurate stone incidence data stratified by age to report [7]. Those countries included Iran, Japan, and the USA. The urolithiasis incidence showed a rise-and-fall pattern which was similar in all three countries. Age at peak incidence was in the 40–49-year-old cohort, except for Japanese women with peak incidence from 50 to 59 years of age. The incidence

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_22,

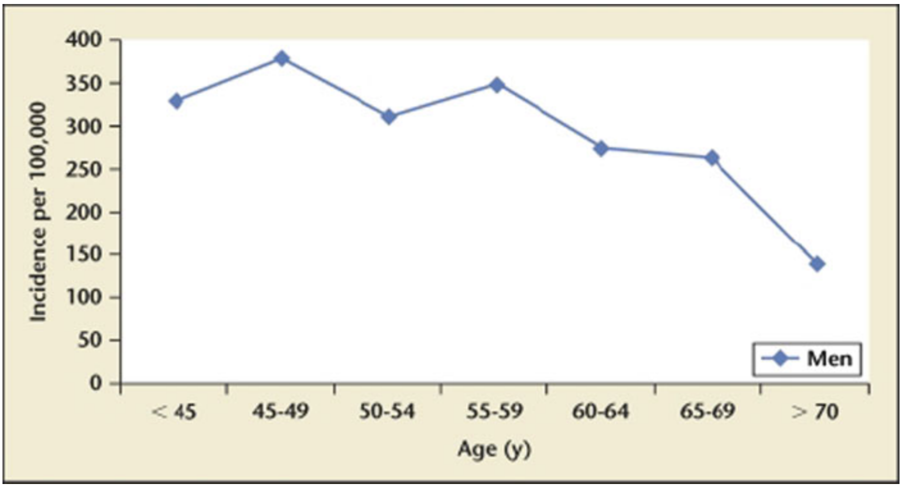


Fig. 22.1 1986 US kidney stone incidence by age group. A rise-and-fall pattern is observed for reported incidence rates in the USA during 1986. Peak incidence is observed between ages 45 and 49 years. (Borrowed from [7])

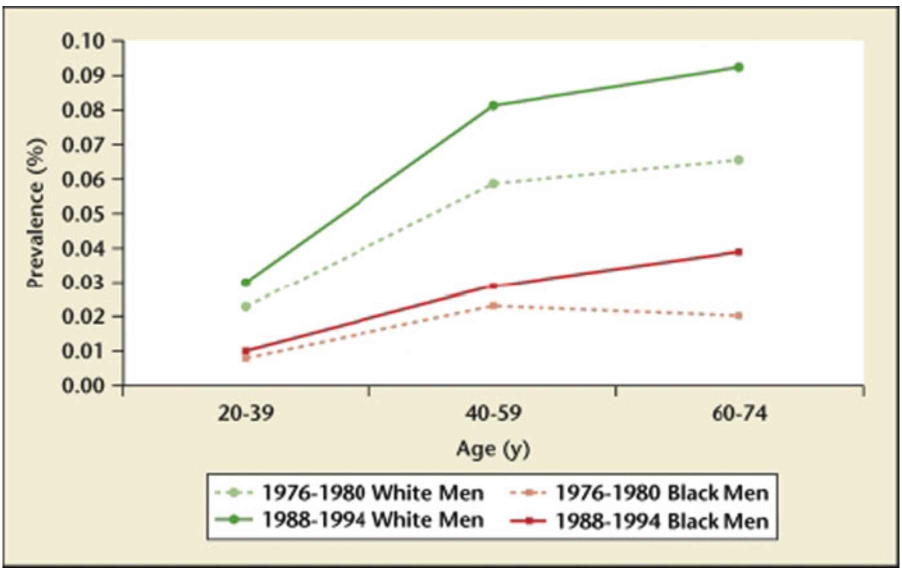


Fig. 22.2 US kidney stone prevalence by race and age group. An increasing prevalence with increasing age is observed in US white and black men for both reporting periods. Prevalence has nearly doubled for black men in the 60- to 74-year-old age group between the two time periods. (Borrowed from [7])

rate continually declined after the peaks with subsequent age groups (Fig. 22.1) [7]. Therefore, it appears that the incidence of urolithiasis is less in the aging population than middle-aged cohorts.

The same global study demonstrated increased prevalence of urolithiasis with increasing age in the countries of Germany, Iceland, Iran, Italy, Greece, Turkey, and the USA (Fig. 22.2) [7]. Earlier prevalence studies between 1976 and 1980 in the USA had shown prevalence rates decreased in women over age 59 and men over the age of 69. However, data after 1991 show continued increasing prevalence rates with increasing age cohorts [1].

The most accurate data we have to date on kidney stone trends in elderly individuals involve two studies from the Urological Diseases in America Project: "Urologic Diseases in America Project: Urolithiasis" by Pearle et al. [8] and "Prevalence of Kidney Stones in the United States" with Scales as lead author [9]. In the first publication, data obtained from the Centers of Medicare and Medicaid Services (CMS) from 1992, 1995, and 1998 showed that hospital admission rates for urolithiasis in Medicare patients aged 65 and older were consistently higher than in the younger age groups throughout the study period [8]. Hospitalization rates decreased approximately 5 % for the Medicare group between 1992 and 1998. This is in contrast to a nearly 15 % drop in hospitalization rates for urolithiasis in a younger, privately insured cohort in the same time frame. The 75–84-year-old group showed the highest rates of admission in all the years of the study. The longest length of hospital stay was in the 85 year and older population at 4.4 days compared to 1.8 days stay in the youngest adult group. Given that urolithiasis treatment has been shifting from inpatient treatment to outpatient management, the lack of significant decrease in inpatient admissions for the over 65 year old individuals suggests a potential increase in prevalence in this population.

In the same study, the hospital outpatient visit rate for urolithiasis in the 65 years and older group increased from 28/100,000 in 1992 to 36/100,000 in 1998 [8]. Medicare physician office visits for nephrolithiasis increased 25 % between 1992 and 1998 for patients older than 65 years of age and peaked in the 65–74-year-old group. As shown by this study, the prevalence of urinary stones in the aging population appears to be increasing in recent years.

Scales et al. reported on the prevalence of kidney stones in the USA by examining the National Health and Nutrition Examination Survey (NHANES) database [9]. The overall lifetime prevalence of kidney stones was 10.6 % in males and 7.1 % in females with lifetime prevalence in individuals over the age of 70 of 18.8 % and 9.4 % in males and females, respectively. The authors concluded that the overall prevalence of stone disease approached 1 in 5 persons in the highest risk groups (non-Hispanic White, males, older) which was a marked increase from the NHANES report in 1994 of 1 in 20 persons [9].

Clinical Presentation

In his manuscript, Gentle stated, "The geriatric stone population is not merely an extension of younger stone forming patients presenting at an older age." [5] His group found geriatric stone formers made up 12 % of the urolithiasis population and that the incidence and recurrence between geriatric and younger stone forming patients was similar, but geriatric patients generally experienced their first stone episode after 50 years of age [5]. A study of emergency room visits in Switzerland confirmed the findings of Gentle that nearly 10 % of urolithiasis patients are geriatric (age > 65) and that more than half of them presented with their first stone episode [10]. The Swiss group also found that stone size, side, and site did not differ between the older and younger groups, but urinary stone disease was more severe in elderly patients. In that study, geriatric patients had a twofold greater likelihood of being hospitalized. Many of the differences in hospitalization rates were attributed to the statistically significantly increased rates of the comorbidities of diabetes mellitus, hypertension, and diuretic use which limited the use of nonsteroidal anti-inflammatory (NSAID) medications for pain control and medical expulsive therapy for spontaneous stone passage [10].

However, the clinical presentation and evaluation of geriatric patients may be different and elderly patients may not present with typical renal colic. In patients older than 65 years of age, abdominal pain is the fourth most common complaint to an emergency department [11]. Often, abdominal pain in an elderly patient may be a vague and nonspecific presentation even in cases which may require acute surgical intervention. Therefore, a CT scan is often obtained to determine the cause of pain. In a prospective study by Hustey et al. exploring the use of abdominal CT scan in older patients with non-traumatic nonspecific abdominal pain, they found that 10 % of the patients had urolithiasis discovered by imaging studies [12].

In a study of Olmstead County, Minnesota, Krambeck et al. found that 16 % of patients presenting with symptomatic kidney stones were older than 60 [13]. Unlike their younger counterparts, older individuals were more likely to present with atypical pain or no pain, fever, gastrointestinal symptoms, pyuria, and urinary tract infection, all of which correlated with increasing age. Like the study by Arampatzis [10], the Olmstead County, Minnesota study showed that older individuals were more likely to be hospitalized for evaluation and older patients were more likely to undergo CT scan evaluation and urological consultation. No difference was found in stone number or location, but older individuals were noted to more often have larger or staghorn calculi on presentation. Due to a size difference at presentation, older individuals were less likely to spontaneously pass a stone and more likely to require surgical intervention [13].

Older individuals are more likely to present with an associated urinary tract infection and stone disease. This finding was noted by Usui et al. in 2003 [14] and confirmed by the recent study by Krambeck [13]. Usui noted a 10.7 % risk of urinary tract infection at time of stone evaluation in patients over 65 years of age, while only 5.1 % of younger patients presenting with stones had an associated UTI [14]. A French study noted that 41 % of first time stone formers were over 60 years of age with an associated urinary tract infection in 24 % of patients [15]. Forty-nine percent of urolithiasis cases after the age of 70 presented with sepsis [15]. Krambeck found that the risk of associated UTI increased with each decade of life [13]. The geriatric population more frequently encountered the complication of bacteremia with stone disease. Two individuals in the Olmstead County study died as a result of bacteremia and acute stone disease and were over 70 years of age [13].

Even though UTI is more common in elderly individuals, most authors believe that this is usually not related to the presence of infected struvite stones as the infectious source. This is based on data that less than 1 % of elderly patients in the study by Gentle et al had struvite stones [5], Krambeck et al. showed no difference in the rate of struvite stones in older adults compared to a younger group [13], and Usui et al. noted only a 4 % rate of struvite stone disease in older stone patients [14].

Overall, the data suggest that older patients may not present with the typical renal colic symptoms classically described in younger patients. Older patients may have no pain, decreased pain, or atypical pain. The diagnosis requires a high level of suspicion for geriatric patients with atypical complaints and associated urological findings. Patients with hematuria or pyuria and those with vague abdominal discomfort not commonly observed with uncomplicated urinary tract infections require additional investigation for a possible obstructing stone. Simply treating a patient for a UTI who may have an obstructing stone can delay diagnosis and treatment and may lead to poorer outcomes. Older individuals with a prior history of stone disease may be more likely to have evaluation for stones on presentation, but a high index of suspicion needs to be maintained even for patients without a previous stone history [13]. One must remember that 50 % of elderly stone patients present with a first time stone episode [5, 10].

Kidney Stone Composition and Urinary Parameters

Stone composition is another parameter that differs between older individuals and younger cohorts. Calcium oxalate is the predominant stone type in both older and younger individuals. However, uric acid stone composition is more common in older patients with a rate around 10–11 %, compared to approximately 5 % in younger stone formers [5, 11]. Hypocitraturia as the isolated urinary abnormality identified on 24-h urine collection appears to be more common in older stone patients than younger individuals (29 % versus 17 %) [5]. Hypocitraturia may be more common in the aging individual due to a mild, physiological metabolic acidosis that is a result of age-dependent renal function decline. Gentle et al. believe that the resultant subclinical decrease in urinary pH may predispose to uric acid stones because a similar serum uric acid and urinary uric acid concentrations were found in the older and younger groups [5].

Hypercalciuria may also be a factor for stone formation in geriatric patients. However, the degree of hypercalciuria decreased with age in a review by Goldfarb and was almost identical in both age groups in the Gentle study [5, 16]. Decreased ambulation is a potential risk factor for hypercalcuria in the geriatric population, which could increase bone resorption and urinary calcium excretion. However, it appears that this likely only contributes to chronically debilitated, bedridden patients and not to a normal ambulatory outpatient geriatric population [5].

The geriatric population has been found to have an increased risk of crystalluria (35 %) compared to younger adults (6 %) [17]. However, other studies did not demonstrate increased amounts of hyperoxaluria in elderly patients [5]. Therefore, the significance of increased crystalluria is unknown.

Much still needs to be determined about the changes that occur in urinary parameters with advancing age. Goldfarb et al. indicated that a primary issue is that stone formation occurs at lower urinary supersaturations in older patients, although the reasons are unclear [16]. As with urinary stone formation during pregnancy, the urinary parameters in aging patients suggest that there are other unknown or unexplored factors that could be the most significant contributors.

The importance of kidney stone development and kidney stone therapy should not be ignored in regard to outcomes for renal function. Individuals with genetic disorders and those with onset of stone disease at a young age are known to have a higher risk of end-stage renal disease. However, a recent large registry cohort study conducted between 1997 and 2009 in Canada demonstrated even patients with only a single kidney stone episode had an adjusted hazard ratio of 2.16 for end-stage renal disease [18]. The absolute increase in numbers was small, but the increased risk was significant. It emphasizes the need for detection, treatment, and prevention of kidney stone complications even in the older patient population to prevent renal function deterioration.

Surgical Management of Stones

Some practitioners are inclined to choose the least invasive surgical option for elderly patients, despite the fact that in some cases these have been shown to have lower success rates compared to more invasive modalities. However, there is evidence that selection of surgical treatment options to treat stones in geriatric patients follows the same distribution as in the younger population. According to the Urologic Diseases in America Project, among Medicare beneficiaries in 1998, shock wave lithotripsy (SWL) comprised 54 % of procedures, ureteroscopy 40 %, percutaneous nephrolithotomy (PCNL) 4 %, and open stone surgery 2 % [8]. The distribution of surgical stone procedures among commercially insured, presumably younger individuals for a comparable time frame (2000) was almost identical. SWL was 55 %, ureteroscopy 40 %, and PCNL 5 %, with the number of open surgical stone procedures too small to reliably report. Notably, the most invasive of the minimally invasive surgical modalities, PCNL, was utilized as frequently among commercially insured individuals as among Medicare beneficiaries. This suggests that the decision regarding the optimal treatment modality for an individual patient was based primarily on patient and stone factors rather than age. According to the Centers for Medicare and Medicaid (CMS), open surgery declined by 63 % (from 4.3 % in 1992 to 1.6 % in 1998). This was similar to the decline seen in the commercially insured population over a similar time period. This trend is consistent with the success of minimally invasive procedures in treating virtually all stones.

The rates of utilization of surgical procedures among Medicare patients remained relatively stable between 1992 and 1998: 10,943–11,738 per 100,000 population for SWL, 8,372–8,839 per 100,000 for ureteroscopy, and 665 to 882 per 100,000 for PCNL. Of note, these rates do not take into account retreatment for the same stone. Because of its higher treatment rate, this affects SWL more than ureteroscopy or PCNL [8].

Interestingly Kerbl and colleagues also reviewed Medicare data from the Health Care Financing Administration (currently CMS) and reported rates and distributions of surgical procedures that conflict with the UDA data [19]. According to their analysis, a 75 % increase in overall stone procedures among Medicare patients occurred between 1988 and 2000. Furthermore, they reported a fourfold increase in the total number of ureteroscopies performed during that time period, as well as an increase in the proportion of ureteroscopic procedures among surgical interventions (9.5 % in 1988 to 22 % in 2000). On the other hand, despite a 1.7-fold increase in the number of SWL procedures performed, the proportion of SWL procedures declined from 72 % to 69 %. Finally, PCNL procedures showed a modest 1.3-fold increase, although the proportion of PCNL procedures remained relatively stable (from 6.0 % to 6.7 %). Explanations for the differences in reported rates and distributions of stone procedures seen in these two datasets are not obvious.

Outcomes for Surgical Stone Procedures in Geriatric Patients

Shock Wave Lithotripsy

SWL is the only noninvasive treatment for upper tract urinary calculi and in many cases the procedure can be performed under intravenous sedation or local anesthesia. Consequently, SWL is an attractive treatment modality for use in the elderly population. However, some reports have suggested outcomes for SWL are age dependent and that stone-free rates are lower and complication rates are higher in the geriatric population. Ackermann and colleagues reviewed 246 patients undergoing SWL with the Dornier HM3 lithotripter and performed multivariable analysis to identify factors predictive of SWL success [20]. Among 160 patients with solitary renal calculi, age was found to be an independent negative predictor of stone free rate, with the poorest results achieved in patients over 60 years of age. Abdel-Khalek and associates also found age $>$40 years to be an independent negative predictor of SWL stone-free rate for renal calculi ($p<0.001$), although the observed difference in stone-free rates among patients $>$40 (84 %) and $\leq$40 years (89 %) was small [21]. On univariate and multivariate analysis of 984 patients with ureteral stones who underwent SWL with the Dornier MFL 5000 lithotripter, these same investigators did not find age to be significantly associated with stone free rate [22].

Ng and colleagues determined that age was a significant predictor of stone free status for renal but not ureteral stones [23]. In a multiple logistic regression model based on a group of 1,498 patients who underwent SWL for 5–15 mm solitary, radio-opaque renal calculi, the authors divided patients into age groups of ≤40, 41–60, and >60 years. Using stone free rates for the ≤40 age group as the referent value, they found adjusted odds ratios of 0.665 (95 % confidence interval (CI) 0.512–0.864, $p=0.002$) for patients 41–60 years of age and 0.629 (95 % CI 0.470–0.841, $p=0.002$) for patients >60 years old. In contrast, age had no effect on stone-free rate among 694 patients undergoing SWL for ureteral stones. Weisenthal and colleagues also found age to be a significant independent predictor of stone-free rate for renal but not ureteral calculi in a multivariate analysis [24]. Ng and coworkers speculated that sclerotic changes in the kidney associated with age may impede transmission of shock waves through the kidney parenchyma and reduce SWL effectiveness for renal but not ureteral calculi.

In contrast, Simunovic and colleagues found no difference in stone free or complication rates among older patients in three age groups, 60–65 ($n=175$), 66–70 ($n=151$), and >70 years ($n=118$) undergoing SWL for renal or ureteral calculi [25]. The groups were comparable with respect to stone size, number of shocks, and number of SWL treatments. No significant differences in 3-month overall stone-free rates were found among the three groups (66 %, 67 %, and 71 %, respectively), nor were there differences in stone-free rates when analyzing only renal or only ureteral stones. Likewise, the rate and spectrum of complications was comparable among groups (complication rates 8 %, 5.3 %, and 4.2 %, respectively). However, unlike other comparative studies, a younger age group was not included in the analysis, and therefore the difference in outcomes between younger and older patients could not be discerned from this study.

Halachmi and Meretyk did not find a difference in stone free or complication rates in patients ≤ 70 ($n = 215$) and those > 70 ($n = 23$) years of age [26]. Despite a substantially greater number of comorbidities in the older group, stone free rates (91 % in each group) and complication rates (1 % in the younger patients and 3.7 % in the older patients) were comparable. In another retrospective review, the outcomes of SWL were analyzed in 130 patients over 70 years of age (mean age 75.1) in whom the mean stone size was 10.2 mm for renal and 8.7 mm for ureteral calculi [27]. All patients underwent continuous ECG monitoring during treatment. With a single treatment stone-free rate of 52 % and no complications, the authors concluded that elderly patients can be safely and successfully treated with SWL without increased risk of complications.

Some investigators have found that SWL-related complications are age dependent. Dhar and coworkers analyzed 317 patients who underwent 415 SWL treatments for renal and proximal ureteral calculi and identified 17 postoperative subcapsular or peri-renal hematomas [28]. Multivariate analysis demonstrated a significantly higher incidence of subcapsular hematomas with age ($p = 0.009$), independent of mean arterial pressure. Indeed, for every 10-year increase in age at treatment, they calculated a 1.67-fold increase in the probability of hematoma formation. It is critical that geriatric patients undergoing SWL discontinue use of any anticoagulant medications prior to treatment.

Knapp and associates used Doppler ultrasound to measure renal resistive indices (RI) in 76 patients immediately before and within 3 h after SWL to identify changes in renovascular resistance [29]. Mean RI increased significantly after SWL compared to baseline (0.6717 versus 0.6203, $p = 0.0001$). Moreover, the authors found a positive linear correlation between age and RI, with 75 % of patients over 60 demonstrating an RI value that exceeded the upper limit of normal (0.7) (mean RI for the group 0.735). In a subsequent study, 57 of the 76 patients were followed with repeat Doppler ultrasound studies and blood pressure measurements for a mean of 26 months (18–31 months) [30]. Among the 20 patients over 60 years of age who were followed longitudinally, 15 demonstrated elevated RI levels and 9 patients had elevated diastolic blood pressure (all of whom had elevated RIs). In contrast only one patient younger than age 60 showed an elevated RI and only one other demonstrated diastolic hypertension. A strong positive correlation between elevated RI and diastolic blood pressure (correlation coefficient 0.903) was demonstrated, and only those nine patients who demonstrated a continued increase in RI after SWL developed hypertension. The authors theorized that the loss of elasticity and increased areas of sclerosis in the kidneys of older patients account for the lower tolerance of the renal vasculature to shock waves, leading to permanent damage resulting in hypertension.

Additional studies are necessary to verify an increased risk of hypertension after SWL in the older population. However, with conflicting reports regarding an age effect on success rates of SWL, an endoscopic approach to treating stones in these patients should at least be considered.

Percutaneous Nephrolithotomy

Percutaneous nephrolithotomy (PCNL) is the treatment of choice for large and/or complex stones. However, PCNL is the most invasive of the surgical treatments for stones now that open stone surgery has all but disappeared from practice. Despite reluctance on the part of some practitioners to perform PCNL on older patients because of concern over an increased risk of complications, the rate of utilization of PCNL among Medicare beneficiaries was not found to be different than the utilization rate among commercially insured, presumably younger, individuals [8].

Stoller and colleagues characterized a cohort of 33 patients aged 65 and older who underwent

42 PCNL procedures and compared them to a group of 160 patients <65 years old undergoing PCNL during the same time period [31]. Staghorn calculi comprised 47 % of stones in the older group and 55 % of stones in the younger group. The transfusion rate was higher in the older group compared to the younger group (26 % versus 14 %, $p<0.01$) despite comparable preoperative hemoglobin levels. A positive preoperative urine culture was documented in 30 % of the older population, and struvite comprised the entire or part of the treated stone in 18 % of patients. Interestingly, the most common stone composition was uric acid (24 %). Complications occurred in 42 % of patients and included fever, collecting system perforation, atrial fibrillation, displacement of nephrostomy tube, and clot retention. Overall, the authors concluded that PCNL was safe and effective in elderly patients, albeit associated with a higher transfusion rate.

In the largest series to date, the Comite Lithiase de l'Association Francaise d'Urologie performed a multicenter retrospective review of 203 patients older than age 70 who underwent 210 PCNL procedures over a 12-year period [32]. Mean stone size was 24 × 15 mm and staghorn calculi comprised 19 % of stones. Comorbidities were present in 68.5 % of patients, and the mean ASA score was 2. Although the overall stone-free rate was 70.8 %, the stone free rate for a subgroup of patients with staghorn stones was only 30.5 %. Among comorbidities, only diabetes mellitus was found to significantly influence stone free rates ($p=0.03$). Excluding two patients with renal failure in whom nephrectomy was performed for bleeding, there was no significant change from baseline for either hemoglobin or creatinine. The authors concluded that PCNL can be performed safely and successfully in elderly patients, with outcomes consistent with those of unselected PCNL series.

A number of investigators have compared outcomes of PCNL in the elderly population with a control group of younger patients undergoing PCNL with generally consistent and comparable results. Sahin and associates compared 27 patients ≥ 60 years of age with 166 younger patients undergoing PCNL [33]. The proportion of staghorn calculi and the mean stone size were comparable between the groups, but the incidence of solitary kidneys was higher in the older group (29 % versus 7 %). There were no significant differences in outcomes between the older and younger groups with regard to success rates (stone free and <4 mm residual fragments, 89 % versus 92 % respectively, $p=0.718$), transfusion rates (21 % versus 18 % respectively, $p=0.662$) or number or spectrum of complications.

Kuzgunbay and coworkers also found no differences in outcomes between a group of 45 patients > 65 years of age and a control group of 37 younger patients between 18 and 36 years of age undergoing PCNL [34]. With a comparable stone burden in both groups, there were no significant differences in operative time (133 versus 146 min), transfusion rates (10.6 % versus 13.5 %), length of hospital stay (3.8 versus 3.9 days), and stone free or success rates (36 % versus 24.3 % stone free, and 53 % versus 37.8 % success rate), respectively, between the older and younger patients. No major complications occurred in either group. Furthermore, the authors found no correlation between the incidence of comorbid conditions and success rates.

Karami and colleagues compared 50 PCNL procedures in elderly patients (>65 years) with 248 PCNLs performed in younger patients (<40 years) [35]. Despite a significantly higher incidence of comorbid conditions at 42 % in the geriatric group compared to 12.5 % in the younger group ($p<0.001$), the rate of complications was not significantly different between the groups. With a comparable stone size in both groups, success rates defined as stone free plus < 4 mm residual fragments were not significantly different with 86 % in the older patients and 90 % in the younger patients ($p=0.45$). Likewise, operative time (75 min versus 76 min), hospital length of stay (3.7 versus 3.8 days), and change in hemoglobin and creatinine from baseline did not differ significantly between the older and younger cohorts. The most common stone composition was calcium oxalate with 58 % among the older patients and 66.5 % in the younger patients. These rates are similar to the general population.

In the largest series comparing PCNL in older and younger patients, Anagnostou and colleagues at the Scottish Lithotriptor Center reviewed their series of 1,058 PCNL procedures performed between 1992 and 2003 [36]. The older group was comprised of 126 patients > 70 years old who underwent 135 procedures, and the younger group consisted of 532 patients between 17 and 69 years old who underwent 644 procedures. The incidence of renal anomalies was similar between the two cohorts. No difference in overall stone-free rates between groups was noted with 60.7 % for the older group versus 53.6 % in the younger group ($p = 0.128$). Likewise, although adverse events occurred more frequently in the older group (14.1 %) compared to the younger group (9.0 %), the difference did not reach statistical significance ($p = 0.073$). These researchers concurred with previous authors that PCNL in the elderly population can be performed as safely and successfully as in the younger population.

In an effort to reduce the morbidity of PCNL, a recent trend has been to use smaller or no nephrostomy tubes post-procedure. Two recent meta-analyses of randomized trials comparing tubeless with standard PCNL found that the tubeless procedure was associated with a shorter hospital stay and reduced pain medication requirements, without an increase in blood loss [37, 38]. Recent investigators further demonstrated that totally tubeless PCNL (no nephrostomy tube or stent) can be performed safely, preserving the advantages of a "tubeless" approach but with even lower pain medication requirements [39–41]. The advantages of totally tubeless PCNL were validated in a group of 60 older patients (≥60 years) who were evenly randomized to totally tubeless versus standard PCNL [42]. The totally tubeless approach was associated with a significantly shorter hospital stay of 1.5 days versus 3.2 days ($p < 0.001$), reduced pain medication requirements of 0.5 mg/kg pethidine versus 1.4 mg/kg ($p < 0.01$), and no difference in bleeding complications or stone-free rates (96 % versus 90 %, respectively). Overall, the safety and efficacy of tubeless or totally tubeless PCNL is likely more closely related to proper intraoperative patient selection than to patient age.

Although most studies have not found higher complication rates in elderly patients undergoing PCNL despite a higher incidence of comorbid conditions, Resorlu and colleagues performed a multicenter study of patients 60 years or older who underwent PCNL to determine if comorbid conditions, assessed by the Charlson Comorbidity Index (CCI), could predict the occurrence of post-PCNL complications [43]. A total of 283 older patients who underwent PCNL were divided into three groups on the basis of their CCI score. (Group 1 = 0 points; Group 2 = 1 point; and Group 3 ≥ 2 points). No statistically significant differences in mean stone size, operative time, length of hospital stay, or stone-free rates were identified among the 3 groups. However, transfusion rates increased with CCI score: 7.6 % for group 1, 11.1 % for group 2, and 23.2 % for group 3 ($p = 0.011$). Furthermore, postoperative medical complications were significantly associated with CCI score ($p < 0.001$): 7.6 % for group 1, 12 % for group 2, and 28.6 % for group 3. Multivariate logistic regression analysis demonstrated that higher CCI score, incidence of bleeding, and long operative time were all significant independent predictors of postoperative medical complications. The authors concluded that elderly patients with high CCI score may be more safely treated conservatively or with less invasive modalities such as ureteroscopy than with PCNL. However, this retrospective study does not take into account the morbidity of leaving stones untreated, or of treating large, potentially infected stones from a retrograde approach. Since most patients undergoing PCNL have large or complex stones, alternative approaches, while "less invasive," may pose a greater risk of complications from incomplete or no stone removal (such as recurrent infection, pain, or obstruction) than from PCNL. Without a randomized trial to compare these treatment modalities in a prospective fashion, the relative risks of these approaches cannot be reliably assumed.

Because of the higher rate of renal functional impairment in geriatric patients, there has been some concern about the effect of PCNL on renal function in this population. Tok and colleagues compared preoperative and 12–24-h postoperative estimated glomerular filtration rate (eGFR) in a group of 64 older (≥65 years) and 647 younger (<65 years) patients undergoing PCNL [44]. Despite a larger mean stone size in the geriatric group compared to the younger group (10.08 mm versus 8.28 mm, $p=0.037$), total operative time was shorter (55.7 min versus 61.3 min, $p=0.036$). The ratio of preoperative to postoperative eGFR was *higher* in the geriatric group compared to the non-geriatric group (1.13 versus 0.98, $p=0.001$), reflecting a 13 % increase in eGFR in the geriatric group and a 2 % decrease in the younger group following surgery. Although these findings suggest that renal function does not decline significantly after PCNL in elderly patients, and PCNL should not be avoided because of concern over renal functional deterioration, the sample size was small and the mean preoperative creatinine was only 1.22 mg/dL.

The effect of PCNL on elderly patients with impaired renal function was explored in a retrospective analysis of 31 patients with a solitary kidney and or chronic renal insufficiency who were at least 2 years post-treatment (mean 41.5 months) from either SWL or PCNL [45]. For patients with a solitary kidney and a creatinine <2 mg/dL, deterioration in renal function was observed in 22 % of SWL patients and 29 % of PCNL patients. In patients with a serum creatinine between 2 and 3 mg/dL, renal functional improvement occurred in all patients. Among five patients with a serum creatinine > 3 mg/dL, four SWL patients demonstrated initial improvement but ultimately developed long-term deterioration of renal function and one PCNL patient showed stabilization of renal function. Unfortunately, with no non-stone forming or unoperated control group, the significance of these findings on the renal functional outcome of PCNL or SWL in geriatric patients cannot be definitively surmised.

Ureteroscopy

The effect of age on ureteroscopy outcomes has not been systematically assessed. However, with an increase in the number of lengthy ureteroscopic procedures associated with expanded indications for ureteroscopy, the impact of longer operative times and duration of irrigation in elderly patients are of increasing interest. Although it is reassuring that Cybulski and colleagues found only a mean of 54 mL of fluid absorption during ureteroscopy with a mean operative time 37 min, it is not clear that fluid absorption increases linearly over time [46]. With longer ureteroscopic procedures and susceptible older patients, fluid absorption could potentially become a more significant problem. The use of ureteral access sheaths has been shown to reduce intrarenal pelvic pressure and may partially obviate the risk [47, 48].

Summary of Surgical Therapy in Older Adults

In summary, surgical procedures for stone disease in the geriatric population can generally be performed safely and efficaciously, and the decision regarding the optimal treatment modality should perhaps be based on stone and patient factors other than age. However, conflicting reports about lower success rates for SWL in older adults and concern about a higher risk of post-SWL hypertension may encourage consideration of endoscopic alternatives in some cases. PCNL has been consistently demonstrated to be safe and effective in the geriatric population, although careful attention to comorbid conditions to assure preoperative optimization and postoperative awareness is essential to minimize the risk of the procedure. However, selection of PCNL should not be avoided because of the greater invasiveness of the procedure. Finally, outcomes of ureteroscopy have not been fully explored in relation to age, but to date there is no reason to expect that carefully performed ureteroscopy poses additional untoward risks in the geriatric population.

Conclusion

The older patient with urolithiasis requires additional consideration in the diagnosis, evaluation, and treatment. As the population ages, physicians can anticipate more clinic visits and operative procedures for kidney stones in the geriatric population. It is important to remember that many older individuals present with their first episode of urolithiasis, and it is not necessarily only previous or chronic stone-forming patients presenting at older ages. Urolithiasis in elderly patients requires a high index of suspicion since presentation may be atypical and older adults can have subtle signs or symptoms of the disease. When diagnosed, urolithiasis in geriatric patients is more often associated with urinary tract infections than in a younger population. Combined with potential medical comorbidities in older patients, delayed treatment of infected stones can lead to worse outcomes.

Age alone should not be the main driving factor in deciding the choice of surgical intervention for urolithiasis. Many studies have shown acceptable surgical outcomes without significantly increased adverse complications in older patients. The main decision on surgical management needs to be based on individual patient factors and stone characteristics. A minimally invasive procedure should be the primary consideration for treatment, but care needs to be taken with the use of SWL in geriatric patients. The older population may need different perioperative care, but geriatric patients still need the appropriate surgical approach based on their stone disease and not on their age.

References

1. Stamatelou KK, Francis ME, Jones CA, et al. Time trends in reported prevalence of kidney stones in the United States: 1976-1994. Kidney Int. 2003;63:1817–23.
2. Payne CK, Babiarz JW, Raz S. Genitourinary problems in the elderly patient. Surg Clin North Am. 1994;74:401–29.
3. Asper R. Epidemiology and socioeconomic aspects of urolithiasis. Urol Res. 1984;12:1–5.
4. Hiatt RA, Dales LG, Friedman GD, et al. Frequency of urolithiasis in a prepaid medical care program. Am J Epidemiol. 1982;115:255–65.
5. Gentle DL, Stoller ML, Bruce JE, et al. Geriatric urolithiasis. J Urol. 1997;158:2221–4.
6. Lieske JC, de la Vegas LS, Slezak JM, et al. Renal stone epidemiology in Rochester, Minnesota: an update. Kidney Int. 2006;69:760–4.
7. Romero V, Akpinar H, Assimos DG. Kidney stones: a global picture of prevalence, incidence, and associated risk factors. Rev Urol. 2010;12:e86–96.
8. Pearle MS, Calhoun EA, Curhan GC, and the Urological Diseases in America Project. Urologic Diseases in America Project: Urolithiasis. J Urol. 2005;173:848–57.
9. Scales CD, Smith AC, Hanley JM, Saigal CS, and the Urologic Diseases in America Project. Prevalence of kidney stones in the United States. Eur Urol. 2012;62: 160–5.
10. Arampatzis S, Lindner G, Irmak F, et al. Geriatric urolithiasis in the emergency department: risk factors of hospitalization and emergency management patterns of acute urolithiasis. BMC Nephrol. 2012;13:117.
11. Wofford JL, Schwartz E, Timerding BL, et al. Emergency department utilization by the elderly: analysis of the National Hospital Ambulatory Medical Care Survey. Acad Emerg Med. 1996;3:694–9.
12. Hustey FM, Meldon SW, Banet GA, et al. The use of abdominal computed tomography in older ED patients with acute abdominal pain. Am J Emerg Med. 2005;23:259–65.
13. Krambeck AE, Lieske JC, Li S, et al. Effect of age on the clinical presentation of incident symptomatic urolithiasis in the general population. J Urol. 2013;189: 158–64.
14. Usui Y, Matsuzaki S, Matsushita K, et al. Urolithiasis in geriatric population. J Exp Clin Med. 2003;28: 81–7.
15. Neuzillet Y, Lechevallier E, Ballanger P, et al. Urinary stones in subjects over the age of sixty. Prog Urol. 2004;14:479–84.
16. Goldfarb DS, Parks JH, Coe FL. Renal stone disease in older adults. Clin Geriatr Med. 1998;14:367–81.
17. Moesch C, Charmes JP, Gaches F, et al. Crystalluria prevalence in the elderly. Eur J Med. 1993;2:512.
18. Alexander RT, Hemmelgarn BR, Wiebe N, et al. Kidney stones and kidney function loss: a cohort study. BMJ. 2012;345:e5287.
19. Kerbl K, Rehman J, Landman J, Lee D, Sundaram C, Clayman RV. Current management of urolithiasis: progress or regress? J Endourol. 2002;16:281–8.
20. Ackermann DK, Fuhrimann R, Pfluger D, Studer UE, Zingg EJ. Prognosis after extracorporeal shock wave lithotripsy of radiopaque renal calculi: a multivariate analysis. Eur Urol. 1994;25:105–9.
21. Abdel-Khalek M, Sheir KZ, Mokhtar AA, Eraky I, Kenawy M, Bazeed M. Prediction of success rate after extracorporeal shock-wave lithotripsy of renal stones–a multivariate analysis model. Scand J Urol Nephrol. 2004;38:161–7.
22. Gomha MA, Sheir KZ, Showky S, Abdel-Khalek M, Mokhtar AA, Madbouly K. Can we improve the prediction of stone-free status after extracorporeal shock wave lithotripsy for ureteral stones? A neural network or a statistical model? J Urol. 2004;172:175–9.
23. Ng CF, Wong A, Tolley D. Is extracorporeal shock wave lithotripsy the preferred treatment option for

elderly patients with urinary stone? A multivariate analysis of the effect of patient age on treatment outcome. BJU Int. 2007;100:392–5.
24. Wiesenthal JD, Ghiculete D, Ray AA, Honey RJ, Pace KT. A clinical nomogram to predict the successful shock wave lithotripsy of renal and ureteral calculi. J Urol. 2011;186:556–62.
25. Simunovic D, Sudarevic B, Galic J. Extracorporeal shockwave lithotripsy in elderly: impact of age and comorbidity on stone-free rate and complications. J Endourol. 2010;24:1831–7.
26. Halachmi S, Meretyk S. Shock wave lithotripsy for ureteral stones in elderly male patients. Aging Male. 2006;9:171–4.
27. Sighinolfi MC, Micali S, Grande M, Mofferdin A, De Stefani S, Bianchi G. Extracorporeal shock wave lithotripsy in an elderly population: how to prevent complications and make the treatment safe and effective. J Endourol. 2008;22:2223–6.
28. Dhar NB, Thornton J, Karafa MT, Streem SB. A multivariate analysis of risk factors associated with subcapsular hematoma formation following electromagnetic shock wave lithotripsy. J Urol. 2004;172:2271–4.
29. Knapp R, Frauscher F, Helweg G, et al. Age-related changes in resistive index following extracorporeal shock wave lithotripsy. J Urol. 1995;154:955–8.
30. Janetschek G, Frauscher F, Knapp R, Hofle G, Peschel R, Bartsch G. New onset hypertension after extracorporeal shock wave lithotripsy: age related incidence and prediction by intrarenal resistive index. J Urol. 1997;158:346–51.
31. Stoller ML, Bolton D, St Lezin M, Lawrence M. Percutaneous nephrolithotomy in the elderly. Urology. 1994;44:651–4.
32. Dore B, Conort P, Irani J, et al. Percutaneous nephrolithotomy (PCNL) in subjects over the age of 70: a multicentre retrospective study of 210 cases. Prog Urol. 2004;14:1140–5.
33. Sahin A, Atsu N, Erdem E, et al. Percutaneous nephrolithotomy in patients aged 60 years or older. J Endourol. 2001;15:489–91.
34. Kuzgunbay B, Turunc T, Yaycioglu O, et al. Percutaneous nephrolithotomy for staghorn kidney stones in elderly patients. Int Urol Nephrol. 2011;43:639–43.
35. Karami H, Mazloomfard MM, Golshan A, Rahjoo T, Javanmard B. Does age affect outcomes of percutaneous nephrolithotomy? Urol J. 2010;7:17–21.
36. Anagnostou T, Thompson T, Ng CF, Moussa S, Smith G, Tolley DA. Safety and outcome of percutaneous nephrolithotomy in the elderly: retrospective comparison to a younger patient group. J Endourol. 2008;22:2139–45.
37. Yuan H, Zheng S, Liu L, Han P, Wang J, Wei Q. The efficacy and safety of tubeless percutaneous nephrolithotomy: a systematic review and meta-analysis. Urol Res. 2011;39:401–10.
38. Wang J, Zhao C, Zhang C, Fan X, Lin Y, Jiang Q. Tubeless vs standard percutaneous nephrolithotomy: a meta-analysis. BJU Int. 2012;109:918–24.
39. Crook TJ, Lockyer CR, Keoghane SR, Walmsley BH. Totally tubeless percutaneous nephrolithotomy. J Endourol. 2008;22:267–71.
40. Gupta V, Sadasukhi TC, Sharma KK, Yadav RG, Mathur R. Tubeless and stentless percutaneous nephrolithotomy. BJU Int. 2005;95:905–6.
41. Aghamir SM, Hosseini SR, Gooran S. Totally tubeless percutaneous nephrolithotomy. J Endourol. 2004;18:647–8.
42. Kara C, Resorlu B, Bayindir M, Unsal A. A randomized comparison of totally tubeless and standard percutaneous nephrolithotomy in elderly patients. Urology. 2010;76:289–93.
43. Resorlu B, Diri A, Atmaca AF, et al. Can we avoid percutaneous nephrolithotomy in high-risk elderly patients using the Charlson comorbidity index? Urology. 2012;79:1042–7.
44. Tok A, Ozturk S, Tepeler A, Tefekli AH, Kazancioglu R, Muslumanoglu AY. The effects of percutaneous nephrolithotomy on renal function in geriatric patients in the early postoperative period. Int Urol Nephrol. 2009;41:219–23.
45. Chandhoke PS, Albala DM, Clayman RV. Long-term comparison of renal function in patients with solitary kidneys and/or moderate renal insufficiency undergoing extracorporeal shock wave lithotripsy or percutaneous nephrolithotomy. J Urol. 1992;147:1226–30.
46. Cybulski P, Honey RJ, Pace K. Fluid absorption during ureterorenoscopy. J Endourol. 2004;18:739–42.
47. Rehman J, Monga M, Landman J, et al. Characterization of intrapelvic pressure during ureteropyeloscopy with ureteral access sheaths. Urology. 2003;61:713–8.
48. Auge BK, Pietrow PK, Lallas CD, Raj GV, Santa-Cruz RW, Preminger GM. Ureteral access sheath provides protection against elevated renal pressures during routine flexible ureteroscopic stone manipulation. J Endourol. 2004;18:33–6.

Sexual Health in Elderly Women

23

Daniel Zainfeld and Priya Padmanabhan

Introduction

Awareness of sexual health and its relevance as an integral component of overall health for both men and women continues to grow throughout the medical field. Management of male sexual health has progressed significantly in recent years with the advent of numerous medications and other treatment modalities. However, older adults, and elderly women in particular, are often overlooked with regard to their sexual health. Myriad reasons contribute to this neglect including hesitancy among older women to seek care related to vaginal or sexual problems and reluctance of physicians to explore these topics with their patients [1]. Female sexual health remains a relatively young scientific field overall and particularly among urologists. Despite growing awareness, there remain significant deficiencies in both recognition and management abilities of physicians with regard to sexual health and dysfunction [2].

Research continues to disprove antiquated ideas that elderly women are generally uninterested in sexual activity, untroubled by its absence, and therefore not often impacted by sexual dysfunction. Improvements in healthcare have extended life expectancies significantly with enhancement in health and overall activity later in life including sexual activity. Sexual activity is an increasingly important factor in the quality of life of elderly women and is often an indicator of overall health and well-being [3, 4]. Prevalence estimates of sexual dysfunction among elderly women have varied greatly between studies. Sexual dysfunction in postmenopausal women has been documented between 68 and 87 % [5]. An increase in the prevalence of sexual dysfunction with advancing age has been well documented [6]. The manifestations of sexual dysfunction vary greatly, presenting a challenge for both diagnosis and treatment, but its prevalence as a significant condition among elderly women is unquestioned.

This chapter will provide an overview of sexual health as it relates to elderly women. This includes the impact of sexual dysfunction on overall health, potential manifestations and available therapies which are essential to providing high-quality care to women of this age group.

Normal Sexual Response in Women

Descriptions of the normal sexual response cycle for both men and women were first published by Masters and Johnson in 1966 in their landmark book, *Human Sexual Response* [7]. They described the sexual response cycle as characterized by four distinct phases including excitement,

D. Zainfeld, M.D. • P. Padmanabhan, M.P.H., M.D. (✉)
Department of Urology, University of Kansas Medical Center, 3901 RAINBOW BLVD, 5027 Sudler Hall, Kansas City, KS 66160, USA
e-mail: ppadmanabhan@kumc.edu

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_23,

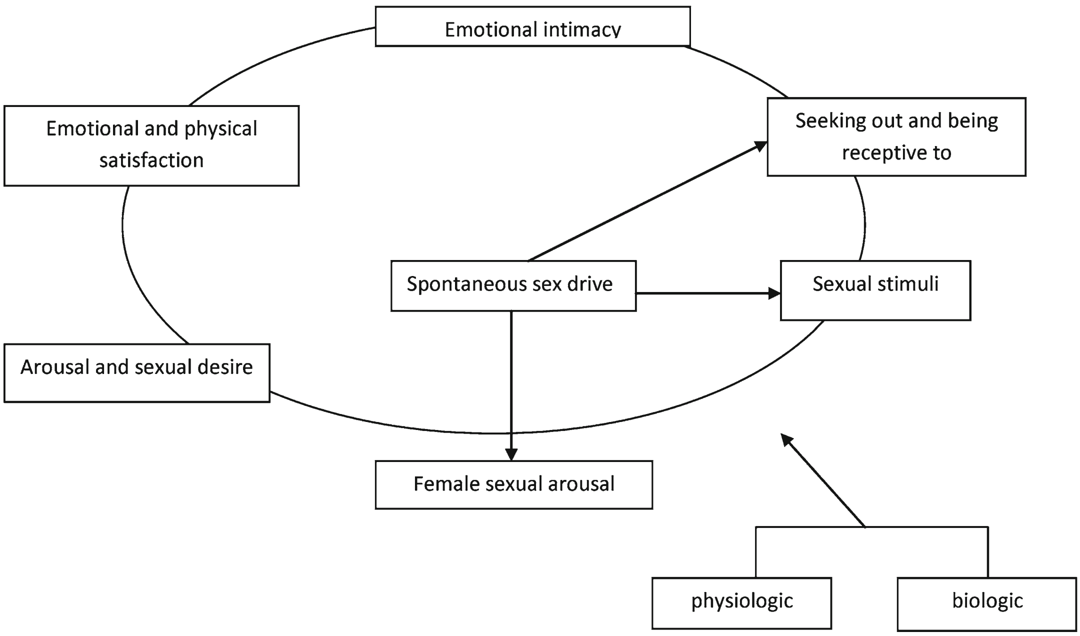


Fig. 23.1 Female sexual response cycle as described by Basson [8]

plateau, orgasm, and resolution, which occur in sequence. This model provides a foundation for understanding of sexual function from which various modifications have subsequently been made. In recognition of the complexities associated with female sexual function and responses, a contemporary model for the female sexual response was introduced in 2000 by Basson [8] (Fig. 23.1). This model emphasizes the complex nature of sexual activity in women, particularly with regard to the importance of emotional intimacy and relationship satisfaction as potential initiation points for sexual activity that may precede desire. Spontaneous sex drive is not a necessary initiation point for sexual function, and as noted by Moore sexual neutrality is a normal variant of female sexual function [9]. This is particularly relevant with regard to elderly women in whom an absence or decrease in spontaneous sex drive may be quite normal.

The female sexual anatomy and physiology has been well described and is not unique to the geriatric patient except for an increased prevalence of pelvic floor disorders including urinary incontinence, pelvic organ prolapse, and fecal incontinence [10]. In addition to minor physical changes, physiologic changes associated with aging can affect the sexual response inhibiting or enhancing sexual function [11]. Elderly women are necessarily in the postmenopausal state. Menopause refers to the cessation of menses, occurring at an average age of 51 years in the USA though there is some variability in reported ages of occurrence with some women experiencing menopause as early as age 40 or as late as age 58. The most notable physiologic finding in menopausal women is the significantly reduced levels of estrogen. Vasomotor symptoms such as hot flashes are among the most recognizable immediate results of decreased levels of estrogen. Estrogen is important with regard to female sexuality for a number of reasons. Chronically diminished levels of estrogen in the postmenopausal state contribute to a variety of changes in the pelvic and vaginal tissues that can negatively impact sexual function. Atrophy of the vaginal tissues, including dryness and thinning of the mucosa, occurs in the absence of adequate levels of estrogen and contributes to significant dyspareunia and other related sexual problems. Decreased libido is a common complaint among postmenopausal and elderly women. The role of estrogen in impacting libido or sexual desire has not been well defined. Estrogen replacement therapy has not been found to significantly improve sexual activity, desire, or pleasure [12]. Interestingly, testosterone has been found to be a key component of sexual health among women as well as men. Libido changes with aging may be closely connected to falling levels of testosterone [5, 13]. Testosterone levels in women decrease progressively with age such that from age 20 to age 40, circulating levels of testosterone have decreased by nearly 50 % [14].

Sexual Dysfunction

Butler and Lewis [15] describes sexuality as the quality or state that comprises sexual desire, arousal, function and activity, physical satisfaction, and emotional intimacy. The broad nature of sexuality has contributed to difficulty in clearly defining and addressing sexual dysfunction and disorders. A classification system was originally developed in 1998 by the American Foundation of Urologic Disease to address this deficiency. Since that time, it has undergone a number of necessary revisions. Foremost among these is the requirement that personal distress results from the sexual symptoms. This is particularly relevant with respect to sexual dysfunction in geriatric patients. In a nationwide study in 2007 including 3,005 US adults (1,550 women and 1,455 men) age 57–85, women were most likely to rate sex as being not at all important, with 41 % of those in the oldest age group (75–85) rating sex as not at all important [16]. This complicates the evaluation and treatment of sexual dysfunction among elderly women and likely contributes to complacency among physicians in assessing for sexual dysfunction in that age group. The most recent revisions to the classification system for female sexual dysfunction and disorders were made in 2004 by the Second International Consultation of Sexual Medicine [17] (Table 23.1).

Prevalence of sexual dysfunction among older women has proven difficult to quantify. This is in large part due to the nuances involved in defining it as previously noted and the variety of definitions and criteria employed in studies that have been conducted. Sexual function and dysfunction is complex, involving interaction between

Table 23.1 Classifications of female sexual dysfunction

Definitions of women's sexual dysfunction (as submitted by the 2nd International Consultation on Sexual Medicine) [17]	
Women's sexual interest/desire disorder	Absent or diminished feeling of sexual interest or desire, absent sexual thoughts or fantasies, and a lack of responsive desire beyond the normative lessening with life cycle and relationship duration
Subjective sexual arousal disorder	Absence of or markedly diminished feelings of sexual arousal from any type of sexual stimulation
Combined genital and subjective arousal disorder	Absence of or markedly diminished feelings of sexual arousal from any type of sexual stimulation as well as complaints of absent or impaired genital sexual arousal
Genital sexual arousal disorder	Complaints of absent or impaired genital sexual arousal which may include minimal vulval swelling or vaginal lubrication from any type of sexual stimulation
Persistent sexual arousal disorder	Spontaneous intrusive and unwanted genital arousal in the absence of sexual interest and desire
Women's orgasmic disorder	Either lack of orgasm, markedly diminished intensity of orgasmic sensations, or marked delay of orgasm despite self-report of high sexual arousal/excitement
Vaginismus	Persistent or recurrent difficulties of the woman to allow vaginal entry of a penis, a finger, and/or any object, despite the woman's expressed wish to do so
Dyspareunia	Persistent or recurrent pain with attempted or complete vaginal entry and/or penile vaginal intercourse

physiologic, psychological, personal, and social factors often unique to each individual. Decline in sexual activity with age and particularly among women has been well documented. Older women in any age category are twice as likely as males to be sexually inactive [18]. Additional studies have demonstrated a progressive decline in sexual activity with age from about 62 % among those aged 57–64 to only 17 % among those aged 75–85 [18]. While rates of sexual activity decline with age, the frequency of sexual activity among those who remain sexually active is maintained. The geriatric cohort over the age of 85 is currently the fastest growing segment of the population. Increasing overall numbers coupled with the knowledge that sexual activity is an increasingly important factor in the quality of life of elderly women emphasize the importance of sexual health in this age group. Despite the large number of women for whom sexual activity is not felt to be important, this still mandates that assessment for and treatment of sexual dysfunction be performed. Sexual dysfunction is known to significantly influence self-esteem and quality of life and to be a source of emotional distress which can lead to relationship problems for women [6]. Sexual dysfunction among women is estimated to have a prevalence from 25 to 63 % [5, 6]. Among postmenopausal women, however, prevalence is significantly higher, impacting as many as 86 % in some studies [6]. US population census data showed nearly ten million women ages 50–74 reported complaints of sexual dysfunction [9, 19]. Lindau and her colleagues found that about 25 % of sexually active adults may avoid sex as a result of a sexual problem [16]. Among elderly women who are sexually active, only about 50 % report a good quality sex life, while the prevalence of bothersome sexual problems has been reported to be greater than 50 % [16, 18].

Most commonly reported sexual problems include lack of interest, difficulties with lubrication, not finding sex pleasurable, and pain [16]. Lack of interest in sex is frequently reported among women of all age groups with a prevalence of 26–49 % which increases with age [5, 18]. As noted earlier, lack of interest in sex must be a source of personal distress for the patient in order to qualify as sexual dysfunction. Dyspareunia or pain during intercourse is also common in the elderly population. Difficulty with lubrication as well as atrophy of pelvic and vaginal tissues occurs in relation to estrogen deficiency in the postmenopausal state. As many as 36–44 % of women have reported difficulty with lubrication for sexual intercourse, and among women over age 57, between 11.8 and 17.8 % report pain during intercourse [18]. Again, the prevalence of these problems increases with age. While difficulty with lubrication and associated pain are problematic in their own right, the discomfort they cause often contributes to additional sexual difficulties including impaired arousal related to anticipated discomfort and anxiety and may lead to decreased libido [5, 20, 21]. The incidence of pelvic floor disorders including pelvic organ prolapse and urinary incontinence is increased in the geriatric population. Nygaard and her colleagues found that one in four women in the USA suffer from symptoms of at least one pelvic floor disorder [22]. Of those women with pelvic floor disorders, as many as 25–50 % report sexual dysfunction [23–26]. Urinary problems including urinary incontinence impact 23–55 % of older women [10, 27]. Urinary incontinence has been shown to negatively impact women's sexual function with 22 % reporting worry that sexual activity may result in urine loss [23]. In addition, pelvic organ prolapse is commonly encountered in the elderly female population and can negatively impact sexual function. Among women affected, greater than 30 % report that symptoms caused by the prolapse interfere with sexual activity [28]. Both incontinence and prolapse can be embarrassing bothersome conditions associated with negative impacts on sexual function, body image, and feelings of sexual attractiveness [10].

Assessment and Diagnosis

Evaluation of the older woman with regard to sexual dysfunction should be performed in a manner similar to that of the general population. Most important is an appreciation of the

Table 23.2 Validated female sexual dysfunction questionnaires

Grade A questionnaires recommended by the 4th International Consultation on Incontinence Committee for Evaluation of Sexual Function and Health in Women with Urinary Symptoms as valid, reliable, and responsive to change following psychometric testing [32]

Questionnaire	Grade	No. of questions	Goal
Golombok Rust Inventory of Sexual Satisfaction (GRISS)	A	28	Self-administered questionnaire assessing quality of heterosexual relationships and function in women currently in relationships
ICIQ-FLUTSsex (BFLUTS)	A	4	Self-administered questionnaire to assess effect of urinary symptoms on sexual function
Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ)	A	31	Self-administered questionnaire to asses sexual function in women with pelvic organ prolapse or incontinence

prevalence of sexual dysfunction and the significant impact this can have in the health, quality of life, and well-being of women. Discussion of sexual health may provide insight into other areas of health as well as sexual expression in geriatric patients and has been reported as predictive of overall health [29].

The initial step involves willingness of physicians and patients alike to confront and address the issue. Unfortunately, physicians often fail to question patients regarding sexual health issues. In one study examining results from the Global Study of Sexual Attitudes and Behaviors, only 9 % of men and women aged 40–80 were asked about their sexual health during medical visits over a 3-year period [30]. Questionnaires provide an effective means of identifying problems and opening conversation between patient and physician. Clegg et al. recommend the routine use of female sexual dysfunction questionnaires as one component of normal female evaluations [31]. The 4th International Consultation on Incontinence Committee on Evaluation of Sexual Function and Health in Women with Urinary Symptoms recommended the use of validated questionnaires in the assessment and care of women [32] (Table 23.2).

Unfortunately, there are no validated questionnaires specific to elderly sexual dysfunction at this time. These questionnaires are useful tools to help in the identification and characterization of sexual dysfunction. However, they cannot and should not replace the complete history and physical examination including a thorough sexual history. The physical examination may reveal problematic atrophic vaginitis or pelvic floor disorders. Among elderly women, the medical history, medications, and social history are of particular significance. The correlation between overall health and sexual function is well established. A number of studies have suggested that women with better functional status and better self-reported overall health are more likely to be sexually active and to have higher levels of sexual satisfaction [10, 18, 33]. An awareness of all medical comorbidities in a patient and their potential impact on sexual function is essential. A variety of medications have demonstrated sexual side effects mandating assessment of current medications in geriatric patients. In particular, diabetes, coronary disease, renal dialysis, cancer, incontinence, and pulmonary disease have all been linked to sexual behavior [10]. Limitations to mobility often contribute to a decrease or absence of sexual function [10, 34]. Mobility issues are particularly problematic as the pathologic process leading to the immobility may contribute to decreased sexual function as well.

An appreciation of the interplay between overall health and sexual function can enhance one's ability to optimize both, especially in geriatric patients. Numerous factors contribute to the presence or absence of sexual activity among older adults. For elderly women, social factors are paramount. The presence of a spouse or partner is the single most influential factor in terms of maintaining sexual activity. A clinic study of patients aged 60 and over revealed that almost 56 % of married women were sexually active compared to about 5 % of unmarried women [34]. However, about 40 % of women in the 75–85-year age group do report having a spouse or other intimate relationship [16]. It is important to elucidate any potential pathologic barriers, including social, physical, or psychological, to sexual activity. It is key to understand that an absence of sexual activity does not equate to sexual dysfunction.

Management

Due to the many causes and manifestations of sexual dysfunction among elderly women, management options are necessarily diverse and must be tailored accordingly to individual patients. Management should begin with a clear understanding of the goals and intentions of treatment with an awareness of the complex interconnections between psychological, social, and physical factors in each patient. Given the established link between overall health status and sexual dysfunction noted earlier, optimization of general health is paramount and should be assessed and encouraged. Often, this may require coordination with other physicians and caregivers.

Symptomatic urogenital atrophy contributing to dyspareunia or other urinary symptoms can be managed with water-based lubricants during intercourse as well as the use of topical estrogen replacement. Topical low-dose estrogen therapy has been demonstrated to be safe and effective for management of irritative vaginal symptoms [35]. Topical estrogen works to significantly improve vaginal atrophy by helping to revascularize the vaginal epithelium and restore pH levels to normal range [36]. As such, topical estrogen therapy should be considered in all elderly women complaining of irritative symptoms or pain with intercourse and evidence of vaginal atrophy on examination. Estrogen use is contraindicated in women with a personal history of uterine cancer. Topical estrogen use has not been shown to increase risk of breast cancer recurrence [37]. However, women with active breast cancer or a personal history of breast cancer should be advised to speak to their oncologist prior to initiating even topical hormone therapy. Exogenous estrogens are typically contraindicated, particularly in women with a history of estrogen-receptor-positive breast cancers.

Among women with pelvic floor disorders including prolapse and bothersome urinary incontinence impacting sexual function, a number of treatment modalities are available. Conservative therapy is often quite effective in terms of improvement in sexual function. Women who are successfully treated for incontinence using only pessaries and pelvic floor muscle exercises have been found to have improvements in sexual function [38]. However, the complex nature of sexual function and dysfunction makes recommendations for aggressive therapy more difficult, particularly with regard to elderly women. Women who underwent surgical correction of urinary incontinence have been shown to experience no changes to libido, arousal, orgasm, and satisfaction while reporting increased coital frequency, decreased fear of incontinence, and embarrassment [39, 40]. In addition, a study using the validated PISQ questionnaire showed correction of pelvic organ prolapse through both vaginal and abdominal approaches improved sexual function [41]. Generalization of these results to a geriatric population requires consideration of inherent risks of surgery and comorbid medical conditions. This suggests that addressing prolapse or urinary incontinence surgically may be a reasonable option in appropriately selected patients with an understanding that outcomes with regard to sexual function may be varied.

Management of sexual dysfunction related to desire or lack of interest is of particular importance given its prevalence among elderly women. When troubling hypoactive sexual desire is present in elderly women, consideration must be given to the potential contributions of social and psychological factors in addition to physiologic changes. Untreated depression should be assessed as this may be a contributing factor in as many as 60 % of women with low desire [42]. Assistance from psychiatrists, psychologists, and sex therapists can be essential in evaluating and treating these women. Psychological therapy including cognitive behavioral therapy and sexual education is among the most useful and successful means of addressing low sexual desire [43]. While post-menopausal women have decreased levels of estrogen and testosterone levels, no direct correlation has been established between either of these hormone concentrations and sexual desire or libido. Systemic estrogen replacement therapy has been found to have no resultant improvement in sexual satisfaction and is not generally recommended to address hypoactive desire. However, additional research in this area among elderly women with sexual dysfunction is needed [44]. Testosterone supplementation remains controversial at this time and is not currently FDA approved for treatment in women. However, a number of studies have demonstrated some efficacy with improvement in sexual function, desire, arousal, and orgasm [45–47].

Conclusion

Sexual health is an important aspect of well-being across the adult life span and remains so among elderly women. The societal cost of sexual dysfunction among older women has not been quantified but is likely to be substantial. Sexual dysfunction is an issue that caregivers must carefully assess for both its impact on the quality of life of patients and its close associations with comorbid disease and overall health. Sexual dysfunction, though varied in its cause, presentation, and effects among elderly women, is highly prevalent and requires careful evaluation and implementation of various methods of treatment. Significant advances have been made, but ongoing work will help to better identify appropriate diagnostic and management techniques as they apply to geriatric female patients.

References

1. Barlow D, Cardozo L, Francis R, et al. Urogenital ageing and its effect on sexual health in older British women. Br J Obstet Gynaecol. 1997;104:87–91.
2. Bachman G. Female sexuality and sexual dysfunction: are we stuck on the learning curve? J Sex Med. 2006;3(4):639–45.
3. Degauquier C, Absil AS, Meuris S, et al. Sexuality of our seniors: happy end or new beginning? Rev Med Brux. 2012;1:40–6.
4. Lindau ST, Gavrilova N. Sex, health, and years of sexually active life gained due to good health: evidence from two US populations based cross sectional surveys of ageing. Br Med J. 2010;340:c810.
5. Ambler DR, Bieber EJ, Diamond MP. Sexual function in elderly women: a review of current literature. Rev Obstet Gynecol. 2012;5(1):16–27.
6. Addis IB, Eeden SK, Wassel-Fyr CL, et al. Sexual activity and function in middle-aged and older women. Obstet Gynecol. 2006;107:755–64.
7. Masters WH, Johnson VE. Human Sexual Response. 1st ed. New York: Little, Brown and Co. 1966.
8. Basson R, Berman J, Burnett A, et al. Report of the International Consensus Development Conference on Female Sexual Dysfunction: definitions and classifications. J Urol. 2000;163:888–93.
9. Moore CK. Female sexual function and dysfunction. In: Kavoussi LR, Novick AC, Partin AW, Peters CA, editors. Campbell-Walsh Urology. 10th ed. Philadelphia, PA: Elsevier; 2012. Chapter 30, p. 823–33.
10. Ratner ES, Erekson EA, Minkin MJ, et al. Sexual satisfaction in the elderly female population: a special focus on women with gynecologic pathology. Maturitas. 2011;70:210–7.
11. Bachmann GA, Leiblum SR. The impact of hormones on menopausal sexuality: a literature review. Menopause. 2004;11:120–30.
12. Shifren JL, Braunstein GD, Simon JA, et al. Transdermal testosterone treatment in women with impaired sexual function after oophorectomy. N Engl J Med. 2000;343(10):682–8.
13. Camacho ME, Reyes-Ortiz CA. Sexual dysfunction in the elderly: age or disease? Int J Impot Res. 2005;17 Suppl 1:S52–6.
14. Davis SR, Guay AT, Shifren JL, et al. Endocrine aspects of female sexual dysfunction. J Sex Med. 2004;1(3):237–53.
15. Butler RN, Lewis MI. Sexuality in old age. In: Tallis RC, Fillit HM, editors. Geriatric medicine and gerontology. London: Churchill Livingstone; 2006. p. 1407–12.
16. Lindau ST, Schumm LP, Laumann EO, et al. A study of sexuality and health among older adults in the United States. N Engl J Med. 2007;357:762–74.
17. Sexual Medicine: Sexual Dysfunctions in Men and Women. 2nd International Consultation on Sexual Medicine. Lue T, Basson R, Rosen R, Giuliano F, Khoury S, Montorsi F, editors. Paris: Editions 21. 2004.
18. Matthias R, Lubben J, Atchison K, et al. Sexual activity and satisfaction among very old adults: results from a community-dwelling medicare population survey. Gerontologist. 1997;37(1):6–14.
19. Shifren JL, Monz BU, Russo PA, et al. Sexual problems and distress in United States women: prevalence and correlates. Obstet Gynecol. 2008;112(5):970–8.
20. Redmund GP. Hormones and sexual function. Int J Fertil Womens Med. 1999;44:193–7.

21. Hofland SL, Powers J. Sexual dysfunction in the menopausal woman: hormonal causes and management issues. Geriatr Nurs. 1996;17:161–5.
22. Nygaard I, Barber M, Burgio K, et al. Prevalence of symptomatic pelvic floor disorders in US women. JAMA. 2008;300(11):1311.
23. Barber M, Visco A, Wyman J, et al. Sexual function in women with urinary incontinence and pelvic organ prolapse. Obstet Gynecol. 2002;99(2):281–9.
24. Handa V, Harvey L, Cundiff G, et al. Sexual function among women with urinary incontinence and pelvic organ prolapse. Am J Obstet Gynecol. 2004;191(3):751–6.
25. Ellerkmann RM, Cundiff GW, Melick CF, et al. Correlation of symptoms with location and severity of pelvic organ prolapse. Obstet Gynecol. 2001;185(6):1332–7.
26. Berglund AL, Fugl KS. Some sexological characteristics of stress incontinent women. Scand J Urol Nephrol. 1996;30(3):207–12.
27. Thomas TM, Plymat KR, Blannin J, et al. Prevalence of urinary incontinence. BMJ. 1980;281:1243–5.
28. Weber AM, Walters MD, Schover LR, et al. Sexual function in women with uterovaginal prolapse and urinary incontinence. Obstet Gynecol. 1995;85(4):483–7.
29. Chen HK, Tseng CD, Wu SC, et al. A prospective cohort study on the effect of sexual activity, libido and widowhood on mortality among the elderly people: 14-year follow-up of 2453 elderly Taiwanese. Int J Epidemiol. 2007;36:1136–42.
30. Moreira ED, Brock G, Glasser DB, et al. Help-seeking behavior for sexual problems: the Global Study of Sexual Attitudes and Behaviours. Int J Clin Pract. 2005;59:6–16.
31. Clegg M, Towner A, Wylie K. Should questionnaires of female sexual dysfunction be used in routine clinical practice? Maturitas. 2012;72:160–4.
32. Incontinence. 4th International Consultation on Incontinence. Abrams P, Cardozo L, Khoury S, Wein A, editors. 4th edition. Paris: Editions 21. 2009.
33. Schover LR. Sexual problems in chronic illness. In: Leiblum SR, Rosen RC, editors. Principles and practice of sex therapy. New York, NY: Guilford; 2000. p. 398–422.
34. Diokno A, Brown M, Herzog A. Sexual function in the elderly. Arch Intern Med. 1990;150:197–200.
35. Rioux JE, Devlin C, Gelfand MM, et al. 17beta-estradiol vaginal tablet versus conjugated equine estrogen vaginal cream to relieve menopausal atrophic vaginitis. Menopause. 2000;7(3):156–61.
36. Nappi RE, Davis SR. The use of hormone therapy for the maintenance of urogynecological and sexual health post WHI. Climacteric. 2012;15:267–74.
37. Dew JE, Wren BG, Eden JA. A cohort study of topical vaginal estrogen therapy in women previously treated for breast cancer. Climacteric. 2003;6(1):45–52.
38. Handa V, Whitcomb E, Weidner A, et al. Sexual function before and after non-surgical treatment for stress urinary incontinence. Female Pelvic Med Reconstr Surg. 2011;17(1):30–5.
39. Pauls R, Silva WA, Rooney C, et al. Sexual function after vaginal surgery for pelvic organ prolapse and urinary incontinence. Obstet Gynecol. 2007;197(6):622–7.
40. Ghezzi F, Serati M, Cromi A, et al. Impact of tension-free vaginal tape on sexual function: results of a prospective study. Int Urogynecol J Pelvic Floor Dysfunct. 2006;17(1):54–9.
41. Komesu Y, Rogers R, Kammerer D, et al. Posterior repair and sexual function. Obstet Gynecol. 2007;197(1):101–6.
42. Basson R, Schultz WW. Sexual sequelae of general medical disorders. Lancet. 2007;369:597–611.
43. Bhasin S, Basson R. Sexual dysfunction in men and women. In: Melmed S, Polonsky K, Larsen P, Kronenberg H, editors. Williams textbook of endocrinology. 12th ed. Philadelphia, PA: Elsevier; 2011. p. 778–816.
44. Hays J, Ockene JK, Brunner RL, et al. Women's Health Initiative Investigators. Effects of estrogen plus progestin on health-related quality of life. N Engl J Med. 2003;348:1839–54.
45. Somboonporn W, Davis S, Seif MW, et al. Testosterone for peri- and post-menopausal women. Cochrane Database Syst Rev. 2005;(4):CD004509
46. Braunstein GD, Sundwall DA, Katz M, et al. Safety and efficacy of a testosterone patch for the treatment of hypoactive sexual desire disorder in surgically menopausal women: a randomized, placebo-controlled trial. Arch Intern Med. 2005;165(14):1582–9.
47. Shifren JL, Davis SR, Moreau M, et al. Testosterone patch for the treatment of hypoactive sexual desire disorder in naturally menopausal women: results from the INTIMATE NM1 study. Menopause. 2006;13(5):770–9.

24 Geriatric Sexuality

Philip T. Zhao, Daniel Su, and Allen D. Seftel

Introduction

> *"Fifty marks the beginning of the best years of our lives, including the best sex of our lives."*
>
> *—Dr. Christiane Northrup*

The older population of the USA, aged 65 years or older, numbered 39.6 million in 2009 and is expected to increase to almost 55 million by 2020 [1]. Knowledge regarding sexuality among older Americans is limited as it encompasses aspects including function, behavioral activity, partnership attitudes, and general health [2]. As men and women grow older, they are more susceptible to medical comorbidities that can affect sexual health. Although illness and increasing age can decrease the prevalence of sexual activity, numerous studies show that a substantial number of older people engage in intercourse and other sexual behaviors even into their eighth and ninth decade of life. In a landmark study, Laumann et al. [3] detailed both male and female sexual dysfunction in a younger cohort of men and women. Analysis of data came from the National Health and Social Life Survey, a probability sample study of sexual behavior in a demographically representative 1992 cohort of US adults. Participants included a national probability sample of 1,749 women and 1,410 men aged 18–59 years at the time of the survey. Sexual dysfunction was more prevalent for women (43 %) than men (31 %) and was associated with various demographic characteristics, including age and educational attainment. Lindau et al. examined an older cohort and reported that the frequency of sexual activity in people up to 74 years of age was similar to that reported among adults 18–59 in the 1992 National Health and Social Life Survey. This was despite a significantly higher ratio (>50 %) of bothersome sexual problems [4].

As a result of significant bothersome sexual problems and misconceptions about aging and sex, a quarter of older adults refrain from sexual activity and many of them do not discuss these issues with their physicians. Although there exists a massive and growing market for drugs and devices to improve sexual function and decrease morbidities among the geriatric population, medication and surgery may not be suited for everyone. Therefore, physician knowledge and patient education should play an active role in improving patient counseling and addressing potentially treatable sexual problems.

P.T. Zhao, M.D.
Rutgers Robert Wood Johnson Medical School, 1 Robert Wood Johnson Pl, New Brunswick, NJ 08901, USA

D. Su, M.D.
Division of Urology, Rutgers Robert Wood Johnson Medical School, 1 Robert Wood Johnson Pl, New Brunswick, NJ 08901, USA

A.D. Seftel, M.D., F.A.C.S. (✉)
Division of Urology, Department of Surgery, Cooper University Health Care, Cooper Medical School of Rowan University, 3 Cooper Plz, Marlton, NJ, USA
e-mail: seftel-allen@cooperhealth.edu

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_24,

Sexual Myths of Aging

A significant barrier to adequately diagnosing and treating sexual conditions in older adults are the perpetual myths regarding sex in aging individuals. These include the stereotypical impression of the older individual as slow moving, slow thinking, and one who rarely explores or indulges in his or her sexuality. Contrary to widely held beliefs and cultural and social views, the aging population continues to enjoy their sexuality. Common myths include the view that erectile dysfunction (ED) is a normal part of aging, that old people do not have sexual desires or capabilities, and that elderly people are too frail to attempt intercourse or that their desires are perverse [5]. In addition, the media has perpetuated some of these stereotypes of "dirty old men" and portrayed older adults in a negative light when it comes to their sexuality [5]. They do a disservice not only to the large portion of the country's population who are elderly but also to the medical professionals who help and treat older patients. In order to build a healthy society and integrate our increasingly older population, the public should be open-minded and tolerant of its aging citizens in regard to their sexuality.

There are factors intertwined with aging that influence sexuality that cross gender lines. Many of these issues impact both men and women during the aging process. There are life stressors such as career, finance, physical and mental fatigue, and drug and alcohol abuse that can substantially affect sexuality [6].

Significant emotional and lifecycle disparities exist between men and women as they grow older. Compared to elderly women, older men are generally more prone to be involved in a relationship. One study showed that 78 % of men aged 75–85 were in a spousal or sexual relationship compared to 40 % of the women in the same age group [4]. This wide gap can be attributed to several factors including generally greater longevity in women compared to men. Women were also more likely to rate sex as an unimportant part of life and relationships compared to men. A multinational survey of people 40–80 years of age showed that women prioritize cognitive and emotional aspects of sexuality as well as general happiness as a more important component of subjective sexual well-being [7]. Women also reported a higher proportion of lack of pleasure with sex. Despite the fact that bothersome sexual problems affect men and women equally, women were less likely than men to discuss these problems with their physicians [8]. Issues include patient unwillingness to initiate discussion, poor general communication with the doctor, sex and age differences between the patient and physician, and negative social attitudes about women's sexuality especially at older age [9, 10].

The Sexual Response Cycle in the Aging Patient

The four stages of the sexual response cycle including excitement, plateau, orgasm, and resolution change as people grow older [11, 12]. Excitement depends on a multitude of visual, olfactory, auditory, and memory stimuli. Plateau is defined as the maintenance and intensification of arousal. Orgasm involves the rhythmic muscular contractions typical of climax. Resolution is the state of relaxation after orgasm. These stages change dramatically as men and women age and they impact sexuality at every level [13]. For women, there is prolongation of the excitement and plateau stages as they age. This is associated with increased time to attain sufficient vaginal lubrication and a marked overall decrease in production of lubrication. Orgasmic contractions decrease in quantity and intensity, due to atrophy of the vaginal mucosa and reduced elasticity and muscle tone. There is also a sharp decrease in the length of the resolution stage. Anatomically, there can be significant atrophy of the vaginal tissues, decreased vaginal canal length and width, loss of vulvar tissue, and decrease in size of the clitoris. Estrogen levels fall sharply and play a dominant role in changes in female sexual function after menopause. In some postmenopausal women, the loss of reproductive capacity either diminishes interest in sexual intercourse or increases the eagerness to engage in sexual activities because the fear of pregnancy is gone [13].

In elderly men [14], all four stages of sexual response decrease with advancing age. More time is required for penile stimulation in order to obtain and maintain a sufficient erection to engage in sex. There is a prolongation of the plateau phase with a shorter transition from orgasm to ejaculation. Orgasms become weaker with shorter intervals and smaller contractions. There is also a significant reduction in the amount of semen volume compared with younger men [15]. Penile detumescence occurs more frequently and rapidly in the resolution phase, and there is a prolonged refractory period between erections [16]. Of course, all of these changes occur in conjunction with decreasing levels of testosterone, which is a primary driver of sexual desire and perhaps sexual function in males.

Psychological Issues

Psychological issues that impact sexuality in the aging population include lifetime sexual experiences, levels of satisfaction pertaining to life, self-esteem and confidence levels, body images, and general attitudes towards sex. Historically, living arrangements and loss of a spouse or significant other have presented challenges and psychological issues to the surviving partner regarding future sexual relationships [17]. Depression affects both males and females and can have lasting psychological implications that substantially decrease interest and ability to engage in a sexual relationship [17].

The Epidemiology of Sexual Dysfunction in the Aging Patient

Descriptions of the incidence and prevalence of sexuality of the aging population are relatively recent. Barriers to accumulating these data include the sensitivity of the subject matter, the difficulties in conducting what may potentially be embarrassing interviews, poor response rate from surveys, and self-reporting biases. In addition to the studies by Laumann and Lindau discussed previously, a large, well-conducted recent report is The Global Study of Sexual Attitudes and Behaviors [7]. This large, multinational study collected data from 27,500 men and women 40–80 years of age using standardized questionnaires. The authors found that more than 80 % of men and 65 % of women had sexual intercourse during the past year. The most common sexual dysfunctions for men were early ejaculation (14 %) and erectile dysfunction (10 %). For women, the lack of sexual desire (21 %), inability to reach orgasm (16 %), and inadequate lubrication (16 %) were the most common sexual problems. Overall 28 % of men and 39 % of women were affected by at least one sexual dysfunction. This study found that sexual desire and activity are in fact widespread among the elderly population. The prevalence of sexual dysfunction was quite high and tends to increase with age, especially in men.

Sexual Dysfunction in the Aging Female

The incidence of sexual dysfunction in the aging female has been much more difficult to characterize. This is mostly due to the ambiguity in the diagnosis of female sexual dysfunction. The previously cited study by Laumann et al. [3] demonstrated that 43 % of women surveyed had sexual dysfunction. Data demonstrated a 22 % prevalence of low sexual desire, 14 % prevalence for arousal problems, and 7 % prevalence of sexual pain. Overall, 57 % reported no sexual dysfunction.

The Global Study of Sexual Attitudes and Behaviors [7] was a multinational study that collected data from 27,500 men and women 40–80 years of age using standardized questionnaires. Among the women participants, the lack of sexual desire (21 %), the inability to reach orgasm (16 %), and inadequate lubrication (16 %) were the most common sexual problems. Quantitative or qualitative criteria for diagnosis of female sexual dysfunction are limited. There are data supporting vaginal atrophy as a cause not only for sexual dysfunction but also for voiding dysfunction in addition to issues with emotional well-being and everyday activity in postmenopausal women [18].

A recent study sought to estimate the prevalence of low sexual desire and hypoactive sexual desire disorder (HSDD) in US women, focusing on their menopausal status [19]. The authors performed a cross-sectional study using a probability sample of households. Participants included 2,207 women aged 30–70 years who were in stable relationships of at least 3 or more months. Interviews were conducted by telephone. The analysis focused on 755 premenopausal women and 552 naturally and 637 surgically menopausal women. Low sexual desire was defined using the Profile of Female Sexual Function desire domain, and HSDD was defined using the Profile of Female Sexual Function and the Personal Distress Scale. The prevalence of low sexual desire ranged from 26.7 % among premenopausal women to 52.4 % among naturally menopausal women. The prevalence of HSDD was highest (12.5 %) among surgically menopausal women. Compared with premenopausal women and adjusting for age, race/ethnicity, educational level, and smoking status, the prevalence ratios for HSDD were 2.3 (95 % CI = 1.2–4.5) for surgically menopausal women and 1.2 (0.5–2.8) for naturally menopausal women. The prevalence ratios for low sexual desire were 1.3 (0.9–1.9) and 1.5 (1.0–2.2) for surgically and naturally menopausal women, respectively.

The recent data from the Rancho Bernardo study were supportive of these findings [20]. A total of 1,303 older women were mailed a questionnaire on general health, recent sexual activity, sexual satisfaction, along with the Female Sexual Function Index questionnaire. A total of 806 of 921 respondents (87.5 %) aged 40 years or more answered questions about recent sexual activity. Median age was 67 years, mean time since menopause was 25 years, most were upper-middle class, 57 % had attended at least 1 year of college, and 90 % reported good to excellent health. Half (49.8 %) reported sexual activity within the past month either with or without a partner. The majority of these women reported arousal (64.5 %), lubrication (69 %), and orgasm (67.1 %) at least most of the time, although one third reported low, very low, or no sexual desire. Although frequency of arousal, lubrication, and orgasm decreased with age, the youngest cohort (<55 years old) and the oldest cohort (>80 years old) reported a higher frequency of orgasm satisfaction. Emotional closeness during sex was associated with more frequent arousal, lubrication, and orgasm. Estrogen replacement therapy did not affect these variables. Overall, two thirds of sexually active women were moderately or very satisfied with their sex life, as were almost half of sexually inactive women [20].

Hormonal Issues in Women: Menopause

Menopause is defined as the permanent cessation of menses usually occurring between 45 and 55 years of age with estrogen deficiency as the primary diagnostic criterion [18, 21]. Symptoms include hot flashes, sexual dysfunction, mood disorders, and urogenital complaints. It also increases the risk for cardiovascular, musculoskeletal, and psychogenic sequelae. Diagnosis is usually made in women with elevated follicle-stimulating hormone (FSH) levels, although FSH is not the most accurate way to assess menopausal status because FSH levels can vary considerably during the transition through menopause [18]. When menopause occurs before the age of 40, it is considered pathologic and a clinical evaluation should be initiated. This is considered premature ovarian failure and is usually secondary to autoimmune oophoritis [18]. Bilateral oophorectomy can also induce menopause.

Although the changes brought on by menopause are, for the most part, considered adverse, some women actually feel relaxed and liberated from the fear of pregnancy. Others experience a psychological decrease of what they consider as their sexuality and femininity. The vaginal changes associated with menopause can cause dyspareunia and worsen the sexual experience for some women. Lower tissue estrogen levels also predispose menopausal women to atrophic vaginitis and more frequent vaginal infections which are associated with itching, burning, and discharge [18, 21].

Estrogen replacement therapy (ERT) had been the mainstay of treatment for menopausal women for decades based on the premise that it safeguards against osteoporosis and cardiovascular disease. However, new data from the Women's Health Initiative E-Alone Trial revealed that ERT may result in increased cardiac events and cerebrovascular disease in healthy women as well as an increased risk of venous thromboembolism [22]. There was also concern regarding ERT predisposing women to higher risks for breast and uterine cancers [23]. Systemic ERT has also been shown to increase rates of stress urinary incontinence in women. Thus, the current focus is treating the sequelae of symptoms, such as osteoporosis, postmenopausal depression, and sexual dysfunctions, without the use of ERT.

Erectile Dysfunction, Ejaculatory Dysfunction, and Hormonal Issues in Men

Erectile dysfunction, the inability to achieve or maintain an erection sufficient for sexual activity, has been thought to account for the majority of sexual dysfunction in aging men. Approximately 152 million men worldwide and as many as 30 million American men are affected by erectile dysfunction. It is projected that as many as 322 million men worldwide are projected to have erectile dysfunction by 2025 [23, 24]. It is estimated that the prevalence of erectile dysfunction is approximately 20 % in men 50–59 years of age. Nearly 18 million American men 40–70 years of age are estimated to be affected with some degree of erectile dysfunction [25, 26]. It has also been demonstrated that the prevalence of erectile dysfunction increases with age [25–28]. Based on the Massachusetts Male Aging Study [28], one of several large, well-done, epidemiologic studies on this topic, the crude incidence rate of erectile dysfunction was 25.9 cases per 1,000 man-years. The annual incidence rate increases with each decade of age and was 12.4 cases per 1,000 man-years for American men 40–49 years of age, 29.8 for men 50–59 years of age, and 46.5 for men 60–69 years of age [28] (Fig. 24.1).

Ejaculatory dysfunction in aging men can be manifest as either rapid or delayed ejaculation. Both entities are difficult to quantitate. Delayed ejaculation, which is currently not well defined in terms of time, in elderly men is most likely a combination of neuropathy of the ejaculatory pathway and a change in the prostatic milieu. Neuropathy may result from diabetes, vitamin deficiency, anatomic spinal issues, central nervous system (CNS) issues, or thyroid disorders. Any prior pelvic surgery that affects the pelvic nerves such as radical prostatectomy or transurethral resection of the prostate can also affect ejaculation. The prostate is predominately a reproductive organ in young men and turns into a less glandular, less secretory, and more fibrotic organ with advancing age. In young men, nonorganic, delayed ejaculation is sometimes thought to be psychogenic in origin; however, it is thought that this is less likely in older men. In general, delayed ejaculation is challenging to treat, as many of the etiological disease processes noted previously are chronic, rendering complete correction of delayed ejaculation less likely.

Premature ejaculation in aging men is also enigmatic [29]. The definition of premature ejaculation is somewhat elusive as worldwide studies reflect the disparity in the "normal" ejaculatory period [30]. In a large, multinational study, the intravaginal ejaculation latency time (IELT), which is considered the sine qua non measurement for rapid ejaculation, had a positively skewed distribution, with a geometric mean of 5.7 min and a median of 6.0 min (range: 0.1–52.1 min). Men from Turkey had the shortest median IELT at 4.4 min. Men from the UK had the longest median IELT at 10.0 min. Circumcision and condom use had no significant impact on the median IELT. Subjects who were discontent with their latency time had slightly lower median IELT values of 5.2 min compared to the median of the general population.

Premature or rapid ejaculation has been historically defined by time. Ejaculation within 1–2 min of erection and psychological or emotional distress are the two primary components of

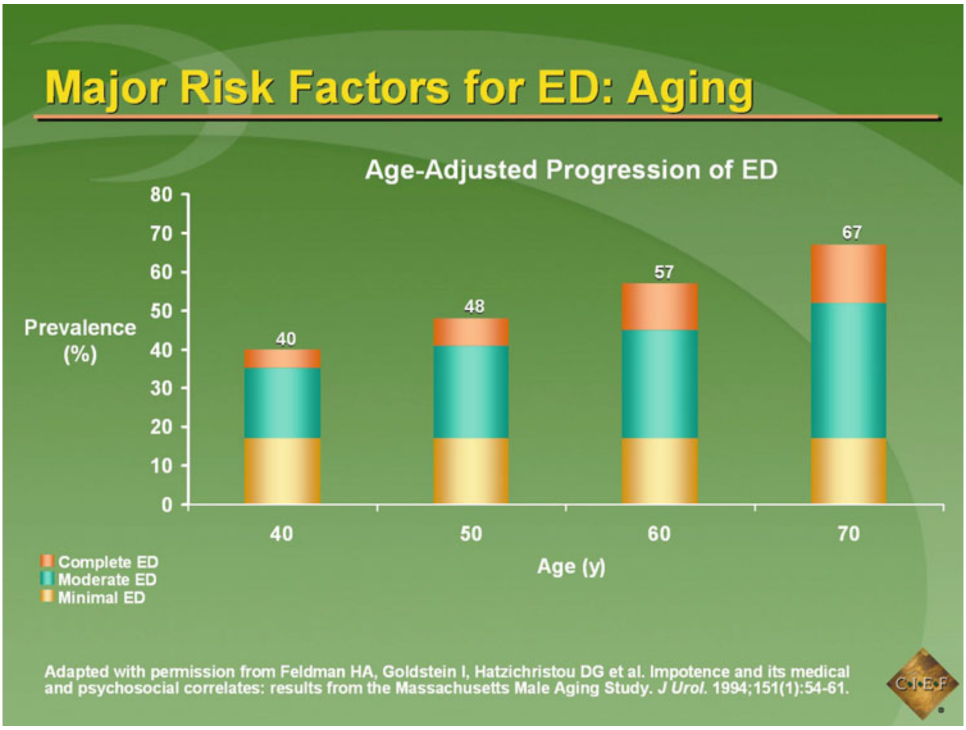


Fig. 24.1 (adapted from [28]): The landmark Massachusetts Male Aging Study (MMAS), a community-based observational study of nearly 3,000 men, aged 40–70 years, clearly established that ED is highly prevalent, age related, and progressive. Subjects ($n=1{,}290$) were asked to respond to a sexual activity questionnaire characterizing their level of ED. *Minimal* ED was defined as "usually able to get or keep an erection"; *moderate*, as "sometimes able"; and *complete*, as "never able to get and keep an erection."[1] Self-rated ED was reflected by higher frequency of erectile difficulty during intercourse, lower monthly rates of sexual activity and erection, and lower satisfaction with sex life and partner. In the MMAS study, 40 % of men were estimated to have ED at age 40, but this increased to 67 % at age 70. Age was the only variable that proved to be a statistically significant predictor of ED ($P<0.0001$)

the current clinical definition. This definition of rapid ejaculation can be independent of vaginal penetration, although intravaginal latency time is often used as the barometer of rapid ejaculation [31].

Rapid ejaculation may be a response to erectile dysfunction which might resolve once the ED is corrected. Alternatively, rapid ejaculation could be lifelong and may only become problematic for older men with advancing age. Rapid ejaculation is thought to be in part partially genetic in younger men. Jern et al. noted a moderate genetic influence (28 %) in rapid ejaculation in a population-based sample of 1,196 Finnish male twins between 33 and 43 years of age [32]. This genetic relationship has not been established in geriatric men.

Hormonal issues in older men can affect sexual desire, erections, and ejaculation [33]. Thyroid disorders are one such example. In one publication, 48 adults including 34 with hyperthyroidism and 14 with hypothyroidism were studied [34]. The mean age was 43.2 ± 12.1 years (range 22–62 years). No significant difference was found in the age at presentation between hyperthyroid and hypothyroid patients. In hyperthyroid men, the prevalence of hypoactive sexual desire (HSD) was 17.6 %, delayed ejaculation (DE) 2.9 %, premature ejaculation (PE) 50 %, and erectile dysfunction (ED) 14.7 %. In hypothyroid men, the prevalence of HSD, DE, and ED were each 64.3 % and PE was 7.1 %. After thyroid hormone normalization in hyperthyroid subjects, PE prevalence fell from 50 to 15 %, whereas DE was improved in half of the treated hypothyroid men. Ejaculation latency time doubled from 2.4 ± 2.1 min before treatment to 4.0 ± 2.0 min after treatment of hyperthyroidism. In contrast, in hypothyroid men, it declined significantly, from 21.8 ± 10.9 min to 7.4 ± 7.2 min ($P < 0.01$ for both groups). Because the cohort in this study was young with a mean age of 43 years, the results may not be fully translatable to older men [34].

Serum testosterone declines with aging in men. This decline, termed "testosterone deficiency" (TD) or hypogonadism, is a subject of major interest. Testosterone deficiency in aging men is a condition associated with a decreased sexual satisfaction and a decline of general well-being [35]. Hypogonadism in men is defined as a clinical syndrome that results from failure of the testis to produce physiological levels of testosterone, leading to androgen deficiency and an abnormal number of spermatozoa due to disruption of one or more levels of the hypothalamic-pituitary-testicular axis.

Abnormalities of the hypothalamic-pituitary-testicular axis at the testicular level cause primary testicular failure, whereas central defects of the hypothalamus or pituitary cause secondary testicular failure. Hypogonadism can also reflect dual defects that affect both the testis and the pituitary. Primary testicular failure results in low testosterone levels, impairment of spermatogenesis, and elevated gonadotropin levels. Secondary testicular failure results in low testosterone levels, impairment of spermatogenesis, and low or low-normal gonadotropin levels. Combined primary and secondary testicular failure results in low testosterone levels, impairment of spermatogenesis, and variable gonadotropin levels, depending on whether primary or secondary testicular failure predominates [35].

Studies have demonstrated that serum testosterone levels decrease at a rate of about 1 % per year after 30 years of age [36, 37]. Harman et al. [36] measured testosterone (T) and sex hormone-binding globulin (SHBG) by radioimmunoassay in stored samples from 890 men in the Baltimore Longitudinal Study on Aging (Fig. 24.2). The authors observed significant, independent, age-invariant, longitudinal effects of age on both T and free T index (free T index = T/SHBG). There was an average change of −0.124 nmol/L per year and −0.0049 nmol T/nmol SHBG per year. Testosterone, but not free T index, also decreased with increasing body mass index. Use of beta-blocking drugs was associated with higher T and higher free T index levels. Using total T criteria, incidence of hypogonadal T levels increased to about 20 % of men over 60 years of age, 30 % in men over 70 years of age, and 50 % in men over 80 years of age. These percentages were even greater when free T index criteria were utilized [36].

Importantly, recent data have suggested that lower serum testosterone levels are associated with morbidity and mortality [38]. These authors used a clinical database to identify men 40 years of age with repeated testosterone levels obtained from October 1, 1994, to December 31, 1999, and without diagnosed prostate cancer. A low testosterone level was defined as a total testosterone level of less than 250 ng/dL (<8.7 nmol/L) or a free testosterone level of less than 0.75 ng/dL (<0.03 nmol/L). Overall, 166 men (19.3 %) were classified as having a low testosterone level, 240 (28.0 %) had an equivocal testosterone level with equal numbers of low or normal levels, and 452 (52.7 %) had a normal testosterone level. The risk for all-cause mortality was estimated using Cox proportional hazards regression models, adjusting for demographic and clinical covariates over a period of 8 years. Testosterone levels differed significantly between the three groups (Fig. 24.3). Men with low testosterone levels were older, had a higher BMI, and had a greater prevalence of diabetes mellitus compared with men with normal testosterone levels. Men with equivocal testosterone levels had a greater BMI than men with normal testosterone levels. Men with low and normal testosterone levels had more testosterone samples obtained than men with equivocal testosterone levels. There were no significant differences between the groups in terms of marital status; medical comorbidity; prevalence of chronic obstructive pulmonary disease (COPD), human immunodeficiency virus (HIV), coronary artery disease (CAD), or hyperlipidemia; or treatment with opiates and glucocorticoids. These

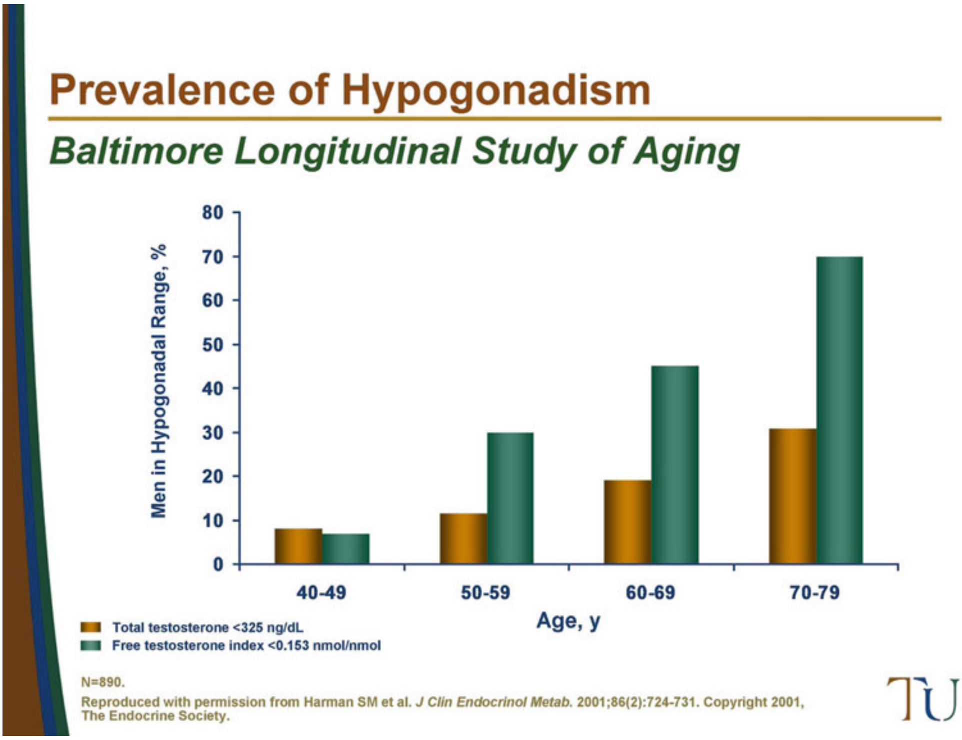


Fig. 24.2 [35] For more than 40 years, the Baltimore Longitudinal Study of Aging has gathered data on a largely middle-class (87 %), white population of men at approximately 2-year intervals. Serum testosterone was measured in stored samples from 890 men in the study. Date-adjusted testosterone and free testosterone index (FTI) values were used to determine the percentage of men in each decade who had hypogonadism. Men were described as hypogonadal if they had at least one visit in that age decade at which testosterone was <325 ng/dL or FTI was <0.153 nmol/nmol. Data for men aged 40–79 years are presented here. According to both criteria, the percentage of men with hypogonadism increased progressively after age 50 years, and the difference between the two criteria expanded with increasing age. The percentage of men classified as hypogonadal according to the FTI tended to be lower for those younger than 50 years and higher for those older than 50 years, compared with the percentage of men classified as hypogonadal according to total testosterone. Of men identified as hypogonadal by either total testosterone level or FTI who had subsequent samples evaluated, 78 % and 97 %, respectively, had total testosterone values that measured in the hypogonadal range at all subsequent visits

data demonstrated that mortality in men with normal testosterone levels was 20.1 % (95 % CI = 16.2–24.1) compared to 24.6 % (95 % CI = 19.2–30.0) in men with equivocal testosterone levels and 34.9 % (95 % CI = 28.5–41.4) in men with low testosterone levels. After adjusting for age, medical comorbidity, and other clinical covariates, low serum testosterone levels continued to be associated with increased mortality (HR 1.88, 95 % CI = 1.34–2.63, $P < 0.001$), while mortality in men with equivocal testosterone levels was not significantly different from men with normal testosterone levels (HR 1.38, 95 % CI = 0.99–1.92, $P = 0.06$).

A decline in serum testosterone in older men may be directly associated with a loss of sexual desire and erectile dysfunction [39, 40]. The authors in the European Male Aging Study (EMAS) study group [39] surveyed a random population sample of 3,369 men between 40 and 79 years of age at eight European centers. Using questionnaires, they collected data about general, sexual, physical, and psychological health. Levels of total testosterone were measured in morning blood samples using mass spectrometry,

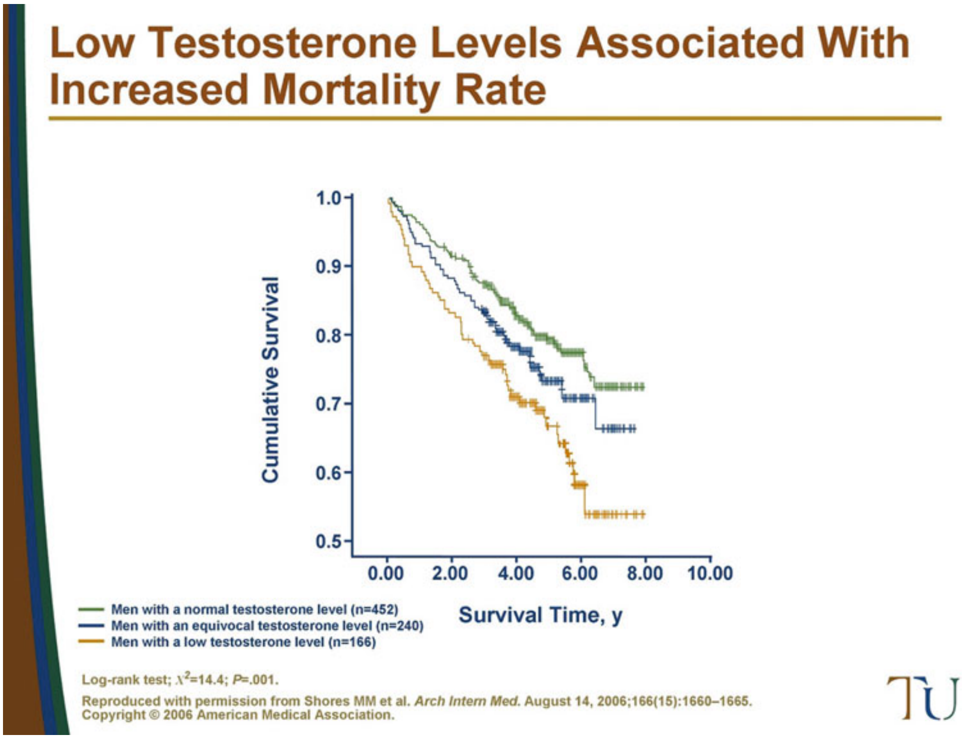


Fig. 24.3 (from [38]) A study was conducted to determine whether low testosterone levels are a risk factor for mortality in men 40 years of age or older. From the clinical database at the Veterans Affairs Puget Sound Health Care System, 858 male veterans who had repeated measurement of testosterone levels and no history of prostate or testicular cancer or antiandrogen treatment were identified. Testosterone levels were categorized as low if total testosterone was <250 ng/dL or free testosterone was <0.75 ng/dL. Testosterone levels were low in 166 men (19.3 %), equivocal (equal number of low and normal levels) in 240 men (28 %), and normal in 452 men (52.7 %). Cox proportional hazards regression models, adjusted for demographic and clinical covariates over an 8-year follow-up period, were used to compare differences in survival times between men with low, equivocal, and normal testosterone levels. As illustrated by the Kaplan–Meier survival analysis, survival times were shorter in men with low or equivocal testosterone levels than in those with normal testosterone levels. All-cause mortality was 34.9 % in men with low testosterone levels, 24.6 % in men with equivocal testosterone levels, and 20.1 % in men with normal testosterone levels

and free testosterone levels were calculated with the use of Vermeulen's formula. Data were randomly split into separate training and validation sets for confirmatory analyses.

In the training set, symptoms of poor morning erection, low sexual desire, erectile dysfunction, inability to perform vigorous activity, depression, and fatigue were significantly related to the serum testosterone level. Increased probabilities of the three sexual symptoms and limited physical vigor were discernible with decreased testosterone levels (ranges, 8.0–13.0 nmol/L or 2.3–3.7 ng/mL for total testosterone and 160–280 pmol/L or 46–81 pg/mL for free testosterone). However, only the three sexual symptoms had a syndromic association with decreased testosterone levels. An inverse relationship between an increasing number of sexual symptoms and a decreasing testosterone level was observed. These relationships were independently confirmed in the validation set, in which the strengths of the association between symptoms and low testosterone levels determined the minimum criteria necessary to identify late-onset hypogonadism. Thus, late-onset hypogonadism can be defined by the presence of at least three sexual symptoms associated with a total testosterone level of less than 11 nmol/L or 3.2 ng/mL and a free testosterone level of less than 220 pmol/L or 64 pg/mL.

Assessment of Sexual Dysfunction in Aging Men and Women

The assessment of male and female sexual function has been challenging. Most regulatory agencies have allowed self-reported, validated instruments to be used as surrogate markers for sexual activity endpoints. Many instruments have been published that meet or fulfill these needs. It is important to bear in mind that to our knowledge, these instruments are not specific to the aging male or female population, but rather are designed for general use. Data regarding elderly men and women has been extrapolated from these instruments.

The instrument that has been most often used to capture the severity of general male sexual function and male erectile function in particular is the International Index of Erectile Function (IIEF) (Fig. 24.4). This instrument was developed as an adjunctive sexual function measure for the sildenafil clinical trials [41] and has since gained universal acceptance as the leading instrument to assess male erectile function. A five-question shorter form was subsequently developed and validated [42] (Fig. 24.5). The IIEF and its shorter version have been used for all the clinical phosphodiesterase type 5 inhibitor trials along with numerous nonindustry sponsored trials. The IIEF contains 15 questions which ask the patient to recall sexual activity for the previous 4 weeks. The 15 questions are answered on a Likert scale which allows the instrument to be graded numerically. Questions 1–5 and 15 are termed the “erectile function domain” of the IIEF.

Male ejaculatory function has been assessed using a variety of instruments. A recent, noteworthy instrument is the Male Sexual Health Questionnaire, which has been shortened to a four-question instrument [43].

Testosterone deficiency in the male can be assessed by a variety of instruments. The Androgen Deficiency in the Aging Male (ADAM) questionnaire is widely used but unfortunately has not been validated [44]. Further, the ADAM questionnaire seems to be sensitive but not specific for the diagnosis of hypogonadism. An answer of YES to questions 1 or 7 or any 3 other questions suggests that the patient may be experiencing androgen deficiency with a low testosterone level. The Aging Males’ Symptom (AMS) questionnaire is often utilized as well [45]. Recently, the NERI hypogonadism screener has been published, but has not yet found its way into routine clinical practice [46].

Female Sexual Function

There are several well-designed, validated instruments that assess female sexual function [47]. One such instrument that seems to be gaining in popularity is the Female Sexual Function Index (FSFI). The FSFI is a brief multidimensional scale for assessing sexual function in women. The scale has undergone psychometric evaluation, including studies of reliability, convergent validity, and discriminant validity. The authors found an FSFI total score of 26.55 to be the optimal cut-point score for differentiating women with and without sexual dysfunction [48] The FSFI has been recently validated for use in cancer survivors [49]. Unfortunately, there was no sexual desire (SD) domain-specific cut point for determining the presence of diminished desire in women with or without a sexual desire problem. Gersterberger et al. noted that the use of a diagnostic cut point of 5 or less on the SD domain of the FSFI as having HSDD and those with SD scores of 6 or more as not having HSDD maximized diagnostic sensitivity and specificity. In the development sample, the sensitivity and specificity for predicting HSDD, with or without other conditions, were 75 % and 84 %, respectively. The corresponding sensitivity and specificity in the validation sample were 92 % and 89 %, respectively [50].

It is important to recognize that many clinicians find these questionnaires somewhat cumbersome to use during the routine office visit. Rather than using the full instrument, many clinicians have adopted their own personal practices and utilize a modified version of a specific instrument.

There are many other instruments that have been developed to assess male and female sexual function. The authors of these fine assessment tools deserve recognition, and we offer our apologies for the inability to include them and credit them in this section due to space limitations. Finally, there are many instruments that evaluate mood, depression, cognition, strength, and quality of life in aging men and women. Discussion of these instruments is beyond the scope of this chapter.

IIEF Questionnaire

Instructions: These questions ask about the effects your erection problems have had on your sex life, over the past 4 weeks. Please answer the following questions as honestly and clearly as possible. In answering these questions, the following definitions apply:

Definitions:

Sexual activity includes intercourse, caressing, foreplay and masturbation

Sexual intercourse is defined as vaginal penetration of the partner (you entered the partner)

Sexual stimulation includes situations like foreplay with a partner, looking at erotic pictures, etc.

Ejaculate is defined as the ejection of semen from the penis (or the feeling of this)

Mark ONLY one circle per question:

1. Over the past 4 weeks, how often were you able to get an erection during sexual activity?

0 No sexual activity
0 Almost always or always
0 Most times (much more than half the time)
0 Sometimes (about half the time)
0 A few times (much less than half the time)
0 Almost never or never

2. Over the past 4 weeks, when you had erections with sexual stimulation, how often were your erections hard enough for penetration?

0 No sexual stimulation
0 Almost always or always
0 Most times (much more than half the time)
0 Sometimes (about half the time)
0 A few times (much less than half the time)
0 Almost never or never

Questions 3, 4 and 5 will ask about erections you may have had during sexual intercourse.

3. Over the past 4 weeks, when you attempted sexual intercourse, how often were you able to penetrate (enter) your partner?

0 Did not attempt intercourse
0 Almost always or always
0 Most times (much more than half the time)
0 Sometimes (about half the time)
0 A few times (much less than half the time)
0 Almost never or never

4. Over the past 4 weeks, during sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?

0 Did not attempt intercourse
0 Almost always or always
0 Most times (much more than half the time)
0 Sometimes (about half the time)
0 A few times (much less than half the time)
0 Almost never or never

Fig. 24.4 IIEF questionnaire

5. Over the past 4 weeks, during sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?

0 Did not attempt intercourse
0 Almost always or always
0 Most times (much more than half the time)
0 Sometimes (about half the time) 0 A few times (much less than half the time)
0 Almost never or never

6. Over the past 4 weeks, how many times have you attempted sexual intercourse?

0 No attempts
0 1-2 attempts
0 3-4 attempts
0 5-6 attempts
0 7-10 attempts
0 11 or more attempts

7. Over the past 4 weeks, when you attempted sexual intercourse how often was it satisfactory for you?

0 Did not attempt intercourse
0 Almost always or always
0 Most times (much more than half the time)
0 Sometimes (about half the time)
0 A few times (much less than half the time)
0 Almost never or never

8. Over the past 4 weeks, how much have you enjoyed sexual intercourse?

0 No intercourse
0 Very highly enjoyable
0 Highly enjoyable
0 Fairly enjoyable
0 Not very enjoyable
0 Not enjoyable

9. Over the past 4 weeks, when you had sexual stimulation or intercourse how often did you ejaculate?

0 Did not attempt intercourse
0 Almost always or always
0 Most times (more than half the time)
0 Sometimes (about half the time)
0 A few times (much less than half the time)
0 Almost never or never

10. Over the past 4 weeks, when you had sexual stimulation or intercourse how often did you have the feeling of orgasm or climax (with or without ejaculation)?

0 No sexual stimulation or intercourse
0 Almost always or always
0 Most times (much more than half the time)
0 Sometimes (about half the time)
0 A few times (much less than half the time)
0 Almost never or never

Questions 11 and 12 ask about sexual desire. Let's define sexual desire as a feeling that may include wanting to have a sexual experience (for example, masturbation or intercourse), thinking about having sex or feeling frustrated due to a lack of sex.

11. Over the past 4 weeks, how often have you felt sexual desire?

0 Almost always or always
0 Most times (much more than half the time)
0 Sometimes (about half the time)
0 A few times (much less than half the time)
0 Almost never or never

Fig. 24.4 (continued)

12. Over the past 4 weeks, how would you rate your level of sexual desire?

0 Very high
0 High
0 Moderate
0 Low
0 Very low or none at all

13. Over the past 4 weeks, how satisfied have you been with you overall sex life?

0 Very satisfied
0 Moderately satisfied
0 About equally satisfied and dissatisfied
0 Moderately dissatisfied
0 Very dissatisfied

14. Over the past 4 weeks, how satisfied have you been with your sexual relationship with your partner?

0 Very satisfied
0 Moderately satisfied
0 About equally satisfied and dissatisfied
0 Moderately dissatisfied
0 Very dissatisfied

15. Over the past 4 weeks, how do you rate your confidence that you can get and keep your **erection**?

0 Very high
0 High
0 Moderate
0 Low
0 Very low

Scoring Algorithm for IIEF

All items are scored in 5 domains as follows:

Domain	**Items**	**Range**	**Score Max Score**
Erectile Function	1, 2, 3, 4, 5, 15	0-5	30
Orgasmic Function	9, 10	0-5	10
Sexual Desire	11, 12	0-5	10
Intercourse Satisfaction	6, 7, 8	0-5	15
Overall Satisfaction	13, 14	0-5	10

Fig. 24.4 (continued)

Pathophysiology of Erectile Dysfunction

The pathophysiology and mechanisms of erectile dysfunction that have been studied in depth and on this topic are abundant in the published literature. Erectile dysfunction is defined as the consistent inability to achieve or maintain an erection adequate for satisfactory sexual function [51]. Age alone is the single most profound variable associated with erectile dysfunction and impotence. Feldman et al. showed that the rate of complete impotence tripled from 5 to 15 % as men aged from 40 to 70 years [28]. After adjustment for age, a higher probability of ED was directly correlated with cardiovascular disease, hypertension, diabetes mellitus (DM), and depression. In contrast, ED was inversely correlated with serum dehydroepiandrosterone (DHEA), high-density lipoprotein cholesterol, and an index of dominant personality. ED can significantly decrease quality of life as well as a man's mental and physical well-being. Although most cases of ED are primarily organic, ED can have a psychogenic etiology as well [28, 51].

ED can be caused by endocrine abnormalities, most commonly DM, but also by hypogonadism and hyperprolactinemia [52–54]. DM causes changes in neurotransmitters like nitric oxide and vasoactive intestinal peptide, resulting in poor erectile ability. Tight glycemic control has been shown to dramatically reduce the prevalence of ED [54–56]. Complications of smooth muscle and endothelial dysfunction are sequelae of DM, which can exacerbate the severity of ED by direct pathophysiologic mechanisms.

Vascular disease and hypertension can worsen the severity of ED and bring an earlier onset of impotence. The primary mechanisms are arterial insufficiency and venous leakage. Atherosclerosis leads to arterial occlusive disease, which can reduce the perfusion pressure and arterial flow to

The International Index of Erectile Function (IIEF-5) Questionnaire

Reprinted by permission from Macmillan Publishers Ltd: Rosen RC, Cappelleri JC, Smith MD, et al. Development and evaluation of an abridged, 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. Int JImpot Res. 1999 Dec;11(6):319-26. © 1999

Over the past 6 months:					
1. How do you rate your **confidence** that you could get and keep an erection?	Very low 1	Low 2	Moderate 3	High 4	Very high 5
2. When you had erections with sexual stimulation, **how often** were your erections hard enough for penetration?	Almost never/never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always/always 5
3. During sexual intercourse, **how often** were you able to maintain your erection after you had penetrated (entered) your partner?	Almost never/never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time)4	Almost always/always 5
4. During sexual intercourse, **how difficult** was it to maintain your erection to completion of intercourse?	Extremely difficult 1	Very difficult 2	Difficult 3	Slightly difficult 4	Not difficult 5

Fig. 24.5 The International Index of Erectile Function (IIEF-5) questionnaire

5. When you attempted sexual intercourse, **how often** was it satisfactory for you?	Almost never/never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always/always 5

IIEF-5 scoring:

The IIEF-5 score is the sum of the ordinal responses to the 5 items.

22-25: No erectile dysfunction

17-21: Mild erectile dysfunction

12-16: Mild to moderate erectile dysfunction

8-11: Moderate erectile dysfunction

5-7: Severe erectile dysfunction

Fig. 24.5 (continued)

the lacunar spaces necessary for penile rigidity. Subsequently, adequate pressure is not achieved within the corpora cavernosa because of excessive venous outflow through the subtunical venules, and thus, no erection occurs [54] (Fig. 24.6).

Other causes of ED include neurologic deficits such as cerebrovascular accidents (CVA), Parkinson's disease, multiple sclerosis, and spinal cord injury. Direct injury to the penis itself either by trauma or by other pathologies like priapism can contribute to varying degrees of ED. Finally, there are several psychogenic causes including anxiety, depression, and stress-related issues that can decrease the strength and duration of an erection or outright prevent initiation of the erection (Table 24.1) [54].

Although the clinical presentation of ED is the same, the diagnosis requires a complete history and a basic genital examination, especially looking for Peyronie's plaque and femoral bruits; evaluating secondary sexual characteristics; and general physical examination including blood pressure assessment. Laboratory values of blood glucose, cholesterol, and testosterone levels usually supplement an evaluation [52].

Pathophysiology of the Role of Hypogonadism in Sexual Dysfunction in Older Men

The effect of hypogonadism on male sexual desire seems to be well established [57]. However, the true contribution of hypogonadism to erectile and ejaculatory function is the subject of intense debate. It is postulated that penile erectile tissue possesses high concentrations of locally synthesized androgens and that testosterone-dependent functions are not a reflection of circulating androgen levels [58]. In animal studies, testosterone deprivation changed the response and structural functionality of erectile tissue [59]. Testosterone is required for adequate function of nitric oxide synthase, which produces nitric oxide necessary

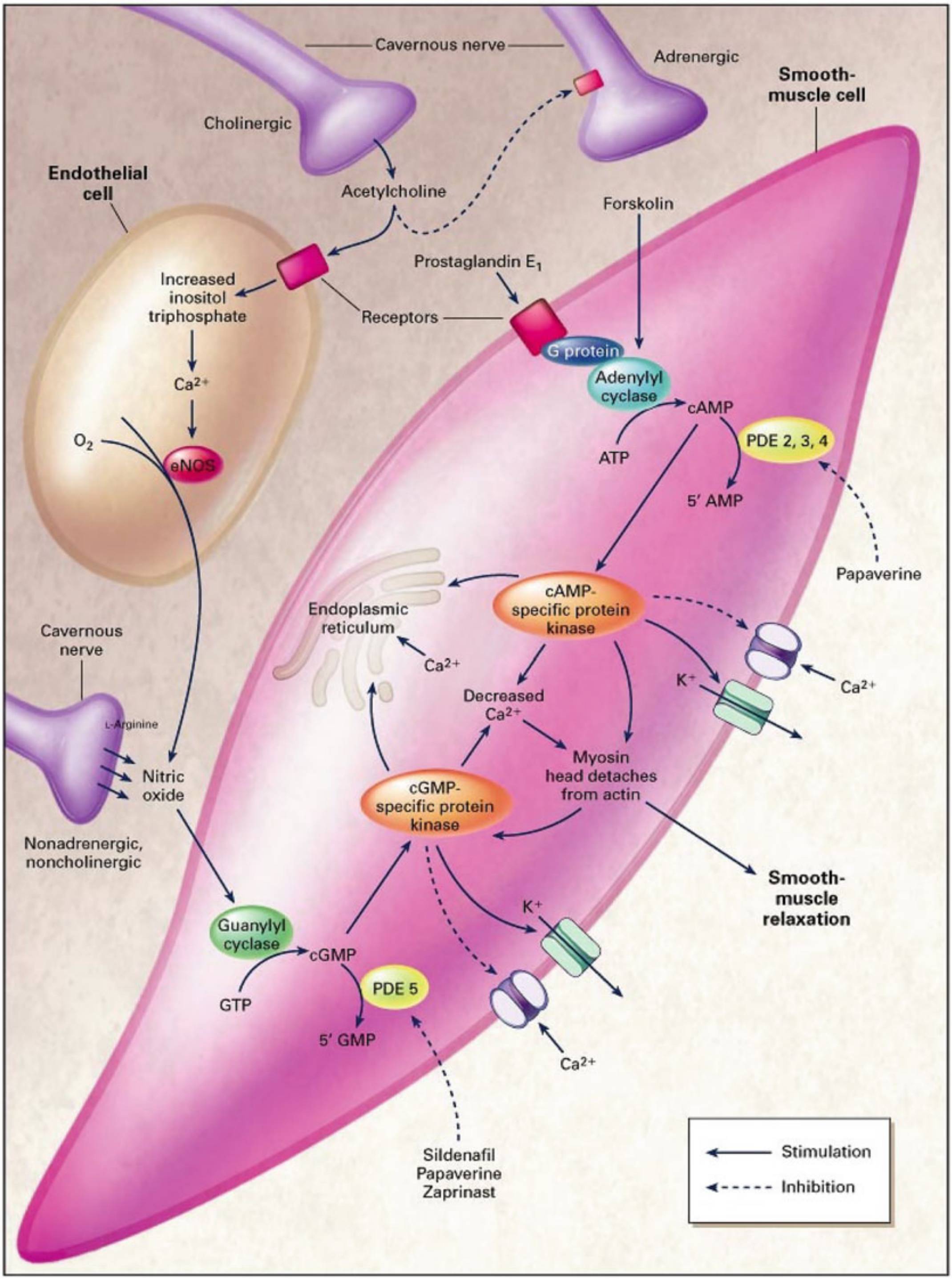


Fig. 24.6 Molecular mechanism of penile smooth muscle relaxation [54]. Cyclic AMP (cAMP) and cyclic GMP (cGMP), the intracellular second messengers mediating smooth muscle relaxation, activate their specific protein kinases, which phosphorylate certain proteins to cause opening of potassium channels, closing of calcium channels, and sequestration of intracellular calcium by the endoplasmic reticulum. The resultant fall in intracellular calcium leads to smooth muscle relaxation. Sildenafil inhibits the action of phosphodiesterase (PDE) type 5, thus increasing the intracellular concentration of cGMP. Papaverine is a nonspecific phosphodiesterase inhibitor. GTP denotes guanosine triphosphate, and eNOS endothelial nitric oxide synthase

Table 24.1 Classification and common causes of erectile dysfunction [54]

Category of erectile dysfunction	Common disorders	Pathophysiology
Psychogenic	Performance anxiety Relationship problems Psychological stress Depression	Loss of libido, overinhibition, or impaired nitric oxide release
Neurogenic	Stroke or Alzheimer's disease Spinal cord injury Radical pelvic surgery Diabetic neuropathy Pelvic injury	Failure to initiate nerve impulse or interrupted neural transmission
Hormonal	Hypogonadism Hyperprolactinemia	Loss of libido and inadequate nitric oxide release
Vasculogenic (arterial or cavernosal)	Artherosclerosis Hypertension Diabetes mellitus Trauma Peyronie's disease	Inadequate arterial flow or impaired venoocclusion
Drug-induced	Antihypertensive and antidepressant drugs Antiandrogens Alcohol abuse Cigarette smoking	Decreased libido Alcoholic neuropathy Vascular insufficiency
Caused by other systemic diseases and aging	Old age Diabetes mellitus Chronic renal failure Coronary heart disease	Usually mutifactorial, resulting in neural and vascular dysfunction

for relaxation of cavernosal endothelial and corporeal smooth muscle resulting in erection [59]. Penile erection can also be mediated through a non-nitric oxide-dependent pathway with the stimulation of cyclic AMP synthesis [60]. Testosterone has also been shown to inhibit detrusor muscle contractions, and thus lower testosterone levels may contribute to detrusor muscle overactivity and lower urinary tract symptoms (LUTS), especially in men with BPH [61, 62].

Lower levels of testosterone also play a significant role in reduced muscle mass, increased fat mass, and weaker bone density as men age. Free testosterone was shown to be the best predictor of loss of muscle mass and strength in the New Mexico Aging Process Study [63]. Sarcopenia eventually leads to frailty and subsequent functional deterioration as well as a substantial decrease in sexual functioning. Objectively, this is measured by unintentional weight loss, exhaustion and fatigue, general muscle weakness, and lower sexual desire. In addition to androgen, other factors including age, caloric intake, and physical activity all play different roles in the pathophysiology of frailty and decreased sexual functionality [64]. In longitudinal studies, the combination of loss of hormones such as testosterone and insulin-like growth factors (IGF-1) and increases in cytokines such as tumor necrosis factor (TNF-alpha) and interleukins (IL-6) provides the mechanism for the reduced muscle mass and strength [65]. Testosterone has a direct effect on osteoblasts which contributes to maintenance of increased bone mineral density [66]. However, the exact interactions between these hormones and their receptor activity, and how other pathways may contribute to muscle decline and higher rates of hip fractures, are not well understood.

With respect to hypogonadism, decreased energy levels and impaired sexual performance were the two most important quality-of-life issues for older men in a recent study [67]. Dacal et al. demonstrated that lowering testosterone medically in patients with prostate cancer receiving androgen deprivation resulted in a sharp deterioration of quality of life [67]. This encompasses not only the lower physical and sexual activity in older adults but also poorer cognition, less coordination, and less satisfaction with functionality [68].

Lower testosterone has been correlated with more severe atherosclerotic changes and increased intima-media thickness [69, 70]. Low-dose supplemental testosterone has been shown to decrease the incidence of exercise-induced myocardial infarction and ST segment depression on electrocardiography (ECG) in men with chronic stable angina [71, 72]. It can be inferred from these studies that testosterone may contribute to a beneficial effect on the cardiovascular system. However, in spite of these data, a recent meta-analysis conducted on behalf of the Agency for Healthcare Research and Quality revealed that the efficacy of hormonal treatments and the value of hormone testing in men with ED were inconclusive [73].

Table 24.2 Specialized urologic and radiologic tests for men with erectile dysfunction [54]

Test	Indications
Combined penile injection of a vasodilator and sexual stimulation	Assess penile vascular function Therapeutic test in men who choose intracavernous therapy
Duplex (color) ultrasonography	Assess vascular function and evaluate for Peyronie's disease
Cavernosography	Young men with congenital or traumatic venous leakage
Pelvic arteriography	Young men with traumatic arterial insufficiency
Nocturnal penile monitoring (RigiScan Ambulatory Rigidity and Tumescence System, Timm Medical, Minneapolis)	Differentiate psychogenic from organic erectile dysfunction

Testing for Erectile Dysfunction in Older Men

The diagnostic paradigm for male ED, and specifically for ED in geriatric men, has shifted, and the presumptive etiology is either partly or fully organic in most cases. Historical tests to assess nocturnal erections, such as the snap-gauge and nocturnal penile tumescence test, have fallen by the wayside and are no longer used by most clinicians. Penile duplex Doppler ultrasound is used in conjunction with a penile injection of a vasoactive agent to induce an erection. This test is performed by select clinicians to assess the penile arterial tree and the penile capacity to trap blood under conditions that mimic an erection. Other tests are available as well (Table 24.2) and are utilized for select patients. In light of the fact that most clinicians and patients move forward with oral medications for the treatment of their ED irrespective of etiology, the utility of these tests for the older male with ED is questioned. Nonetheless, penile duplex Doppler is quite helpful in defining a potential vascular cause of the ED when used under the appropriate conditions. Therefore, the diagnosis of male erectile dysfunction is made predominately on the basis of clinical history, with confirmatory testing limited to specific patients.

Testing for hypogonadism should be relatively simple. The diagnosis is made based upon the presence of symptoms, such as low libido, fatigue, and erectile dysfunction, combined with a serum testosterone of less than 300 ng/dL [73]. Mass screening of the population for low T is discouraged. While at face value this diagnosis should be relatively straightforward, the entire disease state, including the diagnosis, has been the subject of recent debate. The assay to diagnose low T has been scrutinized and is under intense review [74]. As it stands now, many of the assays in current use may fall by the wayside. Next, the lower level of normal, 300 ng/dL, has been discussed in depth and is not universally accepted [75]. Currently, many commercial labs have lower thresholds such as 242–262 ng/dL, adding confusion to this issue. Additionally, there has been discussion that hypogonadism in older men, such as those over 65, is a distinct disease state, dissimilar to hypogonadism in younger men [39, 76]. While there are many advocates supporting the position that hypogonadism is highly prevalent in this older age group [76], others suggest that the actual incidence is quite low [39]. Thus, controversy abounds in this field.

Adding further fuel to the fire, the Institute of Medicine published a very thorough review of this topic and offered the following statement in 2003: “Hypogonadism occurs in men of various ages, and most clinical studies of the therapy so far have been in younger hypogonadal men. Less is known about the potential beneficial or adverse effects of testosterone therapy in older males and there have been concerns regarding prostate outcomes” [76].

The diagnosis of ejaculatory dysfunction in the male is based upon history. The questionnaires mentioned above [42, 43] may be useful to assist with this diagnosis. Rapid ejaculation and delayed ejaculation, particularly in elderly men, remain challenging conditions for the clinician.

Diagnostic Evaluation of Female Sexual Dysfunction

The diagnosis of female sexual dysfunction is made based upon history. Questionnaires are available to corroborate the diagnosis of HSDD [47, 48]. There are no currently available FDA-approved treatment options for HSDD, adding clinical challenges to this disease state. Flibanserin (Boehringer Ingelheim), an oral, dual 5-HT1A receptor agonist and 5-HT2A receptor antagonist, was recently not approved by the FDA for the treatment of HSDD in women [77]. The meaning and definition of low serum testosterone levels in women is a challenging area [78]. Normal serum levels of testosterone are not well established [79], and there is no currently available treatment approved by the FDA for women with low testosterone. Intrinsa (Procter & Gamble), a testosterone patch for women, was tested but not approved by the FDA in 2004 [80]. In a 2011 study, LibiGel (BioSante), a testosterone gel for women, failed to meet its study endpoints and thus will most likely not reach the marketplace [81]. Estrogen replacement therapy in postmenopausal or surgically menopausal women has fallen into disfavor based upon cardiovascular and other evidences presented by the WHI reports [22, 82, 83]. Findings from the Women’s Health Initiative (WHI) Estrogen-Alone (E-Alone) trial were published in April 2004. The National Institutes of Health decided to stop this trial early because of an increased risk of stroke and no heart disease benefit in participants assigned to active estrogen pills compared to those assigned to placebo. The E-Alone trial included 10,739 postmenopausal women who were 50–79 years old and already had a hysterectomy when they joined the WHI. In the E-Alone trial, 5,310 women were assigned to take active conjugated equine estrogen pills (CEE or Premarin®) at a dosage of 0.625 mg each day and 5,429 were assigned to take placebo. The major findings from the trial were that estrogen replacement increased the risk of strokes and blood clots in the legs, decreased the risk of hip fractures, and had no clear effect on heart disease or breast cancer. There is also evidence that systemic estrogen replacement increases the risk of stress urinary incontinence.

For breast cancer, these initial findings suggested that women in the active estrogen (CEE) group had a 23 % lower risk of breast cancer compared to those in the placebo group over an average follow-up of 6.8 years. While this difference was not statistically significant, the findings were viewed as surprising, because a significant increase in breast cancer risk was found in the other WHI hormone trial of combined estrogen plus progestin (E+P) in women who had a uterus when they joined the WHI. In the initial E-Alone report, limited data were published from the 218 invasive breast cancers that had been reported [82]. In April 2006, the final report of all breast cancers diagnosed in this study before the E-Alone trial was stopped was published [83]. This report covered an average of 7.1 years of follow-up and analyzed detailed information from all 237 invasive breast cancers that occurred during the trial. Participants in the CEE group had a 20 % lower risk of invasive breast cancer compared to those in the placebo group, similar to the findings in the initial report. Detailed analyses showed no evidence that breast cancer risk shifted during the average 7 years of follow-up in the E-Alone trial. In contrast, in the E+P trial, the increase in risk of breast cancer emerged after 4 years.

Based on these multiple issues, some authorities advocate the use of topical estrogen therapy and, in some cases, topical testosterone in postmenopausal or surgically menopausal women, in lieu of oral preparations [84]. This remains a controversial area.

Treatment of Sexual Dysfunction in Older Women

Based upon the discussion presented previously, there are concerns regarding hormonal replacement therapies for women with hormonally based sexual dysfunction, although there are proponents of topical hormonal replacement therapies. Oral therapy for HSDD was not approved by the FDA as previously noted [77]. There are a group of women who have both urinary incontinence and sexual dysfunction. Surgical or medical correction of the incontinence seems to improve the sexual issues [85, 86]. This is an underappreciated area of medical need for older women interested in restoration of sexual function. Many women report decreasing or stopping sexual activity specifically due to associated urinary leakage during sexual intercourse.

As an example, 157 women complaining of urodynamic stress incontinence underwent a mid-urethral sling (MUS) procedure [86]. All patients answered the Italian translation of FSFI, prior to and 12 months after surgery. The final analysis also included all of the women who were not sexually active at baseline. The prevalence of female sexual dysfunction was evaluated according to the FSFI cutoff point of 26.55. One hundred thirty-three patients completed the study protocol including 105 who underwent a transobturator sling procedure and 28 who had a retropubic procedure. After the 12-month follow-up, 115 of 133 patients (86 %) were dry, 10 improved their symptoms (7.5 %), and the remaining 8 were unchanged (6.0 %). Of the 133 patients, 79 (59 %) reported an active sexual life before surgery, and 44 (41 %) reported they were not sexually active preoperatively. Twelve months after surgery, 22 of the 54 nonsexually active women (40 %) reestablished sexual activity, whereas only 6 of 79 (7.5 %) patients who were sexually active at baseline were no longer sexually active ($P < 0.05$). After adjusting for multiple factors, only age, menopause, and storage symptoms remained significantly correlated as independent variables with the FSFI total score after surgery. These data showed that after a MUS procedure, female sexual function improves. Interestingly, a very relevant percentage of nonsexually active women reported renewed sexual activity after MUS.

Treatment of Erectile Dysfunction in Older Men

There are many treatments for male ED including oral pills, injection of vasoactive agents into the corpus cavernosum, vacuum device therapies, intraurethral therapies, and surgical options [52, 54]. Oral therapies include the phosphodiesterase-5 inhibitor (PDE5i) class of medications (sildenafil, vardenafil, and tadalafil). PDE5 is found in trabecular smooth muscle and it catalyzes the degradation of cGMP, which elevates cytoplasmic calcium concentrations, leading to smooth muscle contraction. PDE5 inhibitors block this mechanism for improvement in erectile function [54]. These classes of medication can substantially and rapidly decrease blood pressure in patients who are concurrently taking nitrates. Therefore, the use of these medications is contraindicated in patients taking any form of nitrate therapy. Historically, the PDE5i have been taken orally, as on-demand medications. This means the oral drug was taken in proximity to the planned sexual event. Tadalafil provides a 36-h activity window, while the other two drugs in the class indicate 4–8-h therapeutic windows. There are ample short-term data which support the safety and efficacy of these drugs [87]. In general, these medications are well tolerated and provide benefit to the majority of men who take them. Most men (50–80 %) will see an improvement in their erectile function. Data, primarily from short-term trials of ≤12-week duration, indicate that PDE5 inhibitors were more effective for improving sexual intercourse success

Table 24.3 Treatment options for men with erectile dysfunction [54]

Treatment	Cost	Advantages	Disadvantages	Recommendation
Psychosexual therapy	$50–$150/session	Noninvasive Partner involved Curative	Time consuming Patient resistance	First-line treatment May be combined with other treatments
Oral sildenafil	$10/dose	Oral dosage Effective	Cardiovascular disease a contraindication in some men; 1-h wait	First-line treatment Contraindicated with nitrates
Transurethral alprostadil	$25/dose	Local therapy Few systemic side effects	Moderately effective (43–60 % with Actis[a]) Requires office training Causes penile pain	Second-line treatment
Intracavernous alprostadil or drug mixtures[b]	$5–$25/dose	Highly effective (up to 90 %) Few systemic side effects	Requires injection High dropout rate Can cause priapism or fibrosis Causes penile pain	Second-line treatment
Vacuum constriction device	$150–$450/device	Least expensive No systemic side effects	Unnatural erection Causes petechiae Causes numbness (20 %) Trapped ejaculation	Second-line treatment
Surgical treatment Prosthesis (all types)	$8, 000–$15, 000	Highly effective	Unnatural erection (semigrid device) Infection Requires replacement in 5–10 years Requires anesthesia and surgery	For men not satisfied with medical treatment
Vascular surgery	$10, 000–$15,000	Curative	Poor results in older men with generalized disease Requires anesthesia	For young men with congenital or traumatic erectile dysfunction

[a]Actis is an adjustable penile-constriction device.
[b]Drug mixtures contain two or three of the following drugs: papaverine, phentolamine, and alprostadil.

(69.0 %) compared to placebo (35.0 %). The proportion of men with improved erections was significantly greater among those treated with PDE5 inhibitors (range, 67.0–89.0 %) than with placebo (range, 27.0–35.0 %) [73]. Interestingly, improvements in erectile function are gauged, in some studies, by an improvement in the IIEF score, among several other questionnaires [87–89]. The improvement in erectile function will often be proportional to the dose of the drug taken. Data suggest that many men discontinue medication use approximately 1 year after starting therapy. It is unclear if this is due to drug cost because many insurance plans do not cover this oral therapy, side effects, lack of efficacy, partner issues, or a combination of these factors [90]. Side effects are generally mild and usually do not cause the patient to cease therapy. The most common side effects include headache, rhinitis, dyspepsia, facial flushing, myalgia, and back pain [87].

Specific data regarding the efficacy and safety of PDE5i in older men is limited. The efficacy and safety of oral sildenafil (Viagra®) for treating ED in men 65 years of age or older were reported in reviews in 2002 and 2005 [91, 92]. In the 2005 review, the authors analyzed data obtained from five double-blind, placebo-controlled studies of the efficacy and tolerability of oral sildenafil taken as required, but not more than once daily, over a 12-week to 6-month period. Two subgroups were evaluated including 411 elderly men with ED of broad-spectrum etiology and 71 men with ED and diabetes. Efficacy was assessed using a global efficacy question, questions 3 and 4 of the International Index of Erectile Function (IIEF), and the five sexual function domains of the IIEF. All efficacy assessments indicated that sildenafil significantly improved erectile function on both groups. The most common adverse events were mild or moderate headache, flushing, and dyspepsia. The rates of discontinuation due to adverse events were low and were comparable to the rates with placebo.

Beyond these oral agents, pharmacologic entities for treatment include intracavernosal injections and intraurethral suppositories. Other nonpharmacologic treatment options include penile implants and vacuum erection pump devices (Table 24.3) [54]. A more invasive surgical option is penile arterial bypass surgery, which has been shown to have long-term success and high overall satisfaction rates in very select patients [54]. However, all invasive treatment options can be limited by patient age, hand dexterity, fear of injections/surgery, lack of spontaneity, risk for penile injuries, priapism and fibrosis, and pain [93]. The optimal treatment plan usually requires a combination of lifestyle changes, psychosocial counseling, sexual techniques, good patient-physician communication, and an appropriate treatment modality.

Penile injections often work well in older men. In one study, between 63 and 85 years of age (mean 67.1 years), 300 men with erectile dysfunction of organic origin were treated with penile injections [93]. Of the total group, 180 men underwent an initial trial with injection of prostaglandin E1 (PE). Subsequently, these 180 men and the other 120 men were treated with a triple combination of papaverine hydrochloride, phentolamine mesylate, and prostaglandin E1 (PPR). The number of responders to the injection of either PE alone or the drug combination was recorded. These authors observed a statistically significant association between the results obtained after the injection of PPR as compared to PE ($P = <0.001$). A functional erection was obtained in 224 of the 300 subjects (74.7 %) after the injection of PPR as compared to 87 of the 180 men (48.3 %) treated with PE alone. The average volume of PPR necessary to obtain a functional erection was 0.35 ± 0.14 mL, whereas that of PE was 1.3 ± 0.3 mL. Thus, it appeared that both PE and PPR yielded functional erections in a significant number of older men with ED.

With respect to the implantation of penile prosthesis in older men, published data suggest that this is a viable option. One retrospective study reviewed results in 174 men who underwent first time placement of a penile prosthesis for treatment of ED between 1990 and 2007 [94]. Of this group, 35 patients were 70 years of age or older at the time of prosthesis implantation. Of these, 18 patients were still alive at the time of follow-up. Using a telephone survey, patients were asked to answer the Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS) as well as the International Index of Erectile Dysfunction (IIEF). In all, 15 of 18 patients were either very or somewhat satisfied (83 %). At follow-up, 11 out of 15 (73 %) patients were using their prosthesis regularly. The mean IIEF and EDITS scores were 21.80 and 75.20, respectively. Thus, it appears in this small study that a penile prosthesis is a viable option for the older male.

Effects of Treating Male Erectile Dysfunction on the Partner and Relationship

Data have emerged that indicate treatment of male ED can lead to varying degrees of improved partner satisfaction as well. In a crossover clinical trial, 100 heterosexual couples in stable relationships, with male partners having ED based on the erectile function subscale of the International Index of Erectile Function, were randomly assigned to receive either sildenafil or tadalafil for 12 weeks, followed by an additional 12 weeks using the alternate drug [95]. Male and female participants completed sexual event diaries during both study phases, and the female participants were interviewed at baseline, midpoint, and end of study. Primary outcome data were the women's final interviews during which they were asked which drug they preferred and their reasons for that preference. A total of 79.2 % of the women preferred their partners' use of tadalafil, while 15.6 % preferred silde-

Table 24.4 Distribution of subjects in a recent clinical trial of daily tadalafil (adapted from [82])

	Placebo	Tadalafil 2.5 mg	Tadalafil 5 mg
Number of patients randomly assigned (*N*)	94	96	97
Age (years), mean (range)	58.8 (29.5–79.9)	59.8 (26.3–82.3)	60.0 (25.5–81.9)
Age >65 [*n*(%)]	29 (31)	38 (40)	32 (33)

nafil. Preference was not affected by age or treatment order randomization. Women preferring tadalafil reported feeling more relaxed, experiencing less pressure, and enjoying a more natural or spontaneous sexual experience as reasons for their choice. Mean number of tablets used, events recorded, events per week, and days between events were not significantly different during each study phase.

Other data have corroborated these findings. A retrospective analysis of data pooled from two multicenter, randomized, double-blind, placebo-controlled trials that included 505 couples compared 373 couples in which the man received tadalafil 5 mg once daily to 132 couples in which the man received placebo for 12 weeks [96]. Individual Sexual Encounter Profile (SEP) diaries were completed independently by the male subject and his female partner after each sexual intercourse attempt. The mean per-subject/per-partner percentage of "yes" responses to SEP diary questions were assessed, as was the agreement between subjects' and partners' responses. Subjects and partners in the tadalafil-treated group reported significantly greater improvements in the man's ability to achieve some erection, vaginal penetration, and overall sexual satisfaction compared with the placebo-treated group ($P<0.001$). For all intercourse attempts, the mean per-couple percentage of agreement for those in the tadalafil and placebo groups, respectively, was high for erection achievement (99.0 % and 96.6 %), vaginal penetration (98.6 % and 97.4 %), and overall satisfaction (84.3 % and 82.8 %). These authors concluded that tadalafil 5 mg taken once daily as treatment for ED improved overall satisfaction for men and their female partners. This analysis demonstrates the high concordance among couples in their responses to the man's treatment for ED.

Daily Oral PDE5i Therapy for Male Erectile Dysfunction

Historically, oral PDE5i were taken on an as-needed or "prn" basis. This meant that the man would take the medication shortly before the anticipated sexual encounter. Recent data have confirmed that oral, daily tadalafil, both 2.5 mg and 5 mg, improved erectile function and might be a reasonable alternative to as-needed dosing [96, 97]. While no specific studies have been performed in geriatric men, older men were included in a clinical trial that examined daily use and they appeared to gain benefit from daily tadalafil (Table 24.4, adapted from [97]). As shown in this dataset, the efficacy and safety of tadalafil, dosed once a day for the treatment of erectile dysfunction, were assessed in a randomized, double-blind, placebo-controlled, parallel-design study at 15 US centers. Following a 4-week treatment-free run-in period, patients were randomly assigned to 24 weeks of treatment with tadalafil 2.5 mg, tadalafil 5 mg, or placebo. Primary efficacy endpoints were change at 24 weeks in International Index of Erectile Function-Erectile Function (IIEF-EF) domain score and mean per-patient percentage "yes" responses to Sexual Encounter Profile diary questions 2 and 3. Tadalafil significantly improved erectile function compared with placebo for all three co-primary efficacy endpoints. Discontinuation rates due to adverse events were 2.1 % for placebo, 6.3 % for tadalafil 2.5 mg, and 4.1 % for tadalafil 5 mg. Treatment-related adverse events occurred in 5 % of men and included nasopharyngitis, influenza, viral gastroenteritis, and back pain. Tadalafil 2.5 mg and 5 mg, dosed once a day for 24 weeks, were both well tolerated and significantly improved erectile function.

Daily dosing with tadalafil has recently changed the ED treatment paradigm. A recent efficacy study of tadalafil administered 5 mg once daily for treating erectile dysfunction included sexual satisfaction and psychosocial outcome measures [98]. Outcome variables included the treatment satisfaction (THX) domain of the Sexual Life Quality Questionnaire, the Self-Esteem and Relationship (SEAR) questionnaire, the Sexual Encounter Profile questions #4 (SEP4) which measures hardness satisfaction and #5 (SEP5) which assesses overall satisfaction, the intercourse satisfaction (IS) and overall satisfaction (OS) domains of the International Index of Erectile Function (IIEF), and partner SEP question #3 (pSEP3) which examines partner satisfaction with intercourse. After a 4-week run-in phase, 264 participants were randomized to receive tadalafil, and 78 were randomized to receive placebo for 12 weeks. Participants and partners were more satisfied with tadalafil (scores of 75 and 73, respectively) than with placebo (scores of 51 and 55, respectively) ($P<0.001$). Statistically significant improvements were observed for sexual relationship, confidence, self-esteem, and overall relationship (SEAR), in addition to IS, OS, SEP5, and pSEP3 for tadalafil compared with placebo ($P<0.001$) correlated with erectile function (EF) improvement as assessed by change from baseline in IIEF-EF score. Tadalafil significantly improved treatment and sexual satisfaction, while improving multiple outcomes measured by SEAR.

Daily PDE5i for Both Erectile Dysfunction and Benign Prostatic Hyperplasia and Lower Urinary Tract Symptoms

As men age, the prostate enlarges and produces a variety of lower urinary tract symptoms (LUTS). LUTS is characterized by urinary frequency, urgency, weak stream, and nocturia [99]. LUTS is prevalent in more than half of men over 50 years of age. BPH and LUTS significantly diminish quality of life in aging men and may worsen to acute urinary retention requiring emergency care. Treatment of LUTS has centered on oral alpha-blockers as first-line therapy [84]. Alpha-blockers include such drugs as doxazosin, terazosin, tamsulosin, alfuzosin, and silodosin [100]. Interestingly, epidemiologic studies indicate a strong association between lower urinary tract symptoms (LUTS) and male sexual dysfunction including both ED and ejaculatory dysfunction, suggesting a common pathophysiologic theme [101, 102]. In addition, both erectile and ejaculatory disorders appear more frequently in men in conjunction with symptoms of moderate to severe LUTS [102]. Although the exact mechanisms of how LUTS affect sexual function are not clear, there appears to be a direct relationship between these entities. This is especially evident when sexual problems are encountered or exacerbated by management of LUTS (Fig. 24.7) [102].

The Multinational Survey of the Aging Male (MSAM-7) was conducted in the USA and six European countries to systematically investigate the relationship between LUTS and sexual dysfunction in older men aged 50–80 years [102]. LUTS and sexual function were assessed using validated symptom scales, including the International Prostate Symptom Score (IPSS) for LUTS and the Danish Prostatic Symptom Score and the IIEF for sexual function. A total of 12,815 surveys were included in the analysis. The men's self-ratings of erectile function were stratified according to the severity of LUTS. An IIEF total score of 26–30 indicates normal erectile function, and a score of 10 or less indicates severe ED. As expected, there was a gradual worsening of erectile function with increased age. However, within each age group, there was a clear, statistically important relationship between the severity of LUTS and erectile capacity. As LUTS worsened, so did erectile function. Moreover, the relationship between sexual problems and LUTS was independent of comorbidities such as diabetes, hypertension, cardiac disease, and hypercholesterolemia [102]. There was a clear age-related decline in male sexual function, both erectile function and ejaculatory function, seen with aging. The decline in sexual function with aging was exacerbated by worsening LUTS. For exam-

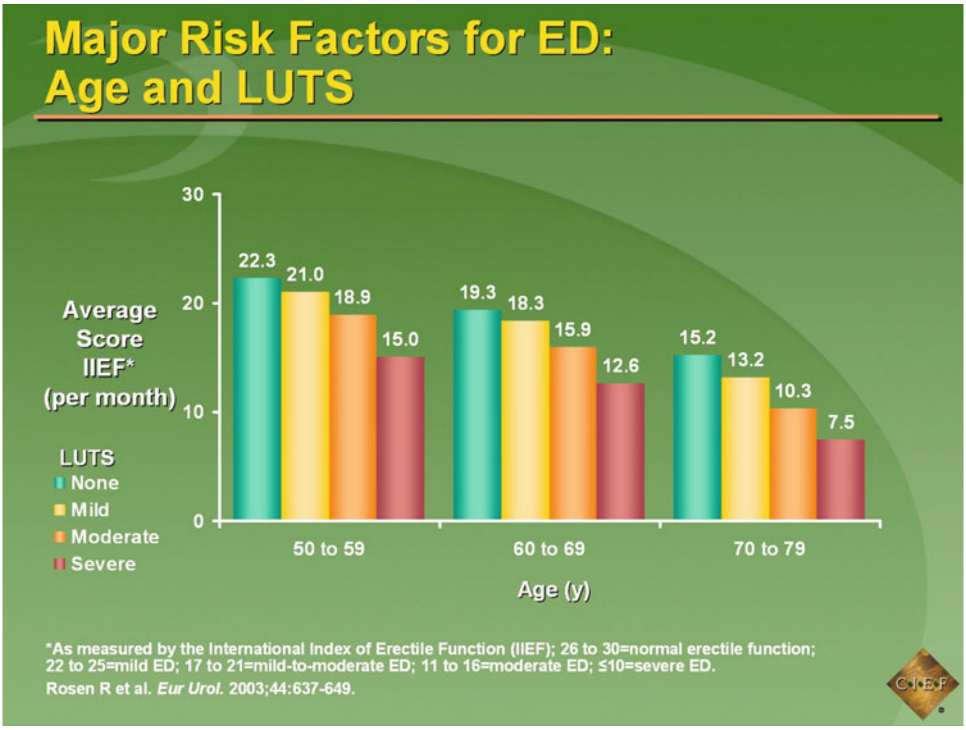


Fig. 24.7 Data shows average score for erectile function (as measured by IIEF) in each age group among men without LUTS (*green column*). As expected, a clear decline in erectile function with increasing age is observed. Within each age group, the average score for erectile function (IIEF) decreases significantly with increasing severity of LUTS. The same relationship holds true for ejaculatory dysfunction. (Adapted from [87], Rosen R et al. *Eur Urol*. 2003;44:637–649)

ple (Fig. 24.6), if a man in the age bracket 50–59 had no LUTS, his erectile function score was quite good at 22.3. As the LUTS take effect, the worsening of the LUTS symptoms then demonstrated that the same man had a worsening of his erectile function. Indeed, with moderate LUTS, the erection score dropped to 18.9, a 15 % decline in erectile function (Fig. 24.7). The clinical implications of these recent studies suggest that a man who presents with LUTS should be carefully evaluated for the presence of sexual problems, and vice versa.

The possible pathophysiologic mechanistic relationship between LUTS and ED is the subject of intense investigation [103]. One plausible common mechanism is that both the prostate and the penis contain phosphodiesterase type 5 (PDE5), and either upregulation of the intrinsic PDE5 enzyme or loss of intrinsic PDE5i protein may cause exacerbation of prostate smooth contraction and penile corpus cavernosum contraction. Excessive contraction prevents the relaxation needed for penile erection and the prostate relaxation needed for the patient to void. The PDE5 and PDE5i mechanisms are well elucidated for the penile corpus cavernosum smooth muscle [54], but are not as clearly defined in the prostate. Both cGMP and PDE5 have recently been identified via immunohistochemistry, mRNA, and Western blot in the rat and human prostate [104–106]. PDE5 inhibitors have been shown to relax prostate tissue in vitro [106, 107].

Uckert et al. [107] performed the following experiments. Using the organ bath technique, the effects of increasing concentrations (1 nM–10 μM) of the PDE5 inhibitors sildenafil, tadalafil, and vardenafil and the PDE4 inhibitors rolipram and RP 73401 on the tension induced by norepinephrine (NE, 40 μM) in prostate strip preparations were investigated. The accumulation of cyclic guanosine monophosphate (cGMP) and cyclic adenosine monophosphate (cAMP) in response to drug exposure was determined by radioimmunoassays. The tension induced by NE was dose dependently reversed by the drugs with the following rank order of efficacy: tadalafil greater than RP 73401 greater than rolipram greater than or equal to vardenafil greater than sildenafil. The maximal reversion of tension values ranged from 52.3 % (tadalafil) to 17 % (sildenafil). Of the PDE inhibitors, only tadalafil induced a 50 % reversion of the initial tension. The most prominent enhancement in tissue cAMP was registered in response to RP 73401 (11-fold), and cGMP levels were significantly elevated by tadalafil, vardenafil, and sildenafil (28-fold, 12-fold, and 3-fold, respectively) [107].

Zhang et al. [106] investigated the effect of testosterone (T) on smooth muscle (SM) contractile and regulatory signaling pathways including PDE5 expression and functional activity in the prostate in three groups of male rats (sham-operated, surgically castrated, and castrated with T supplementation). In vitro organ bath studies, real-time RT-PCR, Western blot analysis, and immunohistochemistry were performed. PDE5 was immunolocalized exclusively in the prostate stroma (Fig. 24.8). The PDE5i zaprinast significantly increased prostate strip relaxation to the nitric oxide donor sodium nitroprusside (SNP) in control but not castrated rats. But SNP alone was more effective on castrated rats, comparable with sham treated with SNP plus zaprinast. T supplementation prevented or restored all of these changes, including SNP and zaprinast in vitro responsiveness. These data show that T positively regulates PDE5 expression and functional activities in prostate, and T ablation not only suppresses prostate size but also reduces prostatic SM contractility, with several potential SM contraction and relaxation pathways implicated. Zaprinast findings strongly suggest a major role for PDE5 and cGMP in this signaling cascade. These data support PDE5 inhibition as a potential mechanism for treatment of BPH.

Tadalafil was recently approved by the FDA for daily use for both BPH and ED [108]. Data suggest [109, 110] that tadalafil can improve LUTS in a similar manner to alpha-blockers (Fig. 24.9), without the alpha-blocker side effects although there are the PDE5i side effects. Tadalafil does not change the PSA at a 1-year time point [112]. Sildenafil and vardenafil also appear to improve both BPH and LUTS symptoms but have not yet cleared the FDA regulatory hurdles for the BPH indication [113, 114].

Treatment of Hypogonadism and Testosterone Replacement in Older Men

The primary treatment for men with symptomatic hypogonadism is testosterone supplementation. There are multiple methods of delivery including injectable, implantable pellets, buccal, transdermal patches, and gels [115]. Although side effects exist, testosterone replacement therapy has been shown to improve muscle mass, energy levels, and bone strength. In older men with significant hypogonadism, testosterone treatment has been effective in enhancing the strength and maintenance of erections [116–120]. In the absence of hypogonadism, testosterone supplementation has been shown to improve the response to sildenafil [118, 119]. Aversa demonstrated that in patients with ED and low-normal androgen levels, short-term testosterone administration increased both total and free testosterone levels and improved the erectile response to sildenafil likely by increasing arterial inflow to the penis during sexual stimulation [121]. Furthermore, one review found that transdermal therapy appears to be more effective than intramuscular delivery methods [122].

As noted previously, controversy exists regarding the lower end of normal for hypogonadism along with the normal levels for the aging male. Seftel et al. attempted to provide guidance regarding the therapeutic targets for T replacement [111] (Fig. 24.9). Hypogonadal male subjects from the Testim phase 3 studies (total

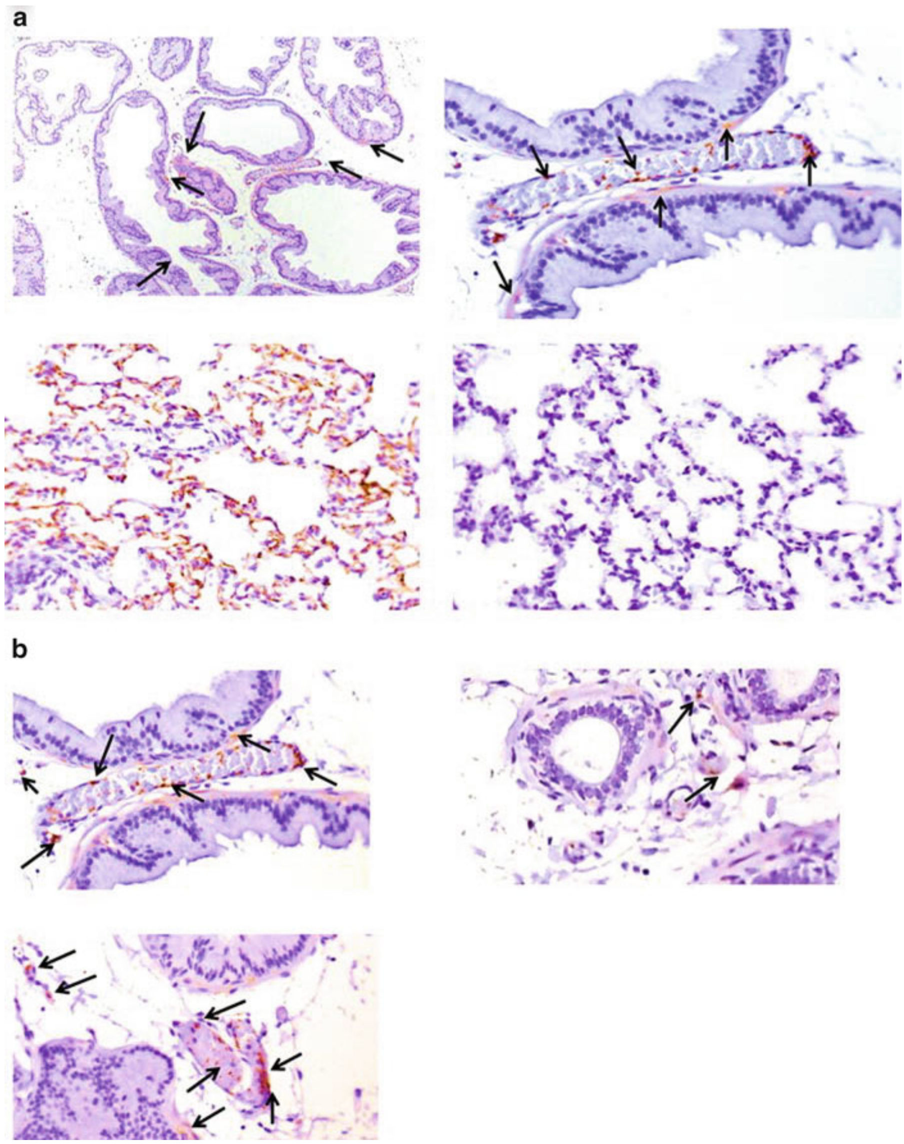


Fig. 24.8 (from [106]) Immunolocalization of phosphodiesterase 5 (PDE5) in rat ventral prostate. (**a**) *Top*: PDE5 positive immunoreactivity in the prostatic stroma from sham-operated rats with magnification ×100 (*left*) and ×400 (*right*). (**a**) *Bottom left*: positive PDE5 control (rat lung, magnification ×400); (**a**) *bottom right*: negative IgG control staining (rat lung, magnification ×400). (**b**) PDE5 immunopositivity in the prostatic stroma from sham (*top left*), castrated (*top right*), and castrated + T (*bottom left*) rats with magnification ×400

T < or = 300 ng/dL, $n = 406$, mean age 58 years) reporting one or more symptoms of low testosterone were randomized to T gel (50 mg/day and 100 mg/day), T patch, or placebo. Twenty-four-hour pharmacokinetic profiles for T were obtained. The three primary endpoints evaluated at 30 and 90 days posttreatment included a significant change in the frequency of intercourse and nighttime erections per 7-day week as well as a change in sexual desire measured on a Likert scale and calculated as a mean daily score. At day 30, a significant increase from baseline in sexual desire was noted for those on 100 mg/day T gel compared with those on 50 mg/day T gel, T

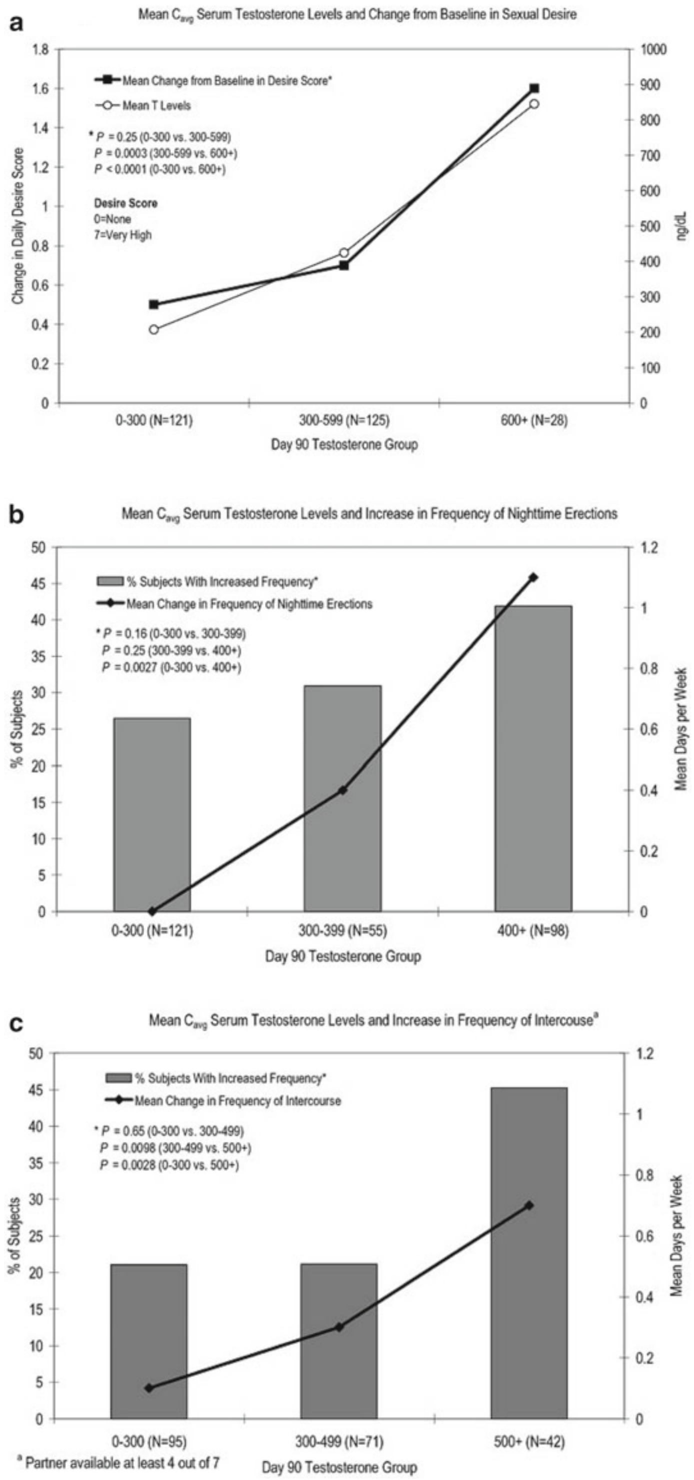


Fig. 24.9 (from [111]) Mean change from baseline for daily sexual desire score and mean C_{avg} (0–24 h) serum testosterone levels (ng/dL); percentage of subjects with increased frequency and mean change in frequency for nighttime erections and intercourse

patch, or placebo (1.2 versus 0.4, 0.7, and 0.4, respectively). A significant increase from baseline in the frequency of nighttime erections was also noted for those on 100 mg/day T gel compared with those on 50 mg/day T gel or placebo. Overall, 51 % of subjects in the 100 mg/day T gel group had an increase in frequency versus 30 % for the 50 mg/day T gel group and 26 % in the placebo group. Finally, a significant increase from baseline in the frequency of intercourse was evidenced for those on 100 mg/day T gel compared with those on T patch or placebo. Of the total sample, 39 % of subjects in the 100 mg/day T gel group had an increase in frequency versus 21 % for the T patch group and 24 % in the placebo group. Similar results were seen for 100 mg/day T gel at day 90 for sexual desire and nighttime erections versus placebo. These data demonstrate a clear relationship between restoring serum T concentrations and improvement in certain parameters of sexual function. We propose that threshold T levels are needed in order to significantly affect improvements in sexual functioning. This threshold level appeared to be approximately 400 ng/dL for nighttime erections, 500 ng/dL for sexual intercourse, and 600 ng/dL for sexual desire. In all three parameters, there was no significant difference in sexual function between the group of subjects with the lowest serum T levels (0–300 ng/dL) and the group of subjects with the next highest serum T level [300–400 ng/dL for nighttime erections, 300–500 ng/dL for sexual intercourse, and 300–600 ng/dL for sexual desire ($P=0.16$)]. The data are depicted in Fig. 24.9.

New formulations of T gels include AndroGel 1.62 %, Testim, Axiron, and Fortesta. Androderm testosterone patches are available as are a buccal preparation, implantable pellets, or standard intramuscular injections [123–125]. Most authorities recommend checking T levels, a hemoglobin and hematocrit level, and a prostate-specific antigen (PSA) level at some designated point after starting T replacement therapy. In addition, a digital rectal examination should regularly be performed as part of clinical follow-up after initiation of T replacement therapy [36].

There is great variability in insurance coverage for T replacement products. Additionally, the FDA has recently issued a "black box" warning regarding the possibility of transference of the T gel once applied by the patient to his body, to a partner, or to a child. This can happen when the T gel is applied to an exposed skin surface and the patient comes into contact with another person. The gels take about 2–6 h to dry once applied to the skin. Appropriate counseling must be provided to the patient when prescribing transdermal T gel replacement therapy [126].

In general, most of the T replacement products are well tolerated by patients. Individual gels may have a side effect specific to its product such as skin irritation, fragrance, a unique application site, or increased time to full absorption. The T patches may also create a bit of skin irritation due to the adhesive but are a reasonable option for the properly selected patient. The buccal preparation is a twice daily application to the inner gum. The T pellets are subcutaneous injections usually performed at 3–4 month intervals. The standard intramuscular injections of T are injected by either the patient or caregiver at 1–3 week intervals. The reader is encouraged to evaluate each specific product to gain familiarity with these compounds.

Treatment endpoints usually include T levels in the therapeutic range and relief of symptoms. T levels can be raised to the higher therapeutic range if symptom relief is not accomplished with initial dosing regimens. The most common T replacement side effects include local skin reactions to the gels, patches, or intramuscular injections; polycythemia; worsening of BPH or LUTS symptoms; increases in serum PSA; pedal edema; gynecomastia; transient oligospermia or azoospermia; and worsening of sleep apnea. While T replacement therapy is contraindicated in men with known prostate cancer, there is a movement afoot to offer T replacement therapy to select men who had undergone treatment for their prostate cancer. This is an extremely controversial topic that is still under investigation [127].

Recent data from the Testosterone in Older Men (TOM) trial has created some concern regarding the beneficial effects of testosterone replacement in older, frail men [128]. These authors studied community-dwelling men, 65 years of age or older, with limitations in mobility and a total serum testosterone level of 100–350 ng/dL (3.5–12.1 nmol/L) or a free serum testosterone level of less than 50 pg/mL (173 pmol/L). These men were randomly assigned to receive placebo gel or testosterone gel, to be applied daily for 6 months. The study premise was that testosterone supplementation has been shown to increase muscle mass and strength in healthy older men. The safety and efficacy of testosterone treatment in older men who have limitations in mobility have not been studied. Adverse events were categorized with the use of the Medical Dictionary for Regulatory Activities classification. The data and safety monitoring board recommended that this trial be discontinued early because there was a significantly higher rate of adverse cardiovascular events in the testosterone group than in the placebo group. A total of 209 men with a mean age of 74 years had been enrolled at the time the trial was terminated. At baseline, there was a high prevalence of hypertension, diabetes, hyperlipidemia, and obesity among the participants. During the course of the study, the testosterone group had higher rates of cardiac, respiratory, and dermatologic events than did the placebo group. A total of 23 subjects in the testosterone group, as compared with five in the placebo group, had cardiovascular-related adverse events. The relative risk of a cardiovascular-related adverse event remained constant throughout the 6-month treatment period. As compared with the placebo group, the testosterone group had significantly greater improvements in leg-press and chest-press strength and in stair climbing while carrying a load. The authors concluded that in this population of older men with limitations in mobility and a high prevalence of chronic disease, the application of a testosterone gel was associated with an increased risk of cardiovascular adverse events. The small size of the trial and the unique population prevent broader inferences from being made about the safety of testosterone therapy.

One must weigh the data presented in the TOM trial with those data provided earlier in this chapter [68–72]. These data suggest that low T is associated with worse long-term morbidity and mortality [38] and T replacement therapy may offer some cardiovascular and cognitive benefit. T replacement therapy appears to offer some metabolic benefits in the areas of cardiovascular disease, diabetes, and the metabolic syndrome [70–72, 129, 130].

Other controversial issues surround patients with late-onset hypogonadism. Some authorities feel that patients with serum total testosterone levels below 8 nmol/L (230 ng/dL) will usually benefit from testosterone treatment. Total testosterone levels between 8 and 12 nmol/L (230–350 ng/dL) warrant repeat measurement of total testosterone with sex hormone-binding globulin (SHBG) to calculate free testosterone or free testosterone by equilibrium dialysis. Total testosterone level above 12 nmol/L (350 ng/dL) may not require substitution [75]. This is another controversial area of study.

Treatment of Ejaculatory Disorders

Ejaculatory disorders have not been particularly well studied in the geriatric population. The two most common ejaculatory disorders include premature ejaculation and delayed ejaculation. Premature ejaculation occurs more commonly in young men compared to elderly men. Treatment of premature ejaculation may include behavioral therapies, sexual therapy, or medications [131, 132]. Antidepressant medications such as dapoxetine and fluoxetine have been used for this purpose [133]. Delayed ejaculation may occur in conjunction with delayed orgasm. In older men, this can sometimes be related to underlying vascular or neurologic conditions. Sexual therapy is often used in the treatment of delayed ejaculation. Some older men may experience retrograde ejaculation, where the semen flows backward into the bladder at the time of ejaculation. This occurs more commonly in men who have undergone transurethral resection of the prostate (TURP) or other surgical therapy for treatment of symptomatic BPH. Some men taking alpha-blocker medications for treatment of BPH may also experience retrograde ejaculation. This occurs because the neck of the bladder does not completely close as usual at the time of orgasm and ejaculation, and the fluid follows the path of least resistance which is directed into the bladder rather than through the urethra. Most men describe that this does not necessarily change the sensation of orgasm. The semen is washed out from the bladder with subsequent urination.

Sexually Transmitted Diseases in Aging Populations

Sexually transmitted diseases (STDs) have become more prevalent as people get older and reengage in sexual activity. The Centers for Disease Control and Prevention (CDC) report that the number of cases of acquired immunodeficiency syndrome (AIDS) has risen from 739 cases in 1999 to 846 in 2009 for adults aged 65 years and older [134]. Although HIV/AIDS transmission through blood transfusions has decreased, other sources of cases by sexual intercourse and multiple sexual partners have increased the number of documented cases [135]. Risk factors for HIV/AIDS in the aging population are the same as those for younger adults including sexual contact, multiple partners, STDs, substance abuse, and intravenous drug use. Older adults were not targeted in the initial public health campaigns designed to increase routine condom use during sexual activity. There has recently been increased recognition of the need to provide public health awareness and access to care across the age continuum.

Older people are especially prone to the sequelae of HIV/AIDS largely because of the decline of humoral- and cell-mediated natural immunity associated with the aging process [12]. The geriatric population is more susceptible to opportunistic infections such as *Mycobacterium tuberculosis*, herpes zoster, and cytomegalovirus. Postmenopausal women are at somewhat higher risk for contracting HIV during sexual intercourse because of decreased lubrication and vaginal wall thinning [136–138]. This may increase risk of viral exposure to the bloodstream. There is also a more aggressive pattern of progression after HIV seroconversion with a lesser response to antiretroviral treatment agents. Comorbidities among older adults may predispose them to an earlier and more rapid demise once infected with HIV as multiple systems may be compromised more quickly. In some cases, older adults may actually die of AIDS before a diagnosis of HIV infection is even made [136]. However, it is also true that with aggressive antiretroviral therapy, many people living with HIV/AIDS are now living longer and are reaching the "geriatric" age group.

Treatment of HIV/AIDS in elderly patients is the same as in the general population. There is a greater propensity for medication interactions and adverse drug reactions because older people are usually taking additional medications for their comorbidities. In older adults, antiretroviral therapies should be started at low dosage and increased gradually under close monitoring. Unfortunately, this patient population sometimes has the combined burden of compromised physical health and compromised cognitive ability to adequately deal with the emotional and psychosocial impact of the initial diagnosis of HIV and the stress of going through the treatment plan [6]. They require additional support and, more importantly, a discussion carefully weighing the risks and benefits of HIV/AIDS treatment in the context of end of life issues.

Because of the significant risks of HIV and other STDs in the geriatric population, it should be stressed to older adults that age in and of itself is not a barrier against these diseases. In the older patient who experiences memory loss, an evaluation for syphilis should be conducted in addition to evaluation for other neurologic conditions [136]. Other more common STDs, such as gonococcal urethritis, vaginitis, trichomoniasis, and chlamydia, are as ubiquitous among the geriatric population as in younger people, and these conditions should be appropriately treated when diagnosed [5]. In nursing homes and assisted living facilities, sexual assault of the cognitively impaired individual should be considered if he or she develops STDs [136]. These various issues and statistics underscore the importance of affirming safer sex practices among the geriatric population by healthcare providers.

Medical Comorbidities and Sexual Health in Older Adults

Comorbid disease processes can have a significant negative impact on sexual health, especially in the geriatric population. Disease states usually cause low energy levels, fatigue, pain, impairment, muscle weakness, and psychological disturbances that hamper a sexual relationship [138]. Conditions requiring surgical intervention can affect anatomic functions including amputations, mastectomy, and bowel or urinary diversions such as colostomy or urostomy. These physical changes can also lead to alterations in body image and lower self-esteem, causing problems with sexual attraction [11]. Frequently, patients are prohibited from significant sexual contact after the resolution of a disease state. Examples include men after radical prostatectomy who are unable to achieve an erection or the patient after myocardial infarction (MI) who is fearful of suffering a recurrent MI during intercourse. Updated guidelines for the clinician have recently been published to assist with the post-MI patient and other patients afflicted with CV disease who wish to resume sexual activity [139]. A cardiovascular evaluation may be required to assess the patients' physical capability and endurance requirements necessary to resume sexual intercourse. Both sexual partners should be cognizant and comfortable with sexual activities after one partner undergoes a life-altering condition or surgery.

After stroke, patients may have paralysis or reduced libido and diminished orgasms. Poststroke weakness can be unilateral and can sometimes be addressed by alternative positioning while engaging in sexual activities [138]. Concerns also exist that medications used to treat certain neurologic conditions may result in sexual dysfunction.

Diabetes mellitus (DM), a significant contributing factor for ED in men, can also negatively impact women's sexuality. DM can cause a decrease of vaginal secretions and reduce libido. Different sequelae of DM such as retinopathy leading to blindness, amputations, renal failure requiring dialysis, peripheral neuropathy, and chronic pain can all hamper sexual functioning [12]. Chronic arthritis can cause pain and joint swelling, limiting range of motion during sex [11]. This may require use of alternate sexual positions or forms of sexual expression.

Postsurgical patients, after any type of surgery, may experience side effects such as pain, scarring, and lymphedema, all of which can interfere with a patient's desire and ability to engage in sexual activities. Partners may also find it difficult to cope with his or her partner's sexual difficulties and inadequacies and may not feel any sexual attraction under those circumstances [140]. There is a heavy toll on both the physical and emotional components of a postsurgical relationship. After hysterectomy, many women found less desire and enjoyment during intercourse, although a minority had improved sexual activity because their prior symptoms and pain were now gone [141].

In men, the most common noncutaneous malignancy is prostate cancer. All treatment modalities including open or robotic radical prostatectomy, external beam radiation, or brachytherapy are associated with a significant concern for incontinence, impotence, and diminished libido [62]. Radical prostatectomy, particularly if it is not done with nerve-sparing technique, may inhibit return of spontaneous erections. In addition, some men may view prostatectomy as an assault on male sexuality and suffer considerable postoperative psychological distress, thereby diminishing sexual desire and function [142, 143]. Urinary incontinence after radical prostatectomy can also negatively impact sexual behavior in older men. Nocturia, bedwetting, and fear of incontinence during sex can all decrease sexual desire and activity. The use of Kegel pelvic floor muscle exercises to improve continence and selective administration of appropriate medications can sometimes lead to improvement in sexual function in older men [143]. Treatment of erectile dysfunction after prostatectomy includes all of the pharmacologic and non-medication options previously described in this chapter.

In addition to organic comorbidities, one must consider chronic psychological diseases associated with sexual dysfunction. Depression and anxiety are serious and prevalent disorders in American men and women [144]. Determination of causality can be challenging, as depression and anxiety can either precede and cause sexual dysfunction or be results of sexual dysfunction. Although psychotherapy and pharmacotherapy can provide substantial relief and clinical improvements, some antidepressants also have sexual side effects such as decreased libido, making these drugs potentially counterproductive in treating sexual dysfunction.

Religious, Social, and Cultural Aspects of Geriatric Sexuality

The influence of religious and cultural factors is also important when considering sexual health in older adults. Religious tenets and philosophies learned during childhood and over a lifetime play a significant role during later adulthood. Some cultures paint sexuality and its expression as a picture of sin and darkness on a religious basis. Others allow for more freedom and insight. In some settings, prior religious teachings can detract older adults from experiencing a satisfactory sexual relationship because of feelings of guilt and repression. This may be true for both sexual intercourse and other forms of sexual expression such as masturbation. Therefore, it is important for urologists and other healthcare providers to address these religious feelings and potential concerns. Providers should attempt to incorporate the treatment of sexual dysfunction as part of health care in a manner that is understanding of and complementary to the patient's religious background and other cultural identity [26].

Sexual orientation is also an important consideration when addressing the sexual health needs of older adults. Most epidemiologic research has demonstrated that up to 10 % of people in populations self-identify as lesbian, gay, or bisexual. Providers need to be aware of healthcare needs that may be unique to older adult lesbians and gay men. Inclusion of the patient's partner in decision making regarding sexual health concerns is extremely important. In addition, transgendered older adults may have sexual health concerns that require medical care. To date, there has been relatively little research published on the urologic and sexual health concerns in the lesbian, gay, bisexual, and transgendered (LGBT) older adult population. Future research will help to address some of these issues. Healthcare providers need to be attuned to the potential sexual health needs in these patients and work to provide culturally sensitive professional care.

Conclusions and Directions for Future Research

Recent years have seen tremendous advances in the treatment of sexual health conditions for patients of all ages. New research will likely continue to advance this field of medicine. Several topics deserve additional research including additional treatments for both erectile dysfunction in men and sexual dysfunction in women. Assessing the sexual response in women with female sexual dysfunctions (FSDs) in clinical trials remains difficult. Outcome measures used by the FDA for female sexual dysfunction drug development remain a significant challenge in the area of female sexual dysfunction [145]. Additional work will also lead to better understanding of the relationship between many of the comorbid conditions of aging and sexual health.

In summary, sexuality plays a vital role in the health and general well-being of many older adults. There are a multitude of physical, psychological, emotional, and spiritual implications of a healthy sex life as men and women age [146]. A healthy sense of sexuality in the aging adult generally provides a more fulfilled lifestyle and can significantly improve quality of life. Although there are challenges and comorbid conditions that can negatively affect sexuality as one ages, those obstacles can often be treated effectively. As more and more Americans live longer, it will become increasingly more important that urologists and other healthcare providers understand that sex life does not disappear with old age and that many elderly people have and enjoy a satisfactory sexual experience. With a balanced and healthy lifestyle, optimal treatment for medical conditions, research and therapeutic advances, and medical breakthroughs, sexual well-being is within reach of many older adults.

References

1. Fowles, DG, Greenberg S. A profile of older Americans: 2010. Administration on Aging, Department of Health and Human Services; 2010.
2. Lindau ST, Laumann EO, Levinson W, Waite LJ (2003) Synthesis of scientific disciplines in pursuit of health: the Interactive Biopsychosocial Model. Perspect Biol Med 46(Suppl 3):S74–86
3. Laumann EO, Paik A, Rosen RC (1999) Sexual dysfunction in the United States: prevalence and predictors. JAMA 281(6):537–44
4. Lindau ST, Schumm P, Laumann EO, Levinson W, O'Muircheartaigh CA, Waite LJ (2007) A study of sexuality and health among older adults in the United States. N Engl J Med 357(8):762–74
5. Rienzo B (1985) The impact of aging on human sexuality. J Sch Health 55(2):66–8
6. Lenahan P, Ellwood A (2004) Sexual health and aging. Clin Fam Pract 6(4):917–39
7. Laumann EO, Paik A, Glasser DB, Kang JH, Wang T, Levinson B, Moreira ED Jr, Nicolosi A, Gingell C (2006) A cross-national study of subjective sexual well-being among older women and men: findings from the Global Study of Sexual Attitudes and Behaviors. Arch Sex Behav 35(2):145–61
8. Nusbaum MRH, Gamble GR, Pathman DE (2002) Seeking medical help for sexual concerns: frequency, barriers, and missed opportunities. J Fam Pract 51:706
9. Lindau ST, Leitsch SA, Lundberg KL, Jerome J (2006) Older women's attitudes, behavior, and communication about sex and HIV: a community-based study. J Womens Health (Larchmt) 15(6):747–53
10. Gott M, Hinchliff S, Galena E (2004) General practitioner attitudes to discussing sexual health issues with older people. Soc Sci Med 58(11):2093–103
11. Kaiser F (1998) Sexuality practice of geriatrics, 3rd edn. WB Saunders, Philadelphia, PA, pp 48–56
12. Ginsberg TB (2006) Aging and sexuality. Med Clin North Am 90(5):1025–36
13. Drench M, Losee R (1996) Sexuality and sexual capacities of elderly people. Rehabil Nurs 21(3): 118–23
14. Jung A, Schill WB (2004) Male sexuality with advancing age. Eur J Obstet Gynecol Reprod Biol 113:123–5
15. Mulligan T, Reddy S, Gulur PV, Godschalk M (2003) Disorders of male sexual function. Clin Geriatr Med 19(3):473–81
16. Masters W, Johnson V (1981) Sex and the aging process. J Am Geriatr Soc 29:385–90
17. Pariser S, Niedermier J (1998) Sex and the mature woman. J Womens Health 7(7):849–59
18. Wilson MM (2003) Menopause. Clin Geriatr Med 19(3):483–506
19. West SL, D'Aloisio AA, Agans RP, Kalsbeek WD, Borisov NN, Thorp JM (2008) Prevalence of low sexual desire and hypoactive sexual desire disorder in a nationally representative sample of US women. Arch Intern Med 168(13):1441–9
20. Trompeter SE, Bettencourt R, Barrett-Connor E (2012) Sexual activity and satisfaction in healthy community-dwelling older women. Am J Med 125(1):37–43 e1
21. Noblett KL, Ostergard DR (1999) Gynecologic disorders. Principles of geriatric medicine and gerontology, 4th edn. McGraw-Hill, New York, NY, pp 797–807
22. Robinson JG, Wallace R, Limacher M, Ren H, Cochrane B, Wassertheil-Smoller S, Ockene JK, Blanchette PL, Ko MG (2008) Cardiovascular risk in women with non-specific chest pain (from the Women's Health Initiative Hormone Trials). Am J Cardiol 102(6):693–9
23. Bernstein L (2006) The risk of breast, endometrial and ovarian cancer in users of hormonal preparations. Basic Clin Pharmacol Toxicol 98(3):288–96
24. Johannes CB, McKinlay JB et al (2000) Incidence of erectile dysfunction in men 40 to 69 years old: longitudinal results from the Massachusetts Male Aging Study. J Urol 163:460–3
25. McKinlay JB et al (2000) The worldwide prevalence and epidemiology of erectile dysfunction. Int J Impot Res 12(Suppl 4):S6–11
26. Hogan R (1982) Influences of culture on sexuality. Nurs Clin North Am 17(3):365–76
27. Laumann EO et al (1994) The social organization of sexuality: sexual practices in the United States. University of Chicago Press, Chicago, IL, p. 370
28. Feldman HA et al (1994) Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. J Urol 151:54
29. Waldinger MD (2008) Recent advances in the classification, neurobiology and treatment of premature ejaculation. Adv Psychosom Med 29:50–69
30. Waldinger MD, McIntosh J, Schweitzer DH (2009) A five-nation survey to assess the distribution of the intravaginal ejaculatory latency time among the general male population. J Sex Med 6(10):2888–95
31. Althof SE, Abdo CH, Dean J, Hackett G, McCabe M, McMahon CG, Rosen RC, Sadovsky R, Waldinger M, Becher E, Broderick GA, Buvat J, Goldstein I, El-Meliegy AI, Giuliano F, Hellstrom WJ, Incrocci L, Jannini EA, Park K, Parish S, Porst H, Rowland D, Segraves R, Sharlip I, Simonelli C, Tan HM, International Society for Sexual Medicine (2010) International Society for Sexual Medicine's guidelines for the diagnosis and treatment of premature ejaculation. J Sex Med 7(9):2947–69
32. Jern P, Santtila P, Witting K, Alanko K, Harlaar N, Johansson A, von der Pahlen B, Varjonen M,

Vikström N, Algars M, Sandnabba K (2007) Premature and delayed ejaculation: genetic and environmental effects in a population-based sample of Finnish twins. J Sex Med 4(6):1739–49
33. Morley JE, Haren MT, Kim MJ, Kevorkian R, Perry HM (2005) Testosterone, aging and quality of life. J Endocrinol Invest 28(3 Suppl):76–80
34. Carani C, Isidori AM, Granata A, Carosa E, Maggi M, Lenzi A, Jannini EA (2005) Multicenter study on the prevalence of sexual symptoms in male hypo- and hyperthyroid patients. J Clin Endocrinol Metab 90(12):6472–9
35. Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS, Montori VM, Task Force Endocrine Society (2010) Testosterone therapy in men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 95(6): 2536–59
36. Harman SM, Metter EJ, Tobin JD, Pearson J, Blackman MR (2001) Longitudinal effects of aging on serum total and free testosterone levels in healthy men. Baltimore Longitudinal Study of Aging. J Clin Endocrinol Metab 86(2):724–31
37. Li JY, Li XY, Li M, Zhang GK, Ma FL, Liu ZM, Zhang NY, Meng P (2005) Decline of serum levels of free testosterone in aging healthy Chinese men. Aging Male 8(3–4):203–6
38. Shores MM, Matsumoto AM, Sloan KL, Kivlahan DR (2006) Low serum testosterone and mortality in male veterans. Arch Intern Med 166(15):1660–5
39. Wu FC, Tajar A, Beynon JM, Pye SR, Silman AJ, Finn JD, O'Neill TW, Bartfai G, Casanueva FF, Forti G, Giwercman A, Han TS, Kula K, Lean ME, Pendleton N, Punab M, Boonen S, Vanderschueren D, Labrie F, Huhtaniemi IT, EMAS Group (2010) Identification of late-onset hypogonadism in middle-aged and elderly men. N Engl J Med 363(2):123–35
40. Isidori AM, Giannetta E, Gianfrilli D, Greco EA, Bonifacio V, Aversa A, Isidori A, Fabbri A, Lenzi A (2005) Effects of testosterone on sexual function in men: results of a meta-analysis. Clin Endocrinol (Oxf) 63(4):381–94
41. Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A (1997) The International Index of Erectile Function (IIEF): a multidimensional scale for assessment of erectile dysfunction. Urology 49(6):822–30
42. Rosen RC, Cappelleri JC, Smith MD, Lipsky J, Peña BM (1999) Development and evaluation of an abridged, 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. Int J Impot Res 11(6):319–26
43. Rosen RC, Catania JA, Althof SE, Pollack LM, O'Leary M, Seftel AD, Coon DW (2007) Development and validation of four-item version of Male Sexual Health Questionnaire to assess ejaculatory dysfunction. Urology 69(5):805–9
44. Tancredi A, Reginster JY, Schleich F, Pire G, Maassen P, Luyckx F, Legros JJ (2004) Interest of the Androgen Deficiency in Aging Males (ADAM) Questionnaire for the identification of hypogonadism in elderly community-dwelling male volunteers. Eur J Endocrinol 151(3):355–60
45. Daig I, Heinemann LA, Kim S, Leungwattanakij S, Badia X, Myon E, Moore C, Saad F, Potthoff P, Thai do M (2003) The Aging Males' Symptoms (AMS) scale: review of its methodological characteristics. Health Qual Life Outcomes 1:77
46. Rosen RC, Araujo AB, Connor MK, Gerstenberger EP, Morgentaler A, Seftel AD, Miner MM, Shabsigh R (2011) The NERI hypogonadism screener: psychometric validation in male patients and controls. Clin Endocrinol (Oxf) 74(2):248–56
47. Meston CM, Derogatis LR (2002) Validated instruments for assessing female sexual function. J Sex Marital Ther 28(Suppl 1):155–64
48. Wiegel M, Meston C, Rosen R (2005) The female sexual function index (FSFI): cross-validation and development of clinical cutoff scores. J Sex Marital Ther 31(1):1–20
49. Baser RE, Li Y, Carter J (2012) Psychometric validation of the Female Sexual Function Index (FSFI) in cancer survivors. Cancer 118(18):4606–18
50. Gerstenberger EP, Rosen RC, Brewer JV, Meston CM, Brotto LA, Wiegel M, Sand M (2010) Sexual desire and the female sexual function index (FSFI): a sexual desire cutpoint for clinical interpretation of the FSFI in women with and without hypoactive sexual desire disorder. J Sex Med 7(9):3096–103
51. Impotence (1993) NIH consensus development panel on impotence. JAMA 270(1):83–90
52. Seftel A, Miner M, Kloner R, Althof S (2007) Office evaluation of male sexual dysfunction. Urol Clin North Am 34(4):463–82
53. Miner M, Seftel AD (2007) Centrally acting mechanisms for the treatment of male sexual dysfunction. Urol Clin North Am 34(4):483–96
54. Lue TF (2000) Erectile dysfunction. N Engl J Med 342:1802–13
55. de Tejada IS, Goldstein I, Azadzoi K, Krane RJ, Cohen RA (1989) Impaired neurogenic and endothelium-mediated relaxation of penile smooth muscle from diabetic men with impotence. N Engl J Med 320:1025–30
56. Rajfer J et al (1992) Nitric oxide as a mediator of relaxation of the corpus cavernosum. N Engl J Med 326:1638
57. Bancroft J (2005) The endocrinology of sexual arousal. J Endocrinol 186:411–27
58. Becker AJ, Uckert S, Stief CG, Scheller F, Knapp WH, Hartmann U, Jonas U (2001) Cavernous and systemic testosterone plasma levels during different penile conditions in healthy males and patients with erectile dysfunction. Urology 58(3):435–40
59. Traish AM, Park K, Dhir V, Kim NN, Moreland RB, Goldstein I (1999) Effects of castration and andro-

gen replacement on erectile function in a rabbit model. Endocrinology 140(4):1861–8
60. Zvara P, Sioufi R, Schipper HM, Begin LR, Brock GB (1995) Nitric oxide mediated erectile activity is a testosterone dependent event: a rat erection model. Int J Impot Res 7(4):209–19
61. Reilly CM, Lewis RW, Stopper VS, Mills TM (1997) Androgenic maintenance of the rat erectile response via a non-nitric-oxide-dependent pathway. J Androl 18(6):588–94
62. Hall R, Andrews PL, Hoyle CH (2002) Effects of testosterone on neuromuscular transmission in rat isolated urinary bladder. Eur J Pharmacol 449(3):301–9
63. Morley JE, Kaiser FE, Perry HM III, Patrick P, Morley PM, Stauber PM, Vellas B, Baumgartner RN, Garry PJ (1997) Longitudinal changes in testosterone, luteinizing hormone, and follicle-stimulating hormone in healthy older men. Metabolism 46(4): 410–3
64. Haren MT, Kim MJ, Tariq SH, Wittert GA, Morley JE (2006) Andropause: a quality-of-life issue in older males. Med Clin North Am 90(5):1005–23
65. Marcell TJ, Harman SM, Urban RJ, Metz DD, Rodgers BD, Blackman MR (2001) Comparison of GH, IGF-I, and testosterone with mRNA of receptors and myostatin in skeletal muscle in older men. Am J Physiol Endocrinol Metab 281(6):E1159–64
66. Benito M, Vasilic B, Wehrli FW, Bunker B, Wald M, Gomberg B, Wright AC, Zemel B, Cucchiara A, Snyder PJ (2005) Effect of testosterone replacement on trabecular architecture in hypogonadal men. J Bone Miner Res 20(10):1785–91
67. Dacal K, Sereika SM, Greenspan SL (2006) Quality of life in prostate cancer patients taking androgen deprivation therapy. J Am Geriatr Soc 54(1):85–90
68. Moffat SD, Zonderman AB, Metter EJ, Blackman MR, Harman SM, Resnick SM (2002) Longitudinal assessment of serum free testosterone concentration predicts memory performance and cognitive status in elderly men. J Clin Endocrinol Metab 87(11):5001–7
69. Dunajska K, Milewicz A, Szymczak J, Jêdrzejuk D, Kuliczkowski W, Salomon P, Nowicki P (2004) Evaluation of sex hormone levels and some metabolic factors in men with coronary atherosclerosis. Aging Male 7(3):197–204
70. Muller M, van den Beld AW, Bots ML, Grobbee DE, Lamberts SW, van der Schouw YT (2004) Endogenous sex hormones and progression of carotid atherosclerosis in elderly men. Circulation 109(17):2074–9
71. Lish KM, Steeds RP, Jones TH, Diver MJ, Channer KS (2000) Low-dose transdermal testosterone therapy improves angina threshold in men with chronic stable angina: a randomized, double-blind, placebo-controlled study. Circulation 102(16):1906–11
72. Malkin CJ, Pugh PJ, Morris PD, Kerry KE, Jones RD, Jones TH, Channer KS (2004) Testosterone replacement in hypogonadal men with angina improves ischaemic threshold and quality of life. Heart 90(8):871–6
73. Bhasin S, Cunningham GR, Hayes FJ (2010) Testosterone therapy in men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 95: 2536–59
74. Vesper HW, Botelho JC, Shacklady C et al (2008) CDC project on standardizing steroid 380 hormone measurements. Steroids 73:1286–92
75. Wang C, Nieschlag E, Swerdloff R et al (2009) Investigation, treatment, and monitoring of 385 late-onset hypogonadism in males: ISA, ISSAM, EAU, EAA, and ASA 386 recommendations. J Androl 30(1–9):387
76. Institute of Medicine. Testosterone and aging: clinical research directions. 2003.
77. Jones JW. Female Viagra ineffective. http://psychcentral.com/news/2010/06/21/female-viagra-ineffective/14803.html
78. Davis SR, Davison SL, Donath S, Bell RJ (2005) Circulating androgen levels and self-reported sexual function in women. JAMA 294(1):91–6
79. Wierman ME, Basson R, Davis SR, Khosla S, Miller KK, Rosner W, Santoro N (2006) Androgen therapy in women: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 91(10): 3697–710
80. Tomaselli KP. Intrinsa stalled by concerns about safety. http://www.ama-assn.org/amednews/2005/01/17/hlsc0117.htm
81. http://www.biosantepharma.com/LibiGel.php
82. http://www.whi.org/findings/ht/ealone_chd.php
83. Stefanick M, Anderson GL, Margolis KL et al (2006) Effects of conjugated equine estrogens on breast cancer and mammography screening in postmenopausal women with hysterectomy. JAMA 295(14):1647–57
84. Buster JE (2010) Transdermal menopausal hormone therapy: delivery through skin changes the rules. Expert Opin Pharmacother 11(9):1489–99
85. Liebergall-Wischnitzer M, Paltiel O, Hochner Celnikier D, Lavy Y, Manor O, Woloski Wruble AC (2012) Sexual function and quality of life of women with stress urinary incontinence: a randomized controlled trial comparing the Paula Method (circular muscle exercises) to pelvic floor muscle training (PFMT) exercises. J Sex Med 9(6):1613–23
86. Filocamo MT, Serati M, Frumenzio E, Li Marzi V, Cattoni E, Champagne A, Salvatore S, Nicita G, Costantini E (2011) The impact of mid-urethral slings for the treatment of urodynamic stress incontinence on female sexual function: a multicenter prospective study. J Sex Med 8(7):2002–8
87. Tsertsvadze A, Fink HA, Yazdi F, MacDonald R, Bella AJ, Ansari MT, Garritty C, Soares-Weiser K, Daniel R, Sampson M, Fox S, Moher D, Wilt TJ (2009) Oral phosphodiesterase-5 inhibitors and

hormonal treatments for erectile dysfunction: a systematic review and meta-analysis. Ann Intern Med 151(9):650–61
88. Goldstein I, Lue TF, Padma-Nathan H, Rosen RC, Steers WD, Wicker PA (1998) Oral sildenafil in the treatment of erectile dysfunction. Sildenafil Study Group. N Engl J Med 338(20):1397–404
89. Brock GB, McMahon CG, Chen KK, Costigan T, Shen W, Watkins V, Anglin G, Whitaker S (2002) Efficacy and safety of tadalafil for the treatment of erectile dysfunction: results of integrated analyses. J Urol 168(4 Pt 1):1332–6
90. Hatzimouratidis K, Hatzichristou DG (2009) Phosphodiesterase type 5 inhibitors: unmet needs. Curr Pharm Des 15(30):3476–85
91. Fink HA, Mac Donald R, Rutks IR, Nelson DB, Wilt TJ (2002) Sildenafil for male erectile dysfunction: a systematic review and meta-analysis. Arch Intern Med 162(12):1349–60
92. Wagner G, Montorsi F, Auerbach S, Collins M (2001) Sildenafil citrate (VIAGRA) improves erectile function in elderly patients with erectile dysfunction: a subgroup analysis. J Gerontol A Biol Sci Med Sci 56(2):M113–9
93. Richter S, Vardi Y, Ringel A, Shalev M, Nissenkorn I (2001) Intracavernous injections: still the gold standard for treatment of erectile dysfunction in elderly men. Int J Impot Res 13(3):172–5
94. Al-Najar A, Naumann CM, Kaufmann S, Steinbach-Jensch A, Hamann MF, Jünemann KP, van der Horst C (2009) Should being aged over 70 years hinder penile prosthesis implantation? BJU Int 104(6): 834–7
95. Conaglen HM, Conaglen JV (2008) Investigating women's preference for sildenafil or tadalafil use by their partners with erectile dysfunction: the partners' preference study. J Sex Med 5(5):1198–207
96. Althof SE, Rubio-Aurioles E, Kingsberg S, Zeigler H, Wong DG, Burns P (2010) Impact of tadalafil once daily in men with erectile dysfunction–including a report of the partners' evaluation. Urology 75(6):1358–63
97. Rajfer J, Aliotta PJ, Steidle CP, Fitch WP III, Zhao Y, Yu A (2007) Tadalafil dosed once a day in men with erectile dysfunction: a randomized, double-blind, placebo-controlled study in the US. Int J Impot Res 19(1):95–103
98. Seftel AD, Buvat J, Althof SE, McMurray JG, Zeigler HL, Burns PR, Wong DG (2009) Improvements in confidence, sexual relationship and satisfaction measures: results of a randomized trial of tadalafil 5 mg taken once daily. Int J Impot Res 21(4):240–8
99. Abrams P (1995) Managing lower urinary tract symptoms in older men. Br Med J 310:1113–7
100. Lepor H, Kazzazi A, Djavan B (2012) α-Blockers for benign prostatic hyperplasia: the new era. Curr Opin Urol 22(1):7–15
101. Braun M, Wassmer G, Klotz T, Reifenrath B, Mathers M, Engelmann U (2000) Epidemiology of erectile dysfunction: results of the 'Cologne Male Survey'. Int J Impot Res 12(6):305–11
102. Rosen R, Altwein J, Boyle P, Kirby RS, Lukacs B, Meuleman E, O'Leary MP, Puppo P, Robertson C, Giuliano F (2003) Lower urinary tract symptoms and male sexual dysfunction: the multinational survey of the aging male (MSAM-7). Eur Urol 44(6):637–49
103. Mouli S, McVary KT (2009) PDE5 inhibitors for LUTS. Prostate Cancer Prostatic Dis 12(4):316–24
104. Uckert S, Oelke M, Stief CG, Andersson KE, Jonas U, Hedlund P (2006) Immunohistochemical distribution of cAMP- and cGMP-phosphodiesterase (PDE) isoenzymes in the human prostate. Eur Urol 49(4):740–5
105. Morelli A, Filippi S, Mancina R, Luconi M, Vignozzi L, Marini M, Orlando C, Vannelli GB, Aversa A, Natali A, Forti G, Giorgi M, Jannini EA, Ledda F, Maggi M (2004) Androgens regulate phosphodiesterase type 5 expression and functional activity in corpora cavernosa. Endocrinology 145(Feb 5):2253–63
106. Zhang X, Zang N, Wei Y, Yin J, Teng R, Seftel A, Disanto ME (2012) Testosterone regulates smooth muscle contractile pathways in the rat prostate: emphasis on PDE5 signaling. Am J Physiol Endocrinol Metab 302(2):E243–53
107. Uckert S, Sormes M, Kedia G, Scheller F, Knapp WH, Jonas U, Stief CG (2008) Effects of phosphodiesterase inhibitors on tension induced by norepinephrine and accumulation of cyclic nucleotides in isolated human prostatic tissue. Urology 71(3):526–30
108. FDA News Release: FDA approves cialis to treat benign prostatic hyperplasia. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm274642.htm
109. Oelke M, Giuliano F, Mirone V, Xu L, Cox D, Viktrup L (2012) Monotherapy with tadalafil or tamsulosin similarly improved lower urinary tract symptoms suggestive of benign prostatic hyperplasia in an international, randomised, parallel, placebo-controlled clinical trial. Eur Urol 61(5):917–25
110. Egerdie RB, Auerbach S, Roehrborn CG, Costa P, Garza MS, Esler AL, Wong DG, Secrest RJ (2012) Tadalafil 2.5 or 5 mg administered once daily for 12 weeks in men with both erectile dysfunction and signs and symptoms of benign prostatic hyperplasia: results of a randomized, placebo-controlled, double-blind study. J Sex Med 9(1):271–81
111. Seftel AD, Mack RJ, Secrest AR, Smith TM (2004) Restorative increases in serum testosterone levels are significantly correlated to improvements in sexual functioning. J Androl 25(6):963–72
112. Donatucci CF, Brock GB, Goldfischer ER, Pommerville PJ, Elion-Mboussa A, Kissel JD, Viktrup L (2011) Tadalafil administered once daily for lower urinary tract symptoms secondary to benign prostatic hyperplasia: a 1-year, open-label extension study. BJU Int 107(7):1110–6
113. McVary KT, Monnig W, Camps JL Jr, Young JM, Tseng LJ, van den Ende G (2007) Sildenafil citrate improves erectile function and urinary symptoms in

men with erectile dysfunction and lower urinary tract symptoms associated with benign prostatic hyperplasia: a randomized, double-blind trial. J Urol 177(3):1071–7
114. Gacci M, Vittori G, Tosi N, Siena G, Rossetti MA, Lapini A, Vignozzi L, Serni S, Maggi M, Carini M (2012) A randomized, placebo-controlled study to assess safety and efficacy of vardenafil 10 mg and tamsulosin 0.4 mg vs. tamsulosin 0.4 mg alone in the treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia. J Sex Med 9(6):1624–33
115. Lunenfeld B, Saad F, Hoesl CE (2005) ISA, ISSAM and EAU recommendations for the investigation, treatment and monitoring of late-onset hypogonadism in males: scientific background and rationale. Aging Male 8(2):59–74
116. Haren M, Chapman I, Coates P, Morley J, Wittert G (2005) Effect of 12 month oral testosterone on testosterone deficiency symptoms in symptomatic elderly males with low-normal gonadal status. Age Ageing 34(2):125–30
117. Kunelius P, Lukkarinen O, Hannuksela ML, Itkonen O, Tapanainen JS (2002) The effects of transdermal dihydrotestosterone in the aging male: a prospective, randomized, double blind study. J Clin Endocrinol Metab 87(4):1467–72
118. Shabsigh R (2005) Testosterone therapy in erectile dysfunction and hypogonadism. J Sex Med 2(6): 785–92
119. Shabsigh R (2003) Hypogonadism and erectile dysfunction: the role for testosterone therapy. Int J Impot Res 15(Suppl 4):S9–13, Review
120. Tariq SH, Haleem U, Omran ML, Kaiser FE, Perry HM III, Morley JE (2003) Erectile dysfunction: etiology and treatment in young and old patients. Clin Geriatr Med 19(3):539–51
121. Aversa A, Isidori AM, Spera G, Lenzi A, Fabbri A (2003) Androgens improve cavernous vasodilation and response to sildenafil in patients with erectile dysfunction. Clin Endocrinol (Oxf) 58(5):632–8
122. Jain P, Rademaker AW, McVary KT (2000) Testosterone supplementation for erectile dysfunction: results of a meta-analysis. J Urol 164(2):371–5
123. Testosterone topical solution (Axiron) for hypogonadism. Med Lett Drugs Ther. 2011;53(1368): 54–5.
124. Kaufman JM, Miller MG, Fitzpatrick S, McWhirter C, Brennan JJ (2012) One-year efficacy and safety study of a 1.62% testosterone gel in hypogonadal men: results of a 182-day open-label extension of a 6-month double-blind study. J Sex Med 9(4):1149–61
125. Seftel A (2007) Testosterone replacement therapy for male hypogonadism: part III. Pharmacologic and clinical profiles, monitoring, safety issues, and potential future agents. Int J Impot Res 19(1): 2–24
126. Testosterone Gel Safety Information. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm161874.htm
127. Morgentaler A (2011) Testosterone and prostate cancer: what are the risks for middle-aged men? Urol Clin North Am 38(2):119–24
128. Basaria S, Coviello A et al (2010) Adverse events associated with testosterone administration. N Engl J Med 363:109–22
129. Dandona P, Dhindsa S (2011) Update: hypogonadotropic hypogonadism in type 2 diabetes and obesity. J Clin Endocrinol Metab 96(9):2643–51
130. Corona G, Monami M, Rastrelli G, Aversa A, Tishova Y, Saad F, Lenzi A, Forti G, Mannucci E, Maggi M (2011) Testosterone and metabolic syndrome: a meta-analysis study. J Sex Med 8(1):272–83
131. Porst H (2011) An overview of pharmacotherapy in premature ejaculation. J Sex Med 8(Suppl 4):335–41
132. Melnik T, Althof S, Atallah AN, Puga ME, Glina S, Riera R (2011) Psychosocial interventions for premature ejaculation. Cochrane Database Syst Rev 8, CD008195
133. McMahon CG (2010) Dapoxetine for premature ejaculation. Expert Opin Pharmacother 11(10):1741–52
134. National Center of Health Statistics. US Department of Health and Human Services Centers for Disease Control and Prevention. AIDS diagnoses by age. 2009. http://www.cdc.gov/hiv/topics/surveillance/basic.htm#aidsage. Accessed 2011.
135. Centers of Disease Control and Prevention, United States. AIDS among persons aged >50 years. 2009. http://www.cdc.gov/hiv/topics/over50/index.htm. Accessed 2011.
136. Senior K (2005) Growing old with HIV. Lancet 5:739
137. Wilson MM (2003) Sexually transmitted diseases. Clin Geriatr Med 19:637–55
138. Kaiser F (2003) Sexual function and the older woman. Clin Geriatr Med 19(3):463–72
139. Levine GN, Steinke EE, Bakaeen FG, Bozkurt B, Cheitlin MD, Conti JB, Foster E, Jaarsma T, Kloner RA, Lange RA, Lindau ST, Maron BJ, Moser DK, Ohman EM, Seftel AD, Stewart WJ, American Heart Association Council on Clinical Cardiology, Council on Cardiovascular Nursing, Council on Cardiovascular Surgery and Anesthesia, Council on Quality of Care and Outcomes Research (2012) Sexual activity and cardiovascular disease: a scientific statement from the American Heart Association. Circulation 125(8): 1058–72
140. Morley JE, Kaiser FE (2003) Female sexuality. Med Clin North Am 87:1077–90
141. Goetsch M (2005) The effect of total hysterectomy on specific sexual sensations. Am J Obstet Gynecol 192:1922–7
142. Anastasiou I, Yiannopoulou KG, Mihalakis A, Hatziandonakis N, Constantinides C (2011) Symptoms of acute posttraumatic stress disorder in prostate cancer patients following radical prostatectomy. Am J Mens Health 5(1):84–9
143. MacDonald R, Fink HA, Huckabay C, Monga M, Wilt TJ (2007) Pelvic floor muscle training to improve urinary incontinence after radical prostatectomy: a systematic review of effectiveness. BJU Int 100(1):76–81

144. Lee CT, Yeh CJ, Lee MC, Lin HS, Chen VC, Hsieh MH, Yen CH, Lai TJ (2012) Leisure activity, mobility limitation and stress as modifiable risk factors for depressive symptoms in the elderly: results of a national longitudinal study. Arch Gerontol Geriatr 54(2):e221–9
145. Kingsberg SA, Althof SE (2011) Satisfying sexual events as outcome measures in clinical trial of female sexual dysfunction. J Sex Med 8(12):3262–70
146. Kingsberg SA (2002) The impact of aging on sexual function in women and their partners. Arch Sex Behav 31(5):431–7

Genitourinary Trauma in Geriatric Patients

25

Joshua A. Broghammer, Andrew P. Windsperger, and Sean P. Elliott

Introduction and Epidemiology of Geriatric Trauma

Every year, millions of people suffer traumatic, unintentional injuries. This not only takes a physical and emotional toll on the victims and their families but also creates a significant economic impact on the healthcare system. In 2011, trauma in the USA accounted for nearly 38 million injury episodes and 180,000 unintentional deaths [1]. Annually, trauma results in two million hospital admissions [2]. In 2010, traumatic injury accounted for nearly 31 % of life years lost, which is more than cancer (17 %) and heart disease (12 %) combined [3]. Traditionally viewed as a disease of the young, unintentional injuries are the leading cause of death in those under the age of 45 [2].

Trauma is less common among those 65 or older but still remains the ninth leading overall cause of death trailing behind heart disease, malignancy, chronic respiratory disease, stroke, Alzheimer's disease, diabetes, influenza, pneumonia, and nephritis [4]. Despite this, over 40,000 seniors die of unintentional injuries annually, which outranks septicemia. The majority of injury-related deaths in the geriatric population result from falls, motor vehicle injuries, and firearm-related suicides [5]. When looking at injury-related deaths, suicide accounts for more than 12 % of all geriatric deaths associated with trauma [6]. Suicide by firearm, poisoning, and suffocation rank fourth, ninth, and tenth, respectively, overall in unintentional injury-related elderly deaths. Homicide is a relatively rare phenomenon in the geriatric population and does not make the top ten causes for injury-related geriatric deaths. In comparison, homicide by firearms alone is the fifth leading cause of injury-related death in the general population.

Unintentional falls account for the greatest number of nonfatal emergency department visits for elderly patients with over 2.3 million visits per year [7]. Motor vehicle collisions rank fourth on the list, which is similar to the remaining driving age population (aged 15 or older) [7], despite stereotypes that older drivers are more unsafe [8]. Unintentional poisoning ranks higher in the elderly population than any other age group [7].

The financial cost of injury is significant. In any given year, approximately 17 % of seniors will present to the emergency department for acute care of unintentional injuries [2]. This percentage is similar across all age groups which are comprised of those aged 10 and older. In 2000, the burden of spending for all injury-related medical services totaled 10 % of the total healthcare expenditures in

J.A. Broghammer, M.D., F.A.C.S. (✉)
A.P. Windsperger, M.D.
Department of Urology, University of Kansas Medical Center, Kansas City, KS, USA
e-mail: jbroghammer@kumc.edu

S.P. Elliott, M.D., M.S., F.A.C.S.
Department of Urology, University of Minnesota Medical Center, Fairview, Minneapolis, MN, USA
e-mail: selliott@umn.edu

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_25,

the USA. That year, the cost of treating geriatric patients alone was 29 billion dollars. Injury-related spending is similar to costs associated with both obesity and smoking [2]. A geriatric patient will be treated in the emergency department for a fall-related injury every 17 s. Every 30 s an elderly patient will die from a fall injury [9]. In 2005, the total cost of fall-related healthcare spending was $23.6 billion. In that same time, fall-related fatalities cost $349 million.

Much of the focus on trauma and injury care is rooted in identification of risk factors, developing prevention efforts, providing education, and ensuring early adoption of preventive measures [2]. Falls are a focus of preventable injury and death among the geriatric population since they are the most frequent injury mechanism to elderly patients [10]. Many interventions have included reduction of psychotropic drugs, strength and balance training, home hazard assessment, correction of cardiac pacing conditions, and treatment of vitamin D with or without calcium supplementation to counter osteoporosis [11]. Elder drivers are also a key focus of injury prevention since motor vehicle trauma is the second highest cause of injury-related death. Motor vehicle deaths per mile traveled increase dramatically in those 75 or older [12]. Attempts at intervention involve neurocognitive testing, screening of vision impairment especially when combined with hearing loss, and implementation of a cognitive training program [13–16].

Outcomes of Geriatric Trauma Patients

The geriatric patient can create a unique and often difficult clinical problem for the trauma team. The outcome of traumatically injured seniors is worse than their younger counterparts with a nearly twofold increased risk of mortality and overall longer hospital stays [17]. Geriatric patients also are more likely to suffer late mortality when compared to younger, injury severity-matched controls [18]. Preexisting conditions play a role in worse outcomes for elder patients presenting with traumatic injuries. The odd ratio for mortality is increased in those with liver dysfunction (5.1), renal disease (3.1), cancer (1.8), and chronic steroid use (1.6) [19]. Some factors influencing mortality in the geriatric population include the need for transfusion and fluid resuscitation [20]. Patients who undergo a general surgical procedure are 2.5 times more likely to die. Injury severity score is likely to predict respiratory complications, while transfusion predicts myocardial infarction, and both transfusion and surgery predict sepsis [20]. The "super elderly" population, or those people defined as age 80 and older, are especially at risk from traumatic injuries. Compared to younger geriatric patients, these "super elderly" patients have an adjusted odds ratio for hospital mortality of 13.4 % versus 7.7 %, were more likely to die from withdrawal of medical support, and have nonroutine discharges [21]. Adjusted risks factors to mortality in the very elderly are head trauma, overall injury severity, and admission to non-verified trauma hospitals [22].

Elderly trauma patients tend to be under triaged upon arrival, which has a profound effect on survival. Approximately 15 % of geriatric patients presenting to the emergency department with an injury severity score (ISS) of >15 were under triaged with an evaluation by emergency department staff and subsequent trauma consultation instead of a full trauma team activation. After risk adjustment, this results in a greater increase in mortality [23]. Early identification of at-risk elderly patients with direct transport to level I trauma centers may reduce complications. Geriatric patients with pelvic fractures initially taken to non-tertiary medical centers had 54 % more complications during the first 2 weeks of hospitalization [24]. Centers with trauma-specific geriatric consultation teams have been shown to have improved outcomes which may account for the differences seen in improvement in care at level 1 trauma centers. Geriatric consultation services are able to offer assistance in the management of delirium, patient disposition, promotion of function and recovery, and geriatric-specific medication changes; decrease inappropriate medications; and assist with pain management [25]. Comparisons to patients admitted prior to implementation of a geriatric trauma consultation service show a reduction in episodes of delirium and decreased discharges to long-term care facilities [26].

Geriatric trauma is a relatively new scientific field, just in its infancy, and the paucity of data makes it difficult to draw conclusions. Prospective trials are needed to develop guidelines and practical management strategies for geriatric patients. The Eastern Association for the Surgery of Trauma (EAST) has developed guidelines for care of elderly trauma patients [27]. Evidence supports direct triage to a trauma center and patients over 55 are often under triaged. Advanced patient age alone is not a poor predictor of outcome if all other factors are equal. Preexisting conditions and complications contribute to greater hospital stays in the elderly population compared to younger patients. A Glasgow Coma Score of <8, base deficit of less than or equal to 6, Trauma Score <7, and respiratory rate < 10 have been shown to have a dismal prognosis, and consideration for limiting aggressive interventions should be undertaken. However, these recommendations are based on Class III data and as a result should be applied cautiously, especially because up to 85 % of geriatric trauma patients will return to independent function after their hospitalization [27].

Geriatric Renal Trauma

Epidemiology, Etiology, and Classification of Renal Injuries

Renal injury comprises the majority of all genitourinary injuries and is present in up to 3 % of all trauma cases [28]. It is the most commonly injured sold organ [29]. The majority (95 %) of renal trauma is caused by blunt abdominal trauma [30], but some series from the military and urban trauma centers overrepresent penetrating mechanisms due to their patient population [31]. Surveying the National Trauma Bank to compare the geriatric population to the remainder of the adult population reveals similar rates of renal injury between both groups [32]. Although the surgical intervention rates were higher in geriatric patients for both blunt (27.3 % versus 17.6 %) and penetrating (40.0 % and 23.1 %) mechanisms, these differences did not prove to be statistically significant.

Renal injuries are classified according to the American Association for the Surgery of Trauma (AAST) (Fig. 25.1) [33]. The classification system has proven to be an excellent predictor in the outcomes of renal trauma [34, 35]. Minor renal injuries are considered grade I–III and consist of contusions (grade I), small laceration (grade II), and lacerations of 1 cm or more which do not involve the collecting system (grade III). Grade IV injuries are comprised of lacerations involving the collecting system or renal vascular injuries with contained hemorrhage. Grade V injuries are life threatening and include disruptions of the renal hilum and shattered kidneys. Recent controversy has surrounded the application of the renal injury grading system as the literature suggests varying outcomes in the nonoperative management of grade V injuries. There is undoubtedly misapplication of the term "shattered kidney" to a kidney with multiple lacerations. Revisions have been proposed to the renal injury classification system to clarify the severity of kidney injury and develop better management strategies in high-grade injuries [36]. In general, geriatric patients have a higher rate of mortality per renal injury grade when compared to non-geriatric patients [32].

Diagnosis of Renal Trauma

Patient history and the mechanism of injury should direct the clinical evaluation of renal trauma. Care and attention should be first paid to core principles of trauma management including airway establishment, fluid resuscitation, and injury assessment. Vital signs should be continuously monitored. Shock is defined as a systolic blood pressure (SBP) less than 90 and needs to be aggressively managed. Rapid deceleration events such as falls from heights, high-impact motor vehicle collisions or those involving pedestrians, blows to the flank, and penetrating injuries with a flank trajectory should all be evaluated [37].

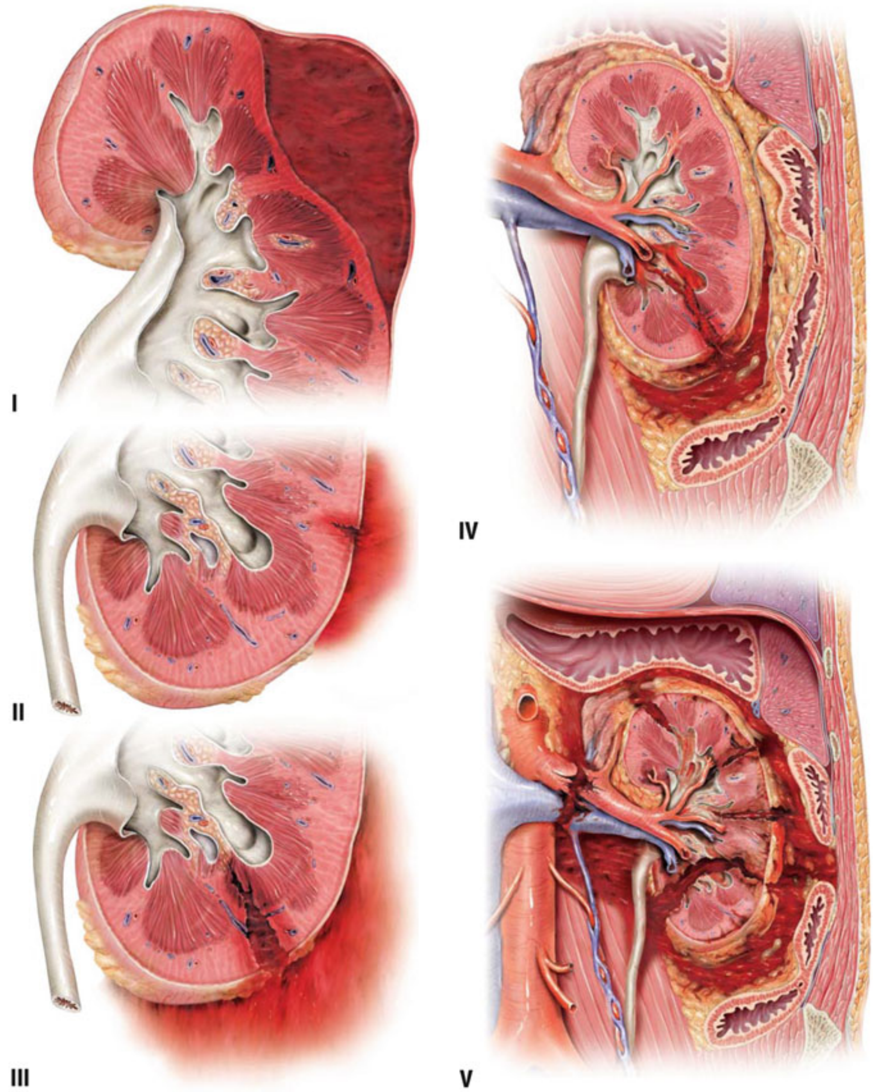


Fig. 25.1 American Association for the Surgery of Trauma (AAST) renal injury grading system [33]. *Picture from Serafetinides E. Renal Trauma. In: Hohenfellner M, Santucci RA, editors. Emergencies in Urology. New York: Springer; 2007: 207, Fig. 15.4.6I–V* (© *Hohenfellner 2007*)

Physical exam findings suggestive of injury include flank or abdominal tenderness, palpable abdominal mass, flank ecchymosis, ipsilateral rib fractures, or entrance/exit wounds of the lower thorax, flank, or upper abdomen/back.

Hematuria is a harbinger of renal injury. Patients should undergo a urinalysis with microscopy to evaluate the presence of blood in the urine. Gross hematuria or the presence of microscopic hematuria associated with an episode of shock necessitates radiological evaluation in the stable patient [29, 38]. Microscopic hematuria is defined as greater than five red blood cells per high-powered field (rbc/hpf). It is important to note that although hematuria predicts renal injury, the degree of hematuria has no correlation to the severity of renal injury [39]. Radiologic evaluation should be considered in those patients with severe associated injuries or those with an injury mechanism suspicious for renal trauma regardless of hematuria status.

The imaging study of choice for the evaluation of renal trauma is the computed tomography (CT) scan which has largely replaced the intravenous pyelogram (IVP) [40]. CT scans should be performed in all patients with suspected renal trauma who are hemodynamically stable. The CT scan should be performed with the administration of intravenous contrast and imaging taken during a venous phase and with 5–10 min delayed studies to allow the excretion of contrast. This is essential to detect grade IV injuries to the collecting system or associated ureteral injuries.

Recent efforts have been made to determine CT findings which may predict those patients that will require operative intervention or treatment with angiographic embolization. Dugi et al. demonstrated three predictive factors for intervention in patients with continued renal bleeding which included medial renal laceration, large perirenal hematoma, and intravascular extravasation of contrast. Hematoma and active extravasation of contrast have been found to be good predictors for renal intervention in other series [41, 42].

Management of Renal Trauma

The management of renal trauma has undergone a paradigm shift over the last several decades. Renal injuries were previously treated with operative intervention, but a growing body of literature has shown that conservative or nonoperative management has proven to be safe and effective [43, 44]. Traditionally, penetrating injuries to the kidney have required exploration, but those patients with adequate injury staging and no additional indications for laparotomy can be monitored [45, 46]. Most renal injuries are low grade and can be managed nonoperatively. Higher grade injuries treated conservatively should be monitored with serial hematocrits and bed rest until gross hematuria resolves. Reimaging grade IV injuries to monitor urine leak has been performed in some series, but management is often dictated by patient symptoms of decreasing hematocrit, fevers, flank pain, etc.

Despite the success of nonoperative management, studies show that nephrectomy remains the most common operation for renal trauma [47]. Exploratory laparotomy and surgical exploration of the kidney are likely to result in unnecessary, iatrogenic nephrectomy. Review of the National Trauma Data Bank by Wessells et al. reveals that the operative rate for renal trauma is 23 % with a resulting nephrectomy rate of 64 % [47]. A more in-depth review of the National Trauma Data Bank looking at outcomes for geriatric renal trauma found that nephrectomy rates for geriatric renal injury patients were nearly double when compared to their non-geriatric counterparts, although these findings were not considered statistically significant [32]. This is somewhat concerning as elderly patients have higher rates of renal insufficiency compared to younger patients. Institutions have shown that adoption of a nonoperative management strategy reduces nephrectomy rates and lowers hospital length of stay [48, 49].

In the modern era, surgical intervention for renal injury should be prompted primarily due to life-threatening hemorrhage. Intervention is required for patients in shock secondary to renal bleeding, intraoperative discovery of an expanding hematoma, or for those patients with persistent transfusion requirements in the face of hemodynamic instability. Other absolute indications for surgery include ureteral pelvic junction injury (Fig. 25.2), renovascular injury, and failure of nonoperative management. Relative indications for surgical exploration include adjacent

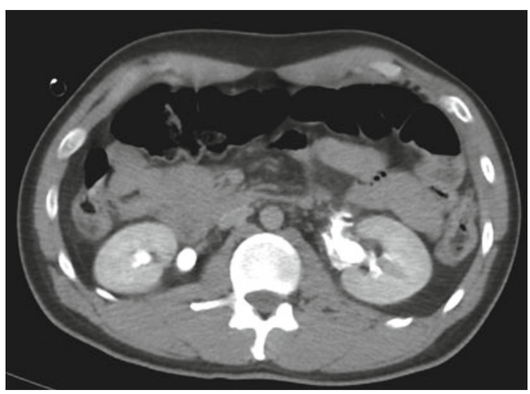


Fig. 25.2 Medial extravasation of contrast from a left kidney indicative of a renal pelvis injury. Note the intact, uninjured renal parenchyma and lack of perinephric hematoma

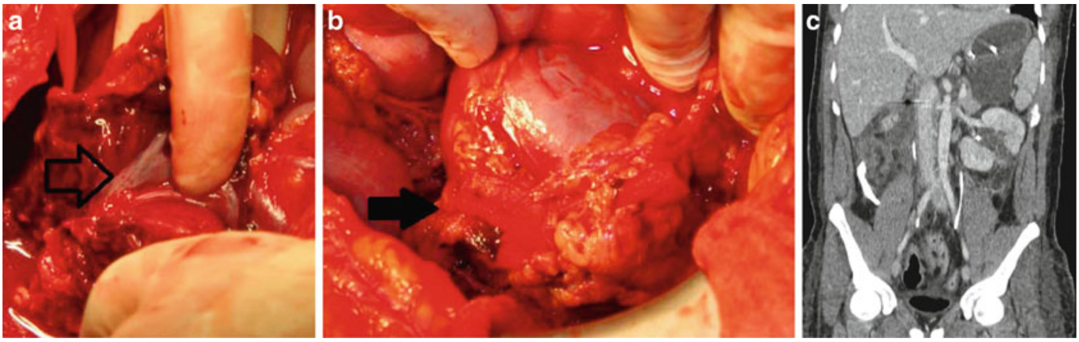


Fig. 25.3 (**a**) Severe grade IV renal injury with exposure of collecting system (*hollow arrow*). (**b**) Grade IV renal injury after repair with a gelatin bolster (*solid arrow*). (**c**) Postoperative CT scan demonstrating repair with gelatin bolster in place. A ureteral stent has been placed to help with renal drainage

organ injury to either bowel or pancreas, as well as devitalized segments of kidney [50–52]. These accompanying injuries increase the risk of infection, prevent renal healing, and may put a patient at risk for failure of conservative treatment.

A one-shot IVP should be considered in those patients brought to the operating room for emergent exploration without proper radiologic staging [53]. This is performed by the injection of 2 mg/kg of intravenous contrast with a 10 min delayed film. Although controversial, it provides information about the presence and function of an uninjured, contralateral kidney. Injury staging with one-shot IVP is often inconclusive but can provide enough information in up to a third of patients to avoid renal exploration [54]. Intraoperative management of renal injuries should consist of examination of the retroperitoneum. Expanding or pulsatile hematomas require surgical exploration. Controversy exists about the need for early vascular control of the aorta and vena cava prior to opening of the retroperitoneum, but one randomized controlled trial does not show an overall benefit [55]. Severe grade V injuries typically result in nephrectomy due to the magnitude of associated bleeding. There are some cases of conservatively managed grade V injuries, but these series should be viewed cautiously as kidneys with multiple, deep lacerations are often misclassified as grade V but do not truly represent "shattered" kidneys. Renovascular injuries are most often treated with nephrectomy due to bleeding but repair of the renal vasculature may be considered in the face of a solitary kidney. Salvage rates remain low at 40 % in the most expert hands [56]. Nephrectomy may be a better option as the complication risk increases up to 15-fold [57].

An attempt should be made at renal salvage and reconstruction when possible [58]. Irreparable renal injury with persistent bleeding should be treated with nephrectomy. Renal exposure is obtained through a midline incision. The colon is mobilized off the underlying Gerota's fascia. Temporary occlusion of the renal hilum is performed to control excess bleeding as needed. Judicious debridement of devitalized tissue is performed. Injuries to the collecting system should be closed in a watertight fashion with small, self-absorbable sutures. The renal parenchyma is reapproximated over a bolster of gelatin or cellulose foam to tamponade bleeding. The renal capsule is then closed over the bolster with self-absorbable 2-0 suture (Fig. 25.3). If the injury is to an upper or lower pole and reconstruction is not possible, a partial nephrectomy is completed with removal of the injured segment and closure of collecting system. The repair is then covered with surrounding omentum to help aid in healing. Retroperitoneal drains should be left to both treat and monitor for urine leaks.

Complications of Renal Trauma

Renal injuries initially managed nonoperatively may require intervention when complications arise. Urinary extravasation is the most common complication and will spontaneously resolve in up to 87 % of patients with grade IV injuries [59]. Those that do not are managed with ureteral stenting. Persistent urinoma can be treated with percutaneous drainage as can perirenal abscess. Delayed renal bleeds have been shown to occur and are often associated with pseudoaneurysm of the renal artery. The majority will respond to angiography with super selective embolization [60, 61]. Regardless of complications, the majority of renal injury results in a salvageable kidney [61].

Geriatric Ureteral Trauma

Epidemiology, Etiology, and Presentation of Ureteral Injuries

The ureters are well protected in the retroperitoneum and injury is unusual, representing 1–3 % of all genitourinary injuries from external violent trauma [62]. Furthermore, only 2–3 % of all gunshot wounds to the abdomen result in ureteral injury [63, 64]. A high index of suspicion is required because no physical findings, laboratory data, or imaging studies are particularly sensitive for the detection of ureteral trauma.

Penetrating trauma is a more frequent etiology of ureteral injury (62–97 %) compared to blunt trauma and is most commonly due to gunshot wound [63, 65–79]. Slightly lower rates of ureteral injury in geriatric patients, with 1.7 % in those >65 years old compared to 2.6 % in those <65 years old, may reflect the lower incidence of firearm trauma in this population [80].

The mechanism of ureteral injury significantly impacts the type of injury and repair. Gunshot wounds result in significant tissue necrosis. Resection of affected ureter can result in a longer defect and a more complex repair. In contrast, blunt ureteral injuries result in avulsion at fixed points along the course of the ureter such as the ureteropelvic junction and can sometimes be managed simply with stenting.

Hematuria is present in only 75 % of cases, making it an insensitive test. In many cases, patients will undergo abdominal imaging with computerized tomography (CT) given hematuria or mechanism. However, it must be remembered to obtain a delayed excretory urogram if a ureteral injury is suspected. When this is properly performed, sensitivity can be as high as 100 % [62, 81]. However, patients with gunshot wound to the abdomen will often proceed directly to the operating room in which case the surgeon must carefully inspect the ureter if there is evidence of trauma in the vicinity of the ureter. In fact, in expert hands, the sensitivity of operative exploration is 89 % [82]. Unfortunately, an on-the-table "one-shot" IVP is not sensitive, with only 7 of 19 positive in a study by Elliott and McAninch [62]. The location of ureteral injury is fully distributed along the course of the ureter, with 37 % involving the upper ureter, 31 % in the middle portion, and 32 % occurring in the lower ureter [62].

The acuity of the patient should be considered in selecting the type of repair. Hypotension is present in 56 % of cases and major organ injury accompanies ureteral injury in 57–87 % [62, 83]. In the setting of gunshot wound, these are typically small or large bowel injuries or vascular injuries. In contrast, with blunt trauma, which is more typical among geriatric patients, these are more likely to be pelvic fractures or vascular injuries [62, 65, 83]. In the acutely ill patient, a heroic attempt at a complex reconstruction such as a Boari flap may not be appropriate and it is sometimes better to ligate the ureter or perform a cutaneous ureterostomy.

Management

Intraoperative Evaluation

When the path of the missile is in proximity of the ureter, the ureter should be mobilized along its course and examined. The wall of the ureter should be inspected for continuity, hemorrhage, and contusion. Neither blind palpation nor the observation of ureteral peristalsis is a reliable indicator of a healthy ureter. A contused ureter after gunshot wound may suffer delayed necrosis for up to 2 cm beyond any evidence of gross injury; therefore, direct inspection is crucial. Dye tests, although helpful, should not be used as a substitute for direct inspection. Indigo carmine or methylene blue can be given intravenously and the ureters inspected for leakage of dye. However, in the hypotensive trauma patient, it is often more expeditious to inject the dye directly into the renal pelvis or in a retrograde fashion if the bladder is open. The link between missed injuries and complications is well established; therefore, a thorough assessment is imperative [62].

Partial ureteral transections due to blunt trauma or stab wound can be closed primarily, but all gunshot wounds or any transection of greater than 50 % require more complex reconstruction. The principles of reconstruction include mobilization of the ureter with preservation of the adventitia, debridement of nonviable tissue to a bleeding edge, and a spatulated, tension-free anastomosis over an internal stent using fine absorbable suture. Omental interposition can be used to separate the repair from associated intra-abdominal injuries or intestinal or vaginal suture lines. The surrounding retroperitoneum should be drained with closed suction drainage.

Distal Ureteral Injuries

Ureteroneocystostomy

Approximately one-third of traumatic injuries occur in the distal ureter. These injuries should, as a rule, be repaired by ureteroneocystostomy. Associated vascular injuries and difficult exposure preclude primary ureteroureterostomy. The damaged distal ureter may be left intact without consequence, unless vesicoureteral reflux is suspected. The spatulated proximal ureter may be reimplanted into the bladder in a refluxing or tunneled manner, but a refluxing anastomosis is quicker and thus most appropriate in geriatric patients (Fig. 25.4). This can usually be done extravesically to minimize morbidity. Bladder drainage is ensured by urethral catheter, suprapubic tube, or both. If using both, then one can be removed when the urine is clear. The remaining catheter can be removed in 7–10 days. If the bladder was opened completely, then a cystogram should be performed before catheter removal. The stent should remain for 4–8 weeks.

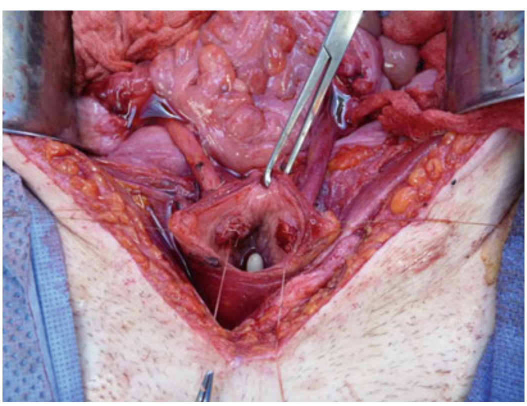


Fig. 25.4 Bilateral ureteroneocystostomies using a refluxing intravesical approach

Vesico-Psoas Hitch

More extensive loss of distal ureteral length can be bridged with a vesico-psoas hitch. The bladder

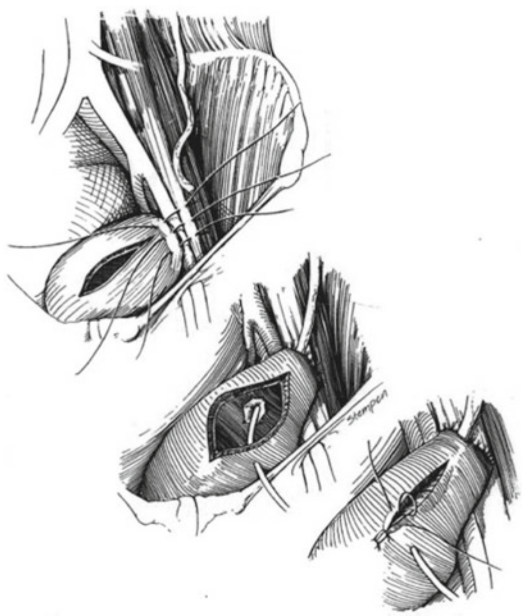


Fig. 25.5 Ureteroneocystostomy with psoas hitch—the bladder is opened and two fingers are inserted to aid retraction of the bladder up to the psoas muscle. Nonabsorbable sutures are placed through the serosa and muscle without entering the mucosa and used to pex the bladder to psoas fascia without injuring the genitofemoral nerve. *Picture from Presti JC, Carroll PR. Ureteral and Renal Pelvic Trauma Diagnosis and Management. In: McAninch JW, editor. Traumatic and Reconstructive Urology. Philadelphia: W.B. Saunders; 1996: 177, Fig. 13-5*

is mobilized in the space of Retzius. Ligating the contralateral superior vesical pedicle aids in mobilization. The bladder is opened vertically and tented up against the ipsilateral psoas muscle by placing two fingers in the bladder. Nonabsorbable monofilament sutures are placed in the bladder wall outside the transitional epithelium and in the psoas muscle away from the genitofemoral nerve (Fig. 25.5). The ureter is reimplanted into the bladder as described above.

Upper and Mid-Ureteral Injuries

Ureteroureterostomy

The length of injury in upper ureteral trauma is frequently short and is usually repaired by ureteroureterostomy (Fig. 25.6) [62, 63, 68, 69, 72, 74, 77–79, 82, 84]. Proximal ureteral stent placement through the half-completed anastomosis is familiar to urologists and is straightforward. Distal placement is more challenging. One can fill the bladder with methylene blue through the urethral catheter and observe reflux of blue urine up the stent. Alternatively, cystoscopy can be done to confirm stent position. An abdominal plain film should be performed postoperatively to confirm stent positioning.

Transureteroureterostomy

Due to the typically short length of ureteral loss, transureteroureterostomy is rarely indicated. Occasionally, after more extensive ureteral loss or when pelvic injuries preclude ureteroneocystostomy, such as with rectal injury, major vascular injury, or extensive bladder injury, transureteroureterostomy is an

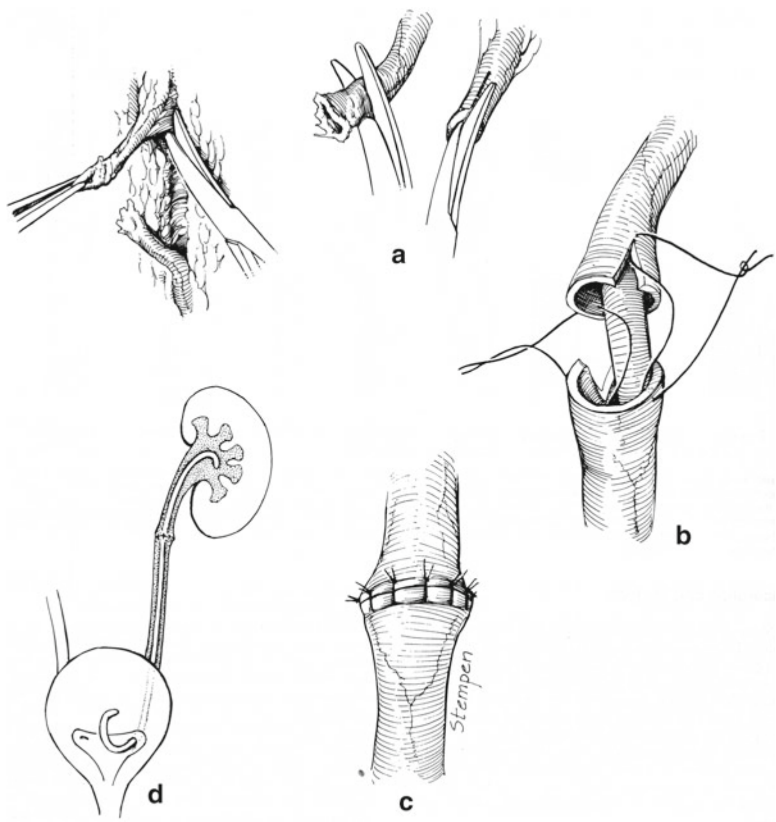


Fig. 25.6 Ureteroureterostomy-steps (from *upper left image*, clockwise) include ureteral moblizaton. (**a**) Debridement and spatulation. (**b**) Alignment of repair over a ureteral stent. (**c**) Closure using fine, interrupted, absorbable suture. (**d**) Completed repair

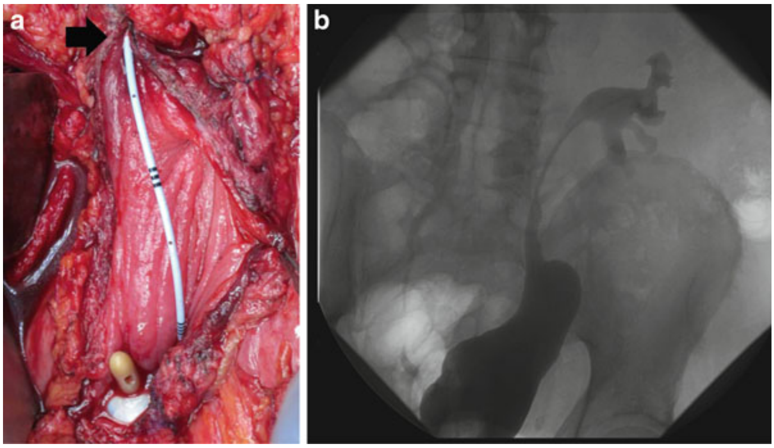


Fig. 25.7 (**a**) Boari flap prior to tubularization. Proximal ureteral anastomosis is designated by the *black arrow*. A ureteral stent crosses the defect. The bladder is marked by the presence of the Foley catheter. (**b**) Boari flap repair seen on cystography

excellent option. The donor ureter should be generously mobilized without compromising the longitudinal adventitial vessels. The donor ureter should be tunneled through the colon mesentery superior to the inferior mesenteric artery in order to avoid kinking. The recipient ureter is not mobilized and a small ellipse is excised from the medial wall. The donor ureter is spatulated and an end to side anastomosis is performed. A double-J stent should be placed from the donor kidney, across the anastomosis, and down to the bladder. Relative contraindications include a history of nephrolithiasis or pelvic radiation.

Repair of Long Segment Ureteral Injury (Boari Flap, Autotransplantation, and Ileal Ureter)

The Boari tubularized bladder flap can bridge long ureteral gaps. However, it is time consuming and thus has little role in the acute trauma setting (Fig. 25.7a+b). Similarly, autotransplantation and ileal ureter are not appropriate in the acute trauma setting. Such extensive ureteral defects should be managed with nephrectomy or, if later reconstruction seems appropriate, temporized with ureteral ligation and a nephrostomy tube. Intraoperative placement of a nephrostomy tube is challenging. It is preferable to await the development of hydronephrosis and place the tube in the radiology suite in about 2 days.

Complications of Ureteral Trauma

Complications occur in approximately 25 % of ureteral injuries [62, 63, 66, 71, 72, 77, 79, 82, 85, 86] and the risk is increased with delayed recognition of ureteral trauma [62, 87]. Prolonged urinary leakage at the anastomosis is the most common acute genitourinary complication. Placing a ureteral stent and a retroperitoneal drain at the time of repair can help prevent urinoma, abscess, or peritonitis that can result from leakage. Delayed recognition of undrained leakage at the anastomosis is associated with additional morbidity such as sepsis, more complicated reconstruction, and prolonged hospital stay [62, 74]. Follow-up can be particularly difficult in the trauma setting and a true assessment of the incidence of long-term complications is difficult. However, innumerable case reports of forgotten ureteral stents after trauma suggest that this is not an uncommon scenario. Non-urologic morbidity and mortality is not uncommon due to the severity of injury in patients with ureteral injury, with geriatric trauma patients being at particularly high risk [80].

Ureteral trauma is rare. Missed ureteral injuries are associated with increased morbidity;

therefore, a high index of suspicion is warranted. The urologist should be familiar with several methods by which to identify a ureteral injury and the evaluation should be tailored to the clinical situation. Most ureteral injuries are short transections and can be repaired with debridement and ureteroureterostomy in the proximal and mid ureter or ureteroneocystostomy in the distal ureter.

Pelvic Ring Fractures and Associated Genitourinary Injuries

Pelvic ring fractures represent a source of substantial morbidity and mortality for patients of all ages but can be particularly devastating to the geriatric trauma patient. Pelvic fractures carry an associated 5–20 % risk of mortality due to hemorrhage and associated organ failure and place genitourinary structures including the bladder and urethra at risk of subsequent injury [88]. Identification of associated injuries, timely management, and aggressive stabilization remain keys to successful management of patients with pelvic ring fractures.

The forces required to cause a pelvic ring fracture are substantial and are often associated with other injuries such as genitourinary injury, intra-abdominal injury, or long bone fracture. Mechanisms of injury include motor vehicle collision, pedestrian versus motor vehicle collision, falls, penetrating trauma, and industrial accidents including pelvic crush injury. In the elderly adult, osteoporotic changes may also predispose to sustaining pelvic fractures from low-impact accidents such as falls from standing height. In fact, blunt trauma from falls has been identified as the leading cause of pelvic fracture in the geriatric population, compared to younger adults where high-impact accidents such as motor vehicle collisions predominate [89, 90].

Epidemiology

The incidence of pelvic fracture rises with increasing age. For the population as a whole, the incidence is 20–37/100,000 per year [91, 92].

Table 25.1 Tile classification system for pelvic fracture (*Reprinted with permission from* [96])

Type A: Stable (posterior arch intact)	
A1	Avulsion injury
A2	Iliac wing or anterior arch fracture caused by a direct blow
A3	Transverse sacrococcygeal fracture
Type B: Partially stable (incomplete disruption of posterior arch)	
B1	Open book injury (external rotation)
B2	Lateral compression injury (internal rotation)
B2-1	Ipsilateral anterior and posterior injuries
B2-2	Contralateral (bucket-handle) injuries
B3	Bilateral
Type C: Unstable (complete disruption of posterior arch)	
C1	Unilateral
C1-1	Iliac fracture
C1-2	Sacroiliac fracture dislocation
C1-3	Sacral fracture
C2	Bilateral, with one side type B and one side type C
C3	Bilateral

In patients >60 years of age, that incidence rises to 92/100,000 per year [93]. This number increases to 446/100,000 per year in patients 85 years of age or older [91]. Sixty-four percent of all pelvic fractures are classified as osteoporotic fractures of those occurring in patients >65 years of age after simple falls. Similarly, 94 % of pelvic fractures sustained in patients over age 60 are defined as osteoporotic fractures [93]. Women suffer pelvic fracture more commonly than men with a ratio of 1.25:1 in ages 60–69 years and 2.7:1 in patients over 80 years of age [93]. An increased incidence of simple falls is seen with advancing age, with 25 % of falls resulting in injury and nearly 6 % leading to osteoporotic fracture [94, 95].

Classification

Pelvic fractures may be classified by one of two systems based upon the mechanism of injury, fracture pattern, and stability. The Tile classification system (Table 25.1) is based upon the integrity and stability of the posterior sacroiliac complex, whereas the Young–Burgess classification system

Table 25.2 Young–Burgess classification system for pelvic fracture (Reprinted with permission from [97])

Anterior–posterior compression (APC)	APC I (stable)	Symphysis widening <2.5 cm
	APC II (partial stability)	Symphysis widening >2.5 cm. Anterior SI joint diastasis
	APC III (complete instability)	Disruption of anterior and posterior SI ligaments (SI dislocation)
Lateral compression (LC)	LC I (stable)	Oblique ramus fracture and ipsilateral anterior sacral ala compression fracture
	LC II (partial stability)	Rami fracture and ipsilateral posterior ilium fracture dislocation (crescent fracture)
	LC III (complete instability)	Ipsilateral lateral compression and contralateral APC (windswept pelvis)
Vertical shear (VS)	VS (complete instability)	Posterior and superior directed force (Malgaigne fracture)
Combined mechanical injury	CM (complete instability)	Combination injury

(Table 25.2) categorizes fractures via direction of force [96–98]. These systems assist in determining appropriate treatment and expected outcome, as well as improving communication of injury pattern. For the purposes of this review, all type 3 injuries, as well as vertical shear and combined mechanical injuries, should be considered the most severe types of pelvic fractures as they are associated with the highest risk of hemorrhage, morbidity, and mortality [96, 98].

Diagnosis

Imaging represents an essential component of evaluation and management of the patient with a pelvic fracture. In the traumatic setting, patients often undergo abdominopelvic imaging as a routine part of the trauma survey. In patients in whom there exists a suspicion for pelvic fracture, plain radiographs of the pelvis and hip may assist in initial diagnosis. Geriatric patients who present for evaluation after falls may endorse inability to bear weight, directed hip pain, or inguinal pain, all of which should prompt evaluation with plain radiographs. For patients with more complex injuries, or for patients with suspected occult injuries not visualized on plain film, computed tomography scans or magnetic resonance imaging may provide additional information. Physical examination findings associated with pelvic fracture such as hematoma or limb shortening may not be present in the elderly patient after simple falls [99].

Initial Management

High-energy, unstable pelvic fractures often require emergency management and intervention. Initial management should be directed toward patient resuscitation and stabilization. Reduction of the pelvic fracture or pelvic fixation may be indicated to limit persistent venous bleeding. Maneuvers may include application of a pelvic binder or pelvic sheet, placement of a pelvic clamp, or temporary external fixation. Conversely, interventional radiologic transcatheter pelvic embolization is often indicated for arterial sources of bleeding [100]. Pelvic fixation provides a limited benefit with regard to hemostasis in patients with an intact pelvic ring [99, 101].

Pelvic Fractures in Geriatric Patients Compared to Younger Adults

Previous research has focused on the key differences in pelvic fractures sustained by younger adults versus geriatric patients as well as differences in outcome. Older patients often have more medical comorbidities that complicate care and resuscitation and may lack the physiologic reserve seen in younger patients in response to injury. In comparison to younger patients, geriatric trauma patients have been reported to have higher rates of morbidity, mortality, and post-injury rehabilitation needs following traumatic accidents [102].

Comorbid conditions and age-related changes may impact outcomes following pelvic fracture in older adults. Osteoporosis has been implicated in the increasing incidence of pelvic fracture in the geriatric trauma patient. Despite this increased susceptibility, osteoporotic pelvic fractures still remain a marker of injury severity in elderly patients [103]. Age-related changes in soft tissue turgor and sarcopenia may lead to impaired mechanisms of tamponade of hemorrhage following pelvic fracture. Atherosclerotic changes associated with advancing age may also impede vasospasm and prolong bleeding. Geriatric patients may also be taking anticoagulants for comorbid conditions leading to additional bleeding concerns. A nearly eightfold increase in odds of pelvic hemorrhage has been described for patients over 55 years of age following pelvic fracture [104]. Comorbid conditions commonly seen in geriatric patients including cardiovascular disease may lead to impaired oxygen delivery and hypoperfusion of tissues following hemorrhage [105].

Pelvic fracture pattern has been shown to differ among younger patients versus elderly cohorts. Studies have demonstrated an increased incidence of up to five times the rate of lateral compression fractures in elderly patients versus younger patients. Pubic rami fractures are also more common in elderly patients. Patients sustaining severe pelvic injuries have been found to require blood transfusion in similar rates when comparing young and elderly patients. However, older patients over age 55 have been found to have significantly higher transfusion requirements following all pelvic fractures, leading some authors to advocate for liberal pelvic angiography and embolization in all elderly patients with significant pelvic trauma [106, 107].

In general, hypovolemic shock, head injury, injury severity score greater than or equal to 16, and higher velocity injury mechanisms carry an increased risk of death following hospital admission for pelvic fracture [108]. Several studies have described an increased risk of mortality from pelvic fracture with advancing age alone being a key independent risk factor. Age also remains a key risk factor for mortality following pelvic fracture, even after adjusting for injury severity score [105, 106]. Higher injury severity scores in elderly patients also predicted worse outcome and higher mortality, as would be expected.

A recent National Trauma Database review of pelvic fracture outcomes divided patients into three categories including younger adults (aged 18–64), elderly patients (aged 65–80), and octogenarians (aged > 80 years) [109]. The authors validated earlier findings of worsening mortality for older patients following pelvic fracture and described a 4.7-fold higher odds ratio of death and 4.57 odds of complication after pelvic fracture compared to younger adults. When comparing elderly patients and octogenarians, octogenarians had an increased odds ratio of mortality and severe complications. Elderly patients and octogenarians were less likely to present with injury severity scores above 16. The authors also noted that between ages 18 and 89 years, there is an approximate 1 % decrease in survivorship for every 10 additional years of age following pelvic fracture [109].

Pelvic Fracture and Genitourinary Injury

High-energy injury resulting in pelvic fracture places patients at risk for injury to genitourinary structures including the bladder and urethra. Injuries to the urethra may result in immediate and long-term sequelae including stricture, hemorrhage, fistula formation, incontinence and impotence, and infectious complications [110]. Bladder injuries, both intra- and extraperitoneal, may result in hemorrhage, infectious complications, and urinary extravasation with risk for fistula formation or urinary ascites [111, 112].

The reported incidence of urinary injury following pelvic fracture varies according to several series. The incidence of male urethral injury following pelvic fracture is estimated to be 1.6–25 %, whereas females have an incidence of <1 %–6 % [113, 114]. Bladder injury following pelvic fracture is associated with an incidence of 4.6–16 % [115]. The incidence of genitourinary injury remains similar across each of the common types of pelvic fracture including lateral compression, anterior–posterior, and vertical shear. In a prospective trial evaluating pelvic fracture subtype and subsequent risk

Table 25.3 Odds ratio of sustaining urethral injury based on underlying fracture patterns adapted from Koraitim et al. [113]

Type of fracture	Odds ratio of urethral injury
Single ramus	0.6
Ipsilateral rami	0.8
Malgaigne's (vertical shear)	3.4
Straddle	3.9
Straddle plus sacroiliac	24

of urethral injury, Koraitim reported the highest risk of urethral injury occurring in straddle fractures with associated diastasis of the sacroiliac joint, followed by straddle fracture alone and Malgaigne fracture (Table 25.3) [113, 116]. Pubic symphysis diastasis and widening of the sacroiliac joint have been reported to be predictors of bladder injury, whereas inferior and superior pubic rami fractures and pubic symphyseal widening are associated with urethral injury [113, 115, 117]. Isolated acetabular fractures are uncommonly associated with urethral or bladder injury [115, 118].

Geriatric Bladder Trauma

Epidemiology, Etiology, and Classification of Injuries

Most bladder injuries (70–88 %) are secondary to blunt rather than penetrating trauma [111, 119, 120]. This is likely to be particularly true of the geriatric trauma patient, in whom penetrating abdominal trauma is less common than in the younger patient. Pooling all ages together, bladder injuries occur in 1.6 % of blunt abdominal trauma [121] with 88–95 % due to pelvic fracture [111, 120]. Concomitant bladder injuries occur in about 5–10 % of all patients with pelvic fractures [122, 123]. Bladder trauma is relatively more common in the geriatric trauma patient compared to the younger trauma patient, representing 30 % of all genitourinary injuries in older adults and only 22 % in the younger cohort [32]. Of all bladder injuries, about 60 % are extraperitoneal, 30 % intraperitoneal, and 10 % are both intra- and extraperitoneal [111, 119, 120]. Associated bladder neck or urethral injury occurs in about 15 % [124–126]. Most of the above data come from single-institution case series at major trauma centers. In contrast, a review of data from the National Trauma Data Bank revealed that only 46 % of all bladder trauma was associated with pelvic fracture and that 86 % was extraperitoneal [127].

Intraperitoneal injuries occur when a blunt force causes a sudden rise in the bladder pressure and the bladder tears at the dome where the wall is relatively thin. The risk of this happening is particularly high when the bladder is full. It is unknown how the thin bladder wall of the elderly woman or the thickened bladder wall of the elderly man with bladder outlet obstruction affects risk of intraperitoneal rupture. Extraperitoneal injuries occur most commonly when a pelvic fracture causes either a laceration at ligament fixations between the bladder and the pelvic bone or a direct puncture injury from a bony fragment. Differentiating intra- from extraperitoneal injury is key, in that it dictates management.

Diagnosis of Bladder Trauma

A diagnosis of bladder injury should be suspected based upon history and mechanism of injury. Bladder trauma should be suspected in patients with lower abdominal trauma, pelvic fracture, penetrating injury with a pelvic trajectory, suprapubic pain, tenderness, or abdominal distension. Gross hematuria on a voided or catheterized specimen is universally present [123, 128]. Gross hematuria in the trauma patient should always prompt cystography. The degree of hematuria does not correlate with extent of injury, and microscopic hematuria should also raise the index of suspicion when correlated with mechanism and associated injuries. Cystography remains the standard when evaluating potential bladder trauma and can be performed as a plain film or a CT cystogram. However, there are key points to avoiding a missed injury in both of these cases. Adequate bladder distention with contrast media that is administered retrograde through a catheter is essential in evaluating for bladder

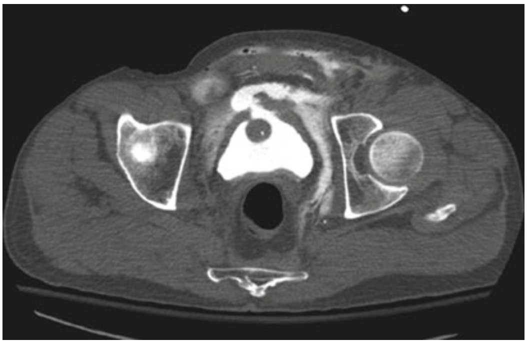


Fig. 25.8 CT cystogram of an extraperitoneal bladder rupture exhibiting the "molar tooth" sign. Lateral extravasation of contrast forms the "roots" of tooth while anterior extravasation forms the "crown"

injury, and a minimum of 350 mL of contrast instilled via gravity fill is recommended. For plain film cystography, it is essential that a post-drainage film or an oblique full film be taken in addition to the standard anteroposterior full film in order to rule out anterior or posterior wall injuries that might be hidden by the overlying contrast within the bladder [129]. For the CT cystogram, full distension with 350 mL of contrast is required, rather than simply clamping the catheter and allowing the intravenous contrast to be excreted into the bladder. The latter technique does not allow adequate bladder distension and is insufficient to rule out a bladder injury [130, 131]. Sonography is not a useful tool in bladder trauma diagnosis [132].

Cystographic images have several unique characteristics. Regardless of plain film or CT cystography, intraperitoneal bladder ruptures depict contrast outlining the intestines and inner lining of the peritoneal cavity. Extraperitoneal bladder ruptures on plain film cystography appear to have a "flame sign." Extraperitoneal ruptures on CT cystography appear as a "molar tooth sign" (Fig. 25.8).

Management

Extraperitoneal bladder injuries may often be managed conservatively with catheter drainage for 7–10 days. A cystogram should be performed at catheter removal to confirm resolution of the injury. Success rate with conservative management is 85 % [120, 133]. Absolute exceptions to conservative management of extraperitoneal injury include concomitant vaginal or rectal injury, intractable hematuria especially if it results in clot obstruction of the catheter, intrusion of bone or a foreign body into the bladder, gunshot wound, concomitant bladder neck injury, and a bladder injury that fails to heal after an adequate period of catheter drainage [133, 134]. Patients with bony fragments protruding into the bladder or adjacent organ injury maintain a higher risk of infection and poor spontaneous healing of the bladder injury [112]. Injuries at the bladder neck have been associated with an increased risk of prolonged urinary extravasation, risk of cavity or abscess formation, and a high risk of incontinence following convalescence [135]. A relative indication for repair includes performing concomitant cystorrhaphy at the time of other procedures such as exploratory laparotomy or open reduction with internal fixation of pelvic fractures. When repairing a posterior bladder laceration due to pelvic fracture, it is best to open the dome of the bladder and repair the injury from inside the bladder. This avoids mobilization of the bladder in the space of Retzius as that would risk liberation of the associated pelvic hematoma.

Intraperitoneal injuries should be expeditiously repaired. The rent in the bladder dome is always large and will not heal with catheter drainage alone. Urinary ascites may lead to peritonitis, abscess, and sepsis. The laceration can be repaired from the outside in one or two layers with absorbable suture. Laparoscopic repair is straightforward and is reasonable in the absence of associated injuries [136]. Foley catheter drainage after repair is needed to assure adequate drainage until the incision is healed. Use of a suprapubic tube is optional and generally does not improve outcomes, but can be used in combination with a urethral catheter to ensure adequate drainage, and provides a means for continuous bladder irrigation if needed.

Geriatric Urethral Trauma

Epidemiology, Etiology, and Classification of Injuries

The rate of urethral injury varies widely according to series and individual institutional reports and differs according to sex. For men, reported incidence of urethra injury with pelvic fracture varies from 1.6 % to up to 25 % [113, 137]. For women, the incidence ranges from 4.6 to 6 %, though there are far fewer reports of female urethral injury following pelvic fracture [138–140]. Male urethral injuries are classified by their location according to the perineal membrane at the junction of the bulbar and membranous portions of the urethra. Injuries distal to the perineal membrane are classified as occurring in the anterior urethra, whereas injuries of the membranous urethra and bulbomembranous junction are categorized as proximal or posterior urethra. Injuries may occur as a direct result of penetrating trauma or direct crush or may be related to the ligamentous support system of the urethra. Puboprostatic ligaments, Denonvilliers' fascia, lateral ligaments, and the endopelvic fascia all comprise portions of the urethral support system, and forces applied to these attachments and the urethra itself during trauma account for subsequent patterns of injury [141].

The American Association for the Surgery of Trauma has developed a grading scale for urethral injuries that includes both anterior and posterior injuries (Table 25.4). Grade I injuries are categorized as stretch injuries of the urethra and demonstrate elongation of the urethra on retrograde urethrography. Grade II injuries are described as urethral contusions and may be associated with blood at the urethral meatus in the absence of extravasation of contrast on urethrography. Grade III injuries show partial urethral disruption, with extravasation of contrast at the injury site with proximal filling of additional portions of the urethra or of the bladder. Complete urethral disruption is given a grade IV and includes extravasation of contrast at the site of injury with no evidence of proximal urethral or bladder filling. Grade V injuries include complete or partial urethral disruptions with concomitant bladder neck injury or injury to contiguous organs including the vagina or rectum [143].

Table 25.4 American Association for the Surgery of Trauma (AAST) urethral injury grading system (Reprinted with permission [142])

Classification of blunt anterior and posterior urethral injury by grade and management options			
Grade	**Description**	**Appearance**	**Management**
I	Stretch injury	Elongation of urethra without extravasation on urethrography	No treatment required
II	Contusion	Blood at the urethral meatus; no extravasation on urethrography	Grades II and III can be managed conservatively with suprapubic cystostomy or urethral catheterization
III	Partial disruption	Extravasation of contrast at injury site with contrast visualized in proximal urethra or bladder	
IV	Complete disruption	Extravasation of contrast at injury site without visualization of proximal urethra or anterior urethra or bladder	Suprapubic cystostomy and delayed repair; primary endoscopic realignment in selected patients with or without delayed repair
V	Complete or partial disruption of posterior urethra with associated tear of the bladder neck, rectum, or vagina	Extravasation of contrast at urethra injury site with/without presence of blood in the vaginal introitus in women; extravasation of contrast at bladder neck during suprapubic cystography with/without rectal or vaginal filling with contrast medium	Primary open repair

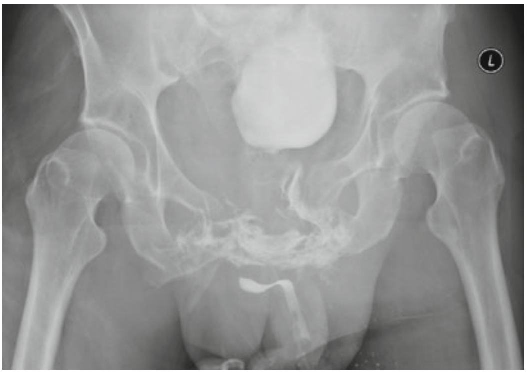


Fig. 25.9 A retrograde urethrogram demonstrating large pubic diastasis, extravasation of contrast, and a complete disruption injury of the membranous urethra with proximal migration of the bladder secondary to pelvic hematoma

Diagnosis of Urethral Trauma

A diagnosis of urethral injury should be suspected based upon history and mechanism of injury. Routine examination of the external genitalia, vagina and introitus, and rectum should be performed, as physical examination findings may raise the index of suspicion for injury. Blood at the urethral meatus; blood at the vaginal introitus, hematuria, and perineal, penile, or labial hematoma; and swelling all require urethral evaluation in order to rule out injury. Blood at the urethral meatus is present in 37–93 % of patients with a posterior urethral injury and in at least 75 % of patients with an anterior urethral injury [142]. Greater than 80 % of females with blood at the vaginal introitus and concomitant pelvic ring injury will have a coexisting urethral injury [114]. Imaging to determine urethral integrity is recommended prior to instrumentation or attempts at catheterization in patients with a high suspicion for injury.

Dynamic imaging including retrograde urethrogram plays an essential role in the diagnosis of urethral injury following pelvic trauma. Retrograde urethrogram should be performed with oblique views of the pelvis in order to evaluate the full length of the urethra (Fig. 25.9). Options for performing retrograde urethrogram include use of a catheter inserted into just the level of the fossa navicularis for injection or use of a Toomey or piston syringe with additional utilization of a gauze sponge for penile retraction and minimization of radiation exposure to the examiner's hands. Imaging may be obtained either via fluoroscopy if the patient remains stable enough for transport or via static imaging obtained in the trauma bay or intensive care unit (ICU). Findings on the retrograde urethrogram may assist in classification of the extent of urethral injury.

Acute Management of Urethral Trauma

Many urethral injuries may be managed via initial urethral or suprapubic catheter drainage, with plans for delayed repair via definitive urethroplasty. Grade I injuries require no directed treatment. Most anterior urethral injuries, including grades II and III injuries, are initially managed with indwelling urethral or suprapubic catheterization followed by delayed repair of any resultant urethral stricture. The standard for posterior urethral injury remains suprapubic cystostomy with delayed repair [141]. Patients with penetrating trauma to the urethra, including gunshot wounds or stab injuries, may be candidates for immediate repair depending on the degree of tissue loss and surrounding tissue damage [144]. Aggressive early operative intervention via primary urethroplasty is not recommended for the vast majority of injuries due to the extent of tissue damage immediately following pelvic trauma [143].

Primary urethral realignment may provide an alternative to delayed urethral reconstruction or improve the technical feasibility of urethroplasty following pelvic trauma. Urethral realignment may be performed up to 7 days following initial injury and is generally recommended after patients have been stabilized and any pelvic hematoma has been allowed to organize. Successful urethral realignment may be achieved by using an antegrade cystoscopic approach via a suprapubic cystotomy and retrograde cystoscopic approach via the urethra. A guidewire is passed between the two cystoscopes with the aid of fluorscopic guidance (Fig. 25.10). Though rates of urethral stricture formation following

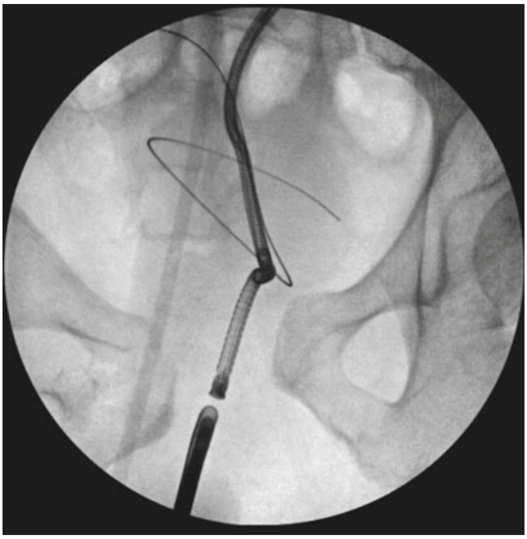


Fig. 25.10 Fluoroscopic images of a primary realignment by the use of one flexible cystoscope placed through the suprapubic cystostomy and a second rigid cystoscope placed through the penile urethra. A guide wire is seen curling in the bladder

primary urethral realignment remain high at 60–80 %, a small percentage of patients may achieve urethral patency via this technique, although close monitoring for failure is recommended [142, 145]. Additionally, primary urethral realignment may assist in performing delayed urethroplasty as the prostate and urethra are brought in closer continuity and alignment following catheter placement. Results of delayed urethroplasty for posterior urethral injuries are excellent with 95 % patency rates [146].

Geriatric Genital Trauma

The incidence of injury for genital trauma in the geriatric population is low when compared to non-geriatric patients (2 % vs. 12 %) [32]. The reason for this is likely due to lack of penetrating gun violence in the elderly population, retirement status reducing the incidence of industrial or farming accidents with mechanical equipment, and decreased use of motorized sport vehicles [147]. When evaluating the geriatric patient with genital trauma, it is important to determine the patient's desire for sexual function, fertility, and status of erectile function since many of these factors decline with age and impact the choice in genital reconstruction. Goals of genital reconstruction should include minimization of further injury, restoration of micturition, prevention of erectile dysfunction, preservation of reproductive function, and adequate cosmesis.

Genital Skin Loss

Most episodes of genital skin loss are caused by machinery related accidents in which mechanical traction removes loosely attached penile and scrotal skin or by genital burns. Treatment begins with debridement of devitalized tissue, copious irrigation, and dressing changes until the wound bed is well healed. Small lacerations can be closed primarily with self-absorbable suture. Up to 50 % of the scrotum can be lost and still closed primarily due to the elastic properties of scrotal skin. Larger wounds may require grafting with extra-genital skin. Circumferential injuries to the penile skin can result in lymphedema, and as such all skin found distal to the injury should be removed. Traditionally, full-thickness, unmeshed grafts have been placed on the penile shaft and split-thickness grafts over the scrotum [148]. Good success has been shown with meshed, unexpanded, split-thickness grafts to the penis [149].

Penile Injury

Penile trauma is less common in geriatric patients. The lack of gun violence reduces penetrating injuries to the penis and the increasing prevalence of erectile dysfunction reduces the rate of penile fractures in the elderly population. General principles of wound care apply to traumatic penile injuries and include judicious debridement of nonviable tissue, irrigation for decontamination, and primary repair of most injuries. Gunshot wounds to the penis should be almost universally explored except in those with superficial injuries [144]. Concomitant injuries to the urethra should be repaired at the same time and have low stricture rates if repaired acutely [150].

Penile fractures typically occur during intercourse when the erect penis slips out of the vagina and strikes the perineum resulting in buckling and tearing of the tunica albuginea of the corpus spongiosum. Physical exam findings include an "eggplant" penis which is a bruising of the penile shaft secondary to extravasation of blood. History of a popping sound and physical exam findings are usually all that are required for diagnosis. Concomitant urethral injuries can occur and are seen with blood at the meatus. Ultrasound and magnetic resonance imaging have been used as adjunctive measures to rule out an injury in equivocal cases but should not be employed routinely [151, 152]. Immediate surgical exploration of the penis should be performed and the tunica albuginea repaired with 3-0 absorbable sutures. Coexisting urethral injuries can be closed with fine absorbable sutures. Nonoperatively managed penile fractures have a greater rate of penile curvature and erectile dysfunction when compared to penile repairs [152, 153].

Penile amputation is a rare event and little is known about phallic amputation in the geriatric age group. The majority of cases stem from self-mutilation related to gender identity issues or acute psychotic episodes. It is imperative that the underlying cause of acute psychosis is addressed to prevent further self-harm. If the severed portion of the penis is recovered, it should be bagged and cooled in an ice water bath, and attempts should be made to reconstruct the penis. Microvascular reconstruction of the dorsal vasculature and nerves has been shown to have better outcomes than macroscopic replantation alone. The urethra is reanastomosed over a catheter with subsequent repair of the corporal bodies. Microscopic anastomosis of the dorsal arteries, the main dorsal vein, and dorsal nerves of the penis is performed [154]. If microsurgical capabilities are not available, macroscopic repair should be attempted. Results are surprisingly good with reasonable return of erections and sexual function.

Testicular Injury

Testicular injuries are uncommon due to mobility of the testicles within the scrotum and protection by the surrounding legs and pelvis. The majority of injuries will present with scrotal ecchymosis and swelling; however, it is important to note that neither corresponds to the degree of testicular injury. Blunt injuries to the testicle resulting in suspected testicular rupture or hematocele formation should be taken to the operating room for assessment of testicular damage [155]. Penetrating wounds to the scrotum with suspected testicular injury should also be universally explored. Equivocal cases or those in which the testicles appear to be uninjured can be assessed successfully with ultrasonography for testicular blood flow and disruption of tunica albuginea [156]. However, treatment should not be delayed based on ultrasound availability. Injuries to the vas deferens are ligated and repaired at a later time if fertility is desired. Any hematocele should be drained and the testicle examined. Minimal debridement of seminiferous tubules is performed and the tunica albuginea is closed primarily with small self-absorbable suture. The majority (75 %) of gunshot wounds to the testes can be salvaged, whereas the majority of lacerations (23 %) are not [147]. Orchiectomy should be reserved only for cases when testicular salvage is not possible.

Conclusions

Geriatric patients present unique challenges to the trauma care team due to the presence of comorbid conditions, increases in mortality, and unique patterns of presentation. Urologists play a key role in the treatment of geriatric urological trauma. Management techniques and surgical reconstruction are similar to techniques used in comparable, younger patients. As the field of geriatric trauma grows, so too must the field of geriatric urology. Outcomes for older patients undergoing treatment for urological injuries will need to be assessed and remain an important potential area for future study.

References

1. Sondik EJ, Madans JH, Gentleman JF. Vital and Health Statistics. Summary Health Statistics for the US Population: National Health Interview Survey, 2011 [Internet]. 2012 February 10, 2013; 10(255). Available from: http://www.cdc.gov/nchs/data/series/sr_10/sr10_255.pdf
2. Gerberding JL, Falk H, Arias I. CDC Injury Factbook: National Center for Injury Prevention and Control, Centers for Disease Control and Prevention; 2006 [cited 2013 February 10]. Available from: http://www.cdc.gov/Injury/publications/FactBook/InjuryBook2006.pdf
3. Life Years Lost to Unintentional Injury, 2010 [Internet]. Centers for Disease Control and Prevention; National Center for Injury Prevention and Control: Web-Based Injury Statistics Query and Reporting System (WISQARS). 2010 [cited February 10, 2013]. Available from: http://webappa.cdc.gov/sasweb/ncipc/ypll10.html
4. 10 Leading Causes of Death by Age Group, United States-2010 [Internet]. Centers for Disease Control and Prevention; National Center for Injury Prevention and Control: Web-Based Injury Statistics Query and Reporting System (WISQARS). 2010 [cited February 10, 2013]. Available from: http://www.cdc.gov/injury/wisqars/pdf/10LCID_All_Deaths_By_Age_Group_2010-a.pdf
5. 10 Leading Causes of Injury Deaths by Age Group Highlighting Unintentional Injury Deaths, United States - 2010 [Internet]. Centers for Disease Control and Prevention; National Center for Injury Prevention and Control: Web-Based Injury Statistics Query and Reporting System (WISQARS). 2010 [cited February 10, 2013]. Available from: http://www.cdc.gov/injury/wisqars/pdf/10LCID_Unintentional_Deaths_2010-a.pdf
6. 10 Leading Causes of Injury Deaths by Age Group Highlighting Violence-Related Injury Deaths, United States - 2010 [Internet]. Centers for Disease Control and Prevention; National Center for Injury Prevention and Control: Web-Based Injury Statistics Query and Reporting System (WISQARS). 2010 [cited February 10, 2013]. Available from: http://www.cdc.gov/injury/wisqars/pdf/10LCID_Violence_Related_Injury_Deaths_2010-a.pdf
7. National Estimates of the 10 Leading Causes of Nonfatal Injuries Treated in Hospital Emergency Departments, United States - 2010 [Internet]. Centers for Disease Control and Prevention; National Center for Injury Prevention and Control: Web-Based Injury Statistics Query and Reporting System (WISQARS). 2010 [cited February 10, 2013]. Available from: http://www.cdc.gov/Injury/wisqars/pdf/National_Estim_10_Leading_Causes_Nonfatal_Injuries_Tx_Hospital-ED_US2010-a.pdf
8. Joanisse M, Gagnon S, Voloaca M. Overly cautious and dangerous: an empirical evidence of the older driver stereotypes. Accid Anal Prev. 2012;45:802–10.
9. Cost of Fall Injuries in Older Persons in the United States, 2005 [Internet]. Centers for Disease Control and Prevention; National Center for Injury Prevention and Control. 2011 [cited February 10, 2013]. Available from: http://www.cdc.gov/homeandrecreationalsafety/falls/data/cost-estimates.html
10. Sleet DA, Moffett DB, Stevens J. CDC's research portfolio in older adult fall prevention: a review of progress, 1985-2005, and future research directions. J Saf Res. 2008;39(3):259–67.
11. Gillespie LD, Gillespie WJ, Robertson MC, Lamb SE, Cumming RG, Rowe BH. Interventions for preventing falls in elderly people. Cochrane Database Syst Rev. 2003;4, CD000340.
12. Older Drivers [Internet]. Centers for Disease Control and Prevention; National Center for Injury Prevention and Control. 2011 [cited February 10, 2013]. Available from: http://www.cdc.gov/Features/OlderDrivers
13. Mathias JL, Lucas LK. Cognitive predictors of unsafe driving in older drivers: a meta-analysis. Int Psychogeriatr IPA. 2009;21(4):637–53.
14. Rubin GS, Ng ES, Bandeen-Roche K, Keyl PM, Freeman EE, West SK. A prospective, population-based study of the role of visual impairment in motor vehicle crashes among older drivers: the SEE study. Investig Ophthalmol Visual Sci. 2007;48(4):1483–91.
15. Green KA, McGwin Jr G, Owsley C. Associations between visual, hearing, and dual sensory impairments and history of motor vehicle collision involvement of older drivers. J Am Geriatr Soc. 2013.
16. Ball K, Edwards JD, Ross LA, McGwin Jr G. Cognitive training decreases motor vehicle collision involvement of older drivers. J Am Geriatr Soc. 2010;58(11):2107–13.
17. Taylor MD, Tracy JK, Meyer W, Pasquale M, Napolitano LM. Trauma in the elderly: intensive care unit resource use and outcome. J Trauma. 2002;53(3):407–14.
18. Perdue PW, Watts DD, Kaufmann CR, Trask AL. Differences in mortality between elderly and younger adult trauma patients: geriatric status increases risk of delayed death. J Trauma. 1998;45(4):805–10.
19. Grossman MD, Miller D, Scaff DW, Arcona S. When is an elder old? Effect of preexisting conditions on mortality in geriatric trauma. J Trauma. 2002;52(2):242–6.
20. Tornetta 3rd P, Mostafavi H, Riina J, Turen C, Reimer B, Levine R, et al. Morbidity and mortality in elderly trauma patients. J Trauma. 1999;46(4):702–6.
21. Bennett KM, Scarborough JE, Vaslef S. Outcomes and health care resource utilization in super-elderly trauma patients. J Surg Res. 2010;163(1):127–31.

22. Meldon SW, Reilly M, Drew BL, Mancuso C, Fallon Jr W. Trauma in the very elderly: a community-based study of outcomes at trauma and nontrauma centers. J Trauma. 2002;52(1):79–84.
23. Rogers A, Rogers F, Bradburn E, Krasne M, Lee J, Wu D, et al. Old and undertriaged: a lethal combination. Am Surg. 2012;78(6):711–5.
24. Garwe T, Roberts ZV, Albrecht RM, Morgan AE, Johnson JJ, Neas BR. Direct transport of geriatric trauma patients with pelvic fractures to a Level I trauma center within an organized trauma system: impact on two-week incidence of in-hospital complications. Am J Surg. 2012;204(6):921–5, discussion 5-6.
25. Fallon Jr WF, Rader E, Zyzanski S, Mancuso C, Martin B, Breedlove L, et al. Geriatric outcomes are improved by a geriatric trauma consultation service. J Trauma. 2006;61(5):1040–6.
26. Lenartowicz M, Parkovnick M, McFarlan A, Haas B, Straus SE, Nathens AB, et al. An evaluation of a proactive geriatric trauma consultation service. Ann Surg. 2012;256(6):1098–101.
27. Jacobs DG. Special considerations in geriatric injury. Curr Opin Crit Care. 2003;9(6):535–9.
28. Wright JL, Nathens AB, Rivara FP, Wessells H. Renal and extrarenal predictors of nephrectomy from the national trauma data bank. J Urol. 2006;175(3 Pt 1):970–5, discussion 5.
29. Alsikafi NF, Rosenstein DI. Staging, evaluation, and nonoperative management of renal injuries. Urol Clin North Am. 2006;33(1):13–9.
30. Krieger JN, Algood CB, Mason JT, Copass MK, Ansell JS. Urological trauma in the Pacific Northwest: etiology, distribution, management and outcome. J Urol. 1984;132(1):70–3.
31. McAninch JW, Carroll PR, Klosterman PW, Dixon CM, Greenblatt MN. Renal reconstruction after injury. J Urol. 1991;145(5):932–7.
32. Bjurlin MA, Goble SM, Fantus RJ, Hollowell CM. Outcomes in geriatric genitourinary trauma. J Am Coll Surg. 2011;213(3):415–21.
33. Moore EE, Shackford SR, Pachter HL, McAninch JW, Browner BD, Champion HR, et al. Organ injury scaling: spleen, liver, and kidney. J Trauma. 1989;29(12):1664–6.
34. Santucci RA, McAninch JW, Safir M, Mario LA, Service S, Segal MR. Validation of the American Association for the Surgery of Trauma organ injury severity scale for the kidney. J Trauma. 2001;50(2):195–200.
35. Shariat SF, Roehrborn CG, Karakiewicz PI, Dhami G, Stage KH. Evidence-based validation of the predictive value of the American Association for the Surgery of Trauma kidney injury scale. J Trauma. 2007;62(4):933–9.
36. Buckley JC, McAninch JW. Revision of current American Association for the Surgery of Trauma Renal Injury grading system. J Trauma. 2011;70(1):35–7.
37. Lynch TH, Martinez-Pineiro L, Plas E, Serafetinides E, Turkeri L, Santucci RA, et al. EAU guidelines on urological trauma. Eur Urol. 2005;47(1):1–15.
38. McAndrew JD, Corriere Jr JN. Radiographic evaluation of renal trauma: evaluation of 1103 consecutive patients. Br J Urol. 1994;73(4):352–4.
39. Federle MP, Brown TR, McAninch JW. Penetrating renal trauma: CT evaluation. J Computer Assisted Tomogr. 1987;11(6):1026–30.
40. Alonso RC, Nacenta SB, Martinez PD, Guerrero AS, Fuentes CG. Kidney in danger: CT findings of blunt and penetrating renal trauma. Radiographics. 2009;29(7):2033–53.
41. Hardee MJ, Lowrance W, Brant WO, Presson AP, Stevens MH, Myers JB. High Grade Renal Injuries: Application of Parkland Hospital Predictors of Intervention for Renal Hemorrhage to a large series of patients with blunt renal trauma. J Urol. 2012;189:1771.
42. Charbit J, Manzanera J, Millet I, Roustan JP, Chardon P, Taourel P, et al. What are the specific computed tomography scan criteria that can predict or exclude the need for renal angioembolization after high-grade renal trauma in a conservative management strategy? J Trauma. 2011;70(5):1219–27, discussion 27-8.
43. Santucci RA, Fisher MB. The literature increasingly supports expectant (conservative) management of renal trauma–a systematic review. J Trauma. 2005;59(2):493–503.
44. Broghammer JA, Fisher MB, Santucci RA. Conservative management of renal trauma: a review. Urology. 2007;70(4):623–9.
45. Voelzke BB, McAninch JW. Renal gunshot wounds: clinical management and outcome. J Trauma. 2009;66(3):593–600. discussion 601.
46. Armenakas NA, Duckett CP, McAninch JW. Indications for nonoperative management of renal stab wounds. J Urol. 1999;161(3):768–71.
47. Wessells H, Suh D, Porter JR, Rivara F, MacKenzie EJ, Jurkovich GJ, et al. Renal injury and operative management in the United States: results of a population-based study. J Trauma. 2003;54(3):423–30.
48. Danuser H, Wille S, Zoscher G, Studer U. How to treat blunt kidney ruptures: primary open surgery or conservative treatment with deferred surgery when necessary? Eur Urol. 2001;39(1):9–14.
49. Hammer CC, Santucci RA. Effect of an institutional policy of nonoperative treatment of grades I to IV renal injuries. J Urol. 2003;169(5):1751–3.
50. Wessells H, McAninch JW. Effect of colon injury on the management of simultaneous renal trauma. J Urol. 1996;155(6):1852–6.
51. Rosen MA, McAninch JW. Management of combined renal and pancreatic trauma. J Urol. 1994;152(1):22–5.
52. Moudouni SM, Patard JJ, Manunta A, Guiraud P, Guille F, Lobel B. A conservative approach to major blunt renal lacerations with urinary extravasation

and devitalized renal segments. BJU Int. 2001; 87(4):290–4.
53. Carpio F, Morey AF. Radiographic staging of renal injuries. World J Urol. 1999;17(2):66–70.
54. Morey AF, McAninch JW, Tiller BK, Duckett CP, Carroll PR. Single shot intraoperative excretory urography for the immediate evaluation of renal trauma. J Urol. 1999;161(4):1088–92.
55. Gonzalez RP, Falimirski M, Holevar MR, Evankovich C. Surgical management of renal trauma: is vascular control necessary? J Trauma. 1999;47(6):1039–42.
56. Brown MF, Graham JM, Mattox KL, Feliciano DV, DeBakey ME. Renovascular trauma. Am J Surg. 1980;140(6):802–5.
57. Knudson MM, Harrison PB, Hoyt DB, Shatz DV, Zietlow SP, Bergstein JM, et al. Outcome after major renovascular injuries: a Western trauma association multicenter report. J Trauma. 2000; 49(6):1116–22.
58. Master VA, McAninch JW. Operative management of renal injuries: parenchymal and vascular. Urol Clin North Am. 2006;33(1):21–31. v-vi.
59. Matthews LA, Smith EM, Spirnak JP. Nonoperative treatment of major blunt renal lacerations with urinary extravasation. J Urol. 1997;157(6):2056–8.
60. Lee DG, Lee SJ. Delayed hemorrhage from a pseudoaneurysm after blunt renal trauma. Int J Urol. 2005;12(10):909–11.
61. Giannopoulos A, Manousakas T, Alexopoulou E, Brountzos E, Papadoukakis S, Kelekis D. Delayed life-threatening haematuria from a renal pseudoaneurysm caused by blunt renal trauma treated with selective embolization. Urol Int. 2004;72(4):352–4.
62. Elliott SP, McAninch JW. Ureteral injuries from external violence: the 25-year experience at San Francisco General Hospital. J Urol. 2003;170(4 Pt 1): 1213–6.
63. Azimuddin K, Milanesa D, Ivatury R, Porter J, Ehrenpreis M, Allman DB. Penetrating ureteric injuries. Injury. 1998;29(5):363–7.
64. Presti Jr JC, Carroll PR, McAninch JW. Ureteral and renal pelvic injuries from external trauma: diagnosis and management. J Trauma. 1989;29(3):370–4.
65. Siram SM, Gerald SZ, Greene WR, Hughes K, Oyetunji TA, Chrouser K, et al. Ureteral trauma: patterns and mechanisms of injury of an uncommon condition. Am J Surg. 2010;199(4):566–70.
66. Perez-Brayfield MR, Keane TE, Krishnan A, Lafontaine P, Feliciano DV, Clarke HS. Gunshot wounds to the ureter: a 40-year experience at Grady Memorial Hospital. J Urol. 2001;166(1):119–21.
67. Peterson NE, Pitts 3rd JC. Penetrating injuries of the ureter. J Urol. 1981;126(5):587–90.
68. Holden S, Hicks CC, O'Brien DP, Stone HH, Walker JA, Walton KN. Gunshot wounds of the ureter: a 15-year review of 63 consecutive cases. J Urol. 1976;116(5):562–4.
69. Liroff SA, Pontes JE, Pierce Jr JM. Gunshot wounds of the ureter: 5 years of experience. J Urol. 1977;118(4):551–3.
70. Stutzman RE. Ballistics and the management of ureteral injuries from high velocity missiles. J Urol. 1977;118(6):947–9.
71. Carlton Jr CE, Scott Jr R, Guthrie AG. The initial management of ureteral injuries: a report of 78 cases. J Urol. 1971;105(3):335–40.
72. Eikenberg H-UaA MA. Gunshot wounds to the ureter. J Trauma. 1976;16(7):562–5.
73. Lankford R, Block NL, Politano VA. Gunshot wounds of the ureter: a review of 10 cases. J Trauma. 1974;14(10):848–52.
74. Campbell Jr EW, Filderman PS, Jacobs SC. Ureteral injury due to blunt and penetrating trauma. Urology. 1992;40(3):216–20.
75. Rober PE, Smith JB, Pierce Jr JM. Gunshot injuries of the ureter. J Trauma. 1990;30(1):83–6.
76. Steers WD, Corriere Jr JN, Benson GS, Boileau MA. The use of indwelling ureteral stents in managing ureteral injuries due to external violence. J Trauma. 1985;25(10):1001–3.
77. Bright 3rd TC, Peters PC. Ureteral injuries due to external violence: 10 years' experience with 59 cases. J Trauma. 1977;17(8):616–20.
78. Ghali AM, El Malik EM, Ibrahim AI, Ismail G, Rashid M. Ureteric injuries: diagnosis, management, and outcome. J Trauma. 1999;46(1):150–8.
79. Palmer LS, Rosenbaum RR, Gershbaum MD, Kreutzer ER. Penetrating ureteral trauma at an urban trauma center: 10-year experience. Urology. 1999;54(1):34–6.
80. Bjurlin MA, Goble SM, Fantus RJ, Hollowell CM. Outcomes in geriatric genitourinary trauma. J Am Coll Surg. 2011;213(3):415–21.
81. Ortega SJ, Netto FS, Hamilton P, Chu P, Tien HC. CT scanning for diagnosing blunt ureteral and ureteropelvic junction injuries. BMC Urol. 2008;8:3.
82. Digiacomo JC, Frankel H, Rotondo MF, Schwab CW, Shaftan GW. Preoperative radiographic staging for ureteral injuries is not warranted in patients undergoing celiotomy for trauma. Am Surg. 2001;67(10):969–73.
83. Best CD, Petrone P, Buscarini M, Demiray S, Kuncir E, Kimbrell B, et al. Traumatic ureteral injuries: a single institution experience validating the American Association for the Surgery of Trauma-Organ Injury Scale grading scale. J Urol. 2005;173(4):1202–5.
84. Brandes SB, Chelsky MJ, Buckman RF, Hanno PM. Ureteral injuries from penetrating trauma. J Trauma. 1994;36(6):766–9.
85. Brandes S, Coburn M, Armenakas N, McAninch J. Diagnosis and management of ureteric injury: an evidence-based analysis. BJU Int. 2004;94(3): 277–89.
86. Velmahos GC, Degiannis E, Wells M, Souter I. Penetrating ureteral injuries: the impact of associ-

ated injuries on management. Am Surg. 1996; 62(6):461–8.
87. Scalea TM, Phillips TF, Goldstein AS, Sclafani SJ, Duncan AO, Atweh NA, et al. Injuries missed at operation: nemesis of the trauma surgeon. J Trauma. 1988;28(7):962–7.
88. Moreno C, Moore EE, Rosenberger A, Cleveland HC. Hemorrhage associated with major pelvic fracture: a multispecialty challenge. J Trauma. 1986;26(11):987–94.
89. Chang TT, Schecter WP. Injury in the elderly and end-of-life decisions. Surg Clin North Am. 2007;87(1):229–45. viii.
90. Alost T, Waldrop RD. Profile of geriatric pelvic fractures presenting to the emergency department. Am J Emerg Med. 1997;15(6):576–8.
91. Melton LJ, Sampson JM, Morrey BF, Ilstrup DM. Epidemiologic features of pelvic fractures. Clin Orthopaed Relat Res. 1981;155:43–7.
92. Ragnarsson B, Jacobsson B. Epidemiology of pelvic fractures in a Swedish county. Acta orthopaedica Scandinavica. 1992;63(3):297–300.
93. Kannus P, Palvanen M, Niemi S, Parkkari J, Jarvinen M. Epidemiology of osteoporotic pelvic fractures in elderly people in Finland: sharp increase in 1970-1997 and alarming projections for the new millennium. Osteoporosis Int. 2000;11(5):443–8.
94. Campbell AJ, Reinken J, Allan BC, Martinez GS. Falls in old age: a study of frequency and related clinical factors. Age Ageing. 1981;10(4):264–70.
95. Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. New Engl J Med. 1988;319(26):1701–7.
96. Tile M. Acute pelvic fractures: I causation and classification. J Am Acad Orthopaed Surg. 1996;4(3): 143–51.
97. Burgess AR, Eastridge BJ, Young JW, Ellison TS, Ellison Jr PS, Poka A, et al. Pelvic ring disruptions: effective classification system and treatment protocols. J Trauma. 1990;30(7):848–56.
98. Canale T, James B. Campbell's operative orthopaedics. 12th ed. Philadelphia: Elsevier; 2012.
99. Krappinger D, Kammerlander C, Hak DJ, Blauth M. Low-energy osteoporotic pelvic fractures. Arch Orthopaed Trauma Surg. 2010;130(9):1167–75.
100. Biffl WL, Smith WR, Moore EE, Gonzalez RJ, Morgan SJ, Hennessey T, et al. Evolution of a multidisciplinary clinical pathway for the management of unstable patients with pelvic fractures. Ann Surg. 2001;233(6):843–50.
101. Wolinsky PR. Assessment and management of pelvic fracture in the hemodynamically unstable patient. Orthoped Clin North Am. 1997;28(3): 321–9.
102. McMahon DJ, Schwab CW, Kauder D. Comorbidity and the elderly trauma patient. World J Surg. 1996;20(8):1113–9, discussion 9–20.
103. Gruen GS, Leit ME, Gruen RJ, Peitzman AB. The acute management of hemodynamically unstable multiple trauma patients with pelvic ring fractures. J Trauma. 1994;36(5):706–11, discussion 11–3.
104. Velmahos GC, Toutouzas KG, Vassiliu P, Sarkisyan G, Chan LS, Hanks SH, et al. A prospective study on the safety and efficacy of angiographic embolization for pelvic and visceral injuries. J Trauma. 2002;53(2):303–8, discussion 8.
105. O'Brien DP, Luchette FA, Pereira SJ, Lim E, Seeskin CS, James L, et al. Pelvic fracture in the elderly is associated with increased mortality. Surgery. 2002;132(4):710–4, discussion 4-5.
106. Henry SM, Pollak AN, Jones AL, Boswell S, Scalea TM. Pelvic fracture in geriatric patients: a distinct clinical entity. J Trauma. 2002;53(1):15–20.
107. Kimbrell BJ, Velmahos GC, Chan LS, Demetriades D. Angiographic embolization for pelvic fractures in older patients. Arch Surg. 2004;139(7):728–32, discussion 32–3.
108. Starr AJ, Griffin DR, Reinert CM, Frawley WH, Walker J, Whitlock SN, et al. Pelvic ring disruptions: prediction of associated injuries, transfusion requirement, pelvic arteriography, complications, and mortality. J Orthopaed Trauma. 2002;16(8):553–61.
109. Matityahu A, Elson J, Morshed S, Marmor M. Survivorship and severe complications are worse for octogenarians and elderly patients with pelvis fractures as compared to adults: data from the National Trauma Data Bank. J Osteopor. 2012;2012:475739.
110. Mundy AR. Pelvic fracture injuries of the posterior urethra. World J Urol. 1999;17(2):90–5.
111. Carroll PR, McAninch JW. Major bladder trauma: mechanisms of injury and a unified method of diagnosis and repair. J Urol. 1984;132(2):254–7.
112. Corriere Jr JN, Sandler CM. Management of the ruptured bladder: seven years of experience with 111 cases. J Trauma. 1986;26(9):830–3.
113. Koraitim MM, Marzouk ME, Atta MA, Orabi SS. Risk factors and mechanism of urethral injury in pelvic fractures. Br J Urol. 1996;77(6):876–80.
114. Perry MO, Husmann DA. Urethral injuries in female subjects following pelvic fractures. J Urol. 1992;147(1):139–43.
115. Aihara R, Blansfield JS, Millham FH, LaMorte WW, Hirsch EF. Fracture locations influence the likelihood of rectal and lower urinary tract injuries in patients sustaining pelvic fractures. J Trauma. 2002;52(2):205–8, discussion 8–9.
116. Bjurlin MA, Fantus RJ, Mellett MM, Goble SM. Genitourinary injuries in pelvic fracture morbidity and mortality using the National Trauma Data Bank. J Trauma. 2009;67(5):1033–9.
117. Basta AM, Blackmore CC, Wessells H. Predicting urethral injury from pelvic fracture patterns in male patients with blunt trauma. J Urol. 2007;177(2):571–5.
118. Morgan DE, Nallamala LK, Kenney PJ, Mayo MS, Rue 3rd LW. CT cystography: radiographic and clinical predictors of bladder rupture. Am J Roentgenol. 2000;174(1):89–95.

119. Cass AS, Luxenberg M. Features of 164 bladder ruptures. J Urol. 1987;138(4):743–5.
120. Corriere Jr JN, Sandler CM. Mechanisms of injury, patterns of extravasation and management of extraperitoneal bladder rupture due to blunt trauma. J Urol. 1988;139(1):43–4.
121. Udekwu PO, Gurkin B, Oller DW. The use of computed tomography in blunt abdominal injuries. Am Surg. 1996;62(1):56–9.
122. Hochberg E, Stone NN. Bladder rupture associated with pelvic fracture due to blunt trauma. Urology. 1993;41(6):531–3.
123. Avey G, Blackmore CC, Wessells H, Wright JL, Talner LB. Radiographic and clinical predictors of bladder rupture in blunt trauma patients with pelvic fracture. Acad Radiol. 2006;13(5):573–9.
124. Belis JA, Recht KA, Milam DF. Simultaneous traumatic bladder perforation and disruption of the prostatomembranous urethra. J Urol. 1979;122(3):412–4.
125. Palmer JK, Benson GS, Corriere Jr JN. Diagnosis and initial management of urological injuries associated with 200 consecutive pelvic fractures. J Urol. 1983;130(4):712–4.
126. Cass AS, Gleich P, Smith C. Simultaneous bladder and prostatomembranous urethral rupture from external trauma. J Urol. 1984;132(5):907–8.
127. Deibert CM, Spencer BA. The association between operative repair of bladder injury and improved survival: results from the National Trauma Data Bank. J Urol. 2011;186(1):151–5.
128. Brewer ME, Wilmoth RJ, Enderson BL, Daley BJ. Prospective comparison of microscopic and gross hematuria as predictors of bladder injury in blunt trauma. Urology. 2007;69(6):1086–9.
129. Sandler CM, Goldman SM, Kawashima A. Lower urinary tract trauma. World J Urol. 1998;16(1):69–75.
130. Doyle SM, Master VA, McAninch JW. Appropriate use of CT in the diagnosis of bladder rupture. J Am Coll Surg. 2005;200(6):973.
131. Horstman WG, McClennan BL, Heiken JP. Comparison of computed tomography and conventional cystography for detection of traumatic bladder rupture. Urol Radiol. 1991;12(4):188–93.
132. Dubinsky TJ, Deck A, Mann FA. Sonographic diagnosis of a traumatic intraperitoneal bladder rupture. Am J Roentgenol. 1999;172(3):770.
133. Cass AS, Luxenberg M. Management of extraperitoneal ruptures of bladder caused by external trauma. Urology. 1989;33(3):179–83.
134. Elliott SP, McAninch JW. Extraperitoneal bladder trauma: delayed surgical management can lead to prolonged convalescence. J Trauma. 2009;66(1):274–5.
135. Mundy AR, Andrich DE. Pelvic fracture-related injuries of the bladder neck and prostate: their nature, cause and management. BJU Int. 2010;105(9):1302–8.
136. Kim FJ, Chammas Jr MF, Gewehr EV, Campagna A, Moore EE. Laparoscopic management of intraperitoneal bladder rupture secondary to blunt abdominal trauma using intracorporeal single layer suturing technique. J Trauma. 2008;65(1):234–6.
137. Brandes S, Borrelli Jr J. Pelvic fracture and associated urologic injuries. World J Surg. 2001;25(12):1578–87.
138. Black PC, Miller EA, Porter JR, Wessells H. Urethral and bladder neck injury associated with pelvic fracture in 25 female patients. J Urol. 2006;175(6):2140–4, discussion 4.
139. Okur H, Kucikaydin M, Kazez A, Turan C, Bozkurt A. Genitourinary tract injuries in girls. Br J Urol. 1996;78(3):446–9.
140. Patil U, Nesbitt R, Meyer R. Genitourinary tract injuries due to fracture of the pelvis in females: sequelae and their management. Br J Urol. 1982;54(1):32–8.
141. Mundy AR, Andrich DE. Urethral trauma. Part I: introduction, history, anatomy, pathology, assessment and emergency management. BJU Int. 2011;108(3):310–27.
142. Martinez-Pineiro L, Djakovic N, Plas E, Mor Y, Santucci RA, Serafetinidis E, et al. EAU guidelines on urethral trauma. Eur Urol. 2010;57(5):791–803.
143. Moore EE, Cogbill TH, Jurkovich GJ, McAninch JW, Champion HR, Gennarelli TA, et al. Organ injury scaling. III: Chest wall, abdominal vascular, ureter, bladder, and urethra. J Trauma. 1992;33(3):337–9.
144. Wessells H, Long L. Penile and genital injuries. Urol Clin North Am. 2006;33(1):117–26. vii.
145. Leddy LS, Vanni AJ, Wessells H, Voelzke BB. Outcomes of endoscopic realignment of pelvic fracture associated urethral injuries at a level 1 trauma center. J Urol. 2012;188(1):174–8.
146. Flynn BJ, Delvecchio FC, Webster GD. Perineal repair of pelvic fracture urethral distraction defects: experience in 120 patients during the last 10 years. J Urol. 2003;170(5):1877–80.
147. Phonsombat S, Master VA, McAninch JW. Penetrating external genital trauma: a 30-year single institution experience. J Urol. 2008;180(1):192–5, discussion 5–6.
148. McAninch JW, Kahn RI, Jeffrey RB, Laing FC, Krieger MJ. Major traumatic and septic genital injuries. J Trauma. 1984;24(4):291–8.
149. Black PC, Friedrich JB, Engrav LH, Wessells H. Meshed unexpanded split-thickness skin grafting for reconstruction of penile skin loss. J Urol. 2004;172(3):976–9.
150. Husmann DA, Boone TB, Wilson WT. Management of low velocity gunshot wounds to the anterior urethra: the role of primary repair versus urinary diversion alone. J Urol. 1993;150(1):70–2.
151. Nomura JT, Sierzenski PR. Ultrasound diagnosis of penile fracture. J Emerg Med. 2010;38(3):362–5.
152. Fedel M, Venz S, Andreessen R, Sudhoff F, Loening SA. The value of magnetic resonance imaging in the diagnosis of suspected penile fracture with atypical clinical findings. J Urol. 1996;155(6):1924–7.

153. Gamal WM, Osman MM, Hammady A, Aldahshoury MZ, Hussein MM, Saleem M. Penile fracture: long-term results of surgical and conservative management. J Trauma. 2011;71(2):491–3.
154. Jezior JR, Brady JD, Schlossberg SM. Management of penile amputation injuries. World J Surg. 2001;25(12):1602–9.
155. Buckley JC, McAninch JW. Diagnosis and management of testicular ruptures. Urol Clin North Am. 2006;33(1):111–6. vii.
156. Guichard G, El Ammari J, Del Coro C, Cellarier D, Loock PY, Chabannes E, et al. Accuracy of ultrasonography in diagnosis of testicular rupture after blunt scrotal trauma. Urology. 2008;71(1):52–6.

26 Preoperative Anesthetic Evaluation and Clinical Decision Making

Ashlie R. Stowers, Susan H. Noorily, Stephen R. Kraus, and Joseph W. Basler

Introduction

In the past decade alone, the portion of the US population aged 65 and over has grown to over 40 million people, representing a 15.1 % increase from 2000 to 2010, and comprising 13 % of the total population. In contrast, the portions of the population under age 18 and age 18–45 increased by only 2.6 % and 0.6 %, respectively. This trend toward an expanding elderly population promises to continue, anticipating the contribution of the aging "Baby Boom" generation, those aged 45–64, who currently make up 26.4 % of the US population [1].

Given that half of all surgical procedures are performed in patients aged 65 years or older [2], healthcare providers involved in the perioperative treatment of patients must be familiar with the issues and concerns particular to geriatric patients. Patients undergoing urologic procedures tend to be older and have an array of complex comorbidities.

A.R. Stowers, M.D. • S.H. Noorily, M.D.
Department of Anesthesiology, University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, TX 78229, USA

S.R. Kraus, M.D., F.A.C.S. • J.W. Basler, M.D. (✉)
Department of Urology, University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, TX 78229, USA
e-mail: krauss@uthsca.edu; basler@uthscsa.edu

Age alone does not imply a level of function. Therefore, providers must determine preoperative functional capacity in each patient in order to meet the postoperative goals of facilitating recovery and avoiding functional decline. Because of age-related and disease-related declines in physiologic function, geriatric patients often take longer to return to their preoperative state and may fail to obtain the same level of function that they had prior to the surgical procedure [3].

The normal aging process involves physiologic changes that occur in all body systems. This ultimately results in a decreased ability to maintain homeostasis as fewer physiologic reserves are available to meet the demands imposed by stressors such as disease, trauma, or surgery. To illustrate this point, age-related decline in hepatic and renal function alters the pharmacokinetic responses to many anesthetic drugs, prolonging their elimination half-time, which predisposes elderly patients to an increased incidence of adverse drug reactions [4]. While these normal physiologic changes result in a gradual decrease in the body's capacity to adapt to physiologic stressors, these effects are commonly compounded by the presence of coexisting disease processes, such as diabetic nephropathy, which greatly increases the risk of postoperative complications related to fluid and electrolyte abnormalities.

Although individual risk correlates with coexisting disease and the specific type of procedure, overall, patients older than 80 years have a

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_26,

higher morbidity (51 %) and mortality (7 %) after surgical procedures than younger patients (28 % and 2.3 % respectively) [5] due to an increased rate of postoperative complications [6]. It has been shown that in patients over 80 years old, there is a 25 % increased 30-day mortality when there are postoperative complications [7–9].

Identifying Patients at High Risk for Complications

One must take into account the nature of the planned surgical procedure including estimated operative time and blood loss, anticipated fluid shifts, and the extent of the patient's preexisting disease in order to identify patient risk factors and perform an appropriate preoperative evaluation.

Rationale for Predicting Risk

Attempting to predict the risk level for a particular surgical procedure can help to determine if a patient is fit enough to undergo the surgery. Based on the extent of the patient's disease and the complexity of the procedure, one may decide that the risks outweigh the potential benefits. For example, a detailed discussion of these concerns may help a patient to decide whether it might be prudent to pursue less aggressive therapy in order to decrease the risk of an adverse outcome. When a patient understands the risks, he or she is better able to make an educated decision about the treatment plan. This is an important part of obtaining proper informed consent.

Predicting a patient's level of risk also helps to establish the degree of perioperative surveillance that may be required. The presence of certain risk factors may guide providers to implement more invasive monitoring techniques requiring placement of arterial lines, central lines, or pulmonary artery catheters which should be discussed during the preoperative evaluation and consent process. It can also help determine the level of postoperative vigilance required such as the need for admission to an intensive care unit for postoperative monitoring.

Table 26.1 American Society of Anesthesiologists (ASA) physical status classification

ASA physical status	
1	A normal healthy patient
2	A patient with mild systemic disease
3	A patient with severe systemic disease
4	A patient with severe systemic disease that is a constant threat to life
5	A moribund patient who is not expected to survive without the operation
6	A declared brain-dead patient whose organs are being removed for donor purposes

The designation "E" can be added to any of the physical status classifications to denote an "emergency" surgery

Reproduced from: (http://www.asahq.org/clinical/physicalstatus.htm)

Classification Systems and Risk Indices

Several different classification systems and risk indices have been developed and studied in an attempt to help providers estimate a patient's level of risk, predict the potential for postoperative complications, and identify those patients who will benefit from special strategies to reduce their risk.

The American Society of Anesthesiologists (ASA) originally developed the ASA Physical Status Classification system in 1941 to describe a patient's overall preoperative physical health status and eventually expanded it to include declared brain-dead organ donors (Table 26.1). It is now widely used to identify those patients at increased risk of adverse perioperative outcomes. Based on the extent of a patient's disease burden, the evaluator assigns the patient an ASA class ranging from 1 to 6, with higher numbers representing worsening medical conditions (see Table 26.1). While the score is irrespective of the planned surgical procedure, emergency surgery is given

Table 26.2 Frailty criteria [12]

Shrinking (weight loss)	Shrinking was defined through self-report as an unintentional weight loss of ≥10 lbs in the last year
Decreased grip strength (weakness)	Weakness was assessed by grip strength and was measured directly with a hand-held JAMAR® dynamometer. Three serial tests of maximum grip strength with the dominant hand were performed, and a mean of the three values were adjusted by gender and body mass index (BMI). Weakness was defined as an adjusted grip strength in the lowest 20th percentile of a community-dwelling population of adults 65 years of age and older. Men met the criteria for weakness if their BMI and grip strength were ≤24 and ≤29 kg; 24.1–26 and ≤30 kg; 26.1–28 and ≤31 kg; >28 and ≤32 kg, respectively. Women met the criteria for weakness if their BMI and grip strength were ≤23 and ≤17 kg; 23.1–26 and ≤17.3 kg; 26.1–29 and ≤18 kg; and >29 and ≤21 kg, respectively
Exhaustion	Exhaustion was measured by responses to the following two statements from the modified 10-item Center for Epidemiological Studies–Depression scale: "I felt that everything I did was an effort" and "I could not get going." Subjects were asked, "How often in the last week did you feel this way?" Potential responses were: 0 = rarely or none of the time (<1 day); 1 = some or a little of the time (1–2 days); 2 = a moderate amount of the time (3–4 days); and 3 = most of the time. Subjects answering either statement with response two or three met the criteria for exhaustion
Low activity	Physical activities were ascertained for the 2 weeks before this assessment using the short version of the Minnesota Leisure Time Activities Questionnaire and included frequency and duration. Weekly tasks were converted to equivalent kilocalories of expenditure, and individuals reporting a weekly kilocalorie expenditure in the lowest 20th percentile for their gender (men, <383 kcal/week; women, <270 kcal/week) were classified as having low physical activity
Slowed walking speed	Slowness was measured by averaging three trials of walking 15 ft. at a normal pace. Individuals with a walking speed <20th percentile, adjusted for gender and height, were scored as having slow walking speed. Men met criteria if height and walk time were ≤173 cm and ≥7 s or >173 cm and ≥6 s, respectively. Women met criteria if height and walk time were ≤159 cm and ≥7 s or >159 cm and ≥6 s, respectively

Each criterion is scored with a 0 or 1

special consideration and is designated by the addition of an "E" to the assigned ASA class. For example, a healthy patient undergoing emergency surgery for testicular torsion would be given an ASA class of 1E. Note that this classification system is considered to be a subjective assessment, given the variability in scoring between evaluators. However, significant correlation exists between the ASA class and the rate of postoperative complications and this has been repeatedly validated [10, 11].

An attempt at predicting the risk of an adverse surgical outcome in an elderly patient should include an assessment of the patient's degree of frailty. One such assessment utilizes a "frailty score" in which the patient is given a score of 0 or 1 based on the absence or presence of each of the following five criteria: unintentional weight loss, decreased grip strength, exhaustion, low physical activity, and slowed walking speed (Table 26.2) [12]. Patients with a score of 2 or 3 are considered intermediately frail while those with a 4 or 5 are considered to be frail. Rather than assessing an individual organ system, the frailty score is thought to represent a patient's overall physiologic reserve and vulnerability to stressors. The addition of the frailty score to other risk models such as ASA score and Lee's revised cardiac risk index (discussed below) may enhance the ability to identify patients at risk. Frail patients have an increase in postoperative complications, longer hospital stays, and are more likely to be discharged to nursing homes or assisted living facilities [12]. Issues related to frailty are discussed in more detail in Chap. 4.

Prediction of Cardiac Risk

One of the most widely used and validated indices which estimates the risk of major cardiac events in stable patients undergoing non-urgent, non-cardiac surgery is the Revised Cardiac Risk Index (RCRI) published in 1999 [13]. Developed by Lee and his colleagues, the RCRI identifies six independent risk factors for increased perioperative cardiac morbidity and mortality including ischemic heart disease, congestive heart failure,

Table 26.3 Revised cardiac risk index [13]

1. High-risk surgical procedures
   - Intraperitoneal
   - Intrathoracic
   - Suprainguinal vascular
2. History of ischemic heart disease
   - History of myocardial infarction
   - History of positive exercise test
   - Current complaint of chest pain considered secondary to myocardial ischemia
   - Use of nitrate therapy
   - ECG with pathological Q waves
3. History of congestive heart failure
   - History of congestive heart failure
   - Pulmonary edema
   - Paroxysmal nocturnal dyspnea
   - Bilateral rales or S3 gallop
   - Chest radiograph showing pulmonary vascular redistribution
4. History of cerebrovascular disease
   - History of transient ischemic attack or stroke
5. Preoperative treatment with insulin
6. Preoperative serum creatinine > 2.0 mg/dL

Risk of major cardiac event

Points	*Class*	*Risk*
0	I	0.4 %
1	II	0.9 %
2	III	6.6 %
3 or more	IV	11 %

Each risk factor is assigned one point

cerebrovascular disease, high-risk surgery, insulin therapy for diabetes mellitus, and preoperative renal insufficiency (Table 26.3).

In a joint effort to provide guidelines to help clinicians determine which patients would benefit from further preoperative cardiovascular evaluation, the American College of Cardiology, and the American Heart Association have established an algorithm that takes into account the urgency and risk level of the proposed non-cardiac surgery as well as the patient's cardiac history, functional capacity, and clinical risk factors as outlined in the RCRI (Fig. 26.1) [14]. An accurate and thorough history will identify patients with an active cardiac condition such as an unstable coronary syndrome, decompensated heart failure, significant arrhythmia, or severe valvular disease (Table 26.4). The presence of any of these active conditions places the patient at high risk and necessitates additional cardiac evaluation with aggressive management and optimization prior to surgery. Functional capacity, measured in metabolic equivalents (METs), is commonly estimated from a patient's ability to perform activities of daily living (ADLs) which can serve as an indicator of the patient's cardiorespiratory reserve (Table 26.5). The established guidelines repeatedly recommend obtaining preoperative cardiac testing only if the results will lead to a change in management [14].

The decrease in cardiopulmonary reserve attributed to the normal aging process makes elderly patients more susceptible to the negative effects of anemia, especially when underlying cardiovascular disease is present. A history of fatigue, dyspnea, angina, tachycardia, palpitations, gross blood loss, or need for prior transfusion may be suggestive of the presence of anemia. Preoperative anemia, defined as a hematocrit level <39 %, is associated with increased risk of 30-day postoperative mortality and cardiac events [15]. Therefore, it is prudent to obtain hemoglobin levels in elderly patients within 30 days prior to undergoing any major elective surgery. If anemia is detected, delay of surgery should be considered to allow sufficient time for the cause to be investigated and treated.

Prediction of Pulmonary Risk

Age-related changes in the respiratory system result in decreased pulmonary reserve in elderly patients. For example, the combination of decreased respiratory muscle strength and increased chest wall stiffness due to cartilage calcification limits vital capacity and tidal volumes. This predisposes the elderly population to an increased risk of postoperative pulmonary complications such as atelectasis, pneumonia, exacerbation of chronic lung disease, and respiratory failure.

The American College of Physicians (ACP) has established guidelines to help clinicians assess patient risk for pulmonary complications and includes strategies to reduce those risks [16]. According to the ACP, chronic obstructive pulmonary disease, age older than 60 years, ASA score of 2 or greater, functional dependency, congestive heart failure and hypoalbuminemia

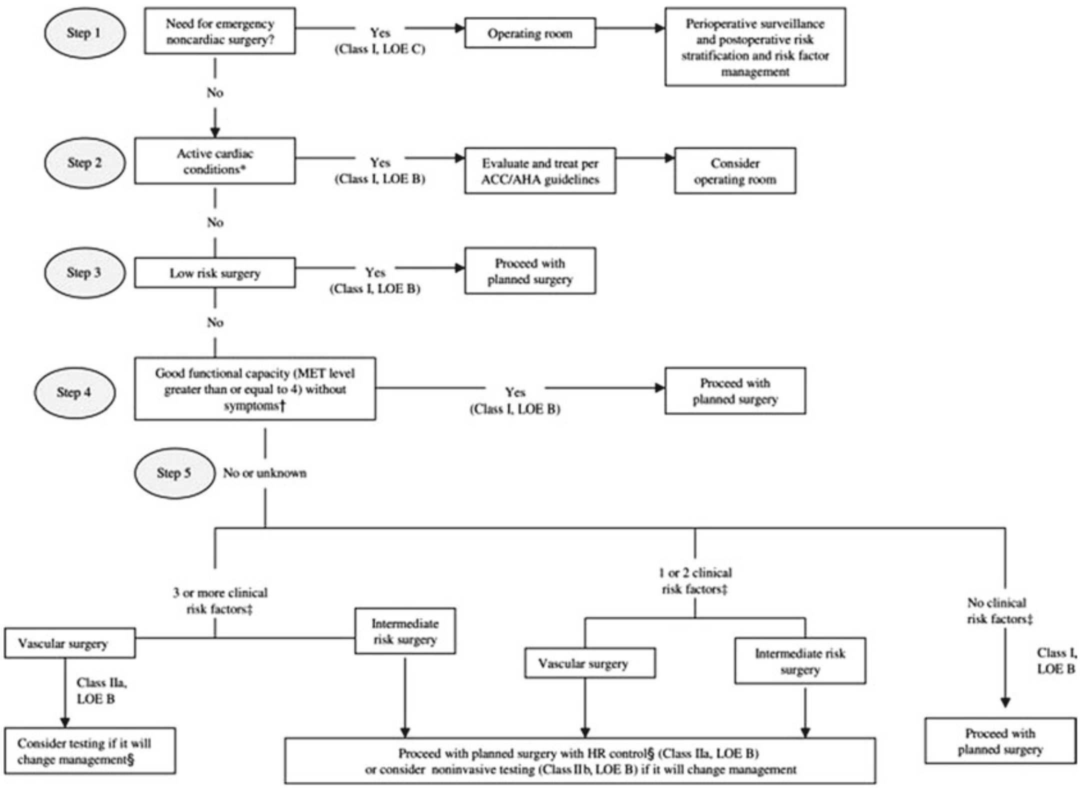


Fig. 26.1 Cardiac evaluation and care algorithm for noncardiac surgery based on active clinical conditions, known cardiovascular disease, or cardiac risk factors for patients 50 years of age or greater [14]

Table 26.4 Active cardiac conditions for which the patient should undergo evaluation and treatment before noncardiac surgery [14]

Condition	Examples
Unstable coronary syndromes	Unstable or severe angina[a] (CCS class III or IV)
	Recent MI[b]
Decompensated Heart Failure (HF) (NYHA functional class IV; worsening or new-onset HF)	
Significant arrhythmias	High-grade atrioventricular block
	Mobitz II atrioventricular block
	Third-degree atrioventricular heart block
	Symptomatic ventricular arrhythmias
	Supraventricular arrhythmias (including atrial fibrillation) with uncontrolled ventricular rate (HR greater than 100 bpm at rest)
	Symptomatic bradycardia
	Newly recognized ventricular tachycardia
Severe valvular disease	Severe aortic stenosis (mean pressure gradient greater than 40 mmHg, aortic valve area less than 1.0 cm^2, or symptomatic)
	Symptomatic mitral stenosis (progressive dyspnea on exertion, exertional presyncope, or HF)

CCS Canadian cardiovascular society, *HF* heart failure, *HR* heart rate, *MI* myocardial infarction, *NYHA* New York heart association

[a]May include “stable” angina in patients who are unusually sedentary

[b]The American College of Cardiology National Database Library defines recent MI as more than 7 days but less than or equal to 1 month (within 30 days)

Table 26.5 Estimated energy requirements for various activities [14]

1 MET	Can you…
	Take care of yourself? Eat, dress, or use the toilet? Walk indoors around the house? Walk a block or 2 on level ground at 2–3 mph (3.2–4.8 kph)?
4 METs	Can you…
	Do light work around the house like dusting or washing dishes? Climb a flight of stairs or walk up a hill? Walk on level ground at 4 mph (6.4 kph)? Run a short distance? Do heavy work around the house like scrubbing floors or lifting heavy furniture? Participate in moderate recreational activities like golf, bowling, dancing, doubles tennis, or throwing a baseball or football?
10 METs	Can you…
	Participate in strenuous sports like swimming, singles tennis, football, basketball, or skiing?

kph kilometers per hour, *MET* metabolic equivalent, *mph* miles per hour
Adapted from Fletcher et al. [14]

(serum albumin level <3.5 g/dL) are identified as significant risk factors for the development of postoperative pulmonary complications. Procedure-related risk factors include emergencies, surgical duration >3 h, use of general anesthesia, as well as abdominal, thoracic, vascular, and head and neck surgery. The risk for pulmonary complications increases as the incision gets closer to the diaphragm. The guidelines clearly state that although preoperative pulmonary function testing may be appropriate in select patients such as those undergoing lung resection, preoperative spirometry, and chest radiographs should not be routinely obtained, as these tests have not been shown to be superior to history and physical examination for predicting pulmonary risk. Further investigations have led to the development of a revised Respiratory Risk Index which identifies a total of 28 independent risk factors for respiratory failure [17]. Notably, it ranks hypoalbuminemia as a less important variable and identifies several new risk factors including hypernatremia (serum sodium level >145 mmol/L), ascites, and preoperative sepsis. A recent prospective multicenter study produced

Table 26.6 STOP-Bang scoring system [25]

1. ***S***noring: Do you *s*nore loudly (louder than talking or loud enough to be heard through closed doors)? Yes No
2. ***T***ired: Do you often feel *t*ired, fatigued, or sleepy during daytime? Yes No
3. ***O***bserved: Has anyone *o*bserved you stop breathing during your sleep? Yes No
4. Blood ***P***ressure: Do you have or are you being treated for high blood *p*ressure? Yes No
5. ***B***MI: *B*MI more than 35 kg/m^2? Yes No
6. ***A***ge: *A*ge over 50 years old? Yes No
7. ***N***eck circumference: *N*eck circumference greater than 40 cm? Yes No
8. ***G***ender: male? Yes No

High risk of OSA: answering yes to three or more items
Low risk of OSA: answering yes to less than three items

a risk index including findings of respiratory infection within 1 month of surgery, anemia, and preoperative SpO2 < 96 % as important risk factors [18]. Other studies have provided evidence supporting pulmonary hypertension and obstructive sleep apnea (OSA) as contributors to increased postoperative pulmonary risk [19–21].

Particular attention must be given to patients known or suspected to have OSA, a very common breathing disorder. OSA involves the partial or complete obstruction of the upper airway during sleep, leading to episodes of oxygen desaturation and hypercapnia. This can result in arousal of the patient in order to restore upper airway patency [22, 23]. Studies indicate the estimated prevalence of OSA to be as high as 20 % in the adult surgical population, with more than 70 % of these patients undiagnosed prior to their preoperative evaluation [23]. Sleep-disordered breathing is more common in elderly patients, with a prevalence of 30–80 % [24]. The STOP-Bang questionnaire was developed as a brief screening tool to identify patients at risk for OSA. Patients answer "yes/no" to the presence of signs and symptoms associated with OSA (Table 26.6) [25].

Prediction of Neurologic Risk

As with other organ systems, the central nervous system (CNS) of the elderly patient is more susceptible to the development of postoperative dysfunction, particularly with respect to cognition.

Changes in cognitive function span the spectrum from emergence delirium seen during or immediately after emergence from general anesthesia and resolving within minutes to hours, to postoperative delirium usually occurring between postoperative days 1 and 3 and resolving within hours to days, to postoperative cognitive decline (POCD) which involves a deterioration in cognition persisting for weeks to months after surgery [26].

Delirium presents as an acute change in mental status with fluctuating severity of mood lability, attention disturbance, disorientation, and memory impairment. Risk factors associated with the development of postoperative delirium include advanced age, baseline functional and cognitive impairment including dementia and depression, history of alcohol abuse, electrolyte disturbances, decreased albumin level, and lower hematocrit [27]. Delirium is discussed in more detail in Chap. 6.

POCD is more difficult to diagnose, requiring valid assessments of both preoperative and postoperative cognitive function. This includes comprehensive neuropsychological testing of attention, perception, learning, memory, verbal abilities, and abstract thinking. POCD can range from mild forgetfulness to severe cognitive impairment, which results in loss of independence and strain on family and social support systems [28]. Recent studies have shown that advanced age is a risk factor for POCD, although major surgery appears to be the principle cause [29].

Interventions Which May Decrease Risk

A major part of mitigating the risk in geriatric surgical patients involves optimizing organ function prior to surgery. Strong consideration should be given to obtaining a preoperative geriatric medicine consultation for those patients with multiple comorbidities. Primary care providers can provide accurate diagnoses and identify treatment plans for common medical problems with perioperative concerns, such as poor blood pressure or glucose control. They can assist with the perioperative management of insulin treatment, taking into account the current insulin dose, level of glucose control, compliance with diabetic diet, and overall health status. Diabetics should be advised not to take oral hypoglycemic medications on the morning of surgery. The primary care provider can initiate beta blocker and/or statin therapy when indicated. These medications can reduce perioperative mortality in some patients [30, 31].

Given the high incidence of polypharmacy in the elderly population, a preoperative geriatric medicine consult provides an important opportunity to review the patient's current medication list. Recent surveys have shown that more than 90 % of people older than 65 years of age take at least one medication per week, 40 % take 5 or more, and 12–19 % take 10 or more medications per week [4]. Preoperative reevaluation may identify prescribed medications that are no longer indicated following resolution of certain health issues. Providers should obtain a thorough history regarding non-prescribed medications, over-the-counter medications, and herbal supplements or vitamins that could potentially contribute to intraoperative or postoperative complications. Issues related to polypharmacy are discussed in more detail in Chap. 5.

Patients must be given clear instructions about which medications to take before and after surgery, and their understanding must be confirmed. In general, patients should continue their normal medications throughout the perioperative period [32]. Some anesthesiologists prefer patients to withhold diuretics, ACE inhibitors, and angiotensin II receptor blockers on the morning of surgery due to the risk of intraoperative hypotension, especially if general anesthesia or major conduction block is planned [33]. Oral hypoglycemic medications are withheld on the day of surgery, and metformin is withheld for 24 h prior to most procedures due to the risk of developing lactic acidosis. Some patients may require preoperative adjustments to their insulin regimen, which can be guided by their primary care provider or anesthesiologist during a preoperative clinic visit [34]. Any decision to stop or withhold antiplatelet agents or anticoagulants including aspirin, clopidogrel, and warfarin should be made in consultation with the prescribing healthcare provider. Nonsteroidal anti-inflammatory drugs (NSAIDs) can be safely withheld prior to surgery, but five elimination half-lives are required

[35]. For example, NSAIDs with a short half-life such as ibuprofen should be discontinued on the day prior to surgery, those with an intermediate half-life such as naproxen should be discontinued 3 days prior, and those with a long half-life such as meloxicam should be stopped for 10 days prior to surgery. Patients on chronic steroid therapy should continue treatment prior to surgery. For those patients on other immunosuppressant medications including methotrexate or tumor necrosis factor (TNF) inhibitors, it is prudent to consult with the prescribing physician regarding the need to interrupt therapy prior to surgery. There is conflicting evidence that these medications retard wound healing and increase the risk of postoperative infection [36]. It is typically recommended that herbal products, including those containing fish oil, ginseng, or garlic, be withheld for at least 2 weeks prior to surgery [37]. When deciding which medications to hold, each should be given consideration based on the patient's individual needs. Those taken on the day of surgery should be taken with a small sip of water, preferably at least 2 h prior to the scheduled procedure. Patients should be specifically counseled on the importance of continuing medications such as beta blockers, anti-reflux medications, and treatments for asthma and thyroid disease on the day of surgery.

Considerations for Patients with Known Cardiac Disease

Given the high level of stress that anesthesia and surgery can pose on the cardiovascular system, it is important to assess the patient's cardiac risk prior to surgery. The presence of significant risk may lead to a delay of an elective procedure, a change in the type of procedure recommended, or pursuit of nonsurgical treatment options. A thorough history and physical exam will identify patients with active cardiac conditions who would benefit from further cardiac testing or treatment of their heart disease prior to surgery [14]. The history should assess exercise tolerance and the presence of angina, palpitations, lightheadedness, syncope, dyspnea on exertion, or paroxysmal nocturnal dyspnea. The physical exam should include measurement of vital signs, auscultation of the heart and lungs, and inspection for distended neck veins, or peripheral edema indicating hypervolemia and possible right ventricular failure. Patients with active or unstable conditions should be referred to a cardiologist for further risk stratification. The cardiologist can also help stabilize and optimize fluid status, blood pressure, and heart rate. Patients who are compliant and medically optimized should continue their current treatment and usually may proceed with the planned surgical procedure.

Prior to interrupting antiplatelet and/or anticoagulant medications in the perioperative period, providers should consider the risks and alternatives of this intervention [35, 38, 39]. Consultation with the patient's cardiologist and/or hematologist is advised when considering withholding these medications or transitioning to a low-molecular weight heparin in patients taking warfarin.

For patients with a pacemaker or implantable cardiac defibrillator (ICD), the provider must determine the type of device, its location (pectoral versus abdominal), battery life, the underlying disease process warranting initial placement of the device, and whether the patient is dependent on the device for safe heart function [40]. This usually requires contacting the cardiologist prior to surgery. The device manufacturer can provide information regarding the effect of placing a magnet over the device and if postoperative interrogation or reprogramming are required. Special consideration is warranted for patients with dual chamber pacemakers who are to undergo extracorporeal shock wave lithotripsy (ESWL). In this case, it is recommended that the device be reprogrammed to the single chamber mode with ventricular-only sensing and pacing, in order to prevent atrial pacing pulses from triggering the lithotripsy generator prematurely. If a patient cannot tolerate the single chamber mode, ESWL should not be performed [41]. For patients with ICDs undergoing ESWL, the tachyarrhythmia detector can be deactivated to prevent delivery of inappropriate shocks. Alternate means of cardiac pacing and external defibrillation should be readily available in all cases because shock waves may cause pacemaker or ICD dysfunction. After ESWL, the device should be reactivated or reprogrammed to its pre-procedure mode and proper function verified because lithotripsy has the potential to permanently damage these devices. Magnetic resonance imaging (MRI) is contraindicated in patients with pacemakers or ICDs. An MRI can change the settings of these devices resulting in dysrhythmias or can cause heating of the lead wires resulting in cardiac tissue damage.

Considerations for Patients with Known Pulmonary Disease

By identifying those patients at increased risk of developing postoperative pulmonary complications, clinicians can develop a strategy to reduce these risks. An effective plan should include postoperative lung expansion techniques such as deep breathing exercises and incentive spirometry, but it may also include preoperative inspiratory muscle training or the use of thoracic epidural analgesia when indicated. These techniques have been shown to decrease rates of pneumonia in postoperative patients [42].

In patients diagnosed with OSA, the use of a continuous-positive airway pressure (CPAP) device should be encouraged to help lessen the degree of upper airway obstruction and resulting atelectasis and hypoxemia [23]. Patients should be instructed to bring their CPAP mask with records of their updated CPAP machine settings on the day of surgery to be used during the recovery period. This may reduce the risk of postoperative complications such as reintubation, delirium or myocardial injury which frequently result in unplanned ICU admissions and longer hospital stays. Providers may want to delay surgery for a sleep consult with polysomnography testing for those patients who would most benefit from the use of CPAP in the perioperative setting. Preoperative identification of patients at risk for OSA will alert providers to prepare for the possibility of difficult airway management.

Smoking cessation should be strongly encouraged. The risks associated with cigarette smoking include decreased mucociliary clearance and immune function with predilection for the development of pneumonia. The greatest benefit results if cessation of smoking occurs at least 6 weeks prior to surgery. However, as little as 48 h of preoperative abstinence is thought to improve mucociliary clearance and decrease carbon monoxide levels, which may help improve pulmonary and cardiovascular function [43].

Antimicrobial therapy should be initiated in some patients presenting with signs or symptoms of a respiratory infection. Delay of elective procedures should be strongly considered when a patient has a respiratory infection given the associated increased airway reactivity and decreased immune function of the respiratory tract in such cases [18]. This predisposes patients to airway compromise from bronchospasm or pneumonia. Some patients with excessive sputum production may benefit from implementation of therapies to improve sputum clearance and decrease airway resistance such as chest physiotherapy or pharmacologic treatments.

Considerations for Patients with Known Cognitive Impairment

Elderly patients with impaired cognition are at risk for adverse perioperative outcomes. An important step in reducing this risk focuses on the prevention of postoperative delirium. First, efforts should be made to optimize the patient's medical condition. This may include controlling or eliminating modifiable risk factors such as respiratory insufficiency, dehydration, malnutrition and electrolyte abnormalities. Second, known delirium triggers such as physical restraints, sensory deprivation, sleep pattern disturbances, and the use of certain sedatives including benzodiazepines and anticholinergics should be avoided [29]. Adequate pain control is crucial; the plan for postoperative analgesia should include non-narcotic modalities in order to avoid the overuse of opioid narcotics.

For high-risk patients, consider obtaining a preoperative geriatric consult to assess functional status and the degree of cognitive impairment prior to surgery. This should include a comprehensive evaluation of the social support systems available to assist with recovery. Based upon factors such as mental status, mobility, fall risk, nutrition and social support, geriatricians can identify those patients who need postoperative home care or rehabilitative services and can assist with disposition planning to nursing homes or other long-term care facilities.

Developing an Anesthetic Plan

During the preoperative evaluation, consider the possible anesthetic techniques based on the history and physical exam and the proposed surgical procedure. The use of local anesthesia should be encouraged whenever possible because this technique has lower postoperative complication rates compared to regional or general anesthesia [44]. Regional anesthesia should be pursued when appropriate unless contraindicated by patient refusal, coagulopathy, severe hypovolemia, or infection at the injection site. Regional anesthesia is associated with fewer pulmonary complications when compared to general anesthesia [45]. It also has the advantage of providing better postoperative pain control, which decreases the dosage requirements for sedatives and narcotics. Limiting exposure to these medications lowers the risk of developing the associated side effects of pruritus, urinary retention, decreased bowel motility, and respiratory depression. Although the use of local or regional anesthesia is encouraged whenever possible, general anesthesia is often required. According to one recent study, the approach to providing general anesthesia, whether through administration of a volatile inhalational gas or through total intravenous anesthesia (TIVA), has not been shown to increase the incidence of delirium in the early postoperative period [46]. At present, there is no evidence that one anesthetic technique is superior to another with respect to cognitive dysfunction in elderly patients [47].

Summary

Surgical care of elderly patients with urologic disorders is common, and the volume of surgical care in this cohort is likely to increase with the aging of the population. Careful preoperative assessment can help to reduce many of the potential risks associated with surgery in older adults. Clinical optimization of underlying comorbid conditions can enhance overall health and reduce rates of perioperative and postoperative complications associated with these other health conditions.

References

1. United States Census Bureau. http://www.census.gov/prod/cen2010/briefs/c2010br-03.pdf. Accessed 20 Sept 2011.
2. Etzioni DA, Liu JH, Maggard MD, et al. The aging population and its impact on the surgery workforce. Ann Surg. 2003;283:170–7.
3. Silverstein JH. The practice of geriatric anesthesia. In: Siverstein JH, Rooke GA, Reves JG, et al., editors. Geriatric anesthesiology. 2nd ed. New York, NY: Springer; 2008. p. 3–14.
4. Barnett SR. Polypharmacy and perioperative medications in the elderly. Anesthesiol Clin. 2009;27:377–89.
5. Turrentine FE, Wang H, Simpson VB, et al. Surgical risk factors, morbidity, and mortality in elderly patients' long term survival. J Am Coll Surg. 2006;203:865–77.
6. Sieber FE, Ryan SR. Preventing postoperative complications in the elderly. Anesthesiol Clin. 2011;29:83–97.
7. Polanczyk CA, Marcantonio E, Goldman L, et al. Impact of age on perioperative complications and length of stay in patients undergoing noncardiac surgery. Ann Intern Med. 2001;134:637–43.
8. Hamel MB, Henderson WG, Khuri SF, et al. Surgical outcomes for patients aged 80 and older: morbidity and mortality from major noncardiac surgery. J Am Geriatr Soc. 2005;53:424–9.
9. Story DA. Postoperative complications in elderly patients and their significance for long-term prognosis. Curr Opin Anaesthesiol. 2008;21:375–9.
10. Rix TE. Pre-operative risk scores for the prediction of outcome in elderly people who require emergency surgery. World J Emerg Surg. 2007;2:16.
11. Peled E, Keren Y, Halachmi S, et al. Patients aged 80 and older undergoing orthopedic or urologic surgery: a prospective study focusing on perioperative morbidity and mortality. Gerontology. 2009;55:517–22.

12. Makary MA, Segev DL, Pronovost PJ, et al. Frailty as a predictor of surgical outcomes in older patients. J Am Coll Surg. 2010;210:901–8.
13. Lee TH, Marcantonio ER, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. Circulation. 1999;100:1043–9.
14. Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for non-cardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association task force on practice guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery): developed in collaboration with the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, and Society for Vascular Surgery. Circulation. 2007;116:1971–96.
15. Wu WC, Schiffner TL, Henderson WG, et al. Preoperative hematocrit levels and postoperative outcomes in older patients undergoing noncardiac surgery. JAMA. 2007;297(22):2481–8.
16. Qaseem A, Snow V, Fitterman N, et al. Risk assessment for and strategies to reduce perioperative pulmonary complications for patients undergoing noncardiothoracic surgery: a guideline from the American College of Physicians. Ann Intern Med. 2006;144:575–80.
17. Johnson RG, Arozulla AM, Neumayer L, et al. Multivariable predictors of postoperative respiratory failure after general and vascular surgery: results from the patient safety in surgery study. J Am Coll Surg. 2007;204:1188–98.
18. Canet J, Gallart L, Gomar C, et al. Prediction of postoperative pulmonary complications in a population-based surgical cohort. Anesthesiology. 2010;113:1338–50.
19. Ramakrishna G, Sprung J, Ravi BS, et al. Impact of pulmonary hypertension on the outcomes of noncardiac surgery: predictors of perioperative morbidity and mortality. J Am Coll Cardiol. 2005;45:1691–9.
20. Hwang D, Shakir N, Limann B, et al. Association of sleep-disordered breathing with postoperative complications. Chest. 2008;133:1128–34.
21. Memtsoudis S, Liu SS, Ma Y, et al. Perioperative pulmonary outcomes in patients with sleep apnea after noncardiac surgery. Anesth Analg. 2011;112:113–21.
22. Caples S, Gami A, Somers V. Obstructive sleep apnea. Ann Intern Med. 2005;142(3):187–97.
23. Adesanya AO, Lee W, Greilich NB, et al. Perioperative management of obstructive sleep apnea. Chest. 2010;138:1489–98.
24. Launois SH, Pepin JL, Levy P. Sleep apnea in the elderly: a specific entity? Sleep Med Rev. 2007;11:87–97.
25. Chung F, Yegneswaran B, Liao P, et al. STOP questionnaire: a tool to screen patients for obstructive sleep apnea. Anesthesiology. 2008;108(5):812–21.
26. Rasmussen LS, Larssen K, Houx P, et al. The assessment of postoperative cognitive function. Acta Anaesthesiol Scand. 2001;45:275–89.
27. Ramaiah R, Lam AM. Postoperative cognitive dysfunction in the elderly. Anesthesiol Clin. 2009;27:485–96.
28. Liu LL, Leung JM. Predicting adverse postoperative outcomes in patients aged 80 years or older. J Am Geriatr Soc. 2000;48:405–12.
29. Silverstein JH, Timberger M, Reich DL, et al. Central nervous system dysfunction after noncardiac surgery and anesthesia in the elderly. Anesthesiology. 2007;106:622–8.
30. Fleisher LA, Beckman JA, Brown KA, et al. ACCF/AHA focused update on perioperative beta blockade incorated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines. Circulation. 2009;120:2123–51.
31. Bakker EJ, Raversbergen NJC, Poldermans D. Perioperative cardiac evaluation, monitoring, and risk reduction strategies in noncardiac surgery patients. Curr Opin Crit Care. 2011;17:409–15.
32. Silverman DG, Rosenbaum SH. Integrated assessment and consultation for the preoperative patient. Med Clin North Am. 2009;93:963–77.
33. Bertrand M, Godet G, Meersschaert K, et al. Should the angiotensin II antagonists be discontinued before surgery? Anesth Analg. 2001;92:26–30.
34. Kohl BJ, Schwartz S. Surgery in the patient with endocrine dysfunction. Med Clin North Am. 2009;93:1031–47.
35. Douketis JD, Berger PB, Dunn AS, et al. The perioperative management of antithrombotic therapy. Chest. 2008;133:299S–339.
36. Harle P, Straub RH, Fleck M. Editorial: elective surgery in rheumatic disease and immunosuppression: to pause or not. Rheumatology. 2010;49:1799–800.
37. Wong A, Townley SA. Herbal medicines and anaesthesia. Cont Edu Anaesthesiol Crit Care Pain. 2011;11:14–7.
38. Dunn AS, Turpie AG. Perioperative management of patients receiving oral anticoagulants. Arch Intern Med. 2003;163:901–8.
39. Hall R, Mazer CD. Antiplatelet drugs: a review of their pharmacology and management in the perioperative period. Anesth Analg. 2011;112:292–318.
40. American Society of Anesthesiologists. Task force on perioperative management of patients with cardiac rhythm management devices: practice advisory for the perioperative management of patients with cardiac rhythm management devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists task force on perioperative management of patients

with cardiac implantable electronic devices. Anesthesiology. 2011;114:247–61.
41. Ubee SS, Kasi VS, Bello D, et al. Implications of pacemakers and implantable cardioverter defibrillators in urological practice. J Urol. 2011;186: 1198–205.
42. Smetana G. Postoperative pulmonary complications: an update on risk assessment and reduction. Cleve Clin J Med. 2009;76(4):60–5.
43. Warner DO. Preoperative smoking cessation: the role of the primary care provider. Mayo Clin Proc. 2005;80:252–8.
44. Paez A, Redondo E, Linares A, et al. Adverse events and readmissions after day-case urological surgery. Int Braz J Urol. 2007;33:330–8.
45. Atanassoff PG. Effects of regional anesthesia on perioperative outcome. J Clin Anesth. 1996;8:446–55.
46. Monk TG, McDonagh D, Martin G, et al (2011) Preoperative cognition, not the type of anesthesia, predicts postoperative delirium. ASA Meeting Abstract A613.
47. Devere R (2012) Dementia insights: cognitive complications of elective surgery and anesthesia. Practical neurology. http://PracticalNeurology.org

Anesthesia for the Geriatric Urologic Patient

27

Jeffrey H. Silverstein

Introduction

Elderly patients have a distinctly increased risk for undergoing anesthesia and surgery. Evaluation of data collected in the 1980s, which still appear valid, suggests that the combination of age and disease load increases the risk for morbidity and mortality [1, 2]. Chronological age on its own is only marginally associated with increased risk. Normative aging can be distinguished from successful aging, which in turn can be separated from age-related disease [3].

Anesthesia involves controlling multiple physiologic processes to permit surgical interventions that normal compensatory mechanisms would not otherwise permit, both due to pain and the physiologic reactions to pain. Anesthesiologists also have expertise in the provision of critical care, the administration of sedation for a variety of less invasive procedures, and the management of postoperative pain and chronic pain syndromes. The primary goal of the anesthesiologist, working with the urologist, is to maintain homeostasis in the face of surgical intervention. Avoiding pain or sensation resulting from a given procedure is the primary goal that assists with control of other physiologic processes such as circulation and respiration. These systems frequently require specific intervention such as mechanical ventilation or vasopressor support for circulation.

Geriatric patients have been described as having a decreased innate capacity to maintain homeostasis. This has been described both in terms of a decrease in reserve function [4] and as homestenosis [5] (Fig. 27.1). The anesthesia team caring for the urologic patient should understand how specific organ systems, particularly the heart, lungs, and brain, function in the aging patient in order to tailor an appropriate anesthetic. In addition to altered physiology, the pharmacology of anesthetic medications, including the pharmacokinetics and pharmacodynamics of many drugs manifest specific age-related alterations.

Approach to the Geriatric Surgical Patient

In assessing a patient, the request for anesthesia services usually specifies a specific operation associated with a diagnosis. Thus, the anesthesiologist does not discern a chief complaint during the pre-anesthesia evaluation. The anesthesiologist's approach to patient evaluation has been described as a vertical- or system-based approach, as opposed the traditional diagnostic approach [4] (Fig. 27.2a, b). The American Society of Anesthesiologists (ASA) physical status classification is assigned following this evaluation (Table 27.1). Although frequently described as a measure of perioperative risk, the primary purpose of this score is to communicate among

J.H. Silverstein, M.D., M.S., A.G.S.F. (✉)
Department of Anesthesiology, Icahn School of Medicine at Mount Sinai, New York, NY, USA
e-mail: Jeff.silverstein@mssm.edu

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_27,

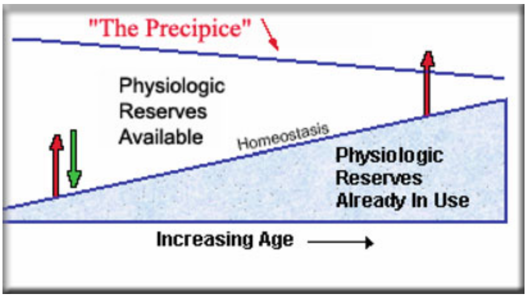


Fig. 27.1 Younger individuals are depicted on the *left* of the schematic and older individuals on the *right*. Homeostasis is now the slanting line that separates physiologic reserves already in use (to maintain homeostasis at rest) from those reserves still available. The precipice is sloping downward, but less steeply. However, the relative distance between homeostasis and a given "precipice" remains the same because of the increased usage of physiologic reserves to maintain homeostasis. [Original material from "Homeostenosis" by George Taffet, MD in collaboration with the University of Oklahoma Reynolds Department of Geriatric Medicine, 2008.]

clinicians. The ASA physical status does not consider age, type of operation, or other nondisease entities, such a frailty that are important modulators of outcomes.

It is now common practice to admit patients to the hospital only on the day surgery after the operation, even for major surgery. This provides the anesthesiologist with a limited opportunity to evaluate the patient and discuss the anesthetic options and the potential perioperative experience with our patients. Preoperative clinics and preoperative telephone interviews provide alternative opportunities to develop an anesthetic plan and establish a rapport with the patient. The preoperative evaluation is an essential process in developing an anesthetic plan and provides an opportunity to answer questions for the patient and family. A consultation from a general internist or specialist is frequently requested as part of the preoperative evaluation. Policies and practices vary as to whether such input is required or even routine. Consultations that indicate that the patient is "cleared" for surgery provide limited useful information. A complete overview of the patient's medical condition, including recent evaluations and medications are considerably more useful to the anesthesiologist and surgeon. The most constructive and useful evaluations provide plans for minimizing risk in the perioperative period, including before, during, and after surgery. The consultants should not make anesthetic choices. Statements such as "cleared for local anesthesia" are inappropriate. Coordinated care involving good communication among the generalist and specialist physicians, the surgeon, the anesthesiologist, and the patient provides the best care for patients.

Plans for the management of the medical problems in the pre and postoperative period should be determined in advance. The team caring for the patient should have a plan for the management of medication regimens such as anti-Parkinsonian medications, anticoagulants, and antidiabetic agents, prior to surgery. Protocols are most effective when agreed upon in advance. When consultation is requested, it should clearly define the issues that need to be addressed and the expected role of the consultant.

Although risk assessment is frequently on the mind of both the patients and physicians, the evaluation and improvement of the patient's medical status prior to surgery, as well as planning for the recovery process, should be the focus of the preoperative assessment. Rarely, the assessment will determine that the proposed surgery is not warranted, but most of the time the objective of risk assessment is to provide a plan for preparing the patient for surgery.

In October of 2012, the American College of Surgeons National Surgical Quality Improvement Program and the American Geriatrics Society published a guideline for preoperative assessment of the geriatric patient assembled through an extensive literature review by an expert panel consisting of multiple specialties, including geriatrics, urology, and anesthesiology [6]. In addition to the history and physical examination described above, this group created a checklist which serves as a reasonable guide for the preparation of elderly patients for urological surgery (Table 27.2).

Evaluation of the cognitive status of a patient involves both the assessment of the capacity to understand the anticipated procedure and to provide a baseline for comparison in the

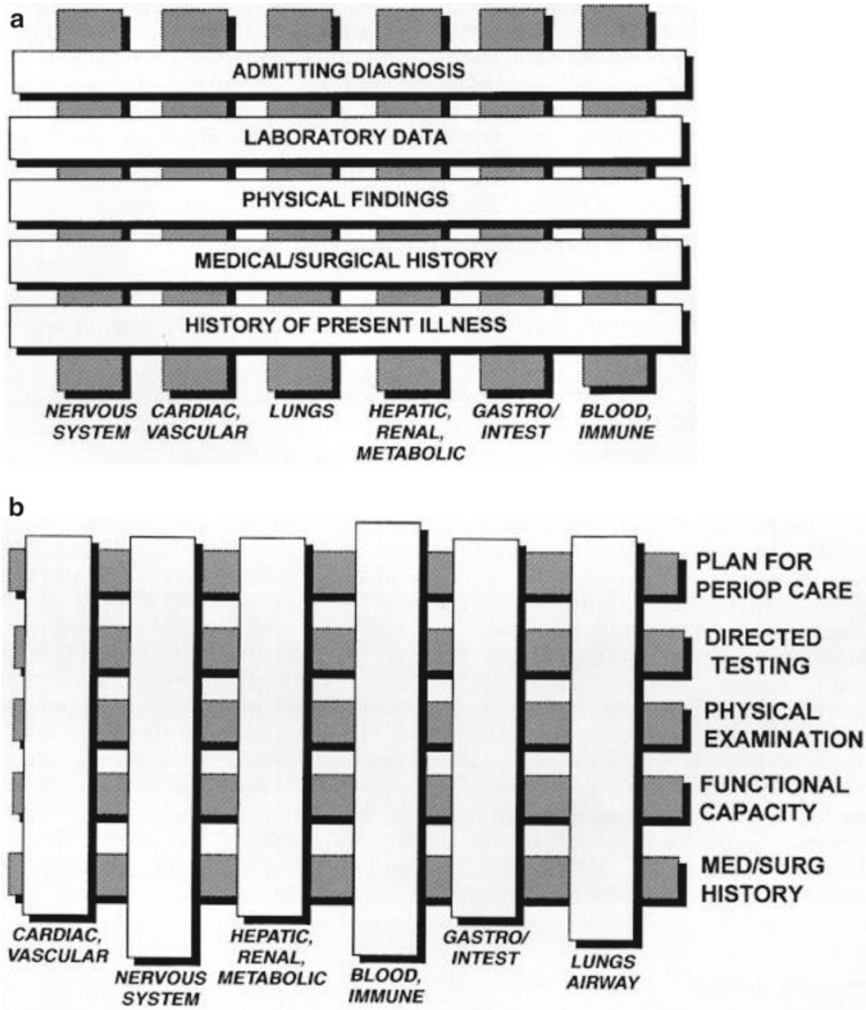


Fig. 27.2 (**a**) The traditional medical approach to diagnosis can be represented as a series of horizontal techniques of inquiry (*open bars*) applied across various organ systems (*shaded bars*) to consolidate data describing the status of different organs into a unified diagnostic entity. (Muravchick S. Preoperative assessment of the elderly patient. Anesthesiol Clin North America. 2000, 18(1): 71–89. (**b**) Organ system-based vertical approach to preoperative assessment of the elderly patient by an anesthesiologist differs from the traditional diagnostic approach because it applies the various techniques of inquiry (*shaded bars*) sequentially to each major organ system (*open bars*) in order to assess organ function and functional reserve. The primary objective of preoperative assessment should be evaluation of physical status, rather than the identification of specific underlying disorders. (Modified from Muravchick S. Preoperative assessment of the elderly patient. Anesthesiol Clin North America. 2000, 18(1): 71–89

postoperative period. One of the problems encountered by older adults in the postoperative period is a change in cognitive function. Understanding these alterations is facilitated by a reasonable preoperative assessment. The American College of Surgeons and American Geriatrics Society (ACS/AGS) guidelines recommend a very brief battery consisting of the Mini-Cog [7]. If an indication of cognitive dysfunction or dementia is evident, a more formal exploration should be pursued. Patients should also be screened for depression and alcohol or other substance abuse.

The American Heart Association (AHA) and American College of Cardiology (ACC) guide-

Table 27.1 ASA physical status classification system

• **ASA Physical Status 1**—A normal healthy patient
• **ASA Physical Status 2**—A patient with mild systemic disease
• **ASA Physical Status 3**—A patient with severe systemic disease
• **ASA Physical Status 4**—A patient with severe systemic disease that is a constant threat to life
• **ASA Physical Status 5**—A moribund patient who is not expected to survive without the operation
• **ASA Physical Status 6**—A declared brain-dead patient whose organs are being removed for donor purposes

The designation 'E' can be added to any of the ASA physical status categories to designate the surgery is being done on an emergency basis

Table 27.2 Checklist for the optimal preoperative assessment of the geriatric surgical patient [6]

In addition to conducting a complete history and physical examination of the patient, the following assessments are strongly recommended:
• 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

lines for the evaluation of cardiac disease in patients undergoing noncardiac surgery are incorporated into the ACS/AGS process [8]. These guidelines integrate surgical severity, type and severity of comorbid disease, and exercise tolerance into a rational approach that suggests who needs to enter an advanced evaluation process. The most recent AHA/ACC guidelines were developed with the idea of limiting the use of noninvasive cardiac testing and to avoid diagnostic procedures with a risk greater than what might be associated with the proposed surgery. With most medical problems the evidence base is limited, so the impact of optimization of medical conditions on postoperative outcome is unknown. Examples include better control of high blood pressure, steroid supplementation and/or taper for a patient with a current exacerbation of reactive airway disease, better control of blood sugar, or consideration of additional therapy for a patient with stable angina. One of the best examples of the difficulties of determining medical optimization and the impact on outcome is the use of beta-blockade for patients with known or suspected coronary heart disease who are not already receiving a beta blocker. The initial studies seemed to indicate few adverse effects from beta-blockade with significant improvements in postoperative cardiac morbidity and mortality [9]. Subsequently, the benefit has been more difficult to determine. Data from the DIPOM trial have documented the risk of perioperative stroke, although associated with a very large preoperative dose of metoprolol (POISE) [10, 11]. While some clinicians continue to champion the use of perioperative beta blockade [12, 13], alternative regimens for minimizing postoperative myocardial mortality are underway (see, for example, POISE 2: http://www.phri.ca/body.cfm?id=392).

In addition to the cardiac guidelines, the ACS/AGS process recommends identifying pulmonary risk and strategies for risk mitigation [6]. These have been conceptually divided into patient-related factors, surgery-related factors, and factors which have traditionally been thought

Table 27.3 Risk factors for postoperative pulmonary complications

Patient-related factors
• Age > 60 years • Chronic obstructive pulmonary disease (COPD) • American Society of Anesthesiologists (ASA) class II or greater • Functional dependence[a] • Congestive heart failure • Obstructive sleep apnea • Pulmonary hypertension • Current cigarette use • Impaired sensorium[b] • Preoperative sepsis • Weight loss ≥ 10 % in 6 months • Serum albumin ≤ 3.5 mg/dL • Blood urea nitrogen (BUN) ≥ 7.5 mmol/L (≥21 mg/dL) • Serum creatinine ≥ 133 mmol/L (≥1.5 mg/dL)
Surgery-related factors
• Prolonged operation ≥3 h • Surgical site[c] • Emergency operation • General anesthesia • Perioperative transfusion • Residual neuromuscular blockade after an operation
Not risk factors
• Obesity • Well-controlled asthma • Diabetes

[a]Total dependence was the inability to perform any activities of daily living. Partial dependence was the need for equipment or devices and assistance from another person for some activities of daily living

[b]Acutely confused or delirious patient who is able to respond to verbal or mild tactile stimulation, or mental status changes or delirium in the context of current illness

[c]Highest risk procedures: upper abdominal, thoracic, neurosurgical, head and neck, vascular (e.g., aortic aneurysm repair)

Note: detailed references for each factor are available in the original publication [6]

to be, but are apparently not risk factors for pulmonary complications (Table 27.3).

In preparing elderly patients for major urologic surgery, the involvement of a geriatrician should be considered. Comprehensive geriatric assessment (CGA) is a generic term for a variety of programs focused on assessment and management of geriatric syndromes. Despite the relatively consistent body of evidence supporting the utility of CGA and other geriatric follow-up programs, they have failed to be instituted on a wide scale [14, 15]. CGA programs are effective at managing multiple medical problems and thus preventing hospital readmission. Whether a geriatrician or other consultant, it is vital to have a systematic means to either implement or reject the recommendations of the consultants. The most developed literature regarding the role of geriatricians in the care of surgical patients has been focused on patients with fractures of the upper femur, but certainly could be expanded to elderly urology patients [16]. There are clear advantages to patients from these models, the key factor being the implementation of the geriatric parts of the care plan. Marcantonio demonstrated the potential for a marked improvement in outcome in a randomized trial of proactive geriatric consultation based on a structured protocol, reducing delirium by over one-third [17]. Some perioperative CGA programs have cut down on length of stay [14]. More complex programs such as the Hospital Elder Life Program are being evaluated for their impact on surgical patients [18]. The ACS/AGS guidelines recommend assessment of functional status and fall risk, assessment of frailty (see below), nutritional status, medication history with an appropriate assessment of polypharmacy issues, and an evaluation of social support systems [6]. All of these assessments are probably most effectively carried out by a geriatrician.

Elderly patients are likely to have advanced directives and "do not resuscitate" (DNR) orders. The approach to these orders should be based on hospital policy and understood by all involved in the patient's care. Cardiac arrests in the operating room do not have the same poor outcome associated with either in or out of hospital arrests and mortality is not necessarily increased in patients with DNR orders [19]. These circumstances should be immediately witnessed and frequently are due to reversible causes such as drug effects or hemorrhage. Many DNR orders proscribe intubation which is standard part of general anesthesia. It is not uncommon to suspend DNR orders in the operating room with reinstitution being either automatic or requiring a physician order [20, 21]. Particularly for a patient at high risk for complications, the DNR orders require review and discussion with the patient. The urologist, anesthesiologist, and other caregivers should all agree as to the approach to be used in advance of any procedure.

Systemic Alterations Associated with Aging

The specific alterations associated with aging that are of particular interest to the anesthesiologist have been reviewed in great depth in recent textbooks [22] and handbooks. A brief overview of these systemic changes is included here to focus on the anesthetic aspects; however, the reader is referred to other chapters in this volume for a more in-depth review of each of these areas.

Cardiac

Patients in the USA and Northern Europe carry a very large burden of cardiac disease, primarily coronary artery disease. The anesthetic implications of coronary artery disease, congestive heart failure, and other specific disease entities which are common in geriatric patients, is beyond the scope of this chapter. The primary age-related alterations in the cardiovascular system, in the absence of coronary artery disease or even hypertension, are thought to evolve primarily from alterations in the aortic root secondary to the continuous distention and contraction associated with each cardiac cycle [23, 24]. With each systole, the aorta expands slightly and then returns to its normal size during diastole. With aging, the elastic properties of the aorta start to change, resulting in a stiffer vessel. This has a number of important consequences including an increase in after-load for the left ventricle and higher systolic pressure, particularly in the aortic root. This also creates an increase in pulse wave velocity and therefore a more rapid return of reflected pulse waves in the vascular system. When a rock is dropped into a calm body of water, the waves expand out from where the rock entered until it encounters an obstacle, at which point reflected waves return to the point of origin. The same process occurs in the cardiovascular system. In younger patients, these reflected waves return during diastole; however, in elderly people with stiffer vessels, these waves return and sum on top of systole, increasing systolic pressure even further. The end result of these alterations is that, even in the absence of disease, a healthy and well-conditioned elderly patient will have some increase in left ventricular size (hypertrophy) and some slowing of ventricular filling. Diastolic relaxation decreased which diminishes early diastolic filling. Ventricular preload becomes more dependent on passive filling produced by both the left atrial pressure and the active filling produced by the atrial contraction. To achieve adequate ventricular filling these must overcome the increased ventricular stiffness and both effects require a full atrium. However, because veins also stiffen with age, atrial blood volume is not so easy to keep constant. The clinical implications are that elderly individuals are somewhat more sensitive to fluid load and they are more prone than young patients to both hypotension and hypertension during surgery.

Consistent with the general idea of loss of reserve function, elderly patients generally cannot increase cardiac output as much as a younger patient might. This results from a combination of left ventricular alterations and a slight decrease in heart rate associated with a limited ability to increase heart rate [25].

Detailed management of the patient with cardiac disease is beyond the scope of this chapter. However, elderly patients with previously placed cardiac stents have become extremely common, and these patients frequently present for urological procedures. There have been a number of cases of sudden death following surgery that have created concern related primarily to the management of anticoagulants in the perioperative period [26]. There is a consistent dilemma between continuing anticoagulant therapy and the potential for operative hemorrhage. As newer drugs, and particularly short acting medications become available, the management of this circumstance will change [27]. Serious consideration needs to be given to maintaining some level of anticoagulation, although the risk of surgical bleeding needs to be considered as well. Clinicians should look to their local cardiologists for up to date management protocols.

Pulmonary

The respiratory system is substantially altered by both aging and general anesthesia [28] (Table 27.2). General anesthesia decreases functional residual capacity by enhancing expiratory muscle tone and diminishing inspiratory muscle tone. Closing capacity increases with age and sighs are suppressed. The combination of increased closing capacity, decreased functional residual capacity, and the loss of sighs increases the already high incidence of atelectasis under general anesthesia. Volatile anesthetics reduce the effectiveness of hypoxic pulmonary vasoconstriction and mechanical ventilation disturbs the normal pattern of diaphragmatic breathing in the supine patient, disturbing normal ventilation/perfusion matching. The use of supplemental oxygen and monitoring with pulse oximetry and frequently with expired gas analysis has markedly decreased the incidence of clinically significant hypoxemia in all age groups. Ciliary function is diminished by both volatile anesthetics and the placement of an endotracheal tube. This effect apparently continues into the postoperative period. Upper airway reflexes are diminished in elderly patients, increasing the risk for silent regurgitation and aspiration. At-risk patients will be challenged postoperatively by drugs that may further depress the airway protective reflexes and impair gastric emptying. Aspiration is much more likely to occur postoperatively than intraoperatively. Elderly patients in general and particularly very frail patients are at increased risk for postoperative ventilatory failure and pneumonia [29]. Unfortunately, there is little in the way of proven effective interventions to prevent pulmonary complications [30, 31].

Renal

Renal function is reported to decrease in older adults with glomerular filtration rates reported to decrease by 10 mL/decade, reaching 50 % by age 80. There is a decrease in total body water, decrease in renal mass of approximately 10 % per decade, and a 20 % loss of renal mass by age 85 [32]. In recent years, it has become apparent that there is considerable variability in these alterations, such that it is probably inappropriate to assess renal function based on age. Rather it is important to estimate or directly measure renal function as some elderly patients will have essentially intact renal function, while others will have significant impairment [33, 34].

Central Nervous System

The healthy elderly patient is cognitively intact. Even these patients manifest an increased sensitivity to a wide variety of anesthetic drugs necessitating a decrease in the dose [35]. This aspect of CNS aging is noted below, but, aside from adjusting medications, there is little that needs to be done specifically. A number of neurodegenerative diseases tend to accumulate in older adults, including Parkinson's disease and the dementias. Patients with motor disorders such as Parkinson's disease are commonly on medications. There needs to be a coherent plan for managing these medications. It is frequently possible to continue medications from the normal regimen up until a procedure and restart them on schedule following surgery. If this is not possible, the primary care physician or neurologist should be consulted for an appropriate plan. An effective recent therapy has been deep brain stimulation (DBS) [36]. When electrocautery is being employed, most experts suggest that the DBS be switched off. These patients are usually quite stiff when the stimulator is off, so the ideal arrangement is to have the device deactivated immediately before surgery and reprogrammed in the Post-Anesthesia Care Unit (PACU) immediately following the procedure.

Musculoskeletal

The loss of muscle mass in the otherwise healthy elderly individual is notable but should not have a major impact on the conduct of urological procedures. There is, however, a syndrome of accelerated sarcopenia referred to as frailty. Although the original descriptions of frailty focused primarily on muscle loss [37, 38], studies of frailty in the perioperative period have focused more on functional definitions [39]. Clinicians have long noted frail elderly patients and worried about their prognosis. Recent studies in surgical patients have demonstrated that the additional use of a frailty index can enhance preoperative risk stratification [40, 41].

Anesthetic Choices for Older Adults

Sedation (Monitored Anesthetic Care)

Sedation involves the reduction of anxiety, usually using medications. The American Society of Anesthesiologists defines three levels of sedation: minimal sedation, moderate sedation/analgesia, and deep sedation/analgesia. Monitored anesthesia care (MAC) is frequently used as a synonym for sedation; however, this is really a term regarding the provision of service. Any level of sedation or no sedation may be provided during MAC.

During a regional anesthetic such as a spinal, epidural, or nerve block, many patients request sedation. They typically prefer not to be aware of the activities in the operating room. Almost always this request can be accommodated. Small quantities of midazolam and fentanyl often suffice, but if higher levels of sedation are desired, typically propofol, either by intermittent bolus or infusion will be used. Interestingly, older patients may fall asleep during epidural or spinal anesthesia in the absence of any sedative medications. Airway obstruction is always a concern when sedation is instituted. Airway obstruction should be manageable by a vigilant and skilled anesthesiologist; however, in the absence of careful monitoring and skilled airway management, airway obstruction can rapidly lead to hypoxia and patient injury. This risk to the patient forms the basis for the recent Joint Commission requirement (Standard PC.13.20) that qualified staff, in addition to the individual performing the procedure, are present to evaluate, monitor, administer medication, assist with the procedure if needed, and recover the patient [42].

Topical Anesthesia

Cystoscopic surgery is frequently undertaken with topical anesthesia inserted into the urethral meatus. This means of anesthesia is usually provided by the urologist with the anesthesiologist providing sedation. The primary issues for the urologist are to have patience in waiting for the local anesthetic to work, which usually requires about 10 min, and to appreciate that there are limits to the total amount of local anesthetic that can be safely administered. Recently, some groups have been using intracorpus spongiosum penile blocks with good results [43].

Regional Anesthesia

Regional anesthesia is the technique of rendering a portion of a patients' body insensate to surgical stimuli. This is accomplished by placing a local anesthetic near the nerves which go to that portion of the body. Local anesthetic agents reversibly inhibit the propagation of electrical potentials along nerves. Anesthesia (loss of sensation) and paralysis (loss of muscle activity) occurs when a local anesthetic agent is applied to a specific nerve or pathway in sufficient concentration. There are two classes of local anesthetics currently in use including aminoester and aminoamide local anesthetics. Unlike cocaine, these agents do not stimulate the sympathetic nervous system and thus do not produce hypertension or local vasoconstriction, nor do they have any abuse potential. The various properties of different local anesthetics are employed in different techniques, including topical anesthesia (surface), infiltration, plexus block, epidural (extradural) block, or spinal anesthesia. The local anesthetic lidocaine is also used as a Class Ib antiarrhythmic drug; however, this drug and all local anesthetics are arrhythmogenic at higher doses. A vitally important safety concept is that all local anesthetics have limited therapeutic windows. Overdosage can result in seizures, cardiac arrhythmias, and resultant death. Elderly patients are not more sensitive to local anesthetics, but, while there are large variations in how aging alters the pharmacokinetics of local anesthetics, aging per se accounts for less than 20 % of variability [44–46].

Field blocks and peripheral nerve blocks should have minimal systemic effects. Care needs to be exerted to avoid intravascular injection of the local anesthetic. There is a potential for allergic reaction to the drug. Local anesthetic gel has been utilized in cystoscopic procedures; however, a recent meta-analysis suggests that there is little benefit to the local anesthetic and that the benefit is essentially limited to the lubricant properties of the gel [47].

Subarachnoid (usually called spinal) and epidural anesthesia are classified as neuraxial blocks. They are complete anesthetics in that no other supplement is necessary, although sedation is often provided at the request of the patient, the surgeon, or perhaps the anesthesiologist. For subarachnoid anesthesia, the local anesthetic is injected into the cerebrospinal fluid where it quickly diffuses into the spinal nerves. This requires passing a needle through the dura and arachnoid membranes, hence the term subarachnoid. At this location, spinal nerves have minimal connective tissue surrounding them; so the anesthetic effectively blocks all nerve fibers, including motor, sensory and sympathetic nerves. An epidural anesthetic deposits the anesthetic agent just outside of the dura and typically involves the placement of a small catheter which can be used for repeated or continuous administration of the drug. Nerves are covered with thick connective tissue sheaths in the epidural space. This slows the onset of the anesthetic. For both subarachnoid and epidural anesthesia, varying the concentration, dose, and volume of the injected local anesthetic permits differential blockade of nerve types. When the purpose is postoperative analgesia, it is desirable to block the pain fibers while sparing motor nerves. Unfortunately, it is difficult to anesthetize pain fibers without also affecting the sympathetic nerves, so blood pressure can still be an issue.

The hemodynamic effects of neuraxial anesthesia stem from the blockade of sympathetic nerves. The level of thoracic dermatomes of sympathetic fibers affected and robustness of the reflex response via the vagus nerve helps to determine the hemodynamic response to neuraxial anesthesia. In the case of spinal anesthesia, the sympathetic fibers may be at least partially blocked for many dermatomes above the level of sensory blockade. A near total sympathectomy is not uncommon with spinal anesthesia. Rooke demonstrated the profound alterations in blood pressure noted in elderly patients as decreased left ventricular filling as blood volume shifted to the legs and mesentery [48]. However, the increase in ejection fraction ameliorated much of the impact on stroke volume and cardiac output.

Spinal and epidural anesthesia can be combined with general anesthesia [49, 50]. This typically involves the provision of primarily a high thoracic epidural anesthetic with the addition of a light general endotracheal anesthetic. The advantage of the technique includes the ability to use considerably less general anesthetic with resultant rapid emergence with the complete absence of pain, because the epidural is still active and will be used to manage postoperative pain. A limitation of the technique includes added difficulty in maintaining blood pressure in the operating room. In addition, it is common to place an epidural catheter for postoperative pain control which will only be activated at the end of surgery. In other words, it is not used at part of the intraoperative anesthetic technique. These methods have been used within the construct of fast-track recovery, in which multiple modalities are used to decrease pain, and mobilize and discharge the patient as soon as possible after major surgery [51, 52].

The advantages of regional anesthesia include profound, complete lack of sensation in the absence of mind-altering medications. Although as described above, sedation is commonly added to a regional block, if a patient prefers and the urologist is agreeable, the patient can be awake during the procedure without untoward sensation. The pain relief lasts into the postoperative period. This depends upon the dosage of anesthetic administered at the time of the procedure. Various local agents and their average durations and maximum doses are listed in (Table 27.4). Catheter techniques such as epidural anesthesia can be continued for prolonged periods of time.

Table 27.4 Local anesthetics commonly used in care of older adults

Local Anesthetics	Duration (hrs)			Max Dose
	Spinal	Epidrual	Peripheral	(mg/kg)
Chloroprocaine 2–3 %	1 to 1.5	0.5 to 1.5		12
Lidocaine 1–2 %	1 to 1.5	1.5 to 2.5	2 to 4	4.5
Mepivacaine 1–1.5 %	1 to 1.5	1 to 3	3 to 5	4.5
Bupivacaine 0.25–0.75 %	1 to 3	3 to 5	6 to 12	3
Ropivacaine 0.2–1 %		2 to 6	5 to 8	3
Tetracaine 1 %	2 to 6			3

Profound spinal and epidural anesthesia produce not only a sensory but also a motor blockade. For patients coming in for ambulatory procedures, the motor blockade must wear off before a patient can walk and therefore be discharged home.

General Anesthesia

General anesthesia involves the administration of medications that render the patient unconscious and, when adequate, unreactive to pain. The primary features of general anesthesia include a lack of consciousness, analgesia or absence of pain, lack of movement in response to painful stimuli, and control of the reflex responses to painful stimuli. Amnesia for intraoperative events is an important aspect of anesthesia. Awareness under anesthesia is a rare but serious complication [53]. Multiple drugs are almost always used to produce specific aspects of general anesthesia.

The electrocardiogram (ECG), blood pressure, and oxygen saturation are always monitored during any type of anesthetic care. For general anesthesia, end tidal carbon dioxide monitoring is required and temperature should be monitored for procedures in excess of 30 min. Intravenous access is universally required as part of anesthetic care. This is routinely used for the administration of fluids and medications and occasionally for the administration of blood products and resuscitation drugs when needed. For major cases, large bore (18 gauge or larger) catheters are inserted into peripheral veins, which can be challenging in elderly patients.

Almost all general anesthetics in geriatric patients are induced with intravenous hypnotic agents. The most common is propofol, however, etomidate, thiopental, and ketamine are viable options. Etomidate and ketamine are generally selected when hemodynamic stability is a greater concern. The suggested induction doses for all sedative hypnotic agents are altered with aging. Patients are usually asked to breathe pure oxygen prior to the induction of anesthesia. The purpose of this maneuver is to replace the nitrogen in the alveoli with pure oxygen. This is important to give the anesthesiologist time to place an appropriate airway device before the oxygen level in the blood starts to fall. Elderly patients take longer to pre-oxygenate and can very quickly become hypoxemic. Maintenance of adequate ventilation via a patent airway is a primary goal of the anesthesiologist. For major cases involving intra-abdominal procedures, unusual positions or prolonged surgery, an endotracheal tube, and positive pressure ventilation are routinely employed. In recent years, alternative airway devices such as the laryngeal mask airway (LMA) have become popular for cases in which positive pressure ventilation is not required. Many urologic procedures on the bladder can easily be accomplished with an LMA. The advantage of the LMA is that it provides a reasonably well-protected airway without requiring a tube in the larynx, a stimulus that sometimes requires a deeper anesthetic than otherwise might be required by the procedure. In the presence of an increased risk of aspiration, most anesthesiologists will not elect an LMA. The choice of device and backup procedures varies with procedure and practitioner. Spontaneous breathing is also feasible and is a potentially desirable alternative to positive pressure ventilation.

Maintaining homeostasis during a procedure requires careful adjustment of the depth of anesthesia. The depth is a balance of the drug effects and the surgical stimulus. The most common symptom of excess anesthesia is hypotension. If the surgical stimulus changes rapidly, a fully anesthetized patient may react by moving or experiencing a change of heart rate. The primary approach to change of heart of anesthesia has been to monitor blood pressure and heart rate. Increases in heart rate and blood pressure generally appear long before a patient would develop any recall of intraoperative events. If the anesthetic gets light, the patient might move in response to a surgical stimulus. Such movement is rarely marked and is not commonly associated with recall by the patient. In recent years, a number of proprietary devices have become available that process electroencephalographic signals to provide a single number between 0 and 100 as an indication of the depth of anesthesia. It is well known that anesthetic requirements for older adults are significantly decreased; however, control of blood pressure can sometimes require more anesthetic than one might expect. These devices seem to suggest that the amount of anesthetic typically used to control blood pressure and heart rate frequently results in extremely deep anesthesia for the brain. There has been some suggestion that excessive depth of anesthesia is associated with poor outcomes [54]. This idea requires prospective validation but may prove a fruitful area of research and guide future geriatric anesthetic care [55].

Most general anesthetics cause a decrease in sympathetic tone that decreases systemic vascular resistance and causes peripheral pooling of blood that lowers cardiac preload. It may also lower heart rate and there is some direct depression of the myocardium. These alterations are often exaggerated in elderly patients, so hemodynamic stability may be more difficult to maintain [25].

Choosing Between Regional Versus General Anesthesia

The choice between regional and general or combined techniques remains primarily a choice of preference by the anesthesiologist and the urologist [56]. Multiple studies designed to show an advantage have come to divergent conclusions. Most of the studies have been focused on orthopedic procedures [57] and Cesearean sections [58], but some have evaluated urologic procedures [59]. Cochrane systematic reviews have failed to delineate a significant advantage for regional over general for Cesarean section deliveries [60]. For hip fracture surgery, the authors concluded that there was insufficient evidence available from trials comparing regional versus general anesthesia to rule out clinically important differences in mortality and the risk of deep venous thrombosis [61]. A recent large retrospective review concluded that regional anesthesia is associated with a lower odds of inpatient mortality and pulmonary complications among all hip fracture patients compared with general anesthesia; however, this may be driven by the selection of anesthetic techniques. Extremely ill patients may have been more likely to receive general anesthesia [57]. On balance, regional anesthetic techniques can be successfully employed in the elderly urologic patient. Certain patients might find this form of anesthesia highly preferable. There is, to date, a lack of significant outcome data that make the choice between regional and general clear when either technique would be applicable.

Because the choice of anesthetic technique may be based on patient preference, it is important to provide patients with comprehensive information and involve them in the decision-making process.

Postoperative Issues in Older Adults

It is important for the anesthesiologist caring for elderly patients to be cognizant of the impact of anesthetic choices and management on the postoperative course of these patients. Postoperative issues are covered in more detail in the following chapter but are briefly mentioned here.

Postoperative Cognitive Alterations

Elderly patients tend to emerge more slowly from general anesthesia. The idea of inadequate emergence has recently been proposed and appears to be associated with longer hospital stays [62].

Emergence delirium is a common problem seen more often in younger patients in which disoriented behavior is encountered in the operating room during emergence from anesthesia. This phenomenon probably does not meet the strict definition of delirium and should probably be referred to as emergence agitation. Postoperative delirium is a loss of orientation that occurs primarily in elderly patients usually at 24–48 h following surgery and anesthesia [63]. To date, there is no clear etiology for delirium. One approach to preventing delirium appears to be high quality cooperation with geriatricians who are paying attention to geriatric issues [17]. Another early study suggested that the level of sedation administered in the operating room was associated with the development of delirium [64]. As delirium is associated with increased mortality and prolonged hospital stays, the need for further research and understanding is clear [63].

Some elderly patients are reported to never be the same after surgery and anesthesia. Prospective studies have defined an incidence of measureable cognitive decline at 1 week and 3 months [65–67]. The finding is most commonly called postoperative cognitive dysfunction (POCD). The long-term implication of these findings is the subject of much controversy [68]. Although of great interest, there is currently no known approach to the prevention of or treatment of POCD. Choice of regional versus general anesthesia does not seem to have an impact on the incidence of POCD [69].

Postoperative Pain

Elderly patients, just as any others who undergo major surgery, will require management of acute postsurgical pain. There is no truth to the myth that elderly patients do not experience postoperative pain. This is important not only in the short term but also to prevent the development of chronic pain, which can be a sequelae of prolonged early acute pain. Opioid analgesics are the most widely used medications for the management of acute postsurgical pain. Opioids bring a number of risks, including the development of opioid-related adverse drug events (ORADEs). Thus, the management of postoperative pain can be a difficult task in elderly patients. Comorbid diseases, concurrent medications, diminished physiological reserve and functional status, and age-related pharmacodynamic and pharmacokinetic changes all complicate the effective treatment of acute pain. Pain assessment in geriatric patients can also be difficult. Selection of analgesic therapy needs to balance these various issues to achieve effectiveness [70].

Urinary Retention

Urologists are frequently called to assess elderly patients with urinary retention in the postoperative period. Urinary retention is particularly common following hernia surgery. Some aspects of anesthesia care, particularly neuraxial anesthesia, may predispose a patient to urinary retention. Catheterization is frequently required, particularly for a bladder containing 600 mL of urine or more. Postoperative urinary retention typically resolves over a few days [71].

Conclusion

Geriatric patients represent the largest growing group of patients in the care of both urologists and anesthesiologists. The better we understand the issues associated with aging and age-related disease, the better the outcomes that can be expected. It is hoped that all practitioners will find these patients to be an exciting and interesting clinical challenge that will engage their attention.

References

1. Tiret L, Desmonts JM, Hatton F, Vourc'h G. Complications associated with anaesthesia: a prospective survey in France. Can Anaesth Soc J. 1986; 33(3 Pt 1):336–44.
2. Li G, Warner M, Lang BH, Huang L, Sun LS. Epidemiology of anesthesia-related mortality in the United States, 1999–2005. Anesthesiology. 2009; 110(4):759–65.

3. Rowe JW, Kahn RL. Successful aging. Gerontologist. 1997;37(4):433–40.
4. Muravchick S. Preoperative assessment of the elderly patient. Anesthesiol Clin North America. 2000;18(1): 71–89. vi.
5. Homeostenosis [homepage on the Internet]. POGOe - Portal of Geriatric Online Education. 2008. Available from: http://www.ouhsc.edu/geriatricmedicine/Education/Homeostenosis/Homeostenosis.htm.
6. Chow WB, Rosenthal RA, Merkow RP, Ko CY, Esnaola NF. American College of Surgeons National Surgical Quality Improvement Program. American Geriatrics Society. Optimal preoperative assessment of the geriatric surgical patient: a best practices guideline from the American College of Surgeons National Surgical Quality Improvement Program and the American Geriatrics Society. J Am Coll Surg. 2012; 215(4):453–66.
7. Borson S, Scanlan J, Brush M, Vitaliano P, Dokmak A. The Mini-Cog: a cognitive 'vital signs' measure for dementia screening in multi-lingual elderly. Int J Geriatr Psychiatry. 2000;15(11):1021–7.
8. American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine, Society for Vascular Surgery, Fleisher LA, Beckman JA, Brown KA, Calkins H, Chaikof EL, et al. ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery. J Am Coll Cardiol. 2009;54(22):e13–118.
9. Poldermans D, Devereaux PJ. The experts debate: perioperative beta-blockade for noncardiac surgery: proven safe or not? Cleveland Clin J Med. 2009;76 Suppl 4:S84–92.
10. POISE Study Group, Devereaux PJ, Yang H, Yusuf S, Guyatt G, Leslie K, et al. Effects of extended-release metoprolol succinate in patients undergoing noncardiac surgery (POISE trial): a randomised controlled trial. Lancet. 2008;371(9627):1839–47.
11. Juul AB, Wetterslev J, Gluud C, Kofoed-Enevoldsen A, Jensen G, Callesen T, et al. Effect of perioperative beta blockade in patients with diabetes undergoing major non-cardiac surgery: randomised placebo controlled, blinded multicentre trial. BMJ. 2006;332(7556):1482. PMCID: PMC1482337.
12. Wallace AW, Au S, Cason BA. Association of the pattern of use of perioperative beta-blockade and postoperative mortality. Anesthesiology. 2010;113(4): 794–805.
13. Wallace AW, Au S, Cason BA. Perioperative beta-blockade: atenolol is associated with reduced mortality when compared to metoprolol. Anesthesiology. 2011;114(4):824–36.
14. Harari D, Hopper A, Dhesi J, Babic-Illman G, Lockwood L, Martin F. Proactive care of older people undergoing surgery ('POPS'): designing, embedding, evaluating and funding a comprehensive geriatric assessment service for older elective surgical patients. Age Ageing. 2007;36(2):190–6.
15. Rubenstein LZ, Joseph T. Freeman Award lecture: comprehensive geriatric assessment: from miracle to reality. J Gerontol A Biol Sci Med Sci. 2004;59(5): 473–7.
16. Heyburn G, Beringer T, Elliott J, Marsh D. Orthogeriatric care in patients with fractures of the proximal femur. Clin Orthop Relat Res. 2004;425: 35–43.
17. Marcantonio ER, Flacker JM, Wright RJ, Resnick NM. Reducing delirium after hip fracture: a randomized trial. J Am Geriatr Soc. 2001;49(5):516–22.
18. Rubin FH, Neal K, Fenlon K, Hassan S, Inouye SK. Sustainability and scalability of the hospital elder life program at a community hospital. J Am Geriatr Soc. 2011;59(2):359–65.
19. Saager L, Kurz A, Deogaonkar A, You J, Mascha EJ, Jahan A, et al. Pre-existing do-not-resuscitate orders are not associated with increased postoperative morbidity at 30 days in surgical patients. Crit Care Med. 2011;39(5):1036–41.
20. Jones JW, McCullough LB. Just how far goes DNR? J Vasc Surg. 2008;48(6):1630–2.
21. Guarisco KK. Managing do-not-resuscitate orders in the perianesthesia period. J Perianesth Nurs. 2004;19(5):300–7.
22. Silverstein JH, Rooke GA, Reves JG, McLeskey CH, editors. Geriatric anesthesiology. 2nd ed. New York, NY: Springer; 2008.
23. Lakatta EG, Levy D. Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises: part I: aging arteries: a "set up" for vascular disease. Circulation. 2003;107(1):139–46.
24. Lakatta EG, Levy D. Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises: part II: the aging heart in health: links to heart disease. Circulation. 2003;107(2):346–54.
25. Rooke GA. Cardiovascular aging and anesthetic implications. J Cardiothorac Vasc Anesth. 2003;17(4): 512–23.
26. Assali A, Vaknin-Assa H, Lev E, Bental T, Ben-Dor I, Teplitsky I, et al. The risk of cardiac complications following noncardiac surgery in patients with drug eluting stents implanted at least six months before surgery. Catheter Cardiovasc Interv. 2009;74(6):837–43.
27. Angiolillo DJ. The evolution of antiplatelet therapy in the treatment of acute coronary syndromes: from aspirin to the present day. Drugs. 2012;72(16):2087–116.
28. Zaugg M, Lucchinetti E. Respiratory function in the elderly. Anesthesiol Clin North America. 2000;18(1): 47–58.
29. Lawrence VA. Predicting postoperative pulmonary complications: the sleeping giant stirs. Ann Intern Med. 2001;135(10):919–21.

30. Lawrence VA, Cornell JE, Smetana GW, American College of Physicians. Strategies to reduce postoperative pulmonary complications after noncardiothoracic surgery: systematic review for the American College of Physicians. Ann Intern Med. 2006;144(8):596–608.
31. Sieber FE, Barnett SR. Preventing postoperative complications in the elderly. Anesthesiol Clin. 2011;29(1):83–97.
32. Muhlberg W, Platt D. Age-dependent changes of the kidneys: pharmacological implications. Gerontology. 1999;45(5):243–53.
33. Pizzarelli F, Lauretani F, Bandinelli S, Windham GB, Corsi AM, Giannelli SV, et al. Predictivity of survival according to different equations for estimating renal function in community-dwelling elderly subjects. Nephrol Dial Transplant. 2009;24(4):1197–205.
34. Pedone C, Corsonello A, Bandinelli S, Pizzarelli F, Ferrucci L, Incalzi RA. Relationship between renal function and functional decline: role of the estimating equation. J Am Med Dir Assoc. 2012;13(1):84.e11–4.
35. Shafer SL. The pharmacology of anesthetic drugs in elderly patients. Anesthesiol Clin North America. 2000;18(1):1–29.
36. Deiner S, Hagen J. Parkinson's disease and deep brain stimulator placement. Anesthesiol Clin. 2009;27(3):391–415.
37. Fried LP, Hadley EC, Walston JD, Newman AB, Guralnik JM, Studenski S, et al. From bedside to bench: research agenda for frailty. Sci Aging Knowledge Environ. 2005;2005(31):e24.
38. Jones DM, Song X, Rockwood K. Operationalizing a frailty index from a standardized comprehensive geriatric assessment. J Am Geriatr Soc. 2004;52(11):1929–33.
39. Sundermann S, Dademasch A, Praetorius J, Kempfert J, Dewey T, Falk V, et al. Comprehensive assessment of frailty for elderly high-risk patients undergoing cardiac surgery. Eur J Cardiothorac Surg. 2011;39(1):33–7.
40. Afilalo J, Mottillo S, Eisenberg MJ, Alexander KP, Noiseux N, Perrault LP, et al. Addition of frailty and disability to cardiac surgery risk scores identifies elderly patients at high risk of mortality or major morbidity. Circ Cardiovasc Qual Outcomes. 2012;5(2):222–8.
41. Sundermann S, Dademasch A, Rastan A, Praetorius J, Rodriguez H, Walther T, et al. One-year follow-up of patients undergoing elective cardiac surgery assessed with the comprehensive assessment of frailty test and its simplified form. Interact Cardiovasc Thorac Surg. 2011;13(2):119–23. discussion 123.
42. Joint Commission on Accreditation of Healthcare Organizations. Correction: Standard PC.13.20, element of performance 3 for ambulatory care. Jt Comm Perspect. 2006;(12):6.
43. Ghosh B, Dorairajan LN, Kumar S, Manikandan R, Muruganandham K, Kumar A. Randomized clinical trial comparing effectiveness of intracorpus spongiosum block versus topical anesthesia for performing visual internal urethrotomy for urethral stricture disease. Urology. 2013;81(1):204–7.
44. Veering BT. Hemodynamic effects of central neural blockade in elderly patients. Can J Anaesth. 2006;53(2):117–21.
45. Simon MJ, Veering BT, Stienstra R, van Kleef JW, Burm AG. Effect of age on the clinical profile and systemic absorption and disposition of levobupivacaine after epidural administration. Br J Anaesth. 2004;93(4):512–20.
46. Simon MJ, Veering BT, Stienstra R, van Kleef JW, Burm AG. The effects of age on neural blockade and hemodynamic changes after epidural anesthesia with ropivacaine. Anesth Analg. 2002;94(5):1325–30.
47. Patel AR, Jones JS, Babineau D. Lidocaine 2% gel versus plain lubricating gel for pain reduction during flexible cystoscopy: a meta-analysis of prospective, randomized, controlled trials. J Urol. 2008;179(3):986–90.
48. 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(1):99–105.
49. Ladjevic N, Likic-Ladjevic I, Dzamic Z, Acimovic M, Dragicevic D, Durutovic O. Combined general and epidural anaesthesia versus general anaesthesia for radical cystectomy. Acta Chir Iugosl. 2007;54(4):89–91.
50. Hong JY, Lee SJ, Rha KH, Roh GU, Kwon SY, Kil HK. Effects of thoracic epidural analgesia combined with general anesthesia on intraoperative ventilation/oxygenation and postoperative pulmonary complications in robot-assisted laparoscopic radical prostatectomy. J Endourol. 2009;23(11):1843–9.
51. Azawi NH, Christensen T, Petri AL, Kehlet H. Prolonged length of hospital stay in Denmark after nephrectomy. Dan Med J. 2012;59(6):A4446.
52. Adamina M, Kehlet H, Tomlinson GA, Senagore AJ, Delaney CP. Enhanced recovery pathways optimize health outcomes and resource utilization: a meta-analysis of randomized controlled trials in colorectal surgery. Surgery. 2011;149(6):830–40.
53. Avidan MS, Jacobsohn E, Glick D, Burnside BA, Zhang L, Villafranca A, et al. Prevention of intraoperative awareness in a high-risk surgical population. N Engl J Med. 2011;365(7):591–600.
54. Sessler DI, Sigl JC, Kelley SD, Chamoun NG, Manberg PJ, Saager L, et al. Hospital stay and mortality are increased in patients having a "triple low" of low blood pressure, low bispectral index, and low minimum alveolar concentration of volatile anesthesia. Anesthesiology. 2012;116(6):1195–203.
55. Monk TG, Weldon BC. Does depth of anesthesia monitoring improve postoperative outcomes? Curr Opin Anaesthesiol. 2011;24(6):665–9.
56. Roy RC. Choosing general versus regional anesthesia for the elderly. Anesthesiol Clin North America. 2000;18(1):91–104. vii.
57. Neuman MD, Silber JH, Elkassabany NM, Ludwig JM, Fleisher LA. Comparative effectiveness of regional versus general anesthesia for hip fracture surgery in adults. Anesthesiology. 2012;117(1):72–92.

58. Mancuso A, De Vivo A, Giacobbe A, Priola V, Maggio Savasta L, Guzzo M, et al. General versus spinal anaesthesia for elective Caesarean sections: effects on neonatal short-term outcome. A prospective randomised study. J Matern Fetal Neonatal Med. 2010;23(10):1114–8.
59. Karacalar S, Bilen CY, Sarihasan B, Sarikaya S. Spinal-epidural anesthesia versus general anesthesia in the management of percutaneous nephrolithotripsy. J Endourol. 2009;23(10):1591–7.
60. Afolabi BB, Lesi FE. Regional versus general anaesthesia for Caesaren section. Cochrane Database Syst Rev. 2012;10:CD004350.
61. Parker MJ, Handoll HH, Griffiths R. Anaesthesia for hip fracture surgery in adults. Cochrane Database Syst Rev. 2004; (4):CD000521.
62. Radtke FM, Franck M, Hagemann L, Seeling M, Wernecke KD, Spies CD. Risk factors for inadequate emergence after anesthesia: emergence delirium and hypoactive emergence. Minerva Anestesiol. 2010; 76(6):394–403.
63. Deiner S, Silverstein JH. Postoperative delirium and cognitive dysfunction. Br J Anaesth. 2009;103 Suppl 1:i41–6.
64. Sieber FE, Zakriya KJ, Gottschalk A, Blute MR, Lee HB, Rosenberg PB, et al. Sedation depth during spinal anesthesia and the development of postoperative delirium in elderly patients undergoing hip fracture repair. Mayo Clin Proc. 2010;85(1):18–26.
65. Monk TG, Weldon BC, Garvan CW, Dede DE, van der Aa MT, Heilman KM, et al. Predictors of cognitive dysfunction after major noncardiac surgery. Anesthesiology. 2008;108(1):18–30.
66. Price CC, Garvan CW, Monk TG. Type and severity of cognitive decline in older adults after noncardiac surgery. Anesthesiology. 2008;108(1):8–17.
67. Moller JT, Cluitmans P, Rasmussen LS, Houx P, Rasmussen H, Canet J, et al. Long-term postoperative cognitive dysfunction in the elderly ISPOCD1 study. ISPOCD investigators. International study of postoperative cognitive dysfunction. Lancet. 1998; 351(9106):857–61.
68. Avidan MS, Xiong C, Evers AS. Postoperative cognitive decline: the unsubstantiated phenotype. Anesthesiology. 2010;113(5):1246–8. author reply 1248–50.
69. Rasmussen LS, Johnson T, Kuipers HM, Kristensen D, Siersma VD, Vila P, et al. ISPOCD2(International Study of Postoperative Cognitive Dysfunction) Investigators. Does anaesthesia cause postoperative cognitive dysfunction? A randomised study of regional versus general anaesthesia in 438 elderly patients. Acta Anaesthesiol Scand. 2003;47(3):260–6.
70. Aubrun F, Marmion F. The elderly patient and postoperative pain treatment. Best Pract Res Clin Anaesthesiol. 2007;21(1):109–27.
71. Darrah DM, Griebling TL, Silverstein JH. Postoperative urinary retention. Anesthesiol Clin. 2009;27(3):465–84.

28 Postoperative Management of the Geriatric Patient

Daniel Ramirez, Vivyenne Roche, and Philippe Zimmern

Introduction

Taking care of the geriatric patient is extremely rewarding, but this population also poses specific challenges, especially in the surgical practice of Urology. Many times the benefits of surgery outweigh the risks. The patient's history needs to be carefully reviewed prior to making any decision for surgical intervention. Some of the most significant concerns include the patient's medical comorbidities, cognitive function, functional status, social support, and living arrangements. Physiological changes of aging, also called "homeostenosis," further diminish their ability to cope with postoperative physiologic stresses. In a study by Polancyzk et al., major postoperative complications and mortality directly increased with advanced age [1]. The first 30 postoperative days carry the most substantial risks, particularly for elderly patients. Hamel et al. showed that patients 80 years and older experiencing postoperative complications after major surgery had a 25 % greater 30-day mortality rate when compared to similar patients without complications [2]. In this patient population, "frailty" denotes specific risks. Frailty is a syndrome that encompasses five elements: weakness, low energy or exhaustion, slowed walking speed, low physical activity, and weight loss. A study by Makary et al. [3] demonstrated frailty as an independent risk factor for postoperative complications, prolonged length of stay after surgery, and higher rates of discharge to assisted living or skilled nursing facility.

Greater awareness and understanding of medical issues in this vulnerable patient population mandate targeting "at-risk" patients and preventing complications in the postoperative period is paramount to ensure postoperative success. In this chapter, we will review the principles of basic postoperative care of the geriatric patient and focus on common and specific postoperative complications unique to this age group.

Prevention of Postoperative Complications

Optimal postoperative care includes proactive management to prevent surgical complications. Specific areas merit attention to promote recovery and decrease complication rates. These include maintenance of mobility and function, prevention of deep venous thromboembolism, medication management, pain control, prevention of constipation and dehydration, and nutritional assessment. There should also be a focus on certain "high-risk" cohorts such as patients with diabetes mellitus and those with chronic respiratory disease.

D. Ramirez, M.D. • P. Zimmern, M.D. (✉)
Department of Urology, UT Southwestern Health Science Center, Dallas, TX, USA
e-mail: Philippe.zimmern@utsouthwestern.edu

V. Roche, M.D.
Department of Internal Medicine, UT Southwestern Health Science Center, Dallas, TX, USA
e-mail: Vivyenne.Roche@UTSouthwestern.edu

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_28,

Table 28.1 Effects of bed rest

Cardiovascular impact response	Musculoskeletal/skin impact
• Obligatory diuresis	• Reduces strength >1 % daily
• Decreases plasma volume	• Causes muscle atrophy
• Impairs baroreceptor	• Decreases aerobic capacity
• Increases venous compliance	• Impairs range of motion of joints
• Decreases cardiac output	• Increases contractures
• Increases resting heart rate	• Accelerates bone loss

Table 28.2 Medications to avoid in older patients [5]

1. Psychiatric medications	(a) Antidepressants (tricyclics, SSRI/SNRI) (b) Anxiolytics (benzodiazepines) (c) Antipsychotics (d) Other (cholinesterase inhibitors/memantine, lithium)
2. Anti-histamines/ Anticholinergics	Diphenhydramine, hydroxyzine Many unrelated drugs have anticholinergic activity such as diphenhydramine, tricyclics, and warfarin
3. Anti-vertigo/ Anti-emetics	Metoclopramide, meclizine, promethazine, prochlorperazine, trimethobenzamide
4. Muscle relaxants	
5. Anti-spasmodics	(a) GI (Donnatal, hyoscyamine, dicyclomine) (b) GU (oxybutynin, tolterodine)
6. Anti-Parkinson's medications	
7. Narcotics	Meperidine
8. Corticosteroids	
9. H2 blockers	Ranitidine, cimetidine
10. Anticonvulsants	
11. Antibiotics	Quinolones, nitrofuantoin

Mobility

Restoring functional status is an essential part of optimal postoperative care. Bed rest significantly impacts the cardiovascular and musculoskeletal systems (Table 28.1). Ascertain the patient's prior functional status before surgery from the patient and their families. After surgery, it is critical to get patients up and begin early mobilization. Write orders for the nursing staff to make the patient sit out of bed three times a day, with assistance if needed. On postoperative rounds, perform "*the Get up and Go test*" [4] which is a quick and straightforward way to assess a patient's functional status. To perform the test, ask the patient to stand up from the bed or chair, walk 10 ft, turn around, and walk back to the bed or chair and sit down. Normally it takes less than 10 s to do this test. If they have difficulty, or they are unsteady, consult physical therapy for gait evaluation and training.

Anticoagulation

Surgical patients are at risk for postoperative thromboembolic disease and should be risk stratified to prevent complications. For low-risk patients who are healthy and mobile undergoing minor procedures including transurethral or other endoscopic urologic procedures, encourage aggressive early ambulation after surgery. For patients at moderate risk undergoing open urologic surgeries, use low molecular weight or unfractionated heparin.

Medication Management

Carefully review the patient's medication regimen prior to admission with the patient, family, or facility. Omission of key medications or dose changes can significantly impact hospitalized patients and cause needless complications. Plan to continue regular medications for chronic diseases such as hypertension, congestive heart failure, or chronic obstructive pulmonary disease. Certain medications are likely to cause unwanted side effects in older patients. The Beers List of medications is a group of potentially inappropriate medications for community-dwelling and nursing home patients. Some medications are placed on this list primarily due to their sedative or anticholinergic properties. Fick et al. describe this comprehensive list of more than 70 medications in the AGS-updated Beers criteria release in April of 2012. Table 28.2 lists medications such as diphenhydramine that should be avoided in older patients [5].

Table 28.3 Table of analgesics indicated and contraindicated in specific organ failures

Drug	Hepatic	Renal	Use in renal failure	Use in dialysis	Use in hepatic failure
Meperidine	Metabolized	Excreted	Use carefully	Use carefully	Use carefully
Morphine	Metabolized	Excreted	Do not use	Do not use	Use carefully Reduce dose
Hydromorphone	Metabolized	Excreted	Use carefully	Use carefully	Use carefully
Oxycodone	Metabolized	Excreted	Not enough data to comment	Not enough data to comment	Not enough data to comment
Codeine	Metabolized	Excreted	Do not use	Do not use	Use carefully
Fentanyl	Metabolized	Excreted	Can be used	Can be used	Can be used
Methadone	Metabolized	Excreted	Can be used	Can be used	Use carefully in severe liver disease

Pain Control

Patients who undergo surgery require pain management. This may be particularly challenging in patients who have delirium or dementia. Inadequate pain treatment in non-demented patients has been shown to cause delirium. Mild pain can be treated with scheduled acetaminophen with as needed analgesics. Nonsteroidal anti-inflammatory drugs such as ketorolac should be avoided or used judiciously in older patients as they may exacerbate congestive heart failure, increase hypertension, and cause gastrointestinal bleeding. Moderate pain may be treated with scheduled oral narcotics, with as-needed doses for breakthrough pain. Severe pain should be treated with higher doses of scheduled narcotics using intravenous administration until the patient has adequate pain control. Dose adjustments may be required for patients with renal or hepatic impairment, and some medications are contraindicated (Table 28.3). Patient-controlled analgesia (PCA) may be very effective in cognitively intact patients but requires an alert cooperative patient. Care should be taken to assure that family members or anyone other than the patient avoid pushing the dosing button on a PCA. This can help to prevent overdosing of analgesic medications. When using narcotics, automatically prescribe a scheduled bowel regimen as constipation should be anticipated.

Constipation

Ensure patients have regular bowel movements after surgery. If patients are constipated, begin a bowel regimen such as docusate sodium one tablet twice a day. If patients are receiving narcotics, then a standardized bowel regimen protocol should be initiated such as docusate with senna two tablets at night, written scheduled, not as needed. Care must be taken in patients who have undergone bowel surgery or in those who have undergone genitourinary reconstruction or diversion using a bowel segment.

Dehydration Prevention

Due to physiologic changes with aging, older patients are very susceptible to dehydration. At baseline they have decreased percentage body water, with delayed and poor thirst perception. They also do not maximally conserve water even in water-deprived states and have impaired antidiuretic hormone (ADH) response to hypovolemia. Older kidneys have impaired renal conservation of sodium and water. In addition, postoperative patients are more likely to have decreased access to water due to impaired mobility. Encourage fluids and free access to water after surgery except in patients who have a history of congestive heart failure. Review fluid administration and volume status daily.

Nutrition

After minor surgery, patients should resume a regular diet. After open urologic surgery, be careful to avoid lengthy periods of nil by mouth in malnourished or frail elderly patients. Patients who are unable to take oral nutrition should have continuous intravenous administration of fluids. Watch for volume overload such as shortness of breath, tachycardia, new onset of basilar crackles and/or edema, particularly in patients with known cardiovascular disease. When bowel sounds are present and the patient is passing flatus, advance from ice chips to liquids and then solids as tolerated. Remember to discontinue IV fluids once oral intake is restored to avoid fluid overload. Restricted diets may exacerbate malnutrition. If ordering oral supplements such as Ensure® or Boost®, order them between meals not with meals as patients should not take the supplements in place of meals but in addition to them. Consider a dietary consult if the patient has diabetes, renal insufficiency, or a delay in return of adequate oral intake.

Diabetes Mellitus

Postoperative hypoglycemia is potentially life threatening and may increase morbidity such as arrhythmias and mortality. Hyperglycemia in observational studies has been associated with increased postoperative wound infection. Hyperglycemia may also lead to significant volume and electrolyte disturbances. The American Diabetes Association recommends fasting glucoses of 140 mg/dL (7.8 mmol/L) for general hospitalized patients, with random glucose readings <180 mg/dL (10 mmol/L).

Chronic Obstructive Pulmonary Disease (COPD)/Asthma/Smoking

Continue pulmonary medications during admission. Pay careful attention to good pulmonary toileting. Encourage patients to do deep breathing and order incentive spirometry, especially if they are at high risk for pulmonary complications. Getting this group of patients mobilized is the key to minimize complications. Keep it simple: get the patient up and out of bed. Assistance with smoking cessation may be beneficial to help reduce rates of smoking behavior after surgery and particularly after hospital discharge.

Acute Postoperative Complications

After reviewing the optimal general postoperative care management of the older patient, we will now address specific acute complications that may arise during the recovery phase.

Delirium

Delirium is a well-recognized, common, postoperative complication. It is not normal for older patients to become acutely confused in the hospital. Patients who have underlying dementia with dehydration, pain, immobility, and/or sleep deprivation are particularly susceptible. Delirium has significant morbidity leading to longer hospital length of stay, closer nursing surveillance, higher hospital costs per day, and a fivefold increase in nursing home placement. In addition it has a case fatality rate of 25–35 %. It can last for weeks to months. Approximately 25 % of patients with delirium continue to have symptoms at 1 month, and 18 % have symptoms at 6 months. Delirium is discussed in more detail in Chap. 6.

As patients with dementia are more likely to develop delirium during hospitalization, baseline screening of cognitive function using the Mini-Cog is useful [6]. To perform the Mini-Cog, ask the patient to repeat 3 words and ask them to draw a clock and put the hands at 11:10. Then, ask them to recall the 3 words without additional prompting. For a clock to be correctly drawn, it must include the circle, all 12 numbers in the correct spatial orientation and rotation around the clock face, and the hands must be set at the correct time, with the hour hand being shorter than the minute hand. Examples of normal and abnormal clocks are shown in Fig. 28.1. Findings consistent with dementia include inability to recall all three items regardless of the clock drawing result or the inability to recall 1 or 2 items together with an abnormal clock drawing result. If patients are able to recall 1 or 2 items and have a normal clock drawing result, they are generally not demented. This test takes less than 3 min to perform and can easily be incorporated into

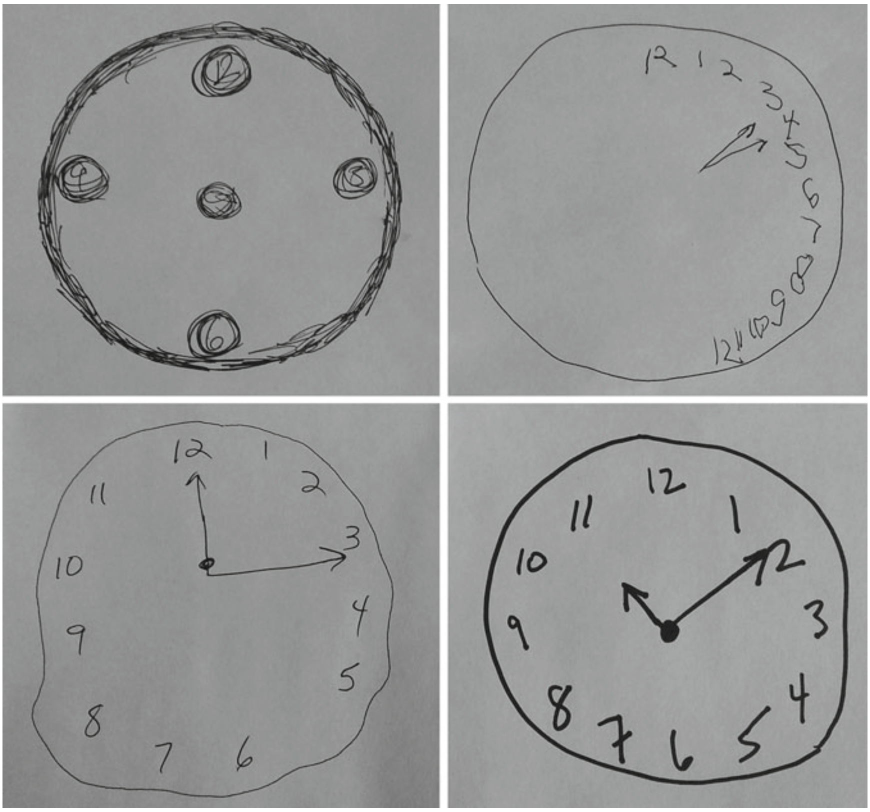


Fig. 28.1 Examples of the clock-drawing test (part of the Mini-Cog). *Upper Left*: Abnormal clock. Note the patient has perseverated on drawing the *circle shapes*, but only four numbers are included and no hands are shown to indicate time. *Upper Right*: Abnormal clock. Note the absence of any numbers on the left side of the clock, the duplication of the number 12, and the incorrect placement of hands. These types of errors may occur with hemispheric stroke and associated lateral inattention. *Lower Left*: Abnormal clock. Note the incorrect spatial orientation of the numbers 5, 6, and 7 and the incorrect placement of hands. *Lower Right*: Normal clock. Note that all numbers are present in the correct spatial orientation, and the hands are set correctly as instructed to indicate the time of 11:10

routine clinical practice. Patients who score poorly on the Mini-Cog are more likely to develop delirium during hospitalization.

The Confusion Assessment Method (CAM) is a simple tool that is used to diagnose delirium if a patient develops confusion during hospitalization. It has a sensitivity of 94–100 % and a specificity of 90–95 % [7]. Information can be gathered by direct observation of the patient or with the assistance of a family member or nursing staff. The CAM uses the following four elements to diagnose delirium:

1. Acute onset and fluctuating course
2. Inattention

   And either 3 or 4
3. Disorganized thinking
4. Altered Level of Consciousness (hypoactive or hyperactive).

   To diagnose delirium the patient must demonstrate items 1 **and** 2 and **either** items 3 or 4.

There are three types of delirium, including hypoactive, hyperactive, and a mixed pattern. The hypoactive form is the lethargic, sleepy patient who is difficult to arouse. The hyperactive patient is agitated, anxious, and hypervigilant. The hypoactive form is the most common and, more importantly, it is the most likely type to be overlooked.

Delirium usually has a multifactorial etiology. It can be caused by hyponatremia, poor pain control, and infection in an individual patient [8]. When a patient develops delirium, the clinician must determine the cause(s) and provide appropriate treatment. Nonpharmacologic management should be employed to the extent possible.

These interventions have been shown to reduce the incidence of delirium and are also used to treat delirium if it develops:

- Sleep promotion, uninterrupted sleep, avoidance of sedatives.
- Encourage patients to wear their glasses and hearing aids.
- Monitor fluid and electrolyte balance.
- Provide adequate nutrition.
- Institute early mobilization.
- Avoid restraints (bladder catheters, physical restraints, and chemical restraints such as sedative hypnotic drugs).
- Eliminate unnecessary medications.
- Provide adequate pain control.
- Regulate bowel and bladder function.
- Employ family and staff in frequent orientation (use of clocks and calendars, blinds open during the day, lights off at night, and encourage relatives to stay with patients).

Behavioral treatment of delirium is optimal as outlined above. However, when a delirious patient poses a danger to themselves or others, pharmacological intervention may be required. Haloperidol is the drug of choice. The starting dose is haloperidol 0.25–0.5 mg orally or intramuscularly. Intravenous preparation is not FDA approved. This dose may be repeated 30 min × 1, then again if needed, up to 3–5 mg total in a 24-h period. The half-life of haloperidol is 21 h [8], with peak efficacy at 4–6 h. Haloperidol does not affect the outcome of delirium and is for symptomatic treatment only. If long-term antipsychotics are indicated, then risperidone, olanzapine, or quetiapine may be used. Short-acting benzodiazepines such as lorazepam are preferred for alcohol withdrawal. Benzodiazepines may cause paradoxical agitation and should be stopped, if increased agitation occurs.

Postoperative Bleeding

Symptomatic anemia from acute blood loss following urologic surgery has now become a rare event in the hands of the experienced surgeon. The advent of different approaches, endoscopic procedures, and intraoperative technical advances such as the use of electrocautery, hemostatic agents, and robotic-assisted surgery has greatly minimized this risk. Table 28.4 reviews the classification of hypovolemic shock relative to blood loss as published by Basket et al. in 1990 [9]. Table 28.5 demonstrates the incidence of acute blood loss anemia requiring reintervention and blood transfusion after common urologic procedures in contemporary literature.

Significant intraoperative bleeding and postoperative acute blood loss anemia can result in acute coronary syndrome and death in high risk patients [10]. A lower threshold for transfusion is recommended, when the patient has a history of cardiovascular disease or poorly controlled diabetes. While a specific hemoglobin value is not established for patients with acute blood loss anemia and coexisting coronary artery disease, a hemoglobin of 10 g/dL is accepted as the threshold for transfusion [11].

The clinical presentation of acute blood loss in older patients may not be straightforward, so maintain a high index of suspicion, especially in patients with limited cardiac reserves and known cardiac risk factors. Significant bleeding can occur in the operating room or en route to the postoperative recovery room. While in the operating room, communication between the anesthesiologist and surgeon is paramount and monitoring serum hemoglobin may be warranted, especially in the setting of unstable vital signs and/or large estimated blood loss. When suspected, a possible mechanism for blood loss must be immediately assessed, as it may be due to misplaced ligatures or hemostatic clips from major blood vessels or unidentified areas of significant bleeding. Prior to closure of the wound, careful exploration and irrigation of the surgical field is extremely important to ensure hemostasis.

If bleeding is suspected postoperatively, initial evaluation of the patient should include a focused history and physical examination, with special attention to the patient's vital signs and postoperative laboratory values. Fatigue,

Table 28.4 Classification of hypovolemic shock according to blood loss

	Class I	Class 2	Class 3	Class 4
Blood loss	<15 % (750 mL)	15–30 % (<1,500 mL)	30–40 % (<2,000 mL)	>40 % (2,000 mL)
Systolic BP	Unchanged	Normal	Decreased	Severe hypotension
Diastolic BP	Unchanged	Increased	Decreased	Severely decreased
Pulse (bpm)	<100	100–120	120 and thready	>120 and very thready
Capillary refill	Normal	Slow (>2 s)	Slow (>2 s)	Undetectable
Respiratory rate	Normal	Normal	>20/min	>20/min
Urine output	>30 mL/h	20–30 mL/h	10–20 mL/h	0–10 mL/h
Extremities	Normal	Pale	Pale	Cold and pale
Complexion	Normal	Pale	Pale	Ashen

Table 28.5 Incidence of reintervention and transfusion associated with common urologic surgeries

Surgery	Reintervention	Transfusion	Study
TURP	2.2–3.5 %	2.0–8.9 %	Gupta et al. [39]
TURBT	0–2.2 %	2.3–3.4 %	Nieder et al. [40]
Laparoscopic radical prostatectomy	0.5 %	5 %	Rassweiler et al. [41]
Open radical prostatectomy	0.5–1.2 %	0.4–2.4 %	Kaufman et al. [12]
Robotic radical prostatectomy	0–0.5 %	1–1.3 %	Bhandari et al. [42]
Laparoscopic partial nephrectomy	0.6–3.5 %	5.2–17.8 %	Desai et al. [43]
Open partial nephrectomy	2.6–7.6 %	5.3–12 %	Steffens et al. [44]
Laparoscopic radical nephrectomy	1.6 %	0.4 %	Willie et al. [45]
Open radical nephrectomy	0–2.7 %	2.4–9.8 %	Shuford et al. [46]

shortness of breath, tachycardia, and tachypnea may indicate the need for transfusion. Consider the patient's ability to compensate for the estimated blood loss. Examine the wound dressings for excessive bleeding and assess any drains in situ for output. Order relevant laboratory tests and compare preoperative and postoperative serum hemoglobin results. Review the medical record for comorbid conditions that may increase morbidity in the setting of acute blood loss. Carefully review the operative report and notify the surgeon of record when persistent bleeding is suspected. The decision for transfusion or surgical intervention is complex and estimated blood loss, vital signs, and noninvasive evaluation with ultrasound and/or CT scanning may demonstrate areas of concern. If clinically unstable, resuscitate the patient and consider emergent re-exploration or angiography if radiologic intervention is appropriate [12, 13]. For example, angiography may diagnose and selectively embolize bleeding vessels after partial nephrectomy.

Postoperative Cardiovascular and Pulmonary Complications

It has been estimated that up to one-third of the postoperative morbidity in geriatric patients is cardiac related, which may only become evident after surgery. Such a high incidence is partially due to age-related changes that predispose an older patient to these complications including lower arterial compliance, increased vascular resistance, and higher systolic pressures [14]. Basal sympathetic output increases can lead to desensitization of the myocardium to beta-adrenergic stimulation [15]. These changes cause progressive ventricular wall thickening, making cardiac output difficult to maintain in times of postoperative stress. Suspect it in patients with multiple risk factors including family history, smoking, hyperlipidemia, diabetes, and decreased functional status. Geriatric patients are more prone to cardiac and pulmonary complications postoperatively than younger patients.

Specific conditions that warrant attention include valvular disease, hypotension, arrhythmias, and congestive heart failure. Aortic stenosis is the most significant valvular disease diagnosed in the elderly population and has been associated with a 13 % incidence of mortality [16]. Hypotension is particularly poorly tolerated in these patients as the myocardium is perfused during diastole, precipitating a sudden ischemic event. Calcifications and fibrotic changes along the Bundle of His predispose to bradyarrhythmias. Most arrhythmias are supraventricular and may be triggered by hypoxia, hypercarbia, or electrolyte abnormalities, especially changes in serum potassium. Atrial fibrillation, the most common arrhythmia, can cause additional postoperative complications such as congestive heart failure, cerebrovascular accidents, cognitive impairment, and renal insufficiency [17]. Patients with coronary artery disease have greater than a 5 % risk of myocardial infarction in the postoperative period. Twenty five percent of patients in this age group are at risk for an ischemic event within the first week after surgery [18, 19].

Perioperative beta blockers have been shown to decrease postoperative cardiac events by opposing exaggerated sympathetic response to pain and fluid shifts which usually cause tachycardia and increased myocardial oxygen demand [20]. It has been shown that patients on statins for greater than 6 months prior to surgery are at decreased risk for atrial fibrillation in the postoperative period, although there are no current data to support starting a patient on a statin to improve outcomes [21].

Older adults frequently have atypical presentation of cardiopulmonary disease including vague complaints such as dizziness, falls, anorexia, and/or delirium. Complaints of dyspnea, cough, chest pain, fever, and palpitations in the postoperative period should be promptly assessed. Chest pain is the most common manifestation of cardiopulmonary disorders, though musculoskeletal pain and gastrointestinal causes should be considered. Myocardial infarction may present without chest pain but rather with altered mental status, acute heart failure, arrhythmia, or hypotension. Determine if symptoms are acute or chronic, cardiopulmonary or other, and benign versus life threatening [22].

Evaluation of new symptoms in elderly postoperative patients should begin with a focused history of symptoms including the onset, location, duration, and radiation of pain if present, a review of the patient's comorbidities, and a thorough medical history. Perform a careful physical examination with particular attention to subtle changes in the patient's vital signs. A respiratory rate greater than 20 breaths per minute should raise the suspicion for a pulmonary cause such as atelectasis, pneumonia, or pulmonary embolism.

Additional evaluation and management depend on the identified etiologies. Initial testing includes complete blood count, basic metabolic profile, oxygenation saturation, and cardiac enzymes. While the complete blood count may show a normal white blood cell count in 50 % of patients with pneumonia, 95 % have a left shift. Order a 12 lead EKG and chest X-ray. If pulmonary embolism is suspected, order a ventilation/perfusion scan or chest-computed tomography angiogram.

A 12-lead electrocardiogram may demonstrate acute ischemia, ventricular strain, arrhythmia, bundle branch block, or left ventricular hypertrophy. Myocardial infarction is indicated by the presence of ST segment elevation greater than 0.1 mV in 2 consecutive leads or by new onset left bundle branch block. Remember, a 12-lead EKG has a sensitivity of only 50 % in patients experiencing an acute myocardial infarction [23, 24]. So order cardiac enzymes concurrently to exclude acute ischemia. If suspected, consult Cardiology immediately as the patient may require thrombolysis or percutaneous coronary intervention (PCI). If anticoagulation is considered, Urology and Cardiology should weigh the benefits and risks together as it may precipitate bleeding in the acute postoperative period.

The Acute Abdomen in the Postoperative Setting

After major laparoscopic or open urologic surgery, assess whether a patient's complaint of abdominal pain is secondary to incisional pain or other serious

Table 28.6 Differential diagnosis in postoperative acute abdominal pain

Intra-abdominal pathology
Generalized peritonitis: perforated bowel, primary infective peritonitis
Localized peritonitis: Meckel's diverticulitis, cholecystitis, appendicitis, abscess, pancreatitis
Disorders of motility: ureteric obstruction, biliary obstruction, intestinal obstruction, urinary retention
Ischemia: mesenteric ischemia, infarction or thrombosis, sickle cell crisis, torsion of omentum, ovarian cyst, or testicle
Other: inflammatory intestinal diseases, peptic ulcer (diverticulitis)
Extra-abdominal pathology
Metabolic: acute adrenal insufficiency, diabetic ketoacidosis, hypercalcemia, thyroid storm
Thoracic: pneumonia, pulmonary embolism, ischemic heart disease, aortic dissection
Neurologic: radiculopathy, herpes zoster, spinal arthritis, tabes dorsalis
Retroperitoneal: masses, hematoma
Abdominal wall: rectal sheath hematoma, incisional pain, herniation

occult pathology. Disorders not related to surgery must be entertained in the differential diagnosis and these are listed in Table 28.6. Delirium may be the only presenting sign of an acute abdominal process, further limiting the surgeon's ability to adequately assess the patient. Cardiac ischemia may mimic abdominal pain and a thorough medical history of atherosclerotic disease should be sought in at-risk patients. As stated earlier, delayed and atypical presentations, blunted ability to communicate, and pharmacologic and physiologic changes may all increase the difficulty to ascertain a diagnosis, leading to higher morbidity and mortality rates [25].

Bowel Obstruction

Types of obstruction are divided into large bowel versus small bowel and functional versus mechanical. Obstruction most commonly occurs in the small bowel due to its small diameter and smooth serosa which make it more vulnerable to adhesions and herniations [26]. The geriatric population is at a threefold greater risk compared to younger patients for developing bowel obstruction [27]. It is the second most common cause, after biliary disease and acute cholecystitis, for emergent surgery in this age group [28]. Patients may present with abdominal colic, distention, nausea and vomiting, and constipation. In cases of large bowel obstruction, nausea, and vomiting usually present later in the disease process. Obstruction may lead to severe complications such as sepsis, ischemia, perforation, dehydration, and death.

Plain films of the abdomen have a sensitivity of 66 % and a specificity of 57 % [29] and demonstrate distended bowel loops with collapse distal to the area of obstruction, air fluid levels, and scarcity of air in the rectum. Distended small bowel classically appears as a stack of coins due to the contours of the plicae circularis. While plain films can help diagnose obstruction, they do not determine the location or etiology. CT scan with oral and intravenous contrast continues to be the study of choice. This may show the location and cause of obstruction such as intramural thickening indicating ischemia. Ischemia caused by strangulated bowel is more common with closed-loop obstruction and can increase mortality by tenfold [30].

Acute management of bowel obstruction should include NPO status for bowel rest, intravenous hydration, nasogastric decompression, and treatment of symptoms. Consult General Surgery to ensure timely surgical management, particularly in patients with suspected closed-loop obstruction or bowel strangulation.

Impaired transit time is the most common cause of functional bowel obstruction in the postoperative patient. Geriatric patients are at greater risk for ileus secondary to poor mobility and decreased intake of fluids. Ileus may occur at any site along the gastrointestinal tract and is associated with the use of tricyclic antidepressants, anticholinergics, and opioids. This is very important as many patients are started on medications for bladder spasms and narcotics for pain control in the immediate postoperative period. Other causes of ileus include severe infections and critical illness, metabolic abnormalities, neurological disorders, and intra-abdominal inflammation secondary to urine or blood in the peritoneal space. Evaluation and treatment of the ileus should proceed in a similar fashion as for cases of mechanical bowel obstruction. If the patient does not improve with 2–3 days of bowel rest and conservative management, CT scan should be performed. General Surgery should be consulted if mechanical obstruction is suspected.

Inflammatory Causes of Postoperative Abdominal Pain

While the widespread use of histamine-receptor type-2 blockers has decreased the rates of peptic ulcer disease in younger patients, complications and hospitalization in the older population have increased, and overall morbidity from this disease is 100-fold higher in this age group. Typical epigastric pain is not usually the initial symptom in geriatric patients [31]. Older adults most commonly present with an upper gastrointestinal bleed with "coffee ground" emesis or increased nasogastric tube output. Nearly 40 % of these patients take aspirin and NSAIDs on a chronic basis which predisposes them to gastric and duodenal ulceration. Increased age is a known independent risk factor for increased risk of gastroduodenal ulceration with concomitant use of these medications [32]. Another risk factor of peptic ulcer disease is *Helicobacter pylori*. Increased age predisposes patients to colonization with this organism.

If a patient has hematemesis, they should be started on a proton pump inhibitor infusion and a Gastroenterology consult should be obtained. Implement bowel rest and place a nasogastric tube. Perforation occurs in 5–10 % of geriatric patients with peptic ulcer disease. A study by Fenyo showed that 47 % of elderly patients presented with abdominal pain after perforation, while only 21 % presented with an acute abdomen [33]. This makes the diagnosis of perforation more difficult and the mortality rate is 30 % once it occurs. General Surgery should be called immediately if this is suspected.

The most common source of nonsurgical acute abdominal pain in older adults is pancreatitis, and increased age has been shown to be an independent risk factor for progression to systemic inflammatory response, organ dysfunction, and death [34]. The most common cause of pancreatitis in this age group is gallstones. Other causes of pancreatitis in this setting include chronic alcohol use, pancreatic pseudocyst, and iatrogenic trauma to the pancreas during abdominal, retroperitoneal, or pelvic surgery.

Abdominal Wound Dehiscence

Fascial dehiscence has been estimated to occur in 0.4–3 % of patients following laparotomy with a mortality rate of 15–20 % [35]. While wound dehiscence is a rare complication [36], it should be assessed in high-risk individuals, specifically patients with obesity, anemia, hyperbilirubinemia, malnutrition, or in patients who are taking certain medications such as steroids, chemotherapeutic agents, or immunosuppressants. Once a dehisced abdominal wound occurs, prompt management and intervention is required to decrease acute or chronic complications.

Preventing wound dehiscence in the postoperative period is essential. Local factors include surgical technique (incision location, closure, suture material, experience, etc.), wound infection, and mechanical distention. Wound infection is minimized by the judicious use of perioperative intravenous antibiotics. Placing retention sutures may be necessary to prevent dehiscence in high risk patients [37]. In the postoperative period, the most common cause of abdominal wound dehiscence is increased abdominal pressure induced by retching or coughing. Use of antiemetics in the perioperative period is important to prevent this complication. However, it is unwise to use antitussive medications to suppress coughing in the postoperative period, as coughing allows the patient to raise secretions from the upper airways and helps prevent atelectasis. Cough suppression may place the patient at risk for developing a postoperative pneumonia.

Wound dehiscence should be suspected in patients who have any fluid drainage from the wound site. The surgical wound should be inspected for signs of inflammation including tenderness, erythema, induration, and fluid drainage. If wound infection or dehiscence is suspected, the skin and superficial wound should be opened to evaluate the deeper tissues. This may necessitate the removal of sutures or staples. Once the wound is open, the fascia should be palpated for defects and fluid, and if present, sent for culture. If fascial openings are appreciated on examination, patients will need revision surgery.

Fevers

Postoperative fever is an extremely common clinical finding after urologic surgery [47]. Because the etiologies of postoperative fevers are extensive, include the timeframe as certain causes are more common during specific periods (Table 28.7). Remember that older adults may not mount a significant fever response even in the presence of infection due to changes in thermoregulation and age-related changes in immune system function.

Table 28.7 Common fever etiologies according to time frame

Time frame	Etiologies
Immediate: In the operating suite or within hours after surgery	• Medications • Blood products • Malignant hyperthermia • Surgical Site Infections from group A streptococcus (*GAS*) or *Clostridium perfringes* • Preexisting infection
Acute: Within first week after surgery	• Preexisting community acquired infection • Nosocomial Infection (Urinary Tract Infection (UTI) or Ventilator-Acquired Pneumonia (VAP)) • Systemic inflammatory response • Surgical site infection • Venous thromboembolism
Subacute: From 1 to 4 weeks after surgery	• Surgical site infection • Nosocomial Infection (Urinary Tract Infection (UTI), Ventilator-Acquired Pneumonia (VAP) or central venous catheter (CVC) infection • Drug reactions/fever • Intra-abdominal abscesses or hematomas • Venous thromboembolism • Antibiotic-associated diarrhea, *Clostridium difficile*-associated diseases CDAD
Delayed: >1 month after surgery	• Recurrent Cellulitis • "Subacute" infective endocarditis • Coagulase-negative *Staphylococcus sp*. surgical site infection • Contaminated blood product infections • Postpericardiotomy syndrome • Drug fever

JHCME. Perioperative Infections and Fever Module. http://www.jhcme.com [47]

Conclusion

This chapter has addressed the postoperative care of the older patient and focused on the optimal care recommended to proactively prevent complications. Bell et al. issued a list of perioperative competencies that are critical to achieve a satisfactory outcome. For the postoperative course, they emphasized several items including prompt diagnosis and evaluation of delirium, recognition of depression, drug management, and adequate pain control [38]. This valuable effort from a variety of specialists involved in the surgical care of the older patients should facilitate a systematic approach to the postoperative care of these more frail individuals. Once these core competencies are mastered by clinicians and nursing staff and properly communicated to family members, the typical risks of surgery in this elderly group should be significantly reduced. Although this chapter covered many of these issues in great detail and offered a urological perspective actuated by several case scenarios, it will hopefully be a valuable resource to all care providers of geriatric patients.

Clinical Cases

Transurethral Resection of the Prostate (TURP) Complicated by the TUR Syndrome

A 72-year-old man with a history of benign prostatic hyperplasia (BPH) and hypertension underwent transurethral resection of the prostate (TURP) for treatment of bladder outlet obstruction. An hour later in the post-anesthesia care unit, the patient becomes acutely confused with nausea and vomiting. Vital signs are normal. On examination, the patient is confused and is only orientated to person, not place or time. The rest of his exam is unre-

(continued)

(continued)

markable and the urine in his catheter is pink tinged with a moderate bladder irrigation drip. According to the operative report, the procedure was done with a 3 % sorbitol solution for endoscopic irrigation, and the estimated blood loss was 100 mL. Basic metabolic panel and complete blood count demonstrate a serum sodium of 121 mg/dL and a hematocrit of 33.4 %. The patient was started on intravenous normal saline and admitted to the intensive care unit for close monitoring of mental status and serial serum sodium. Intravenous furosemide was administered for treatment of suspected hypervolemia.

You have been called to evaluate the patient.

This patient is suffering from postoperative delirium secondary to hyponatremia associated with the absorption of electrolyte-free solution during endoscopic resection of the prostate, also known as transurethral resection syndrome. The risk of this complication increases with larger prostates, use of continuous irrigation, and a long resection time (generally over 1 h). It is due to fluid absorption into venous sinuses following prostate capsule perforation. This syndrome may present with symptoms ranging from asymptomatic hyponatremia to nausea, vomiting, delirium, convulsions, coma, pulmonary edema, cardiovascular compromise, and death. This spectrum of presentation may make diagnosis difficult. In patients presenting with altered mental status and hyponatremia in the immediate postoperative period after endoscopic surgery, transurethral resection syndrome must be considered. Monitor serial serum sodium and slowly correct it less than 12 mmol/L/day in order to avoid central pontine myelinolysis. Never use hypertonic saline which can also cause this complication.

Robotic-Assisted Radical Prostatectomy Complicated by Pulmonary Edema Secondary to Prolonged Pneumoperitoneum

A previously healthy 68-year-old man underwent robotic-assisted radical retropubic prostatectomy for prostate cancer. Immediately postoperatively, he develops dyspnea with oxygen saturation of 84 % on 6 L of oxygen. You are asked to evaluate the patient. On review of the operative report, intra-abdominal pressure was maintained at 15 mmHg throughout the case but was increased to 22 mmHg for 30 min in order to minimize bleeding during the nerve-sparing portion of the surgery. The anesthesia records indicate the patient's central venous pressure increased from 12 mmHg to 30 mmHg. Estimated blood loss was 800 mL and the patient received 3 L of intravenous crystalloids during the case. On examination in the post-anesthesia care unit, the patient appears to be in moderate distress with a respiratory rate of 24 breaths per minute. His blood pressure and heart rate are stable. The rest of his exam is unremarkable. Arterial blood gas analysis demonstrates the following: pH 7.36, pCO_2 53.4 mmHg, and pO_2 58.9 mmHg. Chest X-ray is shown above (Fig. 28.2).

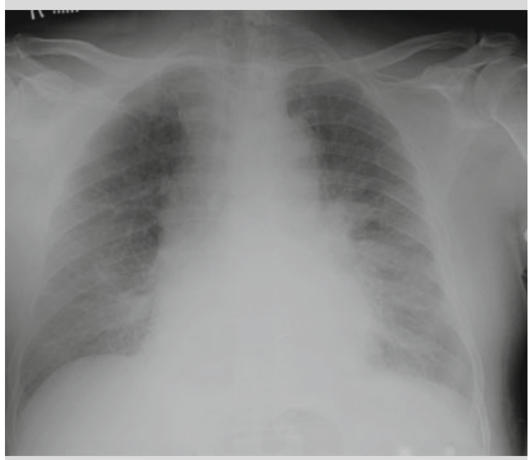


Fig. 28.2 Chest X-ray

(continued)

(continued)

This patient is presenting with pulmonary edema after robotic-assisted prostatectomy. It is important to note the intraoperative events, in this case the need for increased and prolonged pneumoperitoneum and an associated increase in central venous pressure. This chest radiograph demonstrates bilateral basilar infiltrates. Pulmonary edema related to surgery may arise from various factors including cardiac disease and congestive heart failure. Other causes may include intraoperative mechanical obstruction of cardiac output. In this case, prolonged abdominal insufflation increased pressure on the atrial chambers which resulted in diminished venous return and increased central venous pressure; these were most likely the causes of this patient's pulmonary edema. Cardiac pathology must also be ruled out. If the patient's clinical condition does not improve with diuresis and supplemental oxygen, transfer the patient to the intensive care unit and consider endotracheal intubation with ventilator support.

Partial Nephrectomy Complicated by Ileus

A 66-year-old woman underwent left-sided partial nephrectomy through an open flank incision 2 days ago. She has been complaining of nausea and has not been able to tolerate anything by mouth. Vital signs are within normal limits.

You are called to evaluate the patient.

The patient reports vague abdominal pain. On examination, her abdomen is distended with hypoactive bowel sounds. The Jackson–Pratt (JP) drain in her left upper quadrant is filled with 50 mL of straw-colored fluid. The nurse reports that the JP drain output has been over 300 mL daily since surgery. The patient's serum creatinine is 0.9 mg/dL. You send the JP fluid for creatinine content and it returns abnormally high at 36 mg/dL. The primary surgeon was notified and the patient was taken back to the operating room for left ureteral stent placement. Her postoperative intravenous pyelogram (IVP) is shown above (Fig. 28.3).

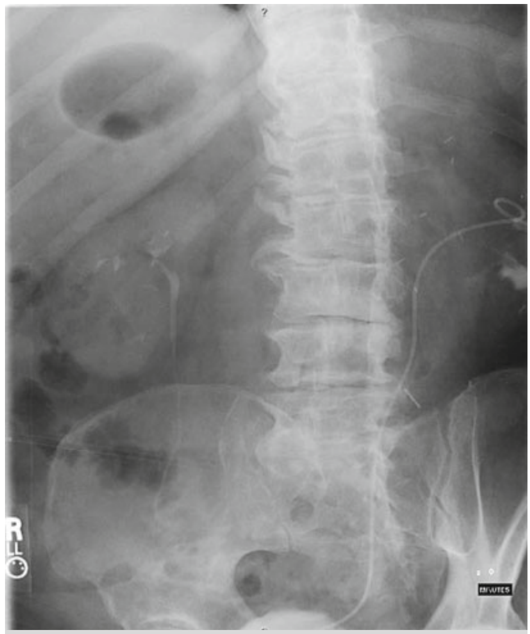


Fig. 28.3 Postoperative intravenous pyelogram (IVP)

This patient presented with a urinary fistula after left-sided partial nephrectomy. If a JP drain is left in place, it is important to assess the daily output and any changes in this over time. If output is higher than expected, evaluate the fluid for creatinine content as it may represent urine. Urinary leakage into the peritoneal space may present as postoperative ileus. If the patient complains of nausea and vomiting with an inability to tolerate an oral diet, a work up for possible postoperative ileus with KUB or CT scan of the abdomen should be considered. In this case, the intravenous pyelogram demonstrates a urine fistula with a left perirenal urinoma. The patient may benefit from placement of a percutaneous drain and possible left ureteral stenting as shown. The majority of urinary fistulas after partial

(continued)

(continued)

nephrectomy resolve spontaneously with percutaneous drainage or stenting.

Radical Cystectomy Complicated by Deep Venous Thrombosis

A 75-year-old man underwent cystoprostatectomy with ileal conduit urinary diversion 8 days ago. He has been eating a regular diet and his pain has been controlled on oral medications. Today on rounds, the patient reports increased left leg swelling and discomfort with ambulation.

You are called to evaluate him.

He denies shortness of breath. Overnight, the patient had a low-grade temperature of 100.8° Fahrenheit. He is saturating at 100 % on room air and his breath sounds are clear. He has +1 pitting edema over his pretibial area on his left lower extremity. No cords are palpated in the leg on examination and no erythema is noted. His laboratory results are normal. Left lower extremity Doppler ultrasound is shown above (Fig. 28.4).

This patient has a left lower extremity deep venous thrombosis. This often presents after the first postoperative week with low grade fevers, lower extremity pain, or swelling. His respiratory status is stable and he does not clinically appear to have a pulmonary embolism at this time. He will need to start anticoagulation for treatment of his deep vein thrombosis. He should initially be started on a heparin infusion or intramuscular enoxaparin injections at a therapeutic dose. Ultimately, he will need to be bridged to warfarin with close monitoring of his prothrombin time (PT) and INR. Patients who are not candidates for anticoagulation with warfarin should be evaluated for placement of an inferior vena caval filter.

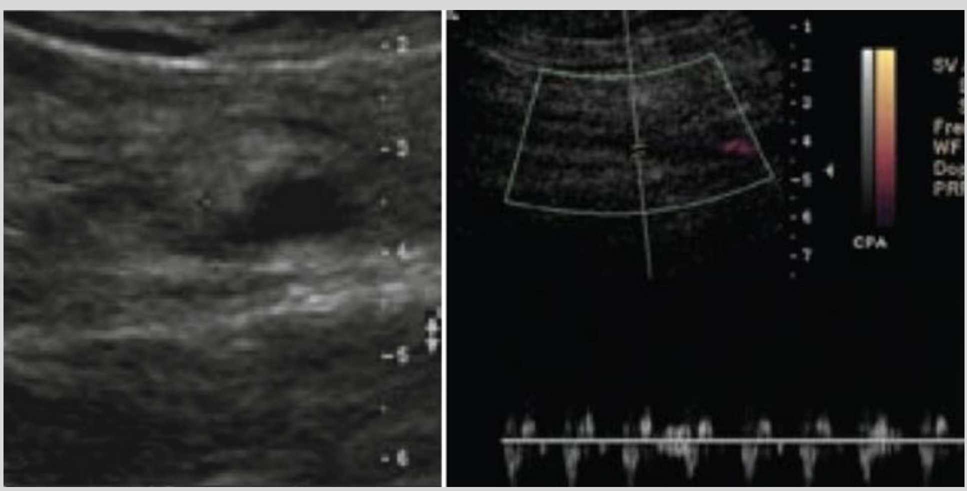


Fig. 28.4 Left lower extremity Doppler ultrasound

References

1. Polanczyk CA, Marcantonio E, Goldman L, Rohde LE, Orav J, Mangione CM, et al. Impact of age on perioperative complications and length of stay in patients undergoing noncardiac surgery. Ann Intern Med. 2001;134(8):637–43.
2. Hamel MB, Henderson WG, Khuri SF, Daley J. Surgical outcomes for patients aged 80 and older: morbidity and mortality from major noncardiac surgery. J Am Geriatr Soc. 2005;53(3):424–9.
3. Makary MA, Segev DL, Pronovost PJ, Syin D, Bandeen-Roche K, Patel P, et al. Frailty as a predictor of surgical outcomes in older patients. J Am Coll Surg. 2010;210(6):901–8.

4. Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc. 1991;39(2):142–8.
5. The American Geriatrics Society 2012 Beers Criteria Update Expert Panel: American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2012; 60(2):616–31.
6. Borson S, Scanlan J, Brush M, Vitaliano P, Dokmak A. TheMini-Cog: a cognitive 'vital signs' measure for dementia screening in multi-lingual elderly. Int J Geriatr Psychiatry. 2000;15(11):1021–7.
7. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegal AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. Ann Intern Med. 1990;113(12):941–8.
8. Marcantonio ER, Goldman L, Mangione CM, Ludwig LE, Muraca B, Haslauer CM, et al. A clinical prediction rule for delirium after elective noncardiac surgery. JAMA. 1994;271(2):134–9.
9. Baskett PJ. ABC of major trauma. Management of hypovolaemic shock. BMJ. 1990;300(6737):1453–7.
10. Carson JL, Duff A, Poses RM, Berlin JA, Spence RK, Trout R, et al. Effect of anaemia and cardiovascular disease on surgical mortality and morbidity. Lancet. 1996;348(9034):1055–60.
11. Tircoveanu R, Van der Linden P. Hemodilution and anemia in patients with cardiac disease: what is the safe limit? Curr Opin Anaesthesiol. 2008;21(1):66–70.
12. Kaufman JD, Lepor H. Reoperation versus observation in men with major bleeding after radical retropubic prostatectomy. Urology. 2005;66(3):561–5.
13. Hedican SP, Walsh PC. Postoperative bleeding following radical retropubic prostatectomy. J Urol. 1994;152(4):1181–3.
14. Lakatta EG, Levy D. Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises: Part I: aging arteries: a "set up" for vascular disease. Circulation. 2003;107(1):139–46.
15. Shulman A, Wolf R. Alcohol ingestion, hormonal changes, and the skin. Clin Dermatol. 1999;17(4):405–9.
16. Goldman L, Caldera DL, Nussbaum SR, Southwick FS, Krogstad D, Murray B, et al. Multifactorial index of cardiac risk in noncardiac surgical procedures. N Engl J Med. 1977;297(16):845–50.
17. Ommen SR, Odell JA, Stanton MS. Atrial arrhythmias after cardiothoracic surgery. N Engl J Med. 1997;336(20):1429–34.
18. Ergina PL, Gold SL, Meakins JL. Perioperative care of the elderly patient. World J Surg. 1993;17(2):192–8.
19. Jin F, Chung F. Minimizing perioperative adverse events in the elderly. Br J Anaesth. 2001;87(4):608–24.
20. Wallace A, Layug B, Tateo I, Li J, Hollenberg M, Browner W, et al. Prophylactic atenolol reduces postoperative myocardial ischemia. McSPI Research Group. Anesthesiology. 1998;88(1):7–17.
21. Alves RJ, Campos RN, Nakiri K. Chronic and regular use of statin prevents atrial fibrillation in period after cardiac surgery. Arq Bras Cardiol. 2010;95(5):614–20.
22. Kurz K, Katus HA, Der GE. akute Thoraxschmerz. [Acute chest pain]. Internist (Berl). 2005;46(9):957–64.
23. Lee TH, Rouan GW, Weisberg MC, Brand DA, Cook EF, Acampora D, et al. Sensitivity of routine clinical criteria for diagnosing myocardial infarction within 24 hours of hospitalization. Ann Intern Med. 1987;106(2):181–6.
24. Giannitsis E, Katus HA. Der akute posteriore Myokardinfarkt. Eine typische Fehldiagnose. [Acute posterior myocardial infarct. A typical diagnostic error]. Internist (Berl). 2002;43(5):618–23.
25. Watters JM, Clancey SM, Moulton SB, Briere KM, Zhu JM. Impaired recovery of strength in older patients after major abdominal surgery. Ann Surg. 1993;218(3):380–90. discussion 90-3.
26. Romano S, Bartone G, Romano L. Ischemia and infarction of the intestine related to obstruction. Radiol Clin North Am. 2008;46(5):925–42.
27. Telfer S, Fenyo G, Holt PR, de Dombal FT. Acute abdominal pain in patients over 50 years of age. Scand J Gastroenterol Suppl. 1988;144:47–50.
28. Hendrickson M, Naparst TR. Abdominal surgical emergencies in the elderly. Emerg Med Clin North Am. 2003;21(4):937–69.
29. Maglinte DD, Balthazar EJ, Kelvin FM, Megibow AJ. The role of radiology in the diagnosis of small-bowel obstruction. AJR Am J Roentgenol. 1997;168(5):1171–80.
30. Qalbani A, Paushter D, Dachman AH. Multidetector row CT of small bowel obstruction. Radiol Clin North Am. 2007;45(3):499–512.
31. Kemppainen H, Raiha I, Sourander L. Clinical presentation of peptic ulcer in the elderly. Gerontology. 1997;43(5):283–8.
32. Griffin MR. Epidemiology of nonsteroidal anti-inflammatory drug-associated gastrointestinal injury. Am J Med. 1998;104(3A):23S–9. discussion 41S-42S.
33. Fenyo G. Acute abdominal disease in the elderly: experience from two series in Stockholm. Am J Surg. 1982;143(6):751–4.
34. Gardner TB, Vege SS, Chari ST, Pearson RK, Clain JE, Topazian MD, et al. The effect of age on hospital outcomes in severe acute pancreatitis. Pancreatology. 2008;8(3):265–70.
35. Swan MC, Banwell PE. The open abdomen: aetiology, classification and current management strategies. J Wound Care. 2005;14(1):7–11.
36. Barker DE, Kaufman HJ, Smith LA, Ciraulo DL, Richart CL, Burns RP. Vacuum pack technique of temporary abdominal closure: a 7-year experience with 112 patients. J Trauma. 2000;48(2):201–6. discussion 206–207.
37. Rucinski J, Margolis M, Panagopoulos G, Wise L. Closure of the abdominal midline fascia: meta-analysis delineates the optimal technique. Am Surg. 2001;67(5):421–6.

38. Bell Jr RH, Drach GW, Rosenthal RA. Proposed competencies in geriatric patient care for use in assessment for initial and continued board certification of surgical specialists. J Am Coll Surg. 2011;213(5):683–90.
39. Gupta N, Sivaramakrishna, Kumar R, Dogra PN, Seth A. Comparison of standard transurethral resection, transurethral vapour resection and holmium laser enucleation of the prostate for managing benign prostatic hyperplasia of >40 g. BJU Int. 2006;97(1):85–9.
40. Nieder AM, Meinbach DS, Kim SS, Soloway MS. Transurethral bladder tumor resection: intraoperative and postoperative complications in a residency setting. J Urol. 2005;174(6):2307–9.
41. Rassweiler J, Stolzenburg J, Sulser T, Deger S, Zumbe J, Hofmockel G, et al. Laparoscopic radical prostatectomy–the experience of the German Laparoscopic Working Group. Eur Urol. 2006;49(1):113–9.
42. Bhandari A, McIntire L, Kaul SA, Hemal AK, Peabody JO, Menon M. Perioperative complications of robotic radical prostatectomy after the learning curve. J Urol. 2005;174(3):915–8.
43. Desai MM, Aron M, Gill IS. Laparoscopic partial nephrectomy versus laparoscopic cryoablation for the small renal tumor. Urology. 2005;66(5 Suppl):23–8.
44. Steffens J, Humke U, Ziegler M, Siemer S. Partial nephrectomy with perfusion cooling for imperative indications: a 24-year experience. BJU Int. 2005;96(4):608–11.
45. Wille AH, Roigas J, Deger S, Tullmann M, Turk I, Loening SA. Laparoscopic radical nephrectomy: techniques, results and oncological outcome in 125 consecutive cases. Eur Urol. 2004;45(4):483–8. discussion 8-9.
46. Shuford MD, McDougall EM, Chang SS, LaFleur BJ, Smith Jr JA, Cookson MS. Complications of contemporary radical nephrectomy: comparison of open vs. laparoscopic approach. Urol Oncol. 2004;22(2):121–6.
47. Carson M, Liu E. Perioperative Infections and Fevers. Johns Hopkins Consultative Medicine Essentials. 2012 http://www.jhcape.com/site/article.cfm?ID=17.

Critical Care in Older Adults

29

David W. Rittenhouse, Niels D. Martin,
and Michael S. Weinstein

Introduction

Geriatric patients comprise a substantial percentage of those requiring admission to an intensive care unit (ICU). It is currently estimated that older adults account for 26–56 % of admissions to the intensive care unit (ICU) and account for 60 % of all ICU days [1, 2]. Older adults also represent one of the fastest growing populations in the USA [2]. As of 2009, there were 39.6 million people greater than age 65 in the USA representing 12.9 % of the population. By the year 2030, the geriatric population is expected to grow to 72.1 million, representing approximately 19 % of the population [3]. Those greater than age 85 constitute the fastest growing subgroup of older adults and are estimated to number 15 million by the year 2025 [2, 4].

This aging population will bring an increase in the number of people suffering from cardiac, pulmonary, and renal disease that will require critical care services. Additionally, the increase in geriatric population will likely incur an increase in the total number of gastrointestinal and genitourinary cancers that are commonly diagnosed in geriatric patients. Data support that the complex operations required for these cancers can be performed safely in older adults and that age alone is not a contradiction to surgery [5]. Following these procedures, patients benefit from ICU admission and perioperative critical care monitoring.

Critical illness is debilitating and recovery nearly always transcends the ICU stay, often requiring specialized care after ICU and hospital discharge. In a study by Udekwu et al. [1], the percentage of elderly patients who were independent decreased after an ICU stay from 84.9 to 72 %; the number of patients who were completely dependent increased from 0 to 3.8 %. Of interest, in this study, the perceived quality of life was not significantly decreased in elderly patients after an ICU stay. These data illustrate the need for social work services and initiatives in patient and family communication to anticipate changes in independence and quality of life that often follow an ICU stay.

At both the individual and population levels, these global geriatric challenges must be met with intensive care and hospital resources that are

D.W. Rittenhouse, M.D. (✉)
Department of Surgery, Jefferson Medical College of Thomas Jefferson University, 1100 Walnut Street, Suite 702, Philadelphia, PA 19107, USA
e-mail: mhpalmer@email.unc.edu

N.D. Martin, M.D., F.A.C.S.
Traumatology, Surgical Critical Care and Emergency Surgery, Hospital of the University of Pennsylvania, 3400 Spruce Street, 5 Maloney, Philadelphia, PA 19104, USA

M.S. Weinstein, M.D., F.A.C.S.
Division of Acute Care, Department of Surgery, Jefferson Medical College of Thomas Jefferson University, 1100 Walnut Street, Suite 702, Philadelphia, PA 19107, USA
e-mail: michael.weinstein@jefferson.edu

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_29,

well equipped with the infrastructure and services to handle the physical and social needs of the elderly population.

Physiology of Aging

To better understand the specific considerations of critical care in the elderly population, the physiological changes associated with aging must be considered. Elderly patients have a decreased physiological reserve [6]. Under unstressed conditions, the elderly patient may function without clinical functional impairment despite the physiological changes of aging that occur in the heart, lungs, and kidneys. However, under times of great stress, such as after an operation, acute illness, or trauma, this decreased physiological reserve can affect the elderly patient's ability to compensate, which can lead to cardiac, pulmonary, or renal failure [7].

Age-Related Cardiovascular Dysfunction

Increased age is a risk factor for the development of cardiovascular disease mainly resulting from the chronic effects of hypertension and atherosclerosis. Cardiovascular disease is the leading cause of mortality and accounts for >40 % of deaths in people >65 years of age [8] and nearly 50 % of all postoperative deaths [9]. This increase in morbidity and mortality from cardiovascular disease results from age-related changes at the histologic level in both the myocardium and the systemic vascular system. With aging, myocardial contractility and ventricular compliance are decreased for any given preload, resulting from progressive loss of myocytes and an increase in the deposition of myocardial collagen [2]. The heart experiences an increase in afterload from loss of collagen in the aorta and systemic arteries causing increased stiffness and decreased distensibility. This secondarily results in higher systolic blood pressure and leads to a decreased peak ejection cardiac output. These changes can also impair coronary perfusion and cause myocardial ischemia and tissue loss during times of increased demand [7].

Age is additionally associated with a decrease in diastolic function, with as many as 50 % of cases of heart failure in geriatric patients resulting from diastolic dysfunction. This dysfunction is a consequence of decreased ventricular compliance and relaxation due to compensatory hypertrophy from long standing hypertension. Because ventricular relaxation allows for coronary perfusion, the heart with diastolic dysfunction is more susceptible to hypoxia [2]. This diastolic dysfunction can be occult, as it can exist in the setting of normal systolic function [10]. A high index of suspicion preoperatively for appropriate risk stratification is prudent in this patient population.

The elderly heart is also susceptible to alterations in the electrical conducting system. Cardiac autonomic tissue is replaced with connective tissue and fat with advancing age. This fibrosis in the conducting tissue, intra-nodal tract, and Bundle of His leads to an increased risk of developing conduction abnormalities such as sick sinus syndrome, atrial arrhythmias, and bundle branch blocks, especially postoperatively or with stress [11, 12].

The elderly heart may also be refractory to increases in catecholamines that are secreted during times of stress or administered for the treatment of shock. This decreased response is thought to occur at the synaptic receptor sites with a decrease in the reuptake of catecholamines [8]. As a consequence, there is a greater dependence on increasing ventricular filling (preload) to augment cardiac output as opposed to catecholamine-induced increased contractility [11]. Increasing preload with volume, however, is not without consequence, as giving extra volume to the elderly heart with preexisting diastolic dysfunction predisposes the patient to the development of pulmonary edema if not done cautiously. Thus, a delicate balance between volume and pressors is prudent.

Age-Related Pulmonary Dysfunction

Changes in the elderly patient's pulmonary physiology that affect the ability to compensate for the stress of acute illness result from alterations in chest wall compliance, respiratory musculature, and lung parenchyma [13]. Increasing age is associated with a stiffening of the thorax that results from costal cartilage calcification and a decrease in the intervertebral disk spaces. These changes in chest wall form lead to an increase in the anterior–posterior diameter of the chest and decreased rib excursion [7]. The elastic recoil properties of the lung also decrease over time from age-related changes in collagen. Aging is additionally associated with weakening of the respiratory muscles [14]. These progressive changes to pulmonary mechanics lead to an increased work of breathing and a progressive decrease in pulmonary function. The forced expiratory volume (FEV1) progressively reduces with age. The FEV1 peaks at age 25 and then declines at a rate of 32 mL per year for men and 25 mL per year for women [14, 15]. This loss of elasticity results in collapse of smaller airways and alveoli, which produces uneven alveolar ventilation and a consequent ventilation perfusion mismatch. This mismatch, in addition to a progressive decrease in alveolar size, reduces the total surface area for gas exchange and accounts for the decline in oxygen tension of 0.3 mmHg per year starting around the age of 30 years [6, 11].

Pulmonary reserve is also compromised by a decreased ability to defend the host against infection. This inability to clear the airways of particulate matter and infectious agents results from a decrease in mucociliary clearance and reduced T cell function. Poor dentition, oropharyngeal colonization, and swallowing dysfunction may afflict elderly patients, with an increased risk for the development of aspiration pneumonia [11].

Finally, age appears to affect central control of ventilation. Elderly patients have a decreased response to hypercarbia and hypoxia, which may mask early respiratory failure, as a patient may appear comfortable despite significant gas exchange abnormalities [16].

Age-Related Renal Dysfunction

Elderly patients have decreased renal function when compared to younger patients. Nephrons progressively become sclerotic with approximately 40 % of nephrons undergoing sclerotic changes from the ages of 25–85 [11]. Renal tubule cells and the afferent and efferent arterioles undergo atrophy which leads to a decrease in renal blood flow by approximately 50 % in the elderly patient [11]. The glomerular filtration rate and creatinine clearance also begin declining after age 50 [6]. By age 80, on average, the glomerular filtration rate has declined by 50 % and the creatinine clearance has declined by 33 % [6]. Paradoxically, serum creatinine levels may be stable or even decreased in older age despite the decrease in creatinine clearance. This is due to decreased lean body mass and decreased creatinine production in advancing age. Therefore, isolated serum creatinine levels should not be used as markers for renal function in elderly patients; instead, creatinine clearance should be calculated.

The ability of the kidney to regulate electrolyte composition and acid–base balance is diminished in the elderly patient, especially when facing a stressor. The decrease in renal tubule function leads to a decrease in the ability of the kidney to conserve sodium and excrete hydrogen ions which lead to derangements in fluid balance and acid–base regulation [17]. Adler et al. showed that elderly patients had a decreased ability to excrete acid when compared to younger patients [18]. Aging kidneys have a decreased ability to compensate for nonrenal losses of sodium and water, which is thought to be in part due to a decrease in the activity of the renin-angiotensin pathway and lessened response of the aging kidney to antidiuretic hormone [11]. These changes in the ability of the aging kidney to regulate electrolytes and acid–base status should be considered when monitoring patients with acute illness in the ICU setting as well as guiding therapies such as medication dosing.

Indications for Postoperative ICU Admission

ICU resources are limited and costly, and thus, great care and thought must be given to for the need for postoperative ICU admission. In determining who qualifies for admission into an ICU, the surgeon must take into consideration the baseline physiological reserve of the patient, preexisting risk factors and comorbidities, the magnitude of the risks of the planned operation, and the need for specialized monitoring and nursing care.

Elective operations are associated with lower morbidity and mortality when compared to emergent operations in the elderly population. This discrepancy is in part from the severity of the illness but also for the ability to plan and physiologically optimize patients prior to elective operations. Liu et al. looked at risk factors in determining perioperative adverse events in 367 octogenarians undergoing noncardiac surgery [19]. The patients in this study had a postoperative in-hospital mortality of 4.6 %, and 26 % of patients suffered an adverse event postoperatively. By multivariate logistic regression, a history of neurological disease ($P=0.0001$), congestive heart failure ($P=0.004$), and a history of arrhythmia ($P=0.01$) increased the odds of adverse postoperative events. These data are in comparison to elderly patients undergoing emergent surgery. Keller et al. studied 100 patients over the age of 70 who underwent emergent operations and found a 31 % morbidity and 20 % mortality [20]. There are clearly many factors that determine which patients will require admission and care in an ICU. Perioperative assessment of the patient's physiological resting state, the acuity and severity of their disease, the invasiveness of the intervention, and the need for increased monitoring all are factors in determining who are admitted to an ICU for critical care.

Postoperative Management

Consideration of how to manage elderly patients in the postoperative setting is a natural extension of the thought process and algorithm that goes into deciding which patients will be cared for in the ICU setting. A structured assessment of the patient's risk factors and common, surgery-specific occurrences must be considered. Two main tenets are to define goals of resuscitation in the postoperative setting and to be prepared for common and expected complications.

Fluid Management

Fluid resuscitation in the elderly population can be quite a challenge given the decreased physiological reserve that elderly patients have in diseased states. The value of a thorough physical exam and history assessment should not be undervalued in the first step of evaluating volume status and thus determining fluid resuscitation strategies. Examining the mucous membranes and turgor of the skin and measuring the pulse contribute in determining how relatively volume resuscitated the patient is. Examination of the extremities for warmth and capillary refill, total fluids in and out, both sensible and insensible, over the course of their preoperative, intraoperative, and postoperative course must be considered. Further, patients undergoing elective operations are often nil per os for at least 8 h prior to the time of operation, and gastrointestinal surgery patients may have had a mechanical bowel preparation prior to the operation. Both of these circumstances can predispose patients to being relatively hypovolemic at the time of elective operation.

Fluid balance in geriatric patients is often a challenge. Changes in myocardial function, vascular responsiveness, and valvular disease lead to a difficult balance between hypovolemia and hypervolemia. Inadequate perioperative resuscitation can lead to hypovolemic shock and acute kidney injury. Excessive volume administration is less tolerated in elderly individuals and can lead to pulmonary edema and the need for prolonged mechanical ventilation. Thus, volume resuscitation is best guided by close attention to endpoints of resuscitation and often requires invasive monitoring.

Invasive Monitoring

Careful consideration must be given to the use of more invasive monitoring in caring for elderly patients. Elderly patients are less able to augment their cardiac output but instead rely on an increase in their systemic vascular resistance [11]. This can give caregivers a false sense of security when patients have a "normal blood" pressure but yet still can be in a pre-shock or shock state of malperfusion. There are various methods of invasive monitoring to assess intravascular volume status and cardiac output to guide fluid and vasopressor therapies. Pulmonary artery catheters are the most invasive of all monitoring techniques. There is much controversy surrounding the use of pulmonary artery catheters in the use of monitoring cardiac output. This controversy has arisen from inconsistent data on the efficacy and safety of using pulmonary artery catheters and whether or not they are beneficial in patient care. Scalea et al. reported the use of early invasive monitoring with pulmonary artery catheters in elderly patients led to early recognition of those patients that were in a state of hypoperfusion and helped to identify which patients required early inotropic and volume support to optimize cardiac output before reaching cardiogenic shock [21]. However, other authors have shown that the use of pulmonary artery catheters in high-risk surgery and in the setting of acute lung injury was associated with no increase in organ function or survival but was associated with increased cost and catheter-associated complications, including arrhythmias and thrombotic events [22–25]. Richards et al. proposed that pulmonary artery catheters may still have a limited use in select circumstances: (1) the diagnosis of right ventricular failure associated with right ventricular afterload, (2) the diagnosis of cardiac etiologies of ventilation liberation failure, (3) goal-directed therapy using SvO2, and (4) validation of newer devices to measure cardiac output [26]. The data remain unclear on defining the patients that will benefit from a pulmonary artery catheter.

Central venous pressure monitoring has long been used as an attempt to gauge volume status and guide fluid therapy. Monitoring the central venous pressure is best utilized in following trends. The number itself is susceptible to fluctuations and is influenced by compliance and changes in right-sided heart pressures as well as pulmonary pressures. Data show that monitoring the central venous pressure with central venous oxygenation monitoring as a tool for achieving early goal-directed therapy may have a benefit in patients suffering from sepsis [27–29].

Less invasive monitors use an arterial line and pulse contour analysis. These monitors estimate stroke volume, and thus cardiac output, based on the contour of the pulse tracing from an arterial line. Additionally the variation in stroke volume with respiration has been demonstrated to be predictive of fluid responsiveness [30]. These techniques operate on the premise that patients who are preload dependent will have a greater difference between minimal and maximal stroke volumes as they vary through the respiratory cycle [31]. Stroke volume varies with changes in intrathoracic pressure with inhalation and exhalation. These techniques have been validated in patients under anesthesia on positive pressure ventilation and may not be as reliable during spontaneous ventilation or when the cardiac rhythm itself is not regular.

Bedside echocardiography, both transthoracic (TTE) and transesophageal (TEE), is being used more frequently by intensivists to monitor cardiac performance and preload. TEE has become more readily available with a commercially available small diameter probe that provides three main views to evaluate cardiac function and preload. Both TTE and TEE are useful for evaluating preload based on the size and compressibility of the inferior or superior vena cava. Cardiac performance is evaluated by direct visualization of all four chambers of the heart. With experience these modalities can be used as less invasive techniques to guide volume and vasopressor support.

No matter what invasive monitoring device is being used, the most important asset in monitoring patients in the ICU is a dedicated and diligent team being attentive to details and constantly reassessing any changes in the patient's condition. Dedicated intensivist presence in the management of critically ill patients has consistently been demonstrated to improve outcomes [32].

Nutritional Assessment and Support

Optimizing nutritional support is of the utmost importance when treating elderly patients in the ICU. Critical illness results in a catabolic state [2].

Elderly patients are less equipped to handle prolonged catabolic periods as muscle mass decreases approximately 40 % from young adulthood to age 80 [33]. Elderly patients are therefore at an increased risk for the development of malnutrition because of this decreased reserve. Studies show that upwards of 65 % of elderly patients suffering from acute illness in an ICU also suffer from malnutrition [2]. Malnutrition in the ICU patient can lead to higher infection rates, slower wound healing, longer mechanical ventilator times, and an increase in mortality [34]. Enteral feeding is the preferred route both for nutritional support and also for maintaining host defense against invasive infections [35]. Enteral feeding is associated with decreased mucosal atrophy which increases the barrier against translocation of enteric pathogens [36].

There are few contraindications to enteral feeding including mechanical bowel obstruction, intestinal anastomotic failure, and high-output enterocutaneous fistula. When enteral nutrition is not an option, parental nutrition should be considered. Parental nutrition is not without its risks. Central line-associated blood stream infection (especially fungemia), hypercapnia, acalculous cholecystitis, hyperglycemia, and fatty liver are not uncommon [37]. While the early use of parenteral nutrition remains controversial, recent data show that the early institution of parenteral nutrition in those patients with relative contraindications to enteral nutrition led to fewer days of invasive ventilation but affected no change in ICU or hospital length of stay or mortality [38].

Acute Pain Management

Assessing pain in geriatric patients is of the utmost importance and is done by means of self-reporting and behavioral or physiological measures [39]. Adequately treating pain leads to decreased splinting after surgery and will lead to less atelectasis and pneumonia. Adequate pain management will lead to earlier ambulation in elderly patients which will decrease their risk for developing atelectasis, pneumonia, and deep venous thrombosis. There are many issues that arise when managing postoperative pain in the elderly patient.

Older adults have an increased response to drugs that affect the central nervous system such as benzodiazepines, anesthetics, and opioids [40]. This exaggerated pharmacodynamic and pharmacokinetic response is thought to be a consequence of age-related changes in the amount of muscle mass and body fat and affect drug distribution and elimination, as do the alterations in renal and hepatic functions associated with age [40]. Elderly patients are frequently on multiple medications that affect the metabolism of benzodiazepines, anesthetics, and opioids.

Traditional intravenous opioids such as morphine given by patient-controlled analgesia (PCA) can be effective in postoperative pain control in elderly patients. Elderly patients have an increased risk of respiratory depression when compared to younger patients. The level of sedation must be carefully monitored in these patients as an indicator of early respiratory depression. Another consideration that must be taken when using a PCA is the ability of elderly patients to maintain the cognition to appropriately use a PCA. Mann et al. showed that approximately 24 % of patients >70 years of age lacked the cognitive capacity to use a PCA [41].

A unique and individualized approach must be used in addressing postoperative pain management in geriatric patients. A multifaceted approach which combines cautious use of both opioid medications and non-opioid medications may be particularly useful.

Postoperative Complications

Myocardial Infarction

Elderly patients, in comparison to their younger counterparts, have limited cardiac reserve that puts them at higher risk when undergoing the stress of an operation or any other illness requiring ICU admission. Myocardial infarction (MI) and ischemia are common postoperative complications that have special considerations when treating elderly patients. First, elderly patients have a high incidence of risk factors for the development of coronary artery disease such as hypertension and diabetes mellitus. In the USA, the incidence and prevalence of acute MI increases with age, with greater than 60 % of acute MIs occurring in patients at least 65 years of age and one third of acute MIs occurring in patients greater than 70 years of age [42]. Further, 60 % of all MI deaths in the USA occur in the 6 % of the population greater than 75 years of age [42]. Given this data, special consideration must be given to this population in diagnosing and treating ischemic cardiac disease.

Elderly patients often have decreased levels of pain perception and therefore have a higher incidence of silent myocardial ischemia that often carries a worse prognosis than in younger patients [43]. The classic symptom of crushing sternal pain decreases with increasing age. Instead, symptoms of dyspnea, worsening neurologic function, increasing confusion, weakness, and worsening heart failure are all more likely to present in elderly patients suffering from myocardial function. The Framingham study showed that myocardial infarction was silent or unrecognized in greater than 40 % of patients greater than 75 years of age [44]. The presenting symptoms can be confusion and altered mental status in >20 % of patients greater than 85 years of age [42]. It is important in the treatment of elderly patients that we consider their functional and physiological status.

Atrial Fibrillation

Atrial fibrillation (AF) is the most common cardiac arrhythmia in patients occurring with an incidence of 1–2 % in the general population [45]. AF is defined as a dyssynchronous beating of the atria, at an increased rate of 350–600 beats per minute that result from any structural or electrophysiological changes to the heart. This fast atrial rate may or may not be associated with a fast ventricular rate. Physiologically, AF results in the loss of the atrial kick in the final phases of ventricular filling, and as a consequence, stroke volume and thus cardiac output decrease. AF can present with palpitations, dizziness, dyspnea, syncope, unstable hemodynamics, tachycardia-induced cardiomyopathy, and stroke; however, many of these patients experience asymptomatic episodes of AF before presenting with actual symptoms [45]. Elderly patients are at an increased risk because of the increased prevalence of structural changes to the elderly patient's heart. AF has a prevalence of 9 % in patients that are ≥80 years of age [46].

Treatment of acute AF initially centers on treating the underlying cause or precipitating factor. Immediate direct current cardioversion is used to treat patients in AF with hemodynamic instability, myocardial infarction, or acute heart failure [47]. Patients that are more stable are treated with respect to rate and rhythm control. Intravenous beta blockers and calcium channel blockers can be used to achieve rate control. The risk of stroke in patients with AF is five times greater than that of the general population. There is a thromboembolic risk to patients who have been in AF for greater than 24 h who undergo cardioversion. In these cases, many cardiologists prefer the treatment strategy of rate control and anticoagulation to avoid multiple cardioversions and the risk of recurrent AF with thromboembolic events. The benefit of anticoagulation to prevent stroke must be carefully balanced with the risk of bleeding in the postoperative state.

Respiratory Failure

Older adults are at an increased risk of respiratory failure when in the face of illness given the limited pulmonary reserve that accompanies aging. This limited pulmonary reserve puts elderly patients at a risk of not being able to ventilate or oxygenate adequately in the face of stress. Respiratory failure requiring mechanical ventilator support can be the primary reason (chronic obstructive pulmonary disease (COPD) exacerbation, pneumonia, pulmonary fibrosis, congestive heart failure) for being admitted to an ICU or can be secondary as a result of another critical illness (acute respiratory distress syndrome, septic shock). Geriatric patients suffer from a disproportionate number of respiratory infections that require ventilator support [48].

Elderly patients have a higher incidence of both nosocomial and community-acquired pneumonias that often have a worse prognosis than younger patients [48]. Geriatric patients also have an increased prevalence of COPD, likely resulting from an increased cumulative exposure to environmental agents [48].

Somme et al. looked at the breakdown of elderly patients admitted to an ICU and looked at three categories by age: 75–79 years ($n=182$), 80–85 years ($n=137$), and >85 years ($n=91$) [49]. The percentage of respiratory failure (total/primary diagnosis) is as follows: 75–79 years (69.2/33 %), 80–85 years (66.4/21.2 %), and >85 years (61.5/24.2 %) [49]. These data illustrate the high percentage of elderly patients with respiratory failure in the ICU setting. However, studies have not shown that age alone is a valid predictor of mortality in patients with respiratory disease and that mortality in these patients is more determined by comorbidities and a patient's underlying health in the response to critical illness with pulmonary disease [48, 50].

These data of respiratory failure in older adults give us insight into caring for elderly patients in the postoperative setting. Intensive care physicians must be diligent and mindful of the decreased pulmonary reserve of elderly patients but consider the patient's overall "clinical picture" in the setting of other comorbidities.

Sepsis

Sepsis is defined as a deleterious host response to infection that can lead to acute organ dysfunction that in turn can lead to septic shock (sepsis accompanied by hypotension that is not reversed with fluid resuscitation) in its most severe form [51]. Data show that elderly patients have a higher incidence of sepsis and have an associated increase in mortality. Angus et al. conducted a cohort study looking at 192,980 patients with the diagnosis of sepsis in 847 hospitals in the USA [52]. Of all of the patients examined, 58.3 % ($n=437,400$) were ≥65 years of age. The incidence of sepsis sharply increased with increasing age. Sepsis occurred with an incidence of 5.3/1,000 patients in the ages 60–64 years and 26/1,000 patients in the age group ≥85 years [52]. Sepsis is also associated with a higher mortality in the elderly population. The overall mortality in patients was 28.5 %. However, in patients ≥85 years, the mortality rose to 38.4 % [52]. Martin et al. published similar data by looking at adults with the diagnosis of sepsis [53]. This study looked at 10,422,301 patients from 500 acute care hospitals in the USA from the years 1979 to 2002. Elderly patients (≥65 years) accounted for 64.9 % of the cases of sepsis. These data revealed that case fatality rates increased linearly by age. A multivariable regression analysis was done that showed age as an independent predictor of mortality (odds ratio, 2.26; 95 % confidence interval, 2.17–2.36) [53]. This study also showed that older adults were more likely to die early in their hospitalization and that elderly survivors were more likely to be discharged to a non-acute healthcare facility [53].

The reason for this increased incidence and mortality in the elderly population when diagnosed with sepsis is thought to be in part to their limited cardiac, pulmonary, and renal reserve in the setting of critical illness. There have also been immunologic explanations to the increased susceptibility. The elderly population has a decline of all immunologic cell lines with age [48]. Elderly patients also have an age-related decrease in polymorphonuclear function [48, 54]. Great diligence must be given to the elderly population when diagnosing and treating sepsis. Sepsis is best treated in these patients by early identification, source control, broad antibiotic coverage, and goal-directed therapies.

Delirium

Delirium is defined as an acute confusional state that occurs in the setting of an organic process such as a medical illness, drug use, or withdrawal [55]. Delirium is differentiated from dementia, another common disease in the geriatric population, by its acute onset, degree of inattention, and an altered level of consciousness [55]. McNicoll et al. looked at the occurrence and clinical course of delirium in the elderly population [55]. This was a prospective cohort study looking at 165 consecutive patients ≥65 years of age who were admitted to an ICU. Delirium was found in 31 % of the study population on initial assessment. Furthermore, of the patients that had a normal mental exam on initial exam, 31 % developed delirium on further assessment. The median time to the development of delirium was 4 days. Patients were followed up to 7 days after discharge from the ICU for analysis. The study found that 40 % of patients still suffered from delirium in the post ICU setting. Patients who suffered from dementia were 40 % more likely to be delirious (relative risk = 1.4, 95 % confidence interval = 1.1–1.7) [55]. Delirium has been shown to be an independent predictor of increased ICU and hospital stay and 6-month mortality rates [11].

Delirium can be caused by the addition of drugs, sleep deprivation, hypoxemia, sepsis, physical restraints, metabolic derangements, endocrine derangements, and fluid and electrolyte imbalances. The best treatment of delirium is to identify and treat the underlying causes and to redirect and engage the patient. When patients present a danger to themselves or others due to delirium, antipsychotics including haloperidol, olanzapine, or quetiapine are the pharmacologic treatment of choice.

For prevention, attention should be paid to the outpatient medication list of a patient as to minimize the number of medications that are dropped from the outpatient to inpatient profile. This is especially important with medications that affect mood and cognition. Avoiding or minimizing the use of benzodiazepines appears to be important in preventing delirium in elderly ICU patients. The most successful strategy in reducing delirium in the ICU has been early and progressive mobilization. To this end many ICUs are focusing on getting patients out of bed and ambulating as early as possible with graded progressive increases in activity. Another factor suggested in preventing delirium is to minimize noise as much as possible in the ICU, especially at night, to reestablish a normal sleep wake cycle.

Palliative and End of Life Care

While most patients survive ICU care, especially following elective surgery, reported mortality in the ICU and following ICU care in geriatric patients varies from 20 to 60 % [56]. In the USA, the percentage of Medicare beneficiaries admitted to intensive care in the last month of life increased from 24.3 % in 2000 to 29.2 % in 2009 [57]. Among those that survive, disability and quality of life outcomes are quite variable [57, 58].

Given this data efforts to integrate palliative care and intensive care have become increasingly prevalent. Palliative care integration aims to improve symptom control throughout the ICU continuum and improve communication regarding prognosis and goals and preferences for treatments. An integrative model has been demonstrated to improve pain and other symptom management; improve family satisfaction [59]; decrease anxiety, depression, and posttraumatic stress disorder in family members of patients who died [60]; shorten time to do not resuscitate status and withdraw burdensome or unwanted therapies [61]; and decrease ICU length of stay without increasing mortality [61–63].

Palliative care integration has several potential components [64]. Engaging ICU teams to focus on aggressive control of pain and other symptoms of suffering is paramount. Early identification of a surrogate decision maker, advanced directives, and code status is recommended within the first 24 h of ICU stay. Early family meetings within the first 3–5 days of ICU play an important role in communicating prognosis and goals of therapy, and patient preferences are the centerpiece of communication efforts.

Conclusion

We have made great strides with advancing technology to allow elderly patients to recover from complex surgeries and critical illness. Thus we need not be any less aggressive medically with elderly patients just because of their biologic age. At the same time, a realistic expectation of prognosis for functional survival will better help align treatments with patient goals and values and potentially avoid unwanted burdensome therapies at the end of life. Critical care medicine plays an important role in the care of geriatric patients, particularly following complex urologic surgery and other therapies.

References

1. Udekwu P, Gurkin B, Oller D, Lapio L, Bourbina J. Quality of life and functional level in elderly patients surviving surgical intensive care. J Am Coll Surg. 2001;193(3):245–9.
2. Menaker J, Scalea TM. Geriatric care in the surgical intensive care unit. Crit Care Med. 2010;38(9 Suppl):S452–9.
3. Aging Statistics, Administration on Aging. http://www.aoa.gov/Aging_Statistics/.
4. U.S. Census Bureau. United States Census 2000. Washington, DC: US Census Bureau; 2000.
5. Ito Y, Kenmochi T, Irino T, et al. The impact of surgical outcome after pancreaticoduodenectomy in elderly patients. World J Surg Oncol. 2011;9:102. doi:10.1186/1477-7819-9-102; 10.1186/1477-7819-9-102.
6. Zoller DP. The physiology of aging. Am Fam Physician. 1987;36(1):112–6.
7. Evers BM, Townsend CM, Thompson JC. Organ physiology of aging. Surg Clin North Am. 1994; 1(74):23–39.
8. Lakatta EG. Age-associated cardiovascular changes in health: impact on cardiovascular disease in older persons. Heart Fail Rev. 2002;7(1):29–49.
9. Goldman L, Caldera DL, Southwick FS, et al. Cardiac risk factors and complications in non-cardiac surgery. Medicine (Baltimore). 1978;57(4):357–70.
10. Tresch DD, McGough MF. Heart failure with normal systolic function: a common disorder in older people. J Am Geriatr Soc. 1995;43(9):1035–42.
11. Marik PE. Management of the critically ill geriatric patient. Crit Care Med. 2006;34(9 Suppl):S176–82. doi:10.1097/01.CCM.0000232624.14883.9A.
12. Morley JE, Reese SS. Clinical implications of the aging heart. Am J Med. 1989;86(1):77–86.
13. Tockman M. Aging of the respiratory system. In: Katlic M, editor. Geriatric surgery, comprehensive care of the elderly patient. Baltimore-Munich: Urban & Schwarzenberg; 1990. p. 75–84.
14. Dhar S, Shastri SR, Lenora RA. Aging and the respiratory system. Med Clin North Am. 1976;60(6): 1121–39.
15. Morris JF, Koski A, Johnson LC. Spirometric standards for healthy nonsmoking adults. Am Rev Respir Dis. 1971;103(1):57–67.
16. Kronenberg RS, Drage CW. Attenuation of the ventilatory and heart rate responses to hypoxia and hypercapnia with aging in normal men. J Clin Invest. 1973;52(8):1812–9.
17. Pisani MA. Considerations in caring for the critically ill older patient. J Intensive Care Med. 2009; 24(2):83–95.
18. Adler S, Lindeman RD, Yiengst MJ, Beard E, Shock NW. Effect of acute acid loading on urinary acid excretion by the aging human kidney. J Lab Clin Med. 1968;72(2):278–89.
19. Liu LL, Leung JM. Predicting adverse postoperative outcomes in patients aged 80 years or older. J Am Geriatr Soc. 2000;48(4):405–12.
20. Keller SM, Markovitz LJ, Wilder JR, Aufses Jr AH. Emergency and elective surgery in patients over age 70. Am Surg. 1987;53(11):636–40.
21. Scalea TM, Simon HM, Duncan AO, et al. Geriatric blunt multiple trauma: improved survival with early invasive monitoring. J Trauma. 1990;30(2):129–34. discussion 134-6.
22. Clermont G, Kong L, Weissfeld LA, et al. The effect of pulmonary artery catheter use on costs and long-term outcomes of acute lung injury. PLoS One. 2011;6(7):e22512.
23. National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network, Wheeler AP, Bernard GR, et al. Pulmonary-artery versus central venous catheter to guide treatment of acute lung injury. N Engl J Med. 2006;354(21):2213–24.
24. Harvey S, Stevens K, Harrison D, et al. An evaluation of the clinical and cost-effectiveness of pulmonary artery catheters in patient management in intensive care: a systematic review and a randomised controlled trial. Health Technol Assess. 2006;10(29):iii–iv, ix–xi, 1–133.
25. Sandham JD, Hull RD, Brant RF, et al. A randomized, controlled trial of the use of pulmonary-artery catheters in high-risk surgical patients. N Engl J Med. 2003;348(1):5–14.
26. Richard C, Monnet X, Teboul JL. Pulmonary artery catheter monitoring in 2011. Curr Opin Crit Care. 2011;17(3):296–302.
27. Levy MM, Dellinger RP, Townsend SR, et al. The surviving sepsis campaign: results of an international guideline-based performance improvement program targeting severe sepsis. Crit Care Med. 2010; 38(2):367–74.
28. Durairaj L, Schmidt GA. Fluid therapy in resuscitated sepsis: less is more. Chest. 2008;133(1):252–63.
29. Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med. 2001;345(19):1368–77.
30. Wiesenack C, Prasser C, Rodig G, Keyl C. Stroke volume variation as an indicator of fluid responsiveness using pulse contour analysis in mechanically ventilated patients. Anesth Analg. 2003;96(5): 1254–7.

31. Greenfield N, Balk RA. Evaluating the adequacy of fluid resuscitation in patients with septic shock: controversies and future directions. Hosp Pract (1995). 2012;40(2):147–57.
32. Pronovost PJ, Angus DC, Dorman T, Robinson KA, Dremsizov TT, Young TL. Physician staffing patterns and clinical outcomes in critically ill patients: a systematic review. JAMA. 2002;288(17):2151–62.
33. Watters JM, Bessey PQ. Critical care for the elderly patient. Surg Clin North Am. 1994;74(1):187–97.
34. Heidegger CP, Darmon P, Pichard C. Enteral vs. parenteral nutrition for the critically ill patient: a combined support should be preferred. Curr Opin Crit Care. 2008;14(4):408–14.
35. Bistrian BR, McCowen KC. Nutritional and metabolic support in the adult intensive care unit: key controversies. Crit Care Med. 2006;34(5):1525–31.
36. Alpers DH. Enteral feeding and gut atrophy. Curr Opin Clin Nutr Metab Care. 2002;5(6):679–83.
37. Phelps SJ, Brown RO, Helms RA, Christensen ML, Kudsk K, Cochran EB. Toxicities of parenteral nutrition in the critically ill patient. Crit Care Clin. 1991;7(3):725–53.
38. Doig GS. Parenteral versus enteral nutrition in the critically ill patient: additional sensitivity analysis supports benefit of early parenteral compared to delayed enteral nutrition. Intensive Care Med. 2013; 39(5):981–2.
39. Falzone E, Hoffmann C, Keita H. Postoperative analgesia in elderly patients. Drugs Aging. 2013; 30(2):81–90.
40. Bowie MW, Slattum PW. Pharmacodynamics in older adults: a review. Am J Geriatr Pharmacother. 2007;5(3):263–303.
41. Mann C, Pouzeratte Y, Boccara G, et al. Comparison of intravenous or epidural patient-controlled analgesia in the elderly after major abdominal surgery. Anesthesiology. 2000;92(2):433–41.
42. Rich MW. Epidemiology, clinical features, and prognosis of acute myocardial infarction in the elderly. Am J Geriatr Cardiol. 2006;15(1):7–11. quiz 12.
43. Gregoratos G. Clinical manifestations of acute myocardial infarction in older patients. Am J Geriatr Cardiol. 2001;10(6):345–7.
44. Kannel WB, Dannenberg AL, Abbott RD. Unrecognized myocardial infarction and hypertension: the Framingham study. Am Heart J. 1985;109(3 Pt 1):581–5.
45. Wadke R. Atrial fibrillation. Dis Mon. 2013; 59(3):67–73.
46. Nantsupawat T, Nugent K, Phrommintikul A. Atrial fibrillation in the elderly. Drugs Aging. 2013;30(8):593–601.
47. Aronow WS. Atrial fibrillation. Heart Dis. 2002;4(2):91–101.
48. Chalfin DB. Outcome assessment in elderly patients with critical illness and respiratory failure. Clin Chest Med. 1993;14(3):583–9.
49. Somme D, Maillet JM, Gisselbrecht M, Novara A, Ract C, Fagon JY. Critically ill old and the oldest-old patients in intensive care: short- and long-term outcomes. Intensive Care Med. 2003;29(12):2137–43.
50. Heuser MD, Case LD, Ettinger WH. Mortality in intensive care patients with respiratory disease. Is age important? Arch Intern Med. 1992;152(8):1683–8.
51. Dellinger RP, Levy MM, Rhodes A, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med. 2013;41(2):580–637.
52. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. Crit Care Med. 2001;29(7):1303–10.
53. Martin GS, Mannino DM, Moss M. The effect of age on the development and outcome of adult sepsis. Crit Care Med. 2006;34(1):15–21.
54. Parrillo JE, Parker MM, Natanson C, et al. Septic shock in humans. Advances in the understanding of pathogenesis, cardiovascular dysfunction, and therapy. Ann Intern Med. 1990;113(3):227–42.
55. McNicoll L, Pisani MA, Zhang Y, Ely EW, Siegel MD, Inouye SK. Delirium in the intensive care unit: occurrence and clinical course in older patients. J Am Geriatr Soc. 2003;51(5):591–8.
56. Sacanella E, Perez-Castejon JM, Nicolas JM, et al. Mortality in healthy elderly patients after ICU admission. Intensive Care Med. 2009;35(3):550–5.
57. Teno JM, Gozalo PL, Bynum JP, et al. Change in end-of-life care for Medicare beneficiaries: site of death, place of care, and health care transitions in 2000, 2005, and 2009. JAMA. 2013;309(5):470–7.
58. Hennessy D, Juzwishin K, Yergens D, Noseworthy T, Doig C. Outcomes of elderly survivors of intensive care: a review of the literature. Chest. 2005;127(5): 1764–74.
59. Stapleton RD, Engelberg RA, Wenrich MD, Goss CH, Curtis JR. Clinician statements and family satisfaction with family conferences in the intensive care unit. Crit Care Med. 2006;34(6):1679–85.
60. Lautrette A, Darmon M, Megarbane B, et al. A communication strategy and brochure for relatives of patients dying in the ICU. N Engl J Med. 2007;356(5):469–78.
61. O'Mahony S, McHenry J, Blank AE, et al. Preliminary report of the integration of a palliative care team into an intensive care unit. Palliat Med. 2010;24(2):154–65.
62. Norton SA, Hogan LA, Holloway RG, Temkin-Greener H, Buckley MJ, Quill TE. Proactive palliative care in the medical intensive care unit: effects on length of stay for selected high-risk patients. Crit Care Med. 2007;35(6):1530–5.
63. Campbell ML, Guzman JA. Impact of a proactive approach to improve end-of-life care in a medical ICU. Chest. 2003;123(1):266–71.
64. Nelson JE, Mulkerin CM, Adams LL, Pronovost PJ. Improving comfort and communication in the ICU: a practical new tool for palliative care performance measurement and feedback. Qual Saf Health Care. 2006;15(4):264–71.

Palliative Care

30

Mary McDonald and Daniel L. Swagerty

Introduction

Urologists, more than ever, are commonly long-term providers of care to their patients over several years, developing meaningful therapeutic relationships. Like many areas of medicine, urology has been successful in curing many of the common acute ailments and now is increasingly faced with managing chronic disease. As part of this aspect of their practice, urologists may find end-of-life care very rewarding. The dying process has become more complex and now takes longer. Patients in the USA now live an average of 30 months after they receive a terminal diagnosis. During those 30 months, patients often receive about 75 % of the health care that they receive during their entire lifetime.

Suffering as well as disease must be addressed during the crucial period of life after it is recognized that a patient has a terminal illness. Sometimes in treating disease, with modern technology, physicians become the source of suffering itself. The wise healthcare provider knows when to transition from cure to palliation. Palliation is about giving our patients the highest quality of life, for as long as possible, even if cure is not possible. We must strive to provide a good death for all our patients.

M. McDonald, M.D.
Department of Community and Family Medicine, Howard University College of Medicine, Washington, DC 20059, USA
e-mail: mary.mcdonald@howard.edu

D.L. Swagerty, M.D., M.P.H., A.G.S.F. (✉)
Department of Family Medicine and Landon Center on Aging, University of Kansas Medical Center, 3901 Rainbow, Kansas City, KS 66103, USA
e-mail: dswagert@kumc.edu

Definition of Palliative Care

The World Health Organization (WHO) definition of palliative care is an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems including physical, psychosocial, and spiritual issues. It is the aggressive treatment of a patient's symptoms, when cure might be possible, in order to provide the greatest quality of life, for as long as possible.

Transitioning from a "Treat to Cure Approach" to a "Palliative Approach"

Advances in urologic care have allowed diseases that were previously acutely terminal to be, for a time, treatable and chronic. Although treatable, the urogenital cancers often defy definitive treatment, and at some point, they reach the eminently terminal phase. The patient's urologist is in the best position to recognize this phase of disease

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_30,

and to transition goals of care to a palliative approach. The primary care provider, in contrast, may await notification from the urologist that the time has come to transition to palliative care.

The transition from a treat and cure approach to a palliative approach is one that may not have received adequate attention in traditional medical training of physicians. It has been surmised that many physicians see death as an indication of their own failing, thus promoting a clinical culture that avoids "giving up" on patients who are unlikely to benefit from any further intervention. In this scenario, patients are subjected to invasive, often uncomfortable, treatments and therapies with little likelihood of benefit that occupy the little remaining time that they have. Deciding to change the goal of care to a palliative approach is entirely different than telling a patient that "there is nothing more I can do for you." The patient is not abandoned in the most vulnerable time of their life but is provided with care that promotes comfort, spiritual health, and psychological well-being.

Palliative care plans are intended to be highly individualized, based on each patient's care goals, quality of life indicators, spiritual beliefs, social support structure, and the circumstances of their medical situation. There are no strictly defined rules that govern the palliative care plan, but the goal of enhanced symptom management versus prolongation of life is the driving force behind all palliative interventions. Although many patients elect for ceasing all invasive procedures in their palliative plan, there are instances when patients undergo palliative surgeries, blood transfusions, radiation therapy, or chemotherapy in order to alleviate symptoms. These decisions are made on a case-by-case basis with symptom management, not prolongation of life, as the indication.

Communication

No one enjoys giving bad news. However, there are proven methods that are effective and can give the physician confidence that they are doing the most professional job possible and provide the most reliable possibility of acceptance from the patient and his or her family. Communicating a terminal diagnosis is a skill developed through experience. The following are recommended steps that can aid in successful, meaningful communications with patients and families.

Steps in Giving Bad News [1]

- *Introduce yourself* and have *others introduce themselves* and state their relationships to the patient.
- *Determine what the patient or family knows*: "What is your understanding of your present condition," or "What have the doctors told you?" (Make no assumptions!)
- Give a "*warning shot!*" "I'm afraid I have some bad news." Then *pause*.
- Present the bad news in a *direct and succinct manner*. Use *lay terms* so there is no misunderstanding.
- Then *sit quietly* for as long as it takes. (It may seem like an eternity!) *Wait* for the patient to respond and take your cue from that.
- If there is no response after a *prolonged silence*, you may gently say something like "Tell me what you are thinking."
- Be *ready for emotions*—feeling angry, sad, numb, fearful, and so on.
- *Validate and normalize* those feelings. It's okay to interject personal statements if appropriate: "I lost my mother last year and know how you feel."
- *Answer questions* and provide information in small chunks. The discussion is like peeling an *onion*. Provide initial information and assess the patient or family's understanding. If they need more information, go to the next layer to meet their needs. Many people won't require a lot of details.
- Assess thoughts of *self-harm*.
- Provide a follow-up plan. This is very important as patient or family will have further questions once the information has "soaked in." "I'll be back in the morning—be sure to write down any questions that you might have."
- Offer to *involve others* including a social worker, chaplain, and other professionals.

Offering realistic prognosis and predicting life expectancy are an essential component for communicating with patients and their families about life-limiting and life-threatening disease. Predicting life expectancy is difficult, but patient and family members frequently ask the physician to give them an estimate of "how long do I have?" Some diagnoses, such as widely metastatic cancers, lend themselves more easily to a terminal designation. Other illnesses, such as a slowly spreading prostate cancer that has had slow progression due to hormonal treatment or brachytherapy, can be more elusive.

The long-standing therapeutic relationships that form during the prolonged treatment of such diseases can also lead the physician to avoid approaching what may be a painful realization. The indicators of the terminal phase of chronic diseases may be difficult to recognize for both patients and physicians. Physicians must routinely evaluate symptoms of disease and functional level of patients to correctly identify when they have reached the terminal phase of their disease. Once a patient has been identified as terminal, avoid using specific timelines as they are unlikely to be accurate. Instead, use general terms that are supported by the following findings [2]:

- Life expectancy of months to years:
  - Increased fatigue
  - Functional decline and decreased ability to perform instrumental activities of daily living (IADLs)
  - Poor response to disease-modifying or curative therapies
- Life expectancy of weeks to months:
  - Increased discomfort
  - Decreased appetite
  - Increased fatigue and sleep
  - Functional decline and decreased ability to perform activities of daily living (ADLs)
  - Talk about dying
- Life expectancy of days to weeks:
  - Very poor oral intake
  - Nausea
  - Rapid or labored respirations
  - Excess pulmonary or gastric secretions
  - Decreased blood pressure
  - Increased pulse
  - Decreased urinary output
- Life expectancy of hours to days:
  - Inability to walk (if previously able)
  - Diaphoresis
  - Poor thermoregulation
  - Dreams or visions of deceased loved ones
  - Disorientation
  - Agitation
  - Picking at clothes or the air

The Palliative Conversation

Having the family unit available to participate in the palliative plan of care is vital as they are important participants in providing for the patient as their health deteriorates. The family unit can more loosely be described as the palliative care team, as many patients will ultimately be cared for by caregivers that are not family members but by other members of their inner social circle. The wishes of the patient are dependent on the willingness or ability of the identified caregivers to provide the care. It is not realistic to devise a palliative care plan that involves participation of caregivers who are not involved in the formation of the plan. The focus of the plan is on the patient, yet these decisions are ultimately made within the context of available resources. The active participation and commitment, along with continual support of the caregiver(s), assures the ultimate success of the care plan.

Frequent assessment of caregiver stress and burden and the recruitment of support services further increase this success. If, for example, a patient's primary goal is to die in their home and the caregiver informs the physician that they are unable to handle the daily services of taking care of an incontinent patient, then an indwelling Foley catheter may be indicated. Despite the risk associated with the placement of a catheter, it allows for the primary goal to be achieved.

Decision-Making Capacity

Patients should be allowed to make decisions for themselves as long as they are physically and cognitively able to do so. However in palliative care, the patient's terminal decline often leaves them ultimately unable to do so. In that case, a surrogate decision-maker is needed to make decisions based on the patient's previous stated wishes or by substituted judgment of what the proxy thinks the patient would want. Capacity is often incorrectly used interchangeably with the term competency. Competency is a legal term and is only decided by a judge, making it an inappropriate term in a medical care context.

The ideal time to discuss end-of-life issues, such as the living will or the durable power of attorney, is early in the illness process. It is then that the patient is best able to communicate their wishes and their decisions, which can then be revisited and confirmed over time. As long as the patient retains their decision-making capacity, they should be the active voice in the care decisions. At times, the proxy decision-maker may need to be reminded of this fact as the physician advocates for their patient's autonomy. For a patient to have decision-making capacity, three things are required:

1. The patient must be able to take in information. This information can be provided verbally, in writing, or by any other form of communication that meets the needs of the patient.
2. The patient must be able to process the information that is pertinent to the particular decision.
3. The patient must be able to communicate their decision back to the healthcare provider or team. This communication can be by any possible method available to the patient.

Decision-making capacity may not be static for a particular patient over time and must be reevaluated with any change of condition, as well as with each new decision. Patients have the right to change their mind over time, but they should be able to explain these changes, and if they cannot, then the decision becomes suspect for being valid. In practice, questioning a patient's decision-making capacity is often triggered by disagreements between physicians, patients, and family members. Both legally and ethically, the medical profession favors a patient's right to self-determination. Patients have the right to make decisions that physicians and family members may think are poor choices. As long as the patient meets the three criteria for decision-making capacity, the patient's wishes should be respected. More complex decisions may require a higher level of decision-making capacity. In these cases, a psychiatry or ethics committee consultation may be helpful.

Goal Setting

Goal setting is the most important part of palliative care. These goals are focused on maximizing the quality of life. Once the goals of care are defined, the treatment plan becomes much more clear. These goals are defined by decisional patients or proxy decision-makers and are based on quality of life indicators and spiritual and cultural beliefs. These goals may be but are not limited to:

- Curative treatment, including aggressive or experimental treatment
- Curative treatment with limits to aggressive treatment, such as no intubation, no feeding tube, and no hospitalization
- Withdrawal of current treatments or interventions
- Vigorous palliative care with focus on quality of life and symptom management [2]

There are questions that the physician can ask to help the patient frame their beliefs and quality of life indicators into palliative care goals, such as:

- What brings you joy? How can we maintain that joy in your life?
- Who are the most important people in your life that you would want to spend the remaining time with?
- Do you feel more comfortable being in the hospital or at your home when you are sick?
- What can you do to make your remaining time more meaningful? What can we do to make this happen?
- What type of help do you see yourself needing in your home?
- What are your fears or concerns about your diagnosis?

Developing Individualized Plans of Care

Once the care goals have been set, the individualized plan of care provides the road map to best achieve those goals. Assuring that the needed resources are available to achieve the goals is an important role of the physician or another member of the multidisciplinary team. Home health services, hospice care, durable medical equipment, and other arrangements ease the burden on patients and family members. The goals of care and the associated care plan may very well change over time as the patient's illness progresses. Their willingness to accept any type of intervention may diminish as their energy deteriorates and symptom management alone becomes the most important intervention.

Communicating Realistic Hope

The physician may have concerns that being honest and truthful about a terminal diagnosis may cause the patient to lose all hope. Hope is what drives one's positive outlook regarding their future. Physicians are obligated to convey the truth to their patients. When physicians avoid being truthful out of fear or discomfort, the patient may well cling to false hope and suffer disappointment, as well as lose opportunity for a more meaningful death. It is only when truth is provided that the patient can transition into their final phase of life.

Patients who have a meaningful therapeutic relationship with their physician are greatly benefitted by the simple assurance that they will not suffer or be abandoned at the end of their life. Such an assurance by their physician usually promotes hope for the patient in their near future. It is detrimental to the therapeutic relationship for the patient to perceive that their physician is not being completely honest with them. Realistic hope is established when patients internalize the nature of their terminal diagnosis, reassess what is important to them, and form realistic goals for the time that they have left. Instead of losing all hope, patients may find themselves empowered by the simplicity and clarity of their life goals and the ability to forgo worry about other more mundane life issues. Some patients may accept the medical facts but cling to hope that a divine miracle will spare their life. It would be inappropriate to find fault with a patient's hope that is based on their personal spiritual belief. In these circumstances, the patient should be encouraged to prepare for the worst but hope (or pray) for the best.

The Hospice Decision

Hospice is a Medicare Part A benefit that is also covered by most private insurance companies. It is the primary method of delivering palliative care in the USA. Hospice services are provided in long-term care facilities, in patient's homes, and in inpatient hospice facilities. With the exception of inpatient hospice, which is intended for patients in the final days of life or requiring emergency stabilization of symptoms, hospice does not cover the day-to-day care of the patient. Ongoing personal care is typically provided by family or nonfamily caregivers in the home or in a long-term care facility. Patients are encouraged to maintain their relationship with their treating physicians, and these physicians are encouraged to continue directing the care of their patients. In cases when patients have been abandoned by their physicians because "there is nothing more I can do for you," the hospice medical director will assume the care of the patient.

Two physicians are required to certify that the patient has a life expectancy of less than 6 months *if* the disease runs its natural course. Patients continue to qualify after the initial 6-month period if the certifying physicians still believe at that time that the patient is likely to die within the next 6 months. There are thousands of hospice organizations in the USA, and they are all required to provide the following medical services:

- Case oversight by a physician, the hospice medical director
- Nursing visits with 24/7 emergency availability
- Social work visits
- Home health aides

- Spiritual care
- Volunteer services
- Bereavement support to the caregivers after the death of the patient
- Medications related to care of the terminal diagnosis (at no cost to the patient)
- Durable medical equipment
- Other services, for example, wound care, physical therapy, etc., related to treatment of the terminal disease

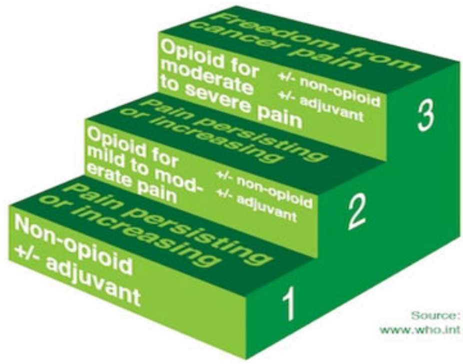


Fig. 30.1 WHO pain relief ladder

Pain Management

Chronic pain, especially in older adults and in end-of-life care, is notoriously undertreated. Most patients are less afraid of death than they are of dying with prolonged intractable pain [3]. The assessment and management of pain is a high priority in palliative medicine. The resistance of some physicians to adequately assess and treat pain may be due to misconceptions about opioid use, such as unsubstantiated fears that opioids cause severe respiratory depression and are thus dangerous. Others may worry that their terminally ill patients will become addicted to opioids or that they have serious side effects. The truth is that opioids are very safe, effective, and well-tolerated medications for pain. The myths about opioid use should not be barriers to patients receiving good pain control at the end of life [4]. This knowledge has changed public expectations, and physicians now face possible legal action for not treating pain adequately [5].

Simple guiding principles for prescribing can assure that opioid use in terminally ill adults is safe and effective in alleviating pain:

1. Stay ahead of the pain with a scheduled dose of narcotic. Long-acting opioids are particularly well suited to achieve steady results and allow for a convenient medication regimen. Escalate the dose if the pain is not controlled.
2. Provide breakthrough pain medication. A short-acting opioid should be given at about 10–20 % of the total daily dose of the long-acting opioid. These as-needed doses can be scheduled prior to activities, wound care, or bathing in anticipation of pain. If the patient is using frequent as-needed doses of opioid, it is appropriate to increase the scheduled long-acting dose.
3. Escalate the dose of the long-acting opioid if the pain is not well controlled. Monitor and reassess the patient frequently and increase the dose, as follows:
   (a) For mild pain, increase the dose by 25 %.
   (b) For moderate pain, increase the dose by 25–50 %.
   (c) For severe pain, increase the dose by 50–100 %.
4. Choose the right pain medication based on the type and severity of pain. The World Health Organization (WHO) recommends a simple yet effective three-step approach for the treatment of pain (Fig. 30.1) [6]:
   (a) Step 1. (Mild pain) Acetaminophen (maximum daily adult dose, 4 g), NSAIDs, or COX-2.
   (b) Step 2. (Mild to moderate pain) Add a weak opioid such as codeine, hydrocodone, or oxycodone.
   (c) Step 3. (Moderate to severe pain) Start morphine, hydromorphone, or fentanyl.
   (d) Pain adjuvants can be added to any of the above steps to enhance analgesia and include corticosteroids, antihistamines, benzodiazepines, NSAIDs, tricyclic antidepressants, and anticonvulsants [6].
   (e) Choose the least invasive route of administration. Oral is usually best. Concentrated

morphine drops (Roxanol 20 mg/mL) are effective and come in low volume.

(f) Manage side effects, like constipation, aggressively and reassess frequently.

(g) Escalation of pain symptoms after pain has been controlled for some time is more likely due to escalation of disease than to true tolerance to opioids.

(h) Use an equianalgesic conversion tool to convert from one opioid preparation to another.

Specific Pain Medications

Morphine

Morphine is the mainstay of pain management and prescribed for moderate to severe pain. It is available in a variety of preparations and methods of delivery, including oral, rectal, parenteral, and intraspinal administration. It is best able to control somatic or visceral pain, but is less effective in treatment of neuropathic pain. Side effects include nausea and vomiting, sedation, drowsiness, somnolence, pruritus, and constipation.

Hydrocodone

Hydrocodone is a step 2 analgesic for moderate to severe pain. It is marketed in combination with acetaminophen or ibuprofen, so the dose is limited by the maximal safe dose of the acetaminophen or ibuprofen. Hydrocodone is available in tablet and liquid form. The side effect profile is the same as morphine.

Oxycodone

Oxycodone is a step 2 analgesic for moderate to severe pain. It is available in tablet and liquid form, as well as in an immediate-acting and sustained-release preparation. Oxycodone is also marketed in combination with acetaminophen, aspirin, or ibuprofen. The side effect profile is the same as morphine.

Methadone

Methadone is a step 2 analgesic for moderate to severe pain. It is available in tablet, injectable, and liquid form and is particularly effective in treating neuropathic pain. Methadone has a very long and variable half-life and is thus difficult to titrate quickly.

Gabapentin

Gabapentin is widely used off-label for the treatment of neuropathic pain. The usual effective dose is 900–3,600 mg daily. It is best to start at 100 mg daily to three times daily and titrate up to effect. It is associated with the side effects of sedation or somnolence, confusion, dizziness, ataxia or abnormal gait, GI upset, and peripheral edema.

Meperidine and Propoxyphene (Demerol, Darvon, and Darvocet)

Meperidine (Demerol) or propoxyphene (Darvon or Darvocet) are not recommended for pain control in older adults due to significantly more central nervous system (CNS) effects and the availability of safer alternatives with equal or superior analgesic action.

Nonpain Symptom Management

Nonpain symptoms, like chronic pain, are notoriously undertreated in older adults and dying patients. At the end of life, most patients experience nonpain symptoms which are amendable to treatment [3]. The assessment and management of these symptoms is a high priority in palliative medicine.

Dyspnea, Air Hunger, and Shortness of Air

Dyspnea is a subjective sensation of uncomfortable breathing and not always associated with signs of tachypnea or hypoxia. Uncomfortable breathing may lead to or be caused by anxiety. It may lead to fear and a decreased quality of life. Common causes of dyspnea include cardiac, pulmonary, infectious, or neoplastic etiologies or can be due to damage from chemotherapy and radiation. Evaluation of the history of symptoms and a focused physical examination can usually identify a specific approach to treatment based on recognizable benefits and burdens, as well as the patient's prognosis, preferences, and care goals.

Nonmedicinal interventions such as repositioning, placement of a fan in the patient's room, relaxation techniques, and the administration of oxygen can be effective approaches with alleviation of symptoms. Medications for alleviating the symptoms of dyspnea are outlined below:

- Opioids—morphine acts centrally to decrease respiratory drive and the subjective sensation of dyspnea. They are the treatment of choice for dyspnea. They may be required on a scheduled basis for persistent symptoms or as needed for intermittent symptoms:
  - For opiate naïve patients:
    Immediate-release morphine, 5–15 mg PO every 4 h
    Sustained-released morphine, 15–30 mg PO every 12 h
    Hydromorphone, 0.5–2 mg PO every 4 h
    Oxycodone, 5–10 mg PO every 4 h
  - For patients who are not opiate naïve:
    Increase opiate dose currently being taken by up to 50 %.
- Other medications useful for dyspnea:
  - Benzodiazepines—addresses the association between dyspnea and anxiety:
    Lorazepam PO/SL/IV, 0.5–1 mg PO every 4 h
  - Bronchodilators for wheezing:
    Albuterol MDI/nebulizer every 4 h
  - Chlorpromazine (Thorazine)—may act synergistically with morphine:
    10–25 mg every 4–6 h
- Treatments for cough:
  - Guaifenesin with dextromethorphan (Robitussin DM).
  - Codeine and hydrocodone—be aware because they cause constipation.
  - Chlorpromazine (Thorazine):
    25 mg PO/IM every 4–6 h for cough triggered by hiccups
- Treatments to dry respiratory/oral secretions:
  - Anticholinergics (scopolamine, atropine, hyoscyamine (Levsin))—be aware of CNS side effects and constipation.
  - Glycopyrrolate (Robinul)—fewer CNS side effects [2].

Fever Near the End of Life

Fever near the end of life may or may not be due to infection. The fever itself typically responds well to acetaminophen, which can be administered PO or PR. Fever is commonly experienced near the end of life and should be included in the discussion of goals of care. This discussion can serve to elicit the patient's wishes regarding evaluation and treatment of fever, as well as provide an opportunity for education of the patient and their family. The reflexive administration of antibiotics in response to fever should be avoided and is only recommended if there is an identified infection for which the benefits of treatment outweigh the burden on the patient, as well as being consistent with the patient's goals of care.

Agitation and Anxiety

Agitation and anxiety may have both physical and psychosocial causes. Some causes of agitation include need for repositioning, urinary retention, fecal impaction, untreated pain, delirium, and environmental factors. In terms of psychosocial etiologies for anxiety and agitation, symptoms can often be alleviated by interviewing the patient and caregivers with focused listening to concerns. Physical examination can identify reversible causes of anxiety and agitation, but often the most effective interventions include a multifactorial approach:

- Environmental modification with repositioning and changes to ambient temperature
- Rectal disimpaction and enemas
- Catheterization of the bladder in cases of urinary retention
- Psychosocial support, including therapeutic touch, listening to concerns and fears, and offering verbal support
- Medications:
  - Neuroleptics for delirium
  - Antidepressants
  - Benzodiazepines for anxiety, not for delirium
  - Morphine for pain and dyspnea

Spiritual and Existential Suffering

Spiritual pain is common, especially at the end of life. Unresolved spiritual or personal conflicts can interfere with the acceptance of death and may lead to immeasurable grief and suffering. Some physicians comfortably perform a spiritual history with their patients, while others prefer to defer this important task to other professionals. Spiritual beliefs are highly personalized and one should avoid making assumptions based on knowledge of religious teachings within a patient's particular faith tradition. Even patients who do not identify with any organized religious group are likely to have core, life-affirming values that guide their decisions. It is very important to uncover these values as they will influence end-of-life decision-making. Pastoral counseling or specific end-of-life spiritual counseling can help address the existential suffering that can interfere with a patient's emotional and spiritual well-being.

Nausea and Vomiting

Nausea is a subjective sensation that is caused by stimulation of the chemoreceptor trigger zone, cerebral cortex, vestibular apparatus, and/or gastrointestinal lining. Vomiting is a neuromuscular reflex that is triggered in the medulla. Transient nausea frequently accompanies the initiation or escalation of opioid dosing, as it stimulates the chemoreceptor trigger zone in the brain. Nausea caused by opioids usually subsides within 7 days and is particularly responsive to treatment with prochlorperazine (Compazine), a potent antidopaminergic, weak antihistamine, and anticholinergic agent.

Vestibular nausea is less common and is associated with a spinning sensation. This sensation is best treated with promethazine (Phenergan), an antihistamine with potent anticholinergic properties and weak antidopaminergic properties. Promethazine is also effective for treating nausea due to gastroenteritis.

Nausea due to constipation and impaction is best treated by correction of the offending condition. Opioids cause constipation by decreasing bowel motility, and the use of a promotility agent, such as sennosides, magnesium hydroxide preparations, or bisacodyl, should always be considered when prescribing opioids. Stool softeners, such as docusate, do not promote GI motility and are less helpful in treatment of constipation due to opioid use. Patients who are unable to evacuate their rectum spontaneously, as can occur in patients who have nerve damage due to pelvic radiation, may benefit from the rectal stimulation achieved by a daily bisacodyl rectal suppository. Other medications that can alleviate nausea include:

- Haloperidol—a potent antidopaminergic agent
- Scopolamine—a potent purely anticholinergic agent

Nonpharmacologic interventions for the alleviation of nausea include:

- Cool damp cloth to the forehead, neck, wrists
- Bland, cool, or room temperature foods
- Decrease noxious stimuli such as odors and noise
- Limit fluids with food
- Fresh air and fan
- Relaxation techniques
- Acupuncture/pressure of transcutaneous electrical nerve stimulator (TENS)—midline wrist, 3 cm from the palmar crease
- Oral care after each emesis [2]

Dizziness

Dizziness is a common and often vague complaint that requires further description of the exact sensation to target effective treatment. Vertigo is a spinning sensation often associated with nausea that can be associated with certain medications, such as amitriptyline or metoclopramide. Avoiding these medications alone can alleviate symptoms of vertigo in many patients. Patients who experience vertigo due to idiopathic vestibular etiologies may benefit from treatment with meclizine (Antivert, 12.5–25 mg three times a day) or scopolamine transdermal patch (every 72 h).

Near syncope can be described as dizziness, and treatment is focused on the likely cause of the sensation. Dizziness encountered upon standing is often due to diminished intravascular fluid volume and can be diminished by discontinuing diuretics, antihypertensives, and sodium restrictions and through oral rehydration. Transfusion is a consideration in anemic patients with symptomatic hypotension.

In general, patients and caregivers can be advised to follow the following recommendations to minimize dizziness:

- Move slowly.
- Avoid swift head movements.
- Avoid looking upward.
- Avoid moving directly from a lying position to a standing position without sitting at the edge of the bed for a full 5 min before rising.

Fatigue

Fatigue is a normal symptom of the dying process and can be appreciable as an early and progressive symptom. Simply reassuring the patient of this fact can allow them to anticipate that slowing down in the final months of life is not a conscious decision or a reflection that they have "given up." Encourage patients to identify the activities in their life that are the most meaningful and rewarding so that they can conserve their limited energy for these purposes. Depression due to, or as the cause of, diminished functional level may improve with the use of antidepressant medications. Low-dose selective serotonin reuptake inhibitors (SSRIs) are well tolerated even in debilitated patients.

The treatment of contributing factors such as anemia or electrolyte imbalances may improve endurance, as can advising the patient to rest between activities. Physical and occupational therapy may have a role in palliative medicine, with a goal of improving quality of life. The use of gait training and positioning and the use of assistive devices may help a debilitated patient conserve energy.

Anorexia

Anorexia is a normal, predictable condition at the end of life and is due to the diversion of oxygen-rich blood supply from the digestive tract (nonessential for life under stress) to the heart and brain. Nonterminal causes of anorexia should be addressed including pain, depression, medications, oral problems, constipation, and other GI problems. Caregivers often gauge an individual's overall well-being by their intake of food and fluids, and this terminal symptom often causes them distress. Anticipatory guidance early in the terminal phase of disease can help alleviate much of the stress associated with anorexia and can avoid the situation where the patient is unduly encouraged to eat and drink despite their lack of interest in food.

The diversion of blood from the digestive tract can lead to significant prolongation in gastric emptying time and decrease in gastrointestinal motility, such that eating normal amounts of food can lead to symptoms of nausea, bloating, and abdominal pain. Forcing oral fluids on a dying patient is associated with increasing gastric secretions and can interfere with the production of natural opioid-like endorphins and diminish overall quality of life. Caregivers should be instructed to adopt a plan of "comfort feeds," an approach that focuses on allowing the patient to eat and drink what they want, how much they want, and when they want. In nonverbal patients, body language such as refusing to open one's mouth or turning away from food or drink when offered should be respected.

Constipation

Constipation is commonly experienced in the end of life due to opioid effect, immobility-associated poor GI motility, dehydration, and anticholinergic medications. Preventing constipation with opioid use is achieved by the concomitant use of bowel stimulants, such as sennosides, magnesium hydroxide preparations, or bisacodyl. Stool softeners (docusate) and fiber preparations do not prevent constipation due to opioids or generalized dysmotility. Even anorexic patients should maintain GI evacuation every 2–3 days to clear GI secretions, desquamation, and bacteria. In patients that are able to accept oral fluids, increasing their intake of fluid may alleviate constipation. Medicines, such as lactulose, sorbitol, and MiraLax, can aid in increasing fluid in the gut. Sitting up, if possible, promotes bowel motility and evacuation. Digital disimpaction or rectal lubricants can also aid with evacuation. Constipation can cause significant suffering, and a high index of suspicion should be maintained in the presence of the following findings:

- Agitation
- Delirium
- Vomiting
- Pain
- Anorexia
- Urinary retention
- New-onset incontinence
- Abdominal distention
- Impaction—evidenced by oozing diarrhea [2]

Delirium

Delirium is an acute confusional state of both impaired cognition and attention, with associated sleep/wake cycle disturbance and psychomotor abnormalities. Perceptual disturbances associated with delirium include visual and auditory illusions, confusion, hallucinations, and paranoia, all of which can be quite troubling to both the patient and caregivers. Patients often have disorganized thought processes and incoherent speech, as well as being disoriented to time. The fluctuating course and rapid onset of delirium help differentiate it from dementia. Delirium is also often worse at night. Psychomotor abnormalities of delirium may be hypoactive or hyperactive. Delirious patients can be either emotionally labile or apathetic.

The causes of delirium are many and commonly occur at the end of life. Causes of delirium include, but are not limited to, metabolic disturbance, vital organ failure, cancer metastasis to the CNS, dehydration, infection and sepsis, fecal impaction, untreated pain, urinary retention, and medication effects. Providing the patient a quiet, well-lit environment with familiar objects may improve symptoms and minimize the need for pharmacologic treatment. Whenever possible, the focus should be on identifying the cause(s) of delirium and minimizing or eliminating their effect. However, this may not be possible in a terminally ill patient, and pharmacologic treatment of the symptom may be warranted to provide the patient and others a safer situation:

- Consider changing to a different narcotic agent.
- Antipsychotics are the medication of choice. Haloperidol (Haldol) 0.5–5 mg, PO or transdermal, two to three times daily can be used for mild delirium. Dosing every 30–60 min may be needed for rapid tranquilization of the severely agitated person with delirium.
- Seroquel, or another atypical antipsychotic, may be useful for patients with extrapyramidal symptoms where haloperidol (Haldol) should be avoided. Seroquel can be started at 25 mg twice daily and titrated up to 100 mg three times daily.
- Benzodiazepines should generally be avoided. In the case of severe anxiety, a benzodiazepine (such as lorazepam, ½–1 mg PO or transdermal, two to three times daily) can be used with an antipsychotic to provide adequate relief.

Diarrhea

Diarrhea is common in the dying patient and has a wide range of causes, including medication effects, GI infections, and idiopathic etiologies. Continuous, oozing diarrhea is frequently found to be due to fecal impaction and is addressed through fecal disimpaction and a promotility bowel regimen. The use of magnesium-based antacids and metoclopramide (Reglan) can lead to diarrhea and should be discontinued. Impaired immunity in frail, debilitated patients leave them susceptible to a host of bacterial infections of the gut. In this case, stool cultures should be obtained to help direct therapy. *Clostridium difficile* infection should be suspected in any patient recently treated with antibiotics and can be treated with metronidazole (Flagyl) 500 mg by mouth every 6 h for 10 days. The oral introduction of probiotics is also thought to be beneficial in the treatment of Clostridium difficile diarrhea. Patients with pancreatic insufficiency due to pancreatitis or pancreatic neoplasm/metastasis may benefit from Pancrease MT (one to three capsules before meals) or pancreatin (one to two tablets before meals). Idiopathic diarrhea is diagnosed by exclusion of other causes and can be treated with several preparations:

- Metamucil
- Kaopectate
- Questran, one packet twice daily
- Diphenoxylate/atropine (Lomotil), two capsules two to four times daily
- Loperamide (Imodium)—for treatment of diarrhea with abdominal cramping: 2–4 mg every 6 h

Besides the immediate discomfort of diarrhea, it may lead to perineal skin breakdown and burning discomfort with defecation. Protective barriers such as A&D ointment, Desitin ointment, Uniderm ointment, and Vaseline applied to the perineal area can prevent these symptoms. Diarrhea can also be associated with dehydration, and care should be taken to provide appropriate fluid replacement as tolerated.

Urinary Incontinence

Urinary incontinence is another normal, predictable occurrence with the dying process, and it can significantly increase caregiver burden. Urologic patients may experience this symptom earlier due to local tumor effects, drug and radiation side effects, infection, and retention with overflow. Chronic indwelling bladder catheter drainage use can be included in the palliative care plan if the known risks are acceptable for the patient and caregivers when balanced by the benefits. New incontinence may be due to acute infection and antibiotic use may be warranted. Detrusor irritability may respond to treatment with medications, such as oxybutynin or antimuscarinic agents.

Depression

Depression may be confused with or masked by symptoms and signs of disease. Preparatory grief refers to the experience of a grief reaction prior to actual death and does not respond to typical treatments for depression. Referral to an experienced grief counselor may benefit patients and caregivers experiencing preparatory grief. Depression (pseudodementia) may mimic dementia, and a high index of suspicion for depressive symptoms should be maintained for patients who are described by their caregivers as experiencing a new onset of dementia near the end of life.

Counseling and reassurance for dying patients is often very helpful to identify causes of psychosocial stress in their lives. Family members, with the patient's permission, should be included in the discussions to allow the patient an opportunity to explore their feelings of loss and their fears. Patients should be reassured that you are dedicated to addressing their physical suffering and that you will not abandon them. One benefit of the patient-centered, palliative plan of care is that it puts the patient in control of planning for their immediate future. This experience of the patient regaining control, when their illness has caused a loss of control and functional independence, can in itself be mood stimulating. Patients should be encouraged to maintain meaningful relationships and activities as well as to share a life review with those close to them. Referral to a psychologist may be of benefit. The use of low-dose selective serotonin reuptake inhibitors (SSRIs) should also be considered.

Nonhealing Wounds

Dying patients are at risk for nonhealing wounds and the development of new wounds for many reasons, including immobility, dehydration, incontinence of the bowel and bladder, immune dysfunction, and malnutrition. Helping the caregivers form realistic expectations regarding wound healing can avoid feelings of failure, anger, and sadness. A more realistic approach to wound care in a dying patient may be to stabilize the wound, reduce pain, reduce bacterial burden, reduce exudate, and eliminate odor. Addressing wound odor is imperative in maintaining the dignity of the patient and affords a more comforting physical environment. Odor can be minimized through mechanical or enzymatic debridement, antibiotics (especially metronidazole gel for anaerobes), papain–urea–chlorophyllin copper sodium (Panafil), charcoal, and/or baking soda-based topicals or kitty litter placed under the bed. Basic principles of wound care should be followed, including:

- Relieving pressure with frequent repositioning and/or low-air-loss mattress and by elevating extremities off the mattress
- Not massaging a pressure area or bony prominence
- Providing nutritional support, if the prognosis warrants
- Protein supplements
- Multivitamins
- Iron
- Vitamin C, 500 mg three times daily
- Zinc, 220 mg two times daily
- Considering Foley catheter, if urine is likely to contaminate a wound

Pruritus

Pruritus is the symptom of itching: an uncomfortable sensation leading to the urge to scratch. This sensation is common in dying patients, especially those with liver disease with jaundice, lymphoma, or renal failure. In fact, patients in the final hours of life sometimes pick at unidentified stimuli on their skin. Basic instructions to caregivers to address itching include:

- Cool, humidified air.
- Avoid hot baths, irritant soaps, and laundry detergent with dyes and scents.
- Lubricate skin with moisturizing lotion.

Several topical treatments can be effective in alleviating the symptom of itching, including:

- 0.1 % triamcinolone cream
- 1.0 % hydrocortisone cream
- Fluorinated steroid creams (Synalar, Lidex)
- 2 % Xylocaine jelly

Systemic treatments to combat itching are effective but associated with side effects and should be prescribed only for widespread symptoms or symptoms with unacceptable response to topical treatment:

- Antihistamines, which have anticholinergic side effects:
  - Hydroxyzine (Atarax), 10–50 mg orally four times daily
  - Diphenhydramine (Benadryl), 25–50 mg orally four times daily
  - Cyproheptadine (Periactin), 4 mg orally four times daily
- Oral steroids, which have the side effects of insomnia, hyperglycemia, psychosis, and delirium:
  - Dexamethasone 4 mg orally daily or twice daily
  - Methylprednisolone taper (Medrol Dosepak)
- Other specific, disease-related treatments are targeted to the offending cause:
  - Candidiasis:
    Miconazole (Micatin) 2 %, topically
    Ketoconazole (Nizoral), 200 mg orally daily
    Fluconazole (Diflucan), 200–400 mg orally daily
  - Jaundice:
    Cholestyramine (Questran), one packet two to three times daily
  - Herpes zoster:
    Acyclovir (Zovirax), 5 % topical ointment
    Acyclovir (Zovirax), 200 mg orally five times daily
  - Mites:
    Kildane (Kwell) lotion and shampoo
    Crotamiton (Eurax) lotion and shampoo

Insomnia

Insomnia is the chronic inability to sleep or to remain asleep throughout the night. Insomnia can be very troubling to patients and lead to daytime somnolence and fatigue, but it can also significantly escalate caregiver burden. Identifying a cause for the disrupted ability to sleep can help the physician advise remedies or strategies to alleviate this symptom. The importance of good sleep hygiene is the first step and includes encouraging consistent sleep routines, relaxation techniques, and environmental modifications to be more conducive to sleep. Unrelieved pain can interfere with the sleep cycle and should be addressed to assure comfort. Leg cramps may be improved with quinine (325 mg orally at bedtime) or gabapentin (Neurontin) (titrated to effect). Night sweats, interfering with sleep, may improve with indomethacin (Indocin) 50 mg orally at bedtime. Despite addressing the above causes of sleep disturbance, some dying patients are chronically bothered by idiopathic insomnia and may benefit from the following medications, if the benefit of refreshing sleep outweighs the medication risk:

- Zolpidem (Ambien), 5–10 mg orally at bedtime
- Lorazepam (Ativan), 0.5–1 mg orally at bedtime, up to 2 mg
- Alprazolam (Xanax), 0.25–0.5 mg orally at bedtime, up to 1 mg
- Trazodone, 25–50 mg orally at bedtime
- Temazepam, 15–30 mg orally at bedtime

Palliative Radiation, Chemotherapy, and Surgery

Palliative Radiation

Radiation can be used as a palliative treatment to improve the quality of life in patients with malignancies by reducing pain, increasing function, and relieving pressure on a vital structure. In fact, 25–40 % of radiation therapy is now used for symptom control rather than for curative treatment [7]. Patients and family members may need to be reoriented to the goal of radiation therapy as it pertains to the patient's palliative care plan. The burden of treatment and side effects must be weighed against the expected response rate to treatment. Common cancer syndromes in which radiation therapy is palliative include the following: [8]

- Painful bone metastasis
- Spinal cord compression
- Superior vena cava syndrome—dyspnea, orthopnea, and venous congestion secondary to tumor impingement
- Brain metastasis
- Obstruction of the esophagus, airway, biliary tract, etc.

Palliative Chemotherapy

Palliative chemotherapy is used solely for the control of symptoms and not for curative treatment. Careful patient selection will minimize the risk of patients pursuing chemotherapy for a cure of their malignancy when the cure rate is negligible. The burden of treatment and toxicity of chemotherapy must be weighed against the probability of symptom improvement if palliative chemotherapy is included in the palliative care plan.

Palliative Surgery

Palliative surgery can be considered in some cases where other treatments have not been effective in providing symptomatic relief. Some patients with urologic conditions could benefit from selective palliative surgical procedures. For example, patients with acute spinal cord compression from bone metastases in cases of advanced prostate cancer may be candidates for spinal decompression surgery, particularly if either radiation therapy or chemotherapy has not been effective. Similarly, patients with advanced kidney cancers who experience intractable pain or uncontrolled bleeding may benefit from either cytoreductive nephrectomy or endovascular embolization.

Summary

While there will always come a time when there is nothing more a physician can do to cure their patient's disease, there will always be something they can do for their patient. They can provide aggressive care to provide comfort. The focus of treatment should be on relieving suffering and improving quality of life for these seriously ill, vulnerable patients. Good end-of-life care is very individual, based upon the patient's philosophy of life and their goals of care. The physician must find out what the patient's goals are and try to satisfy them. Once the patient's philosophy and goals are known, knowing how to care for that individual becomes much easier. At some point, almost everyone begins to see his or her goal as a good and peaceful death.

References

1. Ambuel B. Giving bad and sad news. In: Weissman DE, Ambuel B, editors. Improving end-of-life care: a resource guide for physician education. Milwaukee, WI: The Medical College of Wisconsin; 1999.
2. Old JL, Swagerty DL. A practical guide to palliative care. Philadelphia, PA: Lippincott Williams & Wilkins; 2007.
3. Storey P, Knight CF. Alleviating psychological and spiritual pain in the terminally ill, UNIPAC two. Hospice/Palliative care training for physicians. 2nd ed. Glenview, IL: American Academy of Hospice and Palliative Medicine; 2003. 15.
4. Joranson DE, Ryan KM, Gilson AM, et al. Trends in medical use and abuse of opioid analgesics. JAMA. 2000;283:1710–4.
5. Fishman SM. Legal aspects in pain medicine for primary care physicians. Supplement to Family Practice News. New York, NY: Academy for Healthcare Education; 2006. Available at http://www.AHECME.com
6. WHO Ladder. Cancer pain relief and palliative care. Technical Report Series 804. Geneva: World Health Organization; 1990.
7. Lutz S, Conner S. Radiation oncology and hospice; cornerstones in palliative care. Am Acad Hosp Palliat Med Bull. 2005;6:1–3.
8. Tisdale BA. When to consider radiation therapy for your patient. Am Fam Physician. 1999;59: 1177–89.

31 Healthcare Financing and Public Policy

James M. Dupree and Christopher M. Gonzalez

Introduction

Since 1965, Medicare has provided near universal healthcare coverage for America's seniors. Medicare has several individual components: Part A for inpatient hospital, skilled nursing facility (SNF), and hospice care; Part B for outpatient medical services, supplies, and tests; Part D for prescription drug coverage; and Part C, or Medicare + Choice, as an alternative model for receiving benefits. Each part of Medicare has different benefits and financial structures, all of which are important for urologists to understand as they care for an aging population. The structures of the parts of Medicare affect how seniors interact with their physicians, approach inpatient and outpatient acute and chronic care needs, and obtain prescription medications, durable medical equipment (DME), and supplies.

Over 95 % of seniors use Medicare to help obtain their healthcare services, and many use Medicaid to assist with out-of-pocket costs. This chapter will focus on these two federal entitlement programs. Overall, seniors report being very satisfied with the services they receive in Medicare, and they have excellent access to the current healthcare system. Medicare also helps protect most seniors from undue financial hardships associated with the rising cost of healthcare, although the cost-sharing mechanisms in Medicare can be burdensome to seniors with fewer resources. For seniors with less financial resources, Medicaid often provides important assistance with out-of-pocket cost-sharing expenses. The aim of this chapter is to help the reader navigate through the various origins, terminologies, and components of government healthcare programs for seniors living in the United States in 2014. This chapter also reviews recent changes to the Medicare system and discusses the financial pressures on it from rising healthcare costs and an aging population.

Case

A 76-year-old retired machinist with a history of chronic obstructive pulmonary disease (COPD) and heart failure is admitted to an acute inpatient hospital following an open partial nephrectomy for a 3 cm peripheral, enhancing renal mass. On postoperative day (POD) number one, he has a respiratory event that requires intubation and transfer to the surgical intensive care unit (SICU). He remains on a respirator for 1 week, and after extubation, he develops urinary retention requiring an

(continued)

J.M. Dupree, M.D., M.P.H.
C.M. Gonzalez, M.D., M.B.A., F.A.C.S. (✉)
Department of Urology, Northwestern University, Feinberg School of Medicine, 303 East Chicago Avenue, Tarry 16-703, Chicago, IL 60610, USA
e-mail: jim.dupree@gmail.com; cgonzalez@nmff.org

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_31,

(continued)

indwelling urinary (Foley) catheter and alpha-blocker medical therapy. He is transferred back to the floor but became debilitated during his SICU stay. The physical therapist recommends a SNF after discharge, which occurs on POD number 9, and he stays at the SNF for 2 weeks receiving additional rehabilitation.

While in the SNF, his flank wound opens slightly, requiring wet-to-dry dressing changes; however, he no longer needs a Foley catheter and voids to completion. On discharge from the SNF to home, he remains on alpha-blocker therapy and oral narcotics, and he receives four additional weeks of home healthcare for dressing changes and supplies. He also has outpatient follow-up appointments with his urologist, pulmonologist, and internist. Who pays for the healthcare services required by this elderly male in 2014?

Healthcare Basics

As of 2010, there were 40,267,984 men and women aged 65 or older (referred to as seniors) living in the United States, constituting 13 % of the US population [1]. In 2020, there are projected to be approximately 54.2 million seniors [2], and by 2030, seniors are projected to make up at least 19 % of the population [3].

According to the 2010 Census, the segment of the population aged 65 or older grew 15.1 % over the 10-year period between 2000 and 2010, faster than the growth rate for the entire population under the age of 45 [1]. Much of this growth is a result of the aging of the Baby Boom generation, defined as those born after World War II, from 1946 to 1964 [3]. By 2029, all of the Baby Boomers will be aged 65 or older [4].

Seniors have many unique healthcare characteristics and are at increased risk for many health conditions, including cancer, heart disease, pulmonary disease, and changes in mental status such as dementia [5, 6]. Living with these chronic conditions, along with managing acute changes in health, can be a large financial burden to seniors, most of whom have left the workforce and are living on fixed incomes.

Medicare provides health insurance coverage for over 95 % of seniors [7]. Most of the remaining 5 % of seniors not using Medicare receive health insurance from previous employers. Overall, less than 1 % of seniors in the United States are without some form of health insurance [8, 9]. As of 2008, 10.5 % of private sector employers offered health insurance benefits to retirees, in the form of either Medicare supplemental insurance or primary private insurance [10]. Another government entitlement program, Medicaid, also plays a role in assisting low-income seniors with out-of-pocket costs not covered by Medicare. Medicaid will be described later in this chapter. A minority of seniors also receive some care from the Veterans Health Administration (VHA). Individuals who served active duty in the armed forces and left for reasons other than dishonorable discharge may qualify for VHA benefits. Once enrolled, each veteran is given a priority level based on a variety of factors including, but not limited to, year of service, amount of service-related disabilities, medals received, and income [11]. The VHA uses the priority groups to distribute resources, and a veteran's co-pay for inpatient, outpatient, and prescription drug care will differ depending on his or her priority group [11]. Veterans can obtain more information about their eligibility for VHA care by calling 1-877-222-VETS (8387). According to data from the Federal Interagency Forum on Aging-Related Statistics, in 2011, there were 9.4 million veterans in the USA who were aged 65 and over. Of those, 3.8 million enrolled to receive healthcare from the VHA, and 2.6 million actually received VHA care during the year [12].

Since over 95 % of seniors use Medicare to help obtain their healthcare services (and some use Medicaid to assist with out-of-pocket costs), the remainder of this chapter will focus on these two federal entitlement programs. The few uninsured seniors who are not part of Medicare or do not receive care through employer-sponsored private health plans rely mainly on public hospitals, free clinics, or other federally qualified health center for their healthcare needs. The aim of this chapter is to help the reader navigate through the various origins, terminologies, and components of government healthcare programs for seniors living in the United States in 2014.

Medicare

History

For almost a century, government leaders in the White House and Congress have been concerned about the financial impact of healthcare expenses on seniors. Starting as early as 1915, there were efforts to create a federal safety net to protect seniors from excess financial burdens created by their health conditions [7]. Detailed descriptions of these efforts, as well as the various failed attempts in the early to mid-1900s to provide federal coverage, are well explained elsewhere (http://www.ssa.gov/history/corning.html) and are beyond the scope of this chapter. These early efforts ultimately led to the creation of the Medicare and Medicaid programs.

The Health Insurance for the Aged Act was signed into law in 1965 and created Medicare and Medicaid as titles XVIII and XIX of the Social Security Act, respectively. Medicare was originally structured to provide coverage and benefits similar to the private insurance options available in the mid-1960s [13] and was composed of two parts, A (inpatient hospital care) and B (supplemental medical insurance for physician services and other expenses). Today, Medicare has been expanded through numerous incremental changes including the creation of parts C (Medicare Advantage) and D (prescription drug coverage) (see Table 31.1 for a summary of the current components of the Medicare system). Since 1972, Medicare has also been available to patients with end-stage renal disease, certain disabilities, and those with chronic health conditions; however, those individuals constitute a minority (16.9 %) [4] of Medicare enrollees and are outside the scope of this chapter. Understanding the components of Medicare is important for urologists as they care for an aging population. The structures of the parts of Medicare affect how seniors interact with their physicians, approach inpatient and outpatient acute and chronic care needs, and obtain prescription medications, DME, and supplies.

Eligibility for Medicare

Originally, eligibility for Medicare Part A was tied to age and eligibility for Social Security benefits. Anyone who was aged 65 or older and

Table 31.1 Summary of Medicare parts, coverage, deductibles, and other cost sharing (as of 2012)

	Services covered	Deductible	Other cost sharing
Part A	Inpatient hospital services, skilled nursing facility (SNF) stays, hospice care, some home health services	$1,156 annually for inpatient hospital services	$124 per day for SNF care after 20 days $5 co-pay for outpatient hospice drugs 5 % co-pay for inpatient hospice respite care
Part B	Physician services, supplies, durable medical equipment (DME), physical and speech therapy, outpatient hospital care, ambulatory surgery, laboratory services, outpatient mental health services	$131 annually	$93.50 to $161.40 per month depending on income 20 % co-pay for physician services, physical and occupational therapy, ambulatory surgery services, imaging, DME, and supplies 50 % co-pay for mental health services
Part C (Medicare advantage)	Part A and Part B services, covered through a private insurer	Depends on the individual plan	Depends on the individual plan
Part D	Prescription medication coverage	$32.34 per month, subsidized for low-income individuals	Varies depending on total annual prescription medication expenditures

had paid Social Security taxes for at least 10 years (or 40 fiscal quarters), or who had a spouse that met these criteria, would qualify for Medicare [14]. Eligibility was tied to a history of paying taxes because most seniors lost employer-sponsored healthcare benefits when they retired [13]. Today, seniors who do not qualify for Medicare can pay a monthly premium to enroll in the program as long as they are US citizens or lawful noncitizens who have lived in the country for at least 5 years [8, 14]. This small population of voluntary enrollees is typically composed of seniors who did not accrue 40 quarters of payroll taxes. For 2011, this voluntary monthly premium was $450 for seniors with less than 30 quarters of payroll tax history and $248 for those with a history of paying 30–39 quarters of Medicare payroll taxes [7].

Medicare Part A

Medicare Part A is also known as the Hospital Insurance (HI) program. It is a compulsory program for all seniors who become eligible for Social Security benefits. Seniors become eligible and are enrolled in Part A on the day they turn 65. Part A provides coverage for acute inpatient hospital services, SNF stays, hospice care, and some home health services [13]. Part A is funded through mandatory payroll taxes paid by all workers and their employers. In 1965, the combined tax for employees and employers was 0.7 % of earned income. By 2012 it was 2.9 %, split equally between the employee and employer [13, 15], but in 2013, the tax paid by high-income employees increased by 0.9 % points to 2.35 %; the employer portion remained stable at 1.45 % [16]. The revenues from these taxes account for 84 % of the Part A budget and are put into a Part A trust fund that is used solely to pay for Part A services [15]. It is important to remember that today's tax revenues are being used to pay for services used by today's Medicare beneficiaries. Today's workers are assuming that similar tax revenues will exist when they retire.

Part A also contains cost-sharing measures that beneficiaries either pay out-of-pocket or have covered by supplementary insurance plans (discussed below). For 2012, the Part A annual deductible for inpatient hospital services was $1,156 [16]. Inpatient hospital care costs the senior $992 per stay in the hospital and an additional $248 per day after the first 60 days in the hospital. These costs count towards the annual deductible. For SNFs, days 1–20 are fully covered as long as the SNF stay is preceded by 3 days or more days of an inpatient hospital stay for an acute event [17]. However, beneficiaries must pay $124 per day after 20 days in the SNF. Cost sharing for hospice stay is nominal with a $5 co-pay for outpatient drugs and a 5 % co-pay for inpatient respite care [18]. When summed together, these Part A out-of-pocket expenses can be a considerable financial strain for seniors without supplemental insurance plans.

Medicare Part B

Part B is also known as the Supplementary Medical Insurance (SMI) program. Unlike Part A, Part B is a voluntary program that seniors can elect to enroll in at age 65. Part B covers physician services, supplies, DME, physical and speech therapy, outpatient hospital care, ambulatory surgery, laboratory services, and outpatient mental health services. All citizens and certain legal noncitizens are eligible for Part B, even if they are not automatically eligible for Part A, as long as they pay the monthly premiums [7]. The premiums were $3 per month when the program started in 1966 and now range from $93.50 to $161.40 per month depending on the senior's current income level. Medicare Part B monthly premiums fund 25 % of the annual cost of Part B with the remainder of funding coming from federal income tax revenues on both individuals and corporations [15]. Part B cost sharing is also structured differently from Part A. In addition to the monthly premiums, there is an annual $131 deductible and a 20 % co-pay for physician services, physical and occupational therapy, ambulatory surgery services, imaging, DME, and supplies. There is full coverage for laboratory services and a 50 % co-pay for mental health services.

Medicare Part C (Medicare Advantage)

Medicare Advantage (MA) was created in 1997 as part of the Balanced Budget Act and originally was called Medicare + Choice. It was renamed MA in 2003. MA allows beneficiaries to voluntarily receive their Part A and Part B benefits through a private insurer. The federal government pays the private MA Plan a fixed amount each month to provide Part A and Part B benefits. MA was designed to help reduce Medicare costs to the government by capping federal expenditures and shifting the cost risk to the private MA Plans. For beneficiaries, MA offers the potential for more advantageous cost-sharing arrangements and a wider array of covered services. In 2011, about 25 % of all Medicare beneficiaries were enrolled in an MA Plan [16].

MA Plans differ greatly in their cost-sharing structures; some cover the majority of the above listed Part A and B deductibles, co-pays, and premiums, while others cover only some of those costs. MA programs can be structured as health maintenance organizations (HMOs), preferred provider organizations (PPOs), private fee-for-service (pFFS) plans, and special need plans (SNPs). However, regardless of the structure, all MA Plans must, at a minimum, cover the same basic services as Medicare Part A and B, and all, except for pFFS plans, must include the equivalent of Part D coverage. The MA Plans have the option of providing additional services not covered by Parts A or B; however, this may come at an additional cost for enrollees.

Medicare Part D

Part D is the newest section of Medicare and was signed into law in 2003 by President George W. Bush as part of the Medicare Modernization Act. Part D provides subsidized prescription medication coverage. When Medicare was originally designed, prescription medications were used less frequently than today, and most private insurers at the time did not cover prescription medications. Thus, the benefit was left out of the program. As the practice of medicine has evolved over the past 40 years, the use of prescription medications increased greatly, and seniors began facing large out-of-pocket costs for medications. Prior to implementing Part D, the number one reason seniors did not fill prescriptions was because of this substantial personal cost burden [19]. While Part D is a part of Medicare, the actual medications are obtained through private plans, called prescription drug plans (PDP), that contract with Medicare [16].

Like Part B, Part D is voluntary. It is funded through federal income tax revenues (83 %), Part D premiums (11 %), and state subsidies for "dual-eligible" beneficiaries (discussed later) [15]. Beneficiaries currently pay an average monthly premium of $32.34 for Part D [7]. The premium is subsidized for those with lower income on a sliding scale. There is also a variable coinsurance rate for total annual drug costs above $265, which includes the "doughnut hole" that received so much attention when Part D was introduced. Specifics will differ for each beneficiary, but in general, the first $265 worth of drugs purchased each year is covered by the PDP. Between $265 and $2,400 of annual costs, the beneficiary pays 25 % of the cost. Between $2,400 and $3,850, the beneficiary pays all of the cost (this is the doughnut hole), and above $3,850 of annual drug expenses, the beneficiary pays very little [17]. There have been several changes to the Part D funding structure included in the recent Patient Protection and Affordable Care Act (ACA), and these changes will be discussed later in the chapter.

Supplemental Medicare Insurance

While Medicare helps protect seniors from much of the financial burden associated with healthcare services, there are substantial cost-sharing mechanisms built into the system. Because of these cost-sharing arrangements, many seniors seek out supplemental insurance (SI) to help cover out-of-pocket expenses. Approximately 90 % of Medicare enrollees currently have some form of SI [13]. SI can come from a variety of sources, including former employers, private Medigap plans purchased by the beneficiary, Medicare Advantage, Medicaid, and other sources. Of 2010 Medicare beneficiaries with SI, 33 % received SI through former employers, 25 % through Medigap, 16 % through Medicaid, 13 % through MA, and 2 % through other sources [13]. Studies suggest that those with SI have higher Medicare utilization rates as compared to those without SI [13]. However, SI has proven to be extremely important to Medicare beneficiaries. Medicare enrollees without SI report higher out-of-pocket spending and increased rates of delaying care because of cost concerns, as compared to those with SI [6]. Unfortunately, those at or below the Federal Poverty Line (FPL) are less likely to have SI, even through Medicaid, as compared to those above the FPL [6]. Because of these issues, there are active discussions in policy circles about changing the rules surrounding the availability and cost of SI programs.

Medicaid

Medicaid was implemented simultaneously with Medicare in 1965, yet was designed to provide healthcare access and benefits for the poor, regardless of age. Medicaid has become very important to some older adults because it provides SI for approximately 17 % of Medicare seniors. Most of these individuals qualify for Medicaid because of low income; however, the definition of low income varies from state to state [13]. Medicaid is primarily a state-run program, funded through state tax revenues, and each state sets its own guidelines for eligibility and benefits [20]. However, the Centers for Medicare and Medicaid Services (CMS) offers matching federal funds for states provided they meet certain guidelines about the services and structure of healthcare provided. The amount of matching funds differs for each state on a sliding scale and mostly depends on the state's per capita income and compliance with CMS measures.

Dual Eligibles

Seniors who are eligible for both Medicare and Medicaid benefits are known as "dual eligibles"(DEs). In 2008, approximately 11 % of aged Medicare enrollees were DEs (4.1 million people) [4, 21]. For DE beneficiaries, Medicaid can act as supplemental insurance to provide assistance with Medicare Part A, B, and D premiums, co-pays, and deductibles. Medicaid can also sometimes provide services not covered by Medicare, such as long-term care, dental care, and eyeglasses [22]. This assistance is often necessary for DE seniors because 17 % of all seniors have an annual income below the FPL. Furthermore, in 2002, 46 % of seniors living in the USA had incomes at or below 200 % of the FPL, demonstrating the growing concern for the number of seniors who may become eligible for Medicaid as a source of their SI [13]. The 2011 FPL for a single person in the 48 contiguous states was $10,890. For a family of two, the FPL was $14,710.

DE beneficiaries compromise a complicated set of patients because they tend to have poor health status and limited access to resources. DE beneficiaries tend to have more chronic and mental health problems and a higher rate of living in nursing homes, as compared with other Medicare enrollees [22]. DE also have significantly less financial resources, with 56 % reporting annual incomes of less than $10,000, as compared with 6 % of non-DE Medicare enrollees.

Qualifying for Medicaid can be complicated for seniors as there are multiple pathways for eligibility. Most qualify because their income is at or below 75 % of the FPL. Medicare enrollees can also qualify if they have spent a significant portion of their financial resources on healthcare [22]. If a senior's income is close to or above the FPL, they may also qualify to receive assistance with Medicare premiums. However, they will still likely have to pay out-of-pocket for other Medicare cost-sharing expenses such as co-pays and deductibles [22].

Recent Federal Changes

The ACA was signed into law by President Barack Obama in 2010. It provided the most comprehensive reform to the US healthcare system since Medicare and Medicaid were created in 1965. Several provisions of the ACA were challenged in Federal courts including in the Supreme Court. On June 28, 2012, the Supreme Court released their decision, upholding the constitutionality of the individual mandate in the ACA as a tax that the Congress was authorized to levy. The Supreme Court also allowed for the expansion of Medicaid prescribed in the ACA but ruled that states could decline the expansion, as long as they also declined the new federal funds that accompanied it [23].

For those already on Medicare, one of the biggest changes in the ACA affects Part D cost sharing. Starting in 2012, the "doughnut hole" was reduced. Initially, beneficiaries will receive a 50 % cost discount for out-of-pocket, brand-name medication expenses occurring in the doughnut hole and a 14 % discount for out-of-pocket generic medication expenses in the doughnut hole. The ACA calls for these subsidies to increase through 2020, at which point the doughnut hole will be eliminated. Another provision of the ACA now provides a "welcome to Medicare" exam free of charge to beneficiaries, as well as free annual wellness visits, mammograms, general health screening tests, and preventive care. All of these services required a co-pay prior to the ACA [24].

The ACA also offers structural improvements to citizens younger than 65. The ACA uses incentives to encourage employers to continue to offer health insurance benefits to individuals aged 55–64, even if they are retired. The ACA also eliminates lifetime limits on health insurance coverage and removes preexisting condition limitations that often prevented adults from purchasing individual health insurance products [25].

Challenges for Today's Seniors

Overall, seniors report being very satisfied with their healthcare services and coverage [19]. Much of that fulfillment can be attributed to their near universal access to Medicare [19]. The Commonwealth Fund's 2004 Survey of Older Adults showed that compared with other forms of healthcare insurance coverage, Medicare beneficiaries "have an equal or greater choice of doctors, fill out less paperwork, have fewer problems getting their insurance to pay their doctors, and are equally or more satisfied with the quality of their healthcare and confident in their ability to receive the best medical care available when needed" [19] (see Table 31.2). Despite these positive reports from beneficiaries, there are several issues in Medicare that continue to plague the program and threaten its survivability.

Medicare Costs

Medicare spending is growing at a rate faster than that of the economy [13]. In 2010, Medicare costs accounted for 12 % of total federal spending [18]. According to the Medicare Board of Trustees, Medicare costs are projected to rise from 3.6 % of gross domestic product (GDP) in 2010 to 5.5 % by 2035 and to 6.2 % by 2085 [26]. Healthcare costs are rising at a rapid rate, driven by increasing utilization of services, higher prices, and the use of new technology [15]. Furthermore, the Baby Boomer generation started becoming eligible for Medicare in 2010, thus greatly increasing the rate of Medicare enrollment. This, coupled with the continued retirement of Baby Boomers, has significantly increased the ratio of Medicare beneficiaries to active workers, creating a fiscally unsustainable entitlement program.

Overall, in 2010, Part A accounted for 36 % of total Medicare spending, Part B 27 %, Part C 24 %, and Part D 10 % [18]. In 2004, for the first time, Part A spending exceeded Part A payroll

Table 31.2 Satisfaction rates as percent of individuals aged 50–70 by type of insurance

	Medicare	Employer-sponsored	Individually purchased	Uninsured
"Very satisfied" with their healthcare	60	58	41	23
"Very confident" getting the best medical care	56	52	45	18
Not able to see a needed specialist because of cost	7	7	12	27
Rate current insurance as "excellent" or "very good"	55	57	32	na
"Great deal" of choice in where to go for medical care	52	44	47	na
"Not a problem" filling out paper work for healthcare	70	66	62	na
"Not a problem" getting insurance to pay medical bills	81	75	68	na

taxes collected, and that trend is expected to continue for the foreseeable future. The Medicare Trustees currently expect the Part A trust fund to become insolvent by 2024, meaning that the fund will not have enough reserves to pay benefits [15, 27]. Multiple policy options have been suggested to deal with the imbalance of Medicare expenditures and trust fund incomes. Some suggestions include reducing benefits to Medicare recipients, increasing eligibility age, increasing beneficiary cost sharing, and increasing the Medicare payroll tax for active workers. However, the political will to implement any of these measures has been lacking due to the unpopular ramifications of disrupting this entitlement program for seniors or shifting the enormous cost burden of this program to active workers.

Medicare Parts B and D do not have the same impending insolvency issues that face Part A because Parts B and D were designed to be funded by general income tax revenues and premiums, not through a trust fund. However, as costs for Parts B and D rise, enrollee premiums may need to increase along with general tax revenues in order to sustain Parts B and D [15].

It is important to note that the majority of Medicare spending is concentrated on a minority of beneficiaries. In 2007, the top 10 % of non-MA beneficiaries accounted for 59 % of total Medicare spending [15]. In addition, DE enrollees tend to be high utilizers. Although they constitute only 11 % of aged Medicare beneficiaries, DEs account for about 39 % of all Medicare spending [22]. Not surprisingly, there is increased policy focus on Medicare beneficiaries with high utilization rates, in the hopes of finding ways to decrease costs while maintaining quality. Some of these new policies, such as the Accountable Care Organization shared-savings model and the Hospital Inpatient Value-Based Purchasing program, were implemented in 2011. Other policy ideas are in very early stages of development, and it is unclear what may be offered in the years ahead.

Seniors also face personal financial challenges related to Medicare costs. In 2007, each beneficiary used an average of $18,000 of medical services [15]. About half of these costs were paid by Medicare, with the remaining costs paid by beneficiaries directly or by their SI plans [15]. It is important to note that one in four beneficiaries spends more than 30 % of his or her annual income on cost-sharing expenses [15]. In 2009, healthcare expenditures accounted for 15 % of a Medicare beneficiary's annual budget, which is about three times the proportion of younger individuals' healthcare expenses [16]. Increasing cost sharing, one of the potential policy interventions discussed above, would only add to the already significant financial pressure on seniors.

Medicare Access

Today, Medicare beneficiaries have near universal access to physicians. However, this may not always be the case. The Federal government has made numerous policy changes to Medicare over the past 40 years that have affected physicians, including changes to the physician payment structure and documentation and reporting requirements. In the general press, there are numerous reports of physicians opting out of Medicare [28, 29]. A survey by the Texas Medical Association showed that 172 physicians in Texas opted out of Medicare in 2010 and that 135 opted out in 2009, 151 in 2008, and 70 in 2007 [28]. A 2011 study using the National Ambulatory Medical Care Survey showed a decrease in the percentage of physicians accepting new Medicare patients from 95.5 % in 2005 to 92.9 % in 2008 ($p = 0.01$) [29]. It is unclear how much of this decrease is due to physicians opting out of Medicare versus simply closing their practices to new Medicare referrals.

From the patient perspective, it is uncertain if these rare physician withdrawals from Medicare have started to negatively affect access to services. The Medicare Payment Advisory Commission (MedPAC) is an independent commission designed to advise the Congress about the current state and future direction of the Medicare program. It is comprised of 17 commissioners appointed by the Comptroller General of the USA who are supported by a large research staff. One of their recent reports indicates that 79 % of Medicare patients have "no problem" finding a new primary care provider (PCP), as opposed to 69 % of private insurance patients who reported "no problem" finding a PCP. Access to specialists was easier with 87 % of Medicare patients as compared to 82 % of private insurance patients reporting "no problem" finding a new specialist. Overall, MedPAC found that 85 % of PCPs and 95 % of specialists were willing to accept new Medicare patients. To help prevent further access issues, especially in rural areas, the ACA called for CMS to begin offering a 10 % bonus payment to PCPs and general surgeons practicing in rural areas in 2010 [18].

Sustainable Growth Rate

While Medicare access appears stable at the moment, there are potential Medicare reimbursement changes on the horizon that could drive additional physicians out of the system. One of these possible issues is the Sustainable Growth Rate (SGR) provider reimbursement formula. The SGR was implemented as part of the Balanced Budget Act of 1997 as a means to restrain growth in Medicare physician payment rates. The SGR was tied to the GDP to ensure that physician payment rates would not grow faster than the economy. Unfortunately, practice expenses have risen much faster than GDP, and since 2003, the SGR has prescribed a payment rate cut for physicians. For the past 10 years, the Congress has had to intervene to provide a temporary "Doc Fix" to supersede the SGR payment rate cut [7, 30]. Each of these Congressional interventions has created a cumulative debt. The debt is the amount of money that would have been saved had the SGR payment rates been followed. As of 2011, that cumulative debt is approximately \$300 billion. For 2012, the SGR prescribed an approximately 27 % rate cut for all Medicare physicians. In order to avoid this cut, the Congress again had to pass a 3-month "Doc Fix" in December of 2011 and a 10-month fix in February of 2012. A permanent replacement to the SGR in the year 2012 would cost the government over \$300 billion.

The SGR and the now annual discussions about payment cuts and "Doc Fixes" threaten beneficiaries' access to care. If the prescribed SGR payment rate cut were to become enacted, many physicians might leave Medicare. Also, if the SGR were to be permanently fixed and replaced, some, including MedPAC, have suggested paying for the fix by reducing physician payment rates, either temporarily or permanently. These payment freezes or reductions could also push providers out of the Medicare system, further limiting access for seniors.

Conclusion

Since 1965, Medicare has provided near universal coverage to America's seniors. Medicare has several individual components, each with different benefits and financial structures, all of which are important for urologists to understand as they care for older adults. Seniors have reported being very satisfied with the services they receive in Medicare, and they have excellent access to the current healthcare system. The entitlement program also helps protect most seniors from undue financial hardship associated with the rising cost of healthcare, although the cost-sharing mechanisms in Medicare can be burdensome to seniors with fewer resources. The Medicare system is under tremendous financial pressure because of the rising healthcare costs and an aging population. Moving forward, we must find ways to ensure that seniors maintain access to needed benefits and are protected from burdensome healthcare financial pressures.

Case

Returning to our opening case, the 76-year-old gentleman experienced the following:

– A 10-day inpatient hospital stay following a partial nephrectomy
– A 14-day SNF stay
– Twenty-eight days of home health assistance
– Outpatient prescriptions for alpha-blocker therapy and narcotics
– Outpatient follow-up appointments with his urologist, pulmonologist, and internist

As a retired worker who paid Medicare taxes for over 10 years, he had qualified automatically for Medicare Part A enrollment at age 65, and he had also previously elected to enroll in Part B and D as well. Assuming these are his first healthcare costs of the calendar year, he does not have any Medicare supplementary insurance, and his monthly Part B and D premiums have already been paid, his out-of-pocket healthcare costs for this episode of care are as follows:

- A 10-day inpatient hospital stay following a partial nephrectomy (Part A)
  – $992 for the hospital stay, which goes towards his annual deductible
  – $0 additional costs since his stay was less than 60 days
- A 14-day SNF stay (Part A)
  – $0 since his SNF stay was less than 20 days and was preceded by his acute inpatient hospital stay
- Twenty-eight days of home health assistance
  – $0 for the home health service (Part A).
  – He pays 20 % of the Medicare-approved amount for home health supplies (Part B).
- Outpatient prescriptions for alpha-blocker therapy and narcotics (Part D)
  – $29 for 100 hydrocodone-acetaminophen (generic) tablets
  – $32 for 50 tamsulosin (generic) tablets
- Outpatient follow-up appointments with his urologist, pulmonologist, and internist (Part B)
  – He pays out-of-pocket for the first $131 of care he receives from these physicians. This is his Part B annual deductible.
  – He pays 20 % of Medicare-approved amounts for each outpatient physician visit after his initial $131 outlay.

In total, his expenses are $1,184 plus 20 % of his outpatient physician visits and home health supplies.

References

1. U.S. Census Bureau. Age and sex composition: 2010. C2010BR-03. May 2011. http://www.census.gov
2. Centers for Medicare and Medicaid Services. National health expenditure projections. 2010–2020. http://www.cms.gov
3. National Center for Health Statistics. Health, United States, 2007. Hyattsville, MD: National Center for Health Statistics; 2008.
4. Table 2.1: Medicare enrollment. http://www.cms.gov/MedicareMedicaidStatSupp/08_2011.asp. Accessed 30 Nov 2011
5. Schoenborn CA, et al. Health characteristics of adults aged 55 years and over: United States, 2004–2007. National Health Statistics Reports. No 16. July 8, 2009

6. Rowland D, et al. Medicare, medicaid, and the elderly poor. Healthcare Financ Rev. 1996;18:61–85.
7. Klees BS., et al. Brief summaries of Medicare and Medicaid. Healthcare Financing Review. 2010. Statistical Supplement, Nov 2009
8. Employee Benefits Research Institute. Health insurance and the elderly. August 2003. http://www.ebri.org
9. U.S. Census Bureau. C27001. Health insurance coverage state by sex and age. From 2009 American Community Survey 1-Year Estimates. http://factfinder.census.gov. Accessed 30 Nov 2011
10. 2008 Medical Expenditure Panel Survey-Insurance Component. Table I.A.2.e. http://meps.ahrq.gov/mepsweb/data_stats/summ_tables/insr/national/series_1/2008/tia2e.pdf Accessed 30 Nov 2011
11. US Department of Veterans Affairs. Federal benefits for veterans, dependents and survivors. 2012 Edition. Available at http://www.va.gov/opa/publications/benefits_book.asp (2012). Accessed 15 Sept 2012
12. Federal Interagency Forum on Aging-Related Statistics. Older Americans 2012: Key Indicators of Well-Being. Federal interagency forum on aging-related statistics. Washington, DC: U.S. Government Printing Office. 2012. Available at http://www.agingstats.gov/Main_Site/Data/2012_Documents/docs/EntireChartbook.pdf. Accessed 15 Sept 2012
13. MedPAC. Report to the Congress: context for Medicare payment policy. March 2007. http://www.medpac.gov
14. Medicare part A (Hospital Insurance). http://www.medicare.gov/navigation/medicare-basics/medicare-benefits/part-a.aspx. Accessed 30 Nov 2011
15. Kaiser Family Foundation. Medicare spending and financing. Publication #7305-06. September 2011. http://www.kff.org
16. Kaiser Family Foundation. Medicare at a glance. Publication #1066-14. November 2011. http://www.kff.org
17. MedPAC. Medicare benefit design. MedPAC Medicare basics. October 2007. http://www.medpac.gov
18. Kaiser Family Foundation. Medicare: a primer. Report #7615-03. April 2010. http://www.kff.org
19. Collins SR, et al. Will you still need me? The health and financial security of older Americans. The Commonwealth Fund. Publication #840. June 2005. http://www.cmwf.org
20. Overview Medicaid. http://www.cms.gov. Accessed 29 Nov 2011
21. Table 13.4: Number of Medicaid persons served (beneficiaries), by eligibility group. https://www.cms.gov/MedicareMedicaidStatSupp/09_2010.asp. Accessed 30 Nov 2011
22. Kaiser Family Foundation. Dual eligibles: Medicaid's role for low-income Medicare beneficiaries. Publication #4091-08. May 2011. http://www.kff.org
23. National Federation of Independent Business, et al v. Sebelius, Secretary of Health and Human Services, et al. 567 U.S. 1 (2012)
24. Fact sheet: what the healthcare law does now for people 65+. http://www.aarp.org. Accessed 26 Nov 2011
25. Fact sheet: what the healthcare law does now for people age 50 to 64. January 2011. http://www.aarp.org. Accessed 26 Nov 2011
26. Geithner TF, et al. Trustees report summary. Social Security Administration. http://www.ssa.gov (2011). Accessed 14 Dec 2011
27. Geithner TF, et al. 2011 annual report of the board of trustees of the federal hospital insurance and federal supplementary medical insurance trust funds. Social Security Administration. http://www.ssa.gov (2011)
28. Ackerman T. Texas doctors leaving Medicare hits record high. Houston Chronicle. March 4, 2011
29. Bishop TF, et al. Declines in physician acceptance of Medicare and private coverage. Arch Intern Med. 2011;171:1117–8.
30. Newhouse JP. Medicare's challenges in paying providers. Healthcare Financ Rev. 2005–2006;27:35–44.
31. MedPAC. Medicare advantage program payment system. MedPAC Payment Basics. October 2011. http://www.medpac.gov
32. DeNavas-Walt C, et al. Income, poverty and health insurance coverage in the United States: 2010. U.S. Census Bureau. Publication #60-239. September 2011
33. Congressional Budget Office. The long-term budget outlook. June 2009. http://www.cbo.gov. Accessed 14 Dec 2011
34. Congressional Budget Office. The long-term outlook for healthcare spending. November 2007. http://www.cbo.gov. Accessed 14 Dec 2011
35. Boccuti C, et al. Moving forward from the sustainable growth rate system. Presentation to MedPAC. http://www.medpac.gov. Sept 15, 2011
36. Hargrave E, et al. Retainer-based physicians: characteristics, impact, and policy considerations. MedPAC. No. 10–9. October 2010. http://www.medpac.gov
37. Fiegl C. OIG to study physicians who leave Medicare. American Medical News. October 13, 2011. http://amednews.com. Accessed 14 Dec 2011

The Future of Geriatric Urology

32

Tomas Lindor Griebling

The first use of the term "geriatrics" in a scientific publication was made by Ignatz Leo Nascher, M.D., in a paper from 1909 [1]. At that time, Dr. Nascher was writing to emphasize a need to consider the diagnosis and treatment of medical conditions seen in older adults as a distinct branch of medicine. Over a century later, it is amazing to consider how medicine and healthcare for older adults has changed. Geriatrics is now a recognized specialty, not only in medicine, but across healthcare disciplines including nursing, pharmacy, dentistry, and the various therapy areas.

Multidisciplinary research and clinical care are now the expectation rather than the exception, particularly in geriatrics. Elderly patients frequently have complex and chronic healthcare needs that are often best addressed simultaneously by subspecialists in different fields. There is a growing interest in intraprofessional education and translational research that address the unique conditions and needs of older adults. Over the past 15 years, there has been tremendous growth in the subspecialty areas of geriatrics including the surgical and related medical specialties, in addition to the more traditional areas of internal medicine, family medicine, and psychiatry. Geriatric urology has been extensively involved in these initiatives with regard to education, research, and clinical care [2].

In the USA, several professional organizations including the American Geriatrics Society (AGS) and the Gerontological Society of America (GSA) have long championed the development and dissemination of knowledge related to aging across healthcare and other disciplines. The American Urological Association (AUA), the Geriatric Urological Society (a subspecialty society of the AUA), and the American College of Surgeons have been among the many surgical organizations that have recognized the importance of geriatrics within the surgical specialties. This has included ongoing educational and other programming designed to foster better understanding of geriatrics issues. Healthcare delivery and funding organizations such as the Centers for Medicare and Medicaid Services (CMS), the Department of Veterans Affairs (VA) Medical Centers, and the various state and county entities also play a critical role in the healthcare of older adults in the USA.

Numerous private foundations have provided generous support for research and education of people and programs in aging. Examples include the John A. Hartford Foundation, the Donald W. Reynolds Foundation, and the Atlantic Philanthropies. At a federal level, the National Institute on Aging (NIA), the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), and other member institutes and centers of the National Institutes of Health (NIH)

T.L. Griebling, M.D., M.P.H., F.A.C.S., F.G.S.A., A.G.S.F. (✉)
Department of Urology and The Landon Center on Aging, University of Kansas School of Medicine, 5021 Sudler, Mailstop 3016, 3901 Rainbow Blvd., Kansas City, KS 66160, USA
e-mail: tgriebling@kumc.edu

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0_32,

Table 32.1 New and ongoing questions in geriatric urology

Education
• How can academic urology and geriatrics training programs expand to increase the number of educators and practitioners within the disciplines?
• Can new funding sources be identified and accessed to help support future medical education?
• In light of population demographics, what can be done to stem the growing workforce demands in both urology and geriatrics?
Research
• Are there subclinical changes in aging patients that could predispose them to subsequent urologic health problems?
• Can alternate models of public health awareness alter the development and treatment of urologic conditions in older adults?
• Are there measureable metabolic changes or biomarkers that can predict development of frailty in older adults?
• How do changes in public policy influence urologic healthcare delivery options for older adults?
Clinical care
• What is the role of comprehensive geriatric assessment (CGA) in preoperative evaluation of older adults who need urologic surgery?
• Can selective "prehabilitation" improve clinical outcomes in geriatric patients undergoing urologic surgery?
• Can improved care and prevention measures in young and middle-aged adults slow or eliminate the subsequent of urologic disease in older age?
• What is the clinical impact of published guidelines regarding geriatric and urologic care?
• Does assessment of quality measures for acute hospitalization influence actual clinical outcomes in older urologic patients?

provide valuable support of research efforts in geriatrics and urology. In addition, a variety of disease and condition specific foundations and organizations target issues relevant to geriatric urology. A few examples include the Simon Foundation for Continence, the National Association for Continence, the Urology Care Foundation, and the AGS Foundation for Health in Aging. The efforts of these and other similar organizations are critical in the ongoing development and implementation of education, research, and clinical care in aging, geriatrics, and urology. Numerous other organizations provide excellent resources and contribute to efforts in both urology and geriatrics.

The information contained in this text reflects the current state of the art in the field of geriatric urology. However, as with most similar projects, development of this book has led to many new or previously unanswered questions that will form part of the basis for future scientific enquiry (Table 32.1). These are just a few examples of potential questions in the field of geriatric urology. Many of the questions are practical while others are more rhetorical. In most cases there are no easy answers.

Future Directions

Population analyses and demographic data clearly outline the rapid growth of the aging population in recent years and continued exponential growth in the foreseeable future. Although the population over 65 currently accounts for about 13 % of the total population in the USA, it is estimated that this number will reach at least 20 % by 2030 [3]. In fact, those over the age of 85 currently represent the fastest growing segment of the American population. This trend is occurring essentially worldwide, with the exception of sub-Saharan Africa where life expectancy in many developing countries remains relatively low. Continued expansion of this "oldest-old" population will likely lead to identification of additional unique conditions and challenges. Yoshikawa has recently used the term "gerogeriatrics" to denote the unique aspects of care and research regarding this extremely elderly population [4]. He notes that this group is perhaps among the most vulnerable and in need of healthcare services. However, due to the nature of their conditions and their advanced age, this population also presents some of the greatest challenges to our current base of knowledge and our ability to provide services.

As outlined in this book, many of the most common genitourinary conditions occur with greatest prevalence in the geriatric population. This includes urinary incontinence and other forms of voiding dysfunction, urinary tract infections, pelvic organ prolapse, and most of the genitourinary malignancies. By definition, this makes general urology a specialty with high volumes of geriatric care [2]. Continued growth in the geriatric population will translate into increasing needs for urologists and other urologic healthcare providers well into the future. Issues for future work will be considered within the domains of education, research, and clinical care.

Education

Focused education in geriatrics principles is critical to the development of expertise among clinicians and researchers who are interested in the care of older adults. Excellent programs have been developed and implemented at many institutions across all levels of medical education including undergraduate, postgraduate, and continuing medical education. The American Urological Association (AUA) has included geriatric urology in its annual educational programming, and among the topics within the AUA Core Curriculum for all resident physicians now training in urology [5].

Competency-Based Education

The focus of medical education in general over the past decade has centered on development and attainment of clinical competencies. These are clearly defined components of care that all providers in a given discipline are expected to achieve in order to provide high quality healthcare. Ongoing efforts have led to publication of essential competencies in geriatrics for residents training in internal medicine and family medicine [6]. Recently, a similar proposed set of competencies regarding geriatric patient care have been published for surgical specialists [7]. These include major topics in preoperative, intraoperative, and postoperative care of older adults. Specific competency domains include such areas as understanding complex medication management and avoidance of polypharmacy, evaluation and optimization of complex comorbid disease before and after surgery, transitions of care between healthcare settings, and incorporation of palliative and end-of-life care. Within these and other global domains, practitioners would be expected to have mastered certain specific skills. An example would be to be able to administer and interpret a basic cognitive assessment to screen for cognitive impairment in older adults prior to surgery. This is important because it can help the practitioner identify changes in mental status and cognitive function that could be indicative of subsequent postoperative delirium. Because these types of skills have not always been part of the traditional urology curriculum, there needs to be an increased emphasis on this in future education models. The goal of all of these initiatives is to improve care for our older adult patients. As residency education and program certification move toward evaluation based on milestones, it is hoped that these geriatrics competencies will be incorporated into the new educational model and core curricula.

Workforce Issues

The tremendous growth of the older adult population has become a focus of workforce studies and associated educational needs in both urology and geriatrics. Several researchers have examined current and future workforce trends in urology and other surgical specialties within the context of the growing older adult population. An analysis of predicted surgical workforce needs revealed that nearly 100,000 additional surgeons would be needed in the USA across seven different surgical specialties, including urology, by 2030 [8]. They identified that there are currently about 10,000 urologists practicing in the USA, with a ratio of 3.49 urologic surgeons per 100,000 population in 2005. The number of urologic surgeons needed by 2030 was estimated at 12,048. Urology actually had the second highest calculated percentage shortage at 32.0 % behind only thoracic surgery at 39.0 %. This model assumed that current surgeon to population ratios would remain constant, but total numbers would need to increase in order to meet demand due to population growth. And of course the majority of this population growth is among the geriatric age groups. They also estimated that the total cost to train these additional surgeons would be in the range of $10 billion. Given the continued population growth among older adults, and the current economic crises facing this country, it will be extremely difficult to achieve these goals.

A survey of academic urologic surgeons who are members of the Society of University Urologists revealed that a lack of institutional funding was the main barrier to expanding residency programs or adding additional faculty at their training programs [9]. The use of simulation education was identified as an important component of graduate medical education in urology, and 84 % of respondents indicated that they would expand their simulation facilities if adequate funding was available. Another survey of academic urology department chairs and division heads revealed that there was an extensive need to recruit and retain talented faculty and that the vast majority (71 %) were actively planning to expand their faculties in next 5 years [10]. Identified areas of subspecialty expertise needed among programs included female urology and neurourology (51.7 %), oncology (44.8 %), and pediatrics and general urology (36.8 %). However, the problem remains that the demand for new academic faculty will outstrip supply given the relatively stable number of available residency training positions. Growth in programs will require not only increased patient volumes, which are likely to occur given the population demographics, but also faculty, facilities, and funding. These present real challenges which can limit significant expansion of educational training programs in the future.

There are similar workforce issues facing both primary care and specialty geriatrics. Expansion of academic geriatric medicine training programs has been cited as a critical goal for education of the geriatrics workforce [11]. These authors noted that innovative educational methods will be needed to reach across the healthcare continuum. Lack of adequate reimbursement for clinical care and difficulty recruiting research faculty in geriatrics were cited as barriers to program expansion.

In 2011, the American Geriatrics Society issued a white paper highlighting the need to expand the number of practitioners specializing in geriatrics [12]. Their suggestion was not limited to the traditional areas of internal medicine and family medicine. Rather, they recommended that all member organizations under the aegis of the American Board of Medical Specialties (ABMS) whose members provide care for older adults select and adopt the core competencies appropriate to their specialty. This type of approach could help foster improved understanding and appreciation of geriatrics issues across disciplines and in turn lead to improvements in delivery of quality care for geriatric patients.

A number of unique methods have been identified that can help to address some of the issues associated with the already limited urology and geriatrics workforce. The use of health information technology and electronic medical records has been identified as a particularly valuable tool in care of older adults [13]. Many of the screening instruments used to identify underlying comorbidity and other clinical conditions frequently seen in older adults can be easily incorporated into this type of system. This could potentially improve the rate of administration of these types of instruments by prompting healthcare providers to include these items in their routine examination and work with patients. Clinical guideline information and other best practice recommendations could also be incorporated into these systems to provide easy access to this constantly evolving information for healthcare providers.

Other methods to improve access to care include the use of telemedicine, satellite outreach clinics, and regional centers of excellence. Access to geriatrics expertise in rural settings has been identified as a specific priority [14]. The Veterans Health Administration (VHA) has recently published its strategic plan regarding Geriatrics and Extended Care (GEC) [15]. The goals are to make the system more veteran centric, to provide universal access to care for a panel of essential services among the elderly veteran population, to integrate continuous improvement processes into all aspects of care, and to ensure the VA system was equipped to meet the needs of the growing geriatric patient population.

Nurse practitioners and physician assistants play an important role in the delivery of healthcare across multiple disciplines including urology. Collaboration with these providers will likely expand in the future in order to meet the growing clinical demands. An analysis of the workforce needs specific to pediatric urology has indicated that expanded use of these types of providers could help to substantially enhance the provision of pediatric urology services without requiring a concomitant increase in the number of pediatric urologic surgeons [16]. A recent clinical trial demonstrated that comanagement of common geriatric conditions by nurse practitioners and primary care physicians resulted in improved quality of care using validated endpoint measures [17]. Geriatric urology could likely benefit from similar models of practice delivery and administration.

Research

A full spectrum of research is ongoing in the field of geriatric urology. This includes basic science enquiry, clinical trials and studies of healthcare delivery, outcomes research, economic analyses, studies on public health and social policy, and translational research.

In 2004, the American Geriatrics Society published a treatise outlining a proposed research agenda in the area of geriatrics as it relates to multiple surgical and related medical specialties including urology [18]. A structured review of the published English language literature was used to generate research questions specific to the discipline of geriatric urology. This generated 26 topic specific research questions in the areas of urinary incontinence, urinary tract infections, prostate diseases, genitourinary malignancies, sexual health, stone disease, and renal transplantation. Three key areas for recommended research were also generated. These included a recognized need to better define pathophysiology and natural history of the major urologic conditions that affect older adults, a need to develop and validate predictive models to identify older adults who may be candidates for surgical intervention and optimize their care, and a need to analyze the longitudinal outcomes of various forms of urologic therapy. In 2007, a supplementary volume was published which examined the progress made across these disciplines including geriatric urology in the interim [19]. This analysis identified both progress and continued research needs within the field. Additional research focus questions were added in the areas of male hypogonadism and the assessment of remaining life expectancy. Although great progress has been made in research related to geriatric urology, many of the original questions from both volumes remain valid today.

Several innovative research methods have been developed that may have important implications for urologic healthcare. Although mobility has been measured in a variety of ways, the concept of "life-space" attempts to analyze an older adult's ability to maneuver within the world around them [20, 21]. Life-space measures various spheres of activity ranging from one's bedroom, to multiple rooms in the home, to outdoors in the home area, to the larger community. By identifying the maximum area where a person is able to participate independently, functional status and mobility can be more comprehensively assessed. One study examined life-space in older women undergoing urogynecological and gynecological oncology surgery [22]. Among previously independent community-dwelling older women, life-space was initially reduced in the immediate postoperative period but generally returned to baseline by 6 months. This type of analysis could be used to measure mobility and functional outcomes for older adults in a variety of clinical scenarios.

The National Institute on Aging identified models of healthcare delivery for older adults as an important focus of current and future research [23]. This includes issues related to public health, social services, management of chronic conditions, and intraprofessional healthcare delivery models. Other critical aspects identified in this analysis included models of care management, preventive home visits, proactive rehabilitation, and transitions of care between various care settings. Integration of these types of research will become ever more important in the future. All of these issues are applicable to the field of geriatric urology.

Other researchers have looked at subclinical changes in functional status that may ultimately predispose older adults to healthcare problems and eventual disability [24]. Subclinical functional changes were predictive of difficulties with mobility and other task performance 2 years later. This indicates that efforts to identify and control factors associated with frailty might have important clinical implications. These issues have not been specifically studied in the context of urologic healthcare, but future longitudinal research on this topic may yield interesting findings.

The role of metabolic changes and identification of biomarkers are also popular areas for current translational research. A variety of theories have been proposed to explain both normal aging and development of diseases and pathology associated with the aging process. Dysregulation of normal biochemical and metabolic pathways may be part of the issue. A wide variety of biomarkers are potential predictors of changes associated with aging. In particular, inflammatory biomarkers may be linked to the multidimensional changes seen in older adults [25]. This type of research in urology has been relatively limited with regard to aging, although there is certainly increasing interest on this topic. It is possible that research will demonstrate associations between inflammatory changes due to aging and subsequent development of urologic pathology. This could eventually lead to targeted therapies that could help to slow disease development and progression.

The future for research in geriatric urology is indeed limitless. Numerous questions remain to be addressed in basic science, clinical, outcomes, and policy research.

Clinical Care

In many respects, the ultimate goal of both education and research in medicine is to enhance options for care and improve clinical outcomes. As outlined throughout this textbook, there have been great strides made with regard to clinical care in geriatric urology. This has led to new methods of diagnosis and treatment for many of the conditions treated in older urologic patients. However, several areas of new and future research deserve additional mention.

Postoperative Outcomes

Older adults are at risk for developing a wide variety of postoperative complications. These have been extensively outlined in a number of chapters throughout the book. One recent study examined postoperative delirium in geriatric patients undergoing radical cystectomy for the treatment of muscle invasive bladder cancer [26]. This surgical procedure is unique in urology for several reasons. The underlying disease is often aggressive, and definitive therapy requires a relatively morbid surgical intervention. The incidence and prevalence of muscle invasive bladder cancer is highest in the geriatric population compared to other age groups. These patients frequently have substantial comorbidity that places them at increased risk for complications. Finally, the surgery itself is among the most invasive and challenging procedures done in our specialty. This requires not only removal of the bladder and associated cancer but complex reconstruction of the urinary diversion using a segment of the bowel. Patients are often hospitalized for an extensive time after surgery which in turn predisposes them to complications. This prospective study enrolled 59 patients who were 65 years of age or older and underwent radical cystectomy at a single academic institution. Overall, 49 subjects were evaluable in the analysis. Older age and baseline cognitive impairment were both associated with significantly higher rates of delirium on univariate analysis. However, only older age was found to be predictive of postoperative delirium in the multivariate models. The median age of subjects who experienced delirium was 77.8 years compared to 73.1 years for those who did not develop delirium (OR 1.52; 95 % CI = 1.04–2.22; $p = 0.03$). Those who developed delirium were also more likely to require hospital readmission after initial discharge and to require reoperation for other complications.

Similar future research on issues specific to geriatric urology will be important to help reduce complications and improve clinical outcomes. This includes such topics as perioperative nutritional support, antibiotic administration, surgical approach, and patient selection.

Transitions and Environments of Care

Older patients with urologic problems receive care in a wide variety of settings. Recently, there has been an increased emphasis on improving transitions of care between these different venues in an attempt to reduce hospital readmissions and enhance patient care experiences. This has also become a focus of interest for insurance carriers and public policy makers who are trying to both improve care and reduce costs.

Patterson and colleagues have argued that there needs to be an increased presence of specialists with geriatrics focus and expertise across disciplines and settings including institutional medical directors and others in leadership positions [27]. They identified several target areas that will help in this regard including maintaining a presence in both acute and long-term care settings, expanding the presence of geriatrics in primary care, and moving forward with education, research, and advocacy initiatives. I would argue that these efforts must include urologists, who can advocate on behalf of our older adults patients. Urologic care is provided in a spectrum of settings including ambulatory outpatient clinics, acute care hospitals, and surgery centers. Some urologists provide clinical services in long-term care facilities, skilled care and rehabilitation facilities, and other environments that may have a large presence of older adults.

Interventions to reduce deconditioning and improve functional status and mobility after surgery in older adults have been an important focus for clinical research. Gone are the days of imposed bed rest for most surgical patients. This has led to dramatic reductions in perioperative morbidity including venous thromboembolism, pressure ulcers, falls, and wound complications. Studies have shown that early mobilization and rehabilitation efforts can reduce deconditioning and associated complications [28]. This includes selective use of what has been termed “prehabilitation,” where these types of treatment modalities are implemented prior to surgery in an effort to maximize subsequent outcomes [29]. One of the endpoints frequently assessed in these types of studies is whether patients can be discharged postoperatively from acute care hospitals to home rather than to skilled care nursing facilities. Examination of models of care delivery including both inpatient and outpatient rehabilitation will be important in this regard.

Evidence-Based Medicine, Guidelines and Clinical Recommendations

There has been an encouraging trend toward the popularization of evidence-based medicine across disciplines including both urology and geriatrics. This has helped to improve the quality of knowledge and care delivered by focusing on important clinical questions and outcomes. The use of evidence-based algorithms can help to guide care and improve safety for all patients. This is particularly important for geriatric patients who frequently have multiple and complex comorbidities.

Analysis and understanding of preoperative assessment methods, particularly in relation to surgery in older adults, is extremely important. These factors often play a critical role in helping a surgeon to decide if an older adult patient is a candidate for surgical intervention. The American College of Surgeons and the American Geriatrics Society recently partnered to produce a document regarding best practice guidelines for preoperative clinical assessment in geriatric patients undergoing surgical interventions [30]. This includes consensus statements and evidence-based recommendations in a variety of domains relevant to care of older surgical patients. Specific topics include assessment of cognitive impairment and dementia, decision-making capacity for care, depression, postoperative delirium, alcohol and substance abuse, cardiac and pulmonary evaluations, functional status, mobility and fall risk, frailty, nutritional status, medication management, patient counseling, and preoperative testing. In addition to the evidence used to create these recommendations, practical and validated methods of assessment are outlined in detail. This is particularly valuable for busy clinicians who are working to incorporate these types of evaluations into their daily practices.

A number of studies have examined the role of the comprehensive geriatric assessment (CGA) in older patients undergoing surgery. The CGA includes detailed assessment of function and status across multiple organ systems and clinical domains [31]. Data from this analysis confirmed chronological age is not usually a contraindication to surgery in older adults and that severity of comorbidity is a more valuable predictor of outcomes. It also demonstrated that multidisciplinary perioperative care can improve outcomes in this potentially vulnerable population. Disease-specific analyses of CGA have shown it to be useful for improving clinical outcomes for geriatric patients undergoing surgery for a variety of conditions including colorectal cancer and hip fracture [32, 33]. Future studies will help to better define the role of CGA in urologic surgery cases in older adults.

Adverse events related to medications are common in older adults. This can be due to a variety of factors including drug–drug interactions, drug and disease interactions, polypharmacy, and proper medication selection. The late Dr. Mark Beers was a geriatrician who had a particular interest in this topic, and it was the focus of much of his academic work. The Beers Criteria is a listing of potentially inappropriate medications for use in geriatric patients. The most recent update was published in 2012 and provides an evidence-based examination of the topic [34]. A number of medications used in urologic care are included in the listed recommendations, and readers are encouraged to review and understand these in detail. The ultimate goal of this document is to improve medication selection and treatment for older adults. It is likely that additional guidelines may be developed by various professional organizations regarding numerous aspects of clinical care in older adults. It is crucial that these be evidence based and subject to rigorous standards of development and analysis. If so, they have great potential to improve the quality of care for geriatric patients.

Quality Indicators

A number of variables have been used to assess the concept of quality of care related to surgery. These include length of hospital stay, rates of hospital readmission, reoperation, and discharge location to home versus skilled nursing or long-term care facilities. Other measures also have value in the geriatric population and can be important endpoints for analysis. McGory and colleagues reported on development and validation of quality indicators for older adults undergoing abdominal surgery [35]. Using systematic literature reviews and structured interviews with clinical experts, the panel developed 89 candidate measures, of which 76 were subsequently rated as valid. These included items in seven domains including comorbidity assessment, elderly issues such as cognition, medication use and polypharmacy, patient-to-provider discussions such as preferences about life-sustaining treatments, intraoperative care, postoperative management, and discharge planning regarding transitions of care. Many of these indicators are applicable for older adults undergoing urologic surgery.

Another set of quality indicators that have been developed and validated for use in geriatrics include the Assessing Care of Vulnerable Elders (ACOVE) measures [36]. This includes a number of hospital care measures across a spectrum of clinical and organ-specific systems. According to the quality measures, geriatric patients admitted to acute care hospitals should be assessed for these factors depending on their specific conditions. Examples of topics that are part of the ACOVE set include assessment of nutritional status, pain management, screening for depression, and avoidance of the use of restraints. Other measures assess for the evaluation and treatment of delirium, dementia, pressure ulcers, and urinary incontinence. These measures were developed using published literature for the evidence base and are designed to optimize care and minimize complications. A recent study examined the actual use of these measures in an acute care hospital setting [37]. These researchers found that adherence to these geriatric specific quality measures was lower compared to more general hospital quality indicators. This suggests there may be room for improvement in the utilization of such measures in actual practice. Continued analysis of quality measures and outcomes research will enhance future clinical care for older adults.

Conclusions

This is indeed an exciting time in the realm of geriatric urology. As educational, clinical, and research-based disciplines, both urology and geriatrics have traditionally been leaders in the development and adoption of new methods. This includes use of innovative technology, unique educational models and pedagogy, and new therapeutic options. The growing geriatric population will ensure that our field remains at the forefront of healthcare delivery, public health initiatives, patient advocacy, and public policy. It is my sincere hope that educators, clinicians, and researchers will continue to be attracted to geriatric urology. Future work will enhance our knowledge, expand our treatment armamentarium, and improve the quality of care for the older adult patients that we serve.

References

1. Nascher IL. Geriatrics. NY Med J. 1909;90:358–9.
2. Drach GW, Griebling TL. Geriatric urology. J Am Geriatr Soc. 2003;51:S355–8.
3. U.S. Census Bureau: population projections. Washington, DC: U.S. Department of Commerce. 2013. Available at: http://www.census.gov/population/projections/data
4. Yoshikawa TT. Future direction of geriatrics: 'gerogeriatrics'. J Am Geriatr Soc. 2012;60:632–4.
5. Griebling TL, Drach GW, Pranikoff K, DuBeau CE, Katz P. Geriatric Urology – AUA Core Curriculum. Linthicum, MD: American Urological Association. 2010. Available online at: http://www.auanet.org/eforms/elearning/core/?topic=37. 30 May 2010.
6. Williams BC, Warshaw G, Fabiny AR, et al. Medicine in the 21st century: recommended essential geriatrics competencies for internal medicine and family medicine residents. J Grad Med Educ. 2010;2:373–83.
7. Bell Jr RH, Drach GW, Rosenthal RA. Proposed competencies in geriatric patient care for use in assessment for initial and continued board certification of surgical specialists. J Am Coll Surg. 2011;213:683–90.
8. Williams TE, Satiani B, Thomas A, Ellison EC. The impending shortage and the estimated cost of training the future surgical workforce. Ann Surg. 2009;250:590–7.
9. Gonzalez CM, McKenna P. Challenges facing academic urology training programs: an impending crisis. Urology. 2013;81:475–9.
10. Lightfoot AJ, Rosevear HM, Steers WD, Tracy CR. Current and future need for academic urologists in the United States. J Urol. 2011;185:2283–7.
11. Bragg EJ, Warshaw GA, Meganathan K, Brewer DE. The development of academic geriatric medicine in the United States 2005 to 2010: an essential resource for improving the medical care for older adults. J Am Geriatr Soc. 2012;60:1540–5.
12. Section for Enhancing Geriatric Understanding and Expertise Among Surgical and Medical Specialists (SEGUE), American Geriatrics Society. Retooling for an aging America: building the healthcare workforce. J Am Geriatr Soc. 2011;59:1537–9.
13. Capezuti E. An electronic geriatric specialist workforce: is it a viable option? Geriatr Nurs. 2010;31:220–2.
14. Tumosa N, Horvath KJ, Huh T, et al. Health care workforce development in rural America: when geriatrics expertise is 100 miles away. Gerontol Geriatr Educ. 2012;33:133–51.
15. Shay K, Hyduke B, Burris JF. Strategic plan for geriatrics and extended care in the Veterans Health Administration: background, plan, and progress to date. J Am Geriatr Soc. 2013;61:632–8.
16. Canon S, Basham K, Canon HL, et al. Alternative approaches to expanding pediatric urology services and productivity. J Urol. 2012;188:1639–42.
17. Rueben DB, Ganz DA, Roth CP, et al. Effect of nurse practitioner comanagement on the care of geriatric conditions. J Am Geriatr Soc. 2013;61:857–67.
18. Griebling TL. Geriatric urology. In: Solomon DH, LoCicero J, Rosenthal RA, editors. New Frontiers in Geriatrics Research: An Agenda for Surgical and Related Medical Specialties. New York, NY: American Geriatrics Society; 2004. pp. 269–302. Available online at: http://www.newfrontiers.americangeriatrics.org/
19. Konety B, Drach GW. Geriatric urology. In: LoCicero J, Rosenthal RA, Katlic MR, Pompei P, editors. A Supplement to New Frontiers in Geriatrics Research: An Agenda For Surgical and Related Medical Specialties. New York, NY: American Geriatrics Society; 2007. pp. 259–87. Available online at: http://www.newfrontiers.americangeriatrics.org/

20. Baker P, Bodner E, Allman R. Measuring mobility in community-dwelling older adults. J Am Geriatr Soc. 2003;51:1610–4.
21. Peel C, Baker P, Roth D, et al. Assessing mobility in older adults: the UAB study of aging life-space assessment. Phys Ther. 2005;85:1008–19.
22. Stewart CML, Wheeler II TL, Markland AD, et al. Life-space assessment in urogynecology and gynecological oncology surgery patients: a measure of perioperative mobility and function. J Am Geriatr Soc. 2009;57:2263–8.
23. Liggins C, Pryor L, Bernard MA. Challenges and opportunities in advancing models of care for older adults: an assessment of the National Institute on Aging Research Portfolio. J Am Geriatr Soc. 2010;58:2345–9.
24. Wolinsky FD, Miller DK, Andresen EM, et al. Further evidence for the importance of subclinical functional limitation and subclinical disability assessment in gerontology and geriatrics. J Gerontol B Psychol Sci Soc Sci. 2005;60B:S146–51.
25. Fontana L, Addante F, Copetti M, et al. Identification of a metabolic signature for multidimensional impairment and mortality risk in hospitalized older patients. Aging Cell. 2013;12:459–66.
26. Large MC, Reichard C, Williams JTB, et al. Incidence, risk factors, and complications of postoperative delirium in elderly patients undergoing radical cystectomy. Urology. 2013;81:123–9.
27. Patterson C, Hogan DB, Bergman H. The choices facing geriatrics. Can Geriatr J. 2012;15:24–7.
28. Killewich LA. Strategies to minimize postoperative deconditioning in elderly surgical patients. J Am Coll Surg. 2006;203:735–45.
29. Carli F, Zavorsky GS. Optimizing functional exercise capacity in the elderly surgical population. Curr Opin Clin Nutr Metab Care. 2005;8:23–32.
30. Chow WB, Rosenthal RA, Merkow RP, et al. Optimal preoperative assessment of the geriatric surgical patient: a best practices guideline from the American College of Surgeons National Surgical Quality Improvement Program and the American Geriatrics Society. J Am Coll Surg. 2012;215:453–66.
31. Dewan SK, Zheng SB, Xia SJ. Preoperative geriatric assessment: comprehensive, multidisciplinary and proactive. Eur J Intern Med. 2012;23:487–94.
32. Kristjansson SR, Nesbakken A, Jordhøy MS, et al. Comprehensive geriatric assessment can predict complications in elderly patients after elective surgery for colorectal cancer: a prospective observational cohort study. Crit Rev Oncol Hematol. 2010;76:208–17.
33. Sletvold O, Helbostad JL, Thingstad P, et al. Effect of in-hospital comprehensive geriatric assessment (CGA) in older people with hip fracture. The protocol of the Trondheim Hip Fracture Trial. BMC Geriatr. 2011;11:8.
34. American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2012;2012(60):616–31.
35. McGory ML, Shekelle PG, Rubenstein LZ, et al. Developing quality indicators for elderly patients undergoing abdominal operations. J Am Coll Surg. 2005;201:870–83.
36. Wenger NS, Shekelle PG. Assessing Care of Vulnerable Elders: ACOVE project overview. Ann Intern Med. 2001;135:642–6.
37. Arora VM, Johnson M, Olson J, et al. Using Assessing Care of Vulnerable Elders Quality indicators to measure quality of hospital care for vulnerable elders. J Am Geriatr Soc. 2007;55:1705–11.

Index

T.L. Griebling (ed.), *Geriatric Urology*, DOI 10.1007/978-1-4614-9047-0,