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Editors

Perioperative Care of the Orthopedic Patient

Second Edition

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This book is dedicated to:

Stephen A. Paget, MD (C. Ronald MacKenzie)

David H. Baker, MD, Emeritus Professor of Radiology at Columbia College of Physicians and Surgeons, lifelong mentor, and friend (Charles N. Cornell)

Madhu Mazumdar, PhD, my mentor (Stavros G. Memtsoudis)

Foreword to the Second Edition

Millions of patients worldwide benefit from the significant advances made in orthopedic care over the last half-century. Patients live longer lives, with less pain and greater mobility. Innovations in surgical techniques, perioperative medicine, and anesthesia practice over this time period have helped facilitate this progress. As a consequence of these advances, orthopedic surgical procedures are increasingly extended to a wider range of patients, including the elderly and those with significant medical comorbidities. The opportunities provided by these life-changing procedures, together with the growing need for a multidisciplinary approach to assure optimal outcomes, stimulated the development of the clinical and academic discipline that is perioperative care. At Hospital for Special Surgery, we have been at the forefront of this field. As this second edition demonstrates, we continue to evolve and improve our approach in order to assure optimal outcomes.

The perioperative care of patients presenting for orthopedic surgery requires a team approach, a model of the delivery of care that is coordinated and optimized by a physician-directed, multidisciplinary group working together throughout the perioperative continuum. The process begins with the decision to perform surgery and requires preparation of the patient and an optimization of their general medical condition. Intraoperatively, the most current anesthetic and surgical techniques are utilized to minimize complications and to support the patient's ability to recover from the trauma of surgery. Postoperatively, a seamless transition of care from the recovery room, occasionally the intensive care unit, and then to the hospital floors is achieved by minimizing pain, maximizing the patient's ability to rehabilitate, and ensuring that postoperative medical care mitigates the impact of preexisting comorbidities. This entire continuum is carried out in a safe, cost-efficient, and patient-centered manner. Perioperative care at Hospital for Special Surgery remains premised on these principles.

Our model of care, presented comprehensively in the second edition of this book, is responsible for an unparalleled surgical, medical, and anesthesiologic record of success. As advances in orthopedics continue to challenge those engaged in perioperative care, we will continue to evaluate and adapt our processes. The updates in this edition are illustrative of our effort to address new challenges and persistently refine our system of collaborative care to achieve the highest level of quality and outcomes for all patients. Drs. MacKenzie, Cornell, and Memtsoudis have expertly amended and enhanced their original roadmap and provided an invaluable guide for the perioperative community.

Hospital for Special Surgery
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Preface to the Second Edition

Six years have passed since the publication of our textbook examining the challenges of caring for the orthopedic patient in the surgical setting. The response to this work, the first devoted exclusively to perioperative orthopedic care, has been highly favorable, seemingly striking a cord in the orthopedic, rheumatologic, and perioperative community. Having kept in close contact with contributors, readers, and publishers over the years, we the editors began to feel it is time for a reconsideration of the work, reevaluating its content, addressing perceived weaknesses and omissions, and enhancing its presentation. This second edition is now the product of the efforts of over 70 experts, 19 of whom are new contributors. Each chapter has been reconsidered, updated, and, in a few instances, replaced. Seven new chapters expand the content of the book, filling important gaps of the first edition. One major modification is the new placement of the case studies: formerly presented in an Appendix, they are now at the end of the chapters pertaining to the clinical vignette presented. We remain grateful to the Springer staff, in particular Liz Corra, who has shepherded us through both editions of the book.

In closing, we, as before, take full responsibility for the content of this book and hope it will continue to provide value in the care of the patient undergoing orthopedic surgery.

New York, NY, USA — C. Ronald MacKenzie, MD
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New York, NY, USA — Stavros G. Memtsoudis, MD, PhD, MBA

Preface to the First Edition

Arthritis is the leading cause of disability in the adult US population. Twenty-one percent of adults report physician-diagnosed arthritis, a prevalence projected to increase markedly for the foreseeable future. As conditions for which surgery is often required, the arthritides, in their various presentations, will continue to fuel the need for surgical intervention for years to come. Furthermore, societal demographics underscore the importance of these projections, especially for elderly patient populations, since the elderly are not only the fastest growing segment of Western society, but arthritis as a disease category reaches its peak in older populations. Even today, this is the demographic group that already accounts for the majority of such procedures, particularly total joint arthroplasty.

Medical management in the setting of surgery is a relatively new consultative arena, one spurred on in contemporary times by the aging patient population, a rising prevalence of complex chronic disease, and an ever-expanding surgical armamentarium. Nowhere has the confluence of these forces been more evident than in orthopedic surgery, a highly innovative field, the advances in which continue to enhance the functional capacity and quality of life of patients across the entire span of life.

Although a number of comprehensive textbooks pertaining to perioperative medicine are currently available, none focuses exclusively and comprehensively on the patient undergoing orthopedic surgery. The format of this book was developed with several purposes in mind. A primary goal was the development of the first published comprehensive overview of the challenges presented by the orthopedic surgical environment; as such, the book covers most of the relevant domains of orthopedic surgery. A second ambition was to provide an overview of the innovative and sometimes unique approaches to anesthesia in this patient population. A third objective was a presentation of a general approach to the preoperative evaluation of patients, while the fourth and final aim was to offer an up-to-date review of the disease-specific challenges to the care of patients undergoing surgery, maintaining a particular focus on orthopedic procedures whenever possible. In order to achieve these goals, the book is divided into five primary sections: (1) Preoperative Considerations; (2) Anesthesiologic Management; (3) Medical Management in Specific Clinical Settings; (4) Specific Perioperative Problems in Orthopedic Surgery; (5) Role of Allied Services. The book closes with a chapter providing a number of cases and clinical vignettes illustrating the challenges of caring for patients in the orthopedic surgical setting.

A word about us and our institution also seems appropriate. Hospital for Special Surgery is one of the world's premier hospitals devoted to orthopedic and rheumatologic care. Its functions are supported by 140 inpatient beds, over 60 recovery room/acute carebeds, and 35 in- and outpatient operating rooms. A full complement of orthopedic subspecialties is backed by the Departments of Medicine, Rheumatology, and Perioperative Medicine as well as a 57 member Department of Anesthesiology. Fourteen thousand inpatient and a comparable number of outpatient orthopedic procedures generate over 13,000 preoperative consultations annually. Given this extensive experience, we felt the time was right to contribute in a comprehensive and multidisciplinary way our collective approach to perioperative orthopedic care. The editors, whose tenures at HSS date back 30 years, feel well positioned to lead this effort.

Much has changed since the days during which most of our surgery was conducted on an inpatient basis, all patients admitted (and usually evaluated medically for the first time) the day before their procedure; 5–7 days of postoperative care and rehabilitation generally followed, even after routine total joint arthroplasty. Indeed, the modernization of care, driven though it was by outside forces and unwelcome in its time, has forced greater efficiencies in care, promoted (not stifled) innovation, and lowered cost, while minimizing patient exposure to the hospital environment—all outcomes for the better.

In closing, the editors want to express their gratitude first to the contributors to this book. As a "ground-up" endeavor, we appreciate your efforts, diligence, and particularly your patience. Thanks are also extended to Liz Corra, our development editor at Springer, for her encouragement and endurance. Finally, a word to our readers, ultimately the judges of this effort: we hope you find this reference useful in your daily striving to provide the best possible care for patients. While we take full responsibility for its content, we recognize there may be shortcomings and even important omissions in this first edition. Thus, at a time when knowledge and innovation are advancing medical care on a daily basis, we invite commentary and constructive criticism from the broader perioperative and surgical community. Future editions can only benefit from such collective wisdom.

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Part I

Preoperative Considerations

General Principles and Practices of Perioperative Medicine

1

C. Ronald MacKenzie

Objectives

- To review the rationale for the preoperative medical evaluation
- To review the goals of the preoperative medical evaluation
- To review the literature pertaining to the efficacy of preoperative medical evaluation

Key Points

- Medical evaluation of a patient prior to surgery remains a widespread clinical practice.
- Such consultation is supported by clinical investigation, growing literature, and national conferences.
- The principles and practices of perioperative medicine have been evolving, influenced by the quality movement of the last 15 years.
- An orderly structure for the preoperative evaluation includes: the identification of the nature, severity, and degree of control of all comorbid conditions that may impact perioperative decision-making; the optimization of treatment of all active medical problems; the assessment of anesthesia- and surgery-associated risk; education of patients and families concerning the perioperative experience; and motivation of the patient to commit to preoperative preventive practices.

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Introduction

Growing numbers of patients of ever-increasing age and often advanced medical conditions undergo surgery annually. Owing to developments in surgical technique and advances in the understanding of perioperative medical care, patients of much greater complexity are being considered suitable surgical candidates. Nowhere is this confluence of developments greater than in the field of orthopedics where advances in total joint arthroplasty, spine procedures, and trauma-related surgery have expanded the indications for surgery and pushed the boundaries of perioperative care. As such a familiarity with the literature pertaining to medical care in the perioperative setting is required for those who provide care to the patient undergoing surgery [1–5].

This chapter reviews the clinical domain and literature pertaining to the perioperative medical evaluation emphasizing the patient undergoing orthopedic procedures. Supported by a now extensive literature, a stepwise approach to the preoperative consultation and the assessment of perioperative risk is herein presented.

Preoperative Consultation

As a consequence of medical advances as well as the impact of financial and resource constraints on the medical system at large, the percentage of all surgical procedures performed on an outpatient basis in the USA rose from 20% in 1982 to 60% in 1995, a trend particularly relevant to the arthroscopic techniques of orthopedic surgery [6, 7]. Among the benefits of these developments has been the opportunity to move the preoperative medical evaluation to the outpatient arena as well, often weeks prior to the surgical date. This change in practice has important consequences, enhancing the opportunity for discourse among the physicians, for supplementary consultation and investigation, and for the institution of therapy directed at optimizing the patient's medical status

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prior to surgery. Practiced in this anticipatory manner, the preoperative evaluation becomes a focal point of communication between all professionals involved in caring for the patient, enhancing the deliberative and collaborative nature of the consultative process and ultimately the patient's care.

Depending on the setting and institutional approach to perioperative care, the preoperative consultation may be conducted by an MD (internist, medical subspecialist, hospitalist, or anesthesiologist) or by physician extenders (nurse practitioners, physician assistants) under MD supervision. Owing to the complexity of medicine, especially the growth in pharmacology, challenges of the elderly with their comorbidities and restricted physiologic reserve, and productivity and reimbursement pressures that keep surgeons in the operating room (as opposed to rounding on the floors), surgeons are desirous of a more involved consultant [8]. This may take the form of a more active participation in the patient's care (ordering rather than recommending medications), adopting a comanagement strategy for postoperative care or in some instances assuming full responsibility for the patient after completion of the surgery. Regardless of the institutional model, communication between the referring and consulting physicians remains essential to the provision of optimal perioperative care. Evolving from earlier guidelines regarding effective consultation [9], a conceptual revision stressed such considerations as determining the customer, establishing the urgency, gathering your own information, being brief, being specific and talking to the referring physician, establishing contingency plans, establishing one's turf, teaching with tact, talking with the primary physicians, and providing follow-up [8]. While each of these tenants is central to the whole, the first priority is to insure clarity regarding the question asked, as a lack of transparency about the stimulus for the consultation is sure to get the process off on the wrong foot.

Given its elemental purpose, consultation as a practice is essentially the provision of advice regarding diagnosis and management. In the context of general medical care, it affords an opportunity to initiate or modify treatment whether primary or secondary (preventive). Although the goals may be of shorter term in the preoperative setting, such consultations can still be most complex, taxing the knowledge and skill of the medical consultant and anesthesiologist alike. Further, the role of the preoperative medical consultant may subsume even broader responsibilities, going beyond the evaluation of the patient's current medical status. Additional responsibilities, germane to the preoperative setting, include the estimation of the patient's risk for surgery, decisions regarding the need for additional testing prior to surgery, and the preoperative optimization of the patient's medical condition, the purpose of which is to reduce the risk of postoperative complications [10]. Further, in the domain of orthopedics, the assessment of bone quality is a new and increasingly appreciated preoperative consideration, highly relevant in the setting of spine and hip surgery. This emerging topic is extensively reviewed in Chap. 30.

The success of this process therefore depends on a number of elements including a thorough knowledge of those illnesses which impact upon surgical outcome, an understanding of the surgical procedure and anesthetic strategies that might be employed, and an integration of a management plan across the range of physicians and other professional staff who will be caring for the patient [10]. Implicit is the need for effective communication, as the consultant's clinical judgment will impact outcome only if the recommendations are conveyed and then implemented effectively.

Finally a word about the concept of surgical "clearance" is in order. Though widely ensconced in the clinical vernacular, this notion has been decried by the perioperative medical community citing its lack of specification and that the term "cleared" implies that patients will not experience postoperative complications, a sequel that can never be guaranteed [10]. As you will see shortly, the term "optimized for surgery" is more appropriate and better aligned with the goals of preoperative consultation. What are these goals and how do we approach them?

Goals of the Preoperative Medical Consultation

The goals of the preoperative medical evaluation are as follows:

- Identification of the nature, severity, and degree of control of all *comorbid conditions* that may affect perioperative clinical decision-making and medical care
- *Optimization* of the treatment of all active medical problems
- Assessment of anesthesia- and surgery-associated *risk* (magnitude and type)
- *Education* of patients and families concerning the perioperative experience
- Motivation of the patient to commit to preoperative *preventive* practices

Identification of Conditions that Affect Postoperative Outcome

The needs of the patient in the perioperative context depend on a number of considerations notably age, comorbidity, functional capacity, and the type of anesthesia and surgery to be performed. A complete medical history and physical examination constitute the bedrock preoperative evaluation providing a clinically relevant framework upon which informed decisions concerning the value of additional ancil-

lary testing can be premised. The focus and content of the preoperative history does differ from general medical practice, however. For instance, the indication for any type of surgery is an essential component, as the perioperative risk will vary with the magnitude and urgency of the procedure. Patients should also be asked about their prior experience with surgery and anesthesia. Further, the presence, severity, and stability of all comorbid conditions should be established. In the setting of orthopedic procedures, particularly lower extremity arthroplasty, a patient (or family history) of thromboembolic phenomenon may denote the patient at heightened risk for this well-recognized complication of these procedures. Also relevant to this consideration is the association of various connective tissue diseases with antiphospholipid antibodies, a disorder of (hyper) coagulation that places patients at high thrombotic risk after surgery. This condition presents significant management challenges in the perioperative setting and is reviewed elsewhere (Chap. 24). The use of tobacco, alcohol, and other drugs should also be documented, as should the patient's allergic history. All prescription and over-the-counter medications, including the use of herbs and supplements, should be recorded with their dosages and dosing schedules, as decisions need to be made concerning which therapies should be continued (and which should not) prior to surgery. In addition to a traditional review of systems, certain anesthesia-related checks are also important: these include airway problems and a history of snoring, daytime sleepiness, and hypertension which, if present in the morbidly obese patient, suggest the presence of sleep apnea, a medical problem underappreciated both in the general and perioperative settings (Chap. 19).

An understanding of specific intraoperative events and practices associated with the range of orthopedic procedures cannot be overemphasized when performing preoperative evaluations and may help avoid delays and cancellations on the day of surgery. For example, the simple knowledge of positioning practices may alert the examiner to evaluate the patency of potential femoral vascular grafts, ventriculoperitoneal shunts, and the accessibility of implanted cardiac defibrillators in the prone or lateral position as is utilized for spine and hip procedures, respectively. Further, an appreciation of factors like expected blood loss and specialized ventilation strategies such as one-lung ventilation, will allow for a better assessment of the impact of such an approach on various organs and the ability for any given patient to tolerate such interventions. Lastly, consideration of anesthetic practices for specific procedures (i.e., neuraxial versus general approaches) and their physiologic impact, such as effects on cardiac preload and afterload, should be taken into account when evaluating patients with specific diseases. The effect of prone positioning on positive pressure ventilation may be another example to consider specifically in the obese patient. Thorough evaluation of a patient's possible spinal pathology, including the extent and type of prior back fusions, may avoid confusion on the day of surgery when a neuraxial technique is planned for lower extremity arthroplasty. In selected patients a preoperative consultation with an anesthesiologist may be indicated as to more accurately assess the compatibility of a patient's pathophysiology with an anticipated surgical and anesthetic approach.

Last there has been considerable interest in the estimation of the patient's functional capacity, a surrogate for cardiopulmonary fitness, in the prediction of postoperative outcome [11, 12]. Exercise capacity, quantified in metabolic equivalents (METS), can be easily estimated according to the ability to perform simple everyday tasks of living [10]. Patients with functional limitations so determined have been shown to be at risk for postoperative complications [10]. Although often cited as an easily measured predictor of surgical outcome, the applicability of such assessments is constrained in orthopedic populations, owing to the disability associated with chronic, painful joint conditions.

The physical examination confirms and often amplifies information obtained from the medical history. In the preoperative context, the examination should focus on patient characteristics known to adversely impact upon postoperative course. In addition to the vital signs, body mass index (BMI) should be calculated as this parameter is associated with the development of various chronic diseases, but obesity is also an important independent risk factor for surgery and highly correlated with the underappreciated condition, sleep apnea syndrome. Careful auscultation of the heart is important as the presence of third and fourth heart sounds may indicate left ventricular dysfunction or incipient congestive heart failure while cardiac murmurs imply the presence of valvular heart disease. Depending on the nature and severity of the valvular anomaly, valvular heart disease may compromise cardiac function at times of physiological stress such as surgery. Obesity, large neck circumference, and hypertension predict obstructive sleep apnea; obesity is also associated with insulin resistance and thus diabetes mellitus.

The benefit of preoperative laboratory testing has been examined in many studies, and its benefit (or lack thereof) continues to be widely debated. Several comprehensive reviews pertaining to the commonly performed preoperative studies have been published. Should the determinants of such testing be disease-related or procedure-related? Is the common practice of screening laboratory panels justified in the preoperative setting? With respect to testing when there are no clinical indications, less than 1% of such testing has been shown to provide useful information [13]; indeed, there is evidence that overall this approach may actually be harmful [14]. Not surprisingly, preoperative diagnostic tests ordered as a consequence of a finding uncovered on history and physical examination are more likely to be abnormal [15]; of particular importance is the

previously abnormal result that is associated with new or persistent abnormalities [16]. Finally there is the economics of such testing. Although not extensively examined, one study relevant to the orthopedic population examined the costs associated with routine urinalysis prior to knee arthroscopy; $1.5 million dollars were spent in order to prevent a single urinary tract infection [17].

In response to observations from clinical practice and a literature that fails to demonstrate benefit, support from experienced perioperative clinicians for the global or "shotgun" approach to preoperative testing has waned over time [18]. The establishment of guidelines, the effect of which was to reduce preoperative testing, has been shown to have several advantages These include the standardization of practice, improved efficiency, and a substantial reduction in costs; further, these benefits occur with no adverse effect on outcome [19, 20]. Indeed in studies involving healthy patients undergoing minor procedures (i.e., cataract extraction), routine preoperative laboratory testing appears completely unnecessary [21–23]. Although definitive studies in an orthopedic population have not been conducted, a restrictive preoperative testing model might also apply to many of the minor or regional orthopedic procedures (i.e., hand and foot surgery, arthroscopy). Nonetheless, old practices "die hard" and what appears to be excessive preoperative testing remain a widespread practice. Further, depending on the patient and the nature and magnitude of the surgery, a number of investigations may be considered appropriate and are still commonly performed on patients prior to major surgical procedures.

Optimization of Conditions that May Affect Postoperative Outcome

Patient-related factors, specifically existing medical comorbidities, are now viewed as the most important determinant of postoperative outcome. Part III and Part IV of this book present a comprehensive overview of the perioperative management across the spectrum of chronic medical conditions encountered in orthopedic patients. Optimization of the treatment of these conditions is an important goal of the preoperative evaluation. Common examples of this practice include the control of blood pressure in the patient with hypertension, the resolution of bronchospasm in the asthmatic, the achievement of satisfactory glucose control in the diabetic, electrolyte abnormalities (often medication-induced), and heart rate control in patients with coronary artery disease. Unfortunately, for many relevant conditions (i.e., obesity, smoking practices), time constraints and patient compliance impose substantial obstacles.

In practice, the process of optimization generally involves medication adjustments. Medications may be started, discontinued, or their dosages changed, before or on the day of surgery. Further, because perioperative care is a dynamic process, medication modifications are often required after the surgical procedure as well. The medications involved encompass the entire pharmacopeia, including complementary and alternative therapies. Of note are such pharmacological categories as antihypertensive agents (including beta-blockers), antiarrhythmic agents, statin drugs, bronchodilators, insulin and oral hypoglycemic agents, drugs with effects on coagulation, antidepressants, and analgesics. For example, angiotensin enzyme (ACE) inhibitors and angiotensin receptor antagonists (ARA) are common antihypertensive agents and thus frequently encountered in the preoperative setting. Such medications, which are often combined with a diuretic, are associated with significant hypotension in association with anesthesia and should be held on the day of surgery [24, 25]. Other such disease-related optimization strategies are dealt with in the individual chapters comprising Part III and Part IV of the book.

A decision to hold medication prior to or on the morning of surgery must balance the potential adverse influences of those medications in the short term (in the setting of anesthesia and surgery) versus their long-term indications and benefits. Such decisions must be made on an individual basis. Table 1.1 summarizes these considerations across a range of common medications. The management of anti-rheumatic medications is a unique and relevant subset of this consideration and is dealt with in Chap. 12.

The Assessment of Perioperative Risk

The determinants of perioperative risk fall into four categories [26]. The first and least discussed in the perioperative literature involves various system-related phenomena, including the hospital–institutional model of perioperative care (general vs subspecialty, inpatient vs outpatient, comanagement methodologies), approaches to staffing (nursing, physician assistants, hospitalists), and the role of information systems, all of which are important determinants of outcome. The second category of risk relates to anesthetic management and includes such factors as choice of anesthesia (regional vs general), monitoring techniques, airway considerations, and the approach to postoperative pain control, topics covered in Part II of this book. The third includes the surgery-mediated risks, while the fourth category subsumes those influences arising as a consequence of existing medical comorbidity. The impact of preexisting medical conditions on postoperative complications is a subject about which an extensive literature now exists. Indeed, medical comorbidity is now viewed as the primary determinant of adverse surgical outcome. Apropos of this point, an early study is illustrative. Of 599,548 anesthetics, periopera-

Table 1.1 (A) Medications commonly discontinued several days before surgery. (B) Medications commonly withheld on morning of surgery

Medication	Special considerations and comments
(A) Medications commonly discontinued several days before surgery	
Tricyclic antidepressants	Continue for severe depression
Monoamine oxidase inhibitors (MAOIs)	Continue if severe condition (use MAOI-safe anesthetic that avoids meperidine)
Metformin	May stop 24–48 h to decrease risk of lactic acidosis
Birth control pills, estrogen replacement, tamoxifen	Prolonged risk of thromboembolism, especially after major oncologic and orthopedic surgery. Decision by surgeon or oncologist
Aspirin, clopidogrel (Plavix), cliostazol (Pletal), dipyridamole (Persantine)	May continue in patients with critical need for antithrombotic therapy and/or low risk of significant surgical bleeding. Duration of effect of cilostazol and dipyridamole < clopidogrel, aspirin, and ticlidopine. However, if major concern about intraoperative bleeding, stop for up to 10 days
Warfarin (anticoagulants)	Generally stop for 2–5 days. If high risk of thromboembolism, may replace with heparin or low-molecular-weight heparin
Nonsteroidal anti-inflammatory drugs	May continue for severe inflammatory disorder
Cyclooxygenase type 2 inhibitors	May continue to avoid flare-up (despite potential thrombosis or delayed healing)
Fish oil, vitamin E (>250 U/day), and many herbal medicinals	Potential multisystem (anticoagulant, cardiovascular) effects. Standard vitamins acceptable
(B) Medications commonly withheld on the morning of surgery	
ACE inhibitors, angiotensin receptor blockers	Continue if refractory hypertension, fragile aneurysm, severe congestive heart failure (CHF), valvular insufficiency
Diuretics	May continue for CHF
Phosphodiesterase-5 inhibitors	May predispose to hypotension
Lithium	Interacts with anesthetic agents
Bupropion, trazodone	Predispose to exaggerated sympathetic response
Disulfiram (Antabuse)	Affects metabolism (e.g., phenytoin, warfarin).
Alendronate sodium (Fosamax)	Causes transient esophageal irritation
Particulate antacids	Cause pneumonitis if aspirated
Oral hypoglycemics	Risk of hypoglycemia in fasting patient
Long-acting insulin (no available IV access—e.g., day-of-surgery admission)	May also decrease dose night before surgery if patient is prone to morning hypoglycemia. Initiate tighter control when IV access available
Rapidly acting insulin	Administer preoperatively only if hyperglycemia
Insulin pump	Withhold bolus; may continue basal rate.
Pyridostigmine (for myasthenia gravis)	May complicate use of neuromuscular blocking drugs. Continue if risk of severe weakness or dysphagia
Low-molecular-weight heparin (enoxaparin)	Can replace warfarin; typically withhold for 12–24 h

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tive death was proportionately attributed to anesthesiological practices (1/2680), the surgeon (1/420), and patient comorbidity (1/95) [27]. This, the first paper to feature the key role played by patient comorbidity in surgical outcome, was buttressed by a second report in which patient-related comorbidity was the major contributor to the mortality in 485,850 of surgical procedures [28].

The identification of the factors that may alter the risk associated with surgery has, until recently, been the purview of the anesthesiologist. Surgical practice has, however, changed. An ever-aging patient population, with an increasing burden of medical comorbidity, is now considered as a suitable candidate for surgical intervention. Such patient-related characteristics, coupled with the technical evolution of surgical practice, now require the input other clinical disciplines, specifically internal medicine or the medical subspecialists, professionals who by necessity have entered the perioperative arena and now play a key collaborative role.

The concept of preoperative risk assessment was ushered into clinical practice by anesthesiologists in the 1940s [29]. Discouraged by the complexity of the problem, investigators initially regarded the challenge as too daunting owing to such problems as the magnitude of the data required, practice variation, and to the lack of agreement regarding key definitions and terms. Early investigators did, however, develop a scale for the assessment of the patient's state of health prior to surgery. Indeed, the *American Society of Anesthesiologists (ASA) Physical Status Scale* has proven among the most durable tools of clinical medicine [30]. Employed for decades in the setting of anesthesia and surgery, the ASA scale has high correlation with a patient's postoperative course. Five levels of risk based on the presence of a systemic disturbance (illness or comorbidity) are defined with the associated surgical mortality in parentheses: I absent (0.2%), II mild (0.5%), III severe/non-incapacitating (1.9%), IV incapacitating/threat to life (4.9%), and V moribund/survival <24 h without surgery (NA); the subdesignation E denotes emergency surgery which doubles the risk [31]. First proposed in 1941 [29], a revision of the scale remains in virtual universal use to this day [32]. Although criticized for the vagueness of its criteria, it has proven an extraordinarily enduring assessment tool. The search for more robust surgical prediction methodologies has continued and achieved considerable success. The prodigious literature pertaining to surgical risk prediction, both global and organ-specific risk, is fully reviewed in Chap. 2.

Patient Education and Preventive Practices

Patient education and the introduction of preventive practices represent the final goals of the preoperative evalua-

tion. At our institution, preoperative classes are conducted daily for all patients scheduled for total hip and knee arthroplasty as well as those who are to undergo spinal surgery. These sessions review the entire inpatient and postoperative experience associated with these major orthopedic procedures. Supplemented by a comprehensive guide given to each patient, the classes provide an opportunity for patients and their family members to ask questions of the trained nursing educational leaders about the entire perioperative experience. Studies have been conducted in the orthopedic setting, demonstrating a number of benefits of such educational practices; these include a reduction in surgery-associated anxiety and pain [33] as well as a reduction in length of stay [34].

Arising logically from the educational ethos, the implementation of preventive measures has long been an aspirational element of the preoperative assessment. While the range of putative deterrent interventions and the clinical settings in which they might apply remains poorly characterized, there are few data substantiating the role and effectiveness of such approaches. Smoking cessation has received the most attention, in part because it is a sound health-promoting recommendation in general. Nonetheless, the termination of cigarette smoking is often not practical, as smoking cessation needs to take place many weeks prior to the procedure, generally well before the preoperative consultation takes place. In the realm of orthopedic surgery, however, the opportunity to implement effective prevention is enhanced by the often, elective nature of the procedure. Weight loss is another important target for prevention, as obesity is not uncommon in the orthopedic setting. Indeed, obesity remains a relevant issue with respect to such concerns as prosthetic longevity in the setting of total hip and knee arthroplasty and the long-term results from spinal surgery; obesity as a medical problem remains a major societal challenge fraught with well-known challenges.

Efficacy of Preoperative Consultation

Until recently the efficacy of preoperative assessment has essentially been assumed [35, 36], justified by the aging and increasing complexity of modern-day surgical patients. The anticipated benefits of consultation in the preoperative setting include the documentation of comorbid disease, to optimize such preexisting conditions through the selective performance of additional investigations and timely referral for subspecialty consultation, and the initiation of interventions intended to reduce risk, to anticipate the postoperative needs of the patient and to defer and occasionally cancel surgery [37]. Studies examine a number of aspects of the preoperative consultation including their impact on such adverse outcomes as day of surgery cancellations [38, 39], duration of hospitalization [40, 41], and hospital costs [12, 42] and on patient anxiety [43]. Such studies have focused on quality concerns and the financial impact of preoperative consultation, but there are other important considerations. For example, patient satisfaction is favorably influenced by the preoperative evaluation. In one study patients rated meeting with the anesthesiologist preoperatively a higher priority than that of obtaining information on pain relief, methods of anesthesia, and discussion concerning potential complications of surgery [44].

Data concerning the quality of the preoperative consultation have been published. Observations from the Australian Incident Monitoring Study (AIMS) shed light on this issue [45]. In this study 11% of preoperative assessments were considered either inadequate or incorrect; 3.1% of all adverse postoperative events were judged a direct result of these flawed practices. Among those patients experiencing postoperative complications, the morbidity was considered major and only 5% of such events were considered unpreventable. Another study, of anesthetic-related deaths, further develops this theme. Thirty-nine percent (53/135) of such deaths involved suboptimal preoperative assessment and management [46].

Yet the entrenchment of the preoperative consultation has occurred despite a lack of evidence to support its widespread acceptance. One randomized trial of preoperative medical consultation showed little benefit on postoperative outcome or on quality of care [47]. In another study of 1282 patients undergoing surgery, preoperative consultation resulted in no improvement in quality of care indicators (glucose in the diabetic, DVT prophylaxis, DVT) [48]. Two recent studies have examined the impact of preoperative consultation on a macro level [49, 50]. In these cohort studies, Wijeysundera et al. utilized population-based databases to examine the impact of preoperative anesthesia and medical consultation on a large surgical population (270,000 patients) undergoing a broad range of major procedures. In addition to mortality and length of stay, a number of process-related phenomena were assessed in order to judge how preoperative consultation might influence differentials in outcome.

While modest differences were found according to whether the preoperative consultation was performed by an anesthesiologist or by a medically trained physician, several themes emerged from these reports. First, over the 10-year period (1994–2003) of the study, the rate of preoperative consultation increased from 19% to 53%. Presumably reflecting a perceived benefit of consultation on the part of the referring surgeons, the withdrawal to the operating room by the surgical community is also likely responsible. Among the medical consultations, the majority (94.2%) were performed in the outpatient setting, generally about 2 weeks before the surgery. Consultation was associated with higher

rates of preoperative testing, the preoperative use (new) of beta-blockers and statin drugs, and preoperative cardiac interventions suggesting an active engagement in decision-making by the preoperative physicians. In terms of benefit, however, the results were disappointing. Regardless of who performed the consultation (anesthesiologist vs medical physician), no reduction in mortality could be shown; indeed, patients undergoing preoperative medical consultation had a modest increase in 1-year mortality. Length of stay was also longer (+0.67 days) in patients who underwent medical consultation (though −0.35 days shorter in those who saw an anesthesiologist prior to surgery). Given the support and general belief in the practice of preoperative consultation, these results were surprising, and the authors posit a number of potential explanations for their findings. These include the association of consultation with an apparent decrease in the use of epidural anesthesia, the higher use of beta-blockers (now believed to increase the rate of stroke after surgery), and the fact that the study population did not include patients whose surgery had been cancelled, nor were those undergoing urgent/emergent procedures considered. In addition, perhaps those surgeons who felt comfortable managing medical comorbidities on their own provided superior perioperative care, thus diluting the impact of the preoperative consultation.

So what additional approaches to care might be of incremental benefit? In addressing this question, Weed brings us back to one of the foundational elements of effective consultation, that is, communication [51]. Citing Chassin, a leader in the quality movement, Weed shows that the "beneficial effect of process" emphasizes how the achievement of optimal outcomes (i.e., postoperative complications) is inextricably a function of the process used to deliver medical care. Thus, the preoperative consultation in itself is not sufficient. Success requires the fastidious attention to the implementation of the preoperative recommendations. Comanagement, a strategy of perioperative care that emphasizes the active participation of the medical consultant, may provide an effective template [52–54]. However, the experience with this model in the orthopedic and other surgical settings has been mixed and generated commentary of a cautionary nature [55].

Summary

The medical evaluation of a patient prior to surgery remains a widespread clinical practice. Although, as discussed previously, the overall utility of such assessments remains to be demonstrated, the enduring and widespread support for such consultation is supported by clinical investigation and growing literature, even national conferences. Owing to this widespread acceptance, the underpinning of perioperative medicine, its principles and practices, is evolving influenced by the quality movement of the last 15 years. This chapter provides a general overview and approach to the patient in the perioperative setting and offers a template not only for this book but for clinical practice as well.

Summary Bullet Points

- The preoperative medical evaluation offers an important opportunity for communication between all professionals involved in the care of the surgical patient.
- The term surgical "clearance" should be replaced by the notion of preoperative "optimization" for surgery.
- The goals of the preoperative evaluation include the evaluation and optimization of patient comorbidity, the assessment of surgical risk, and to provide an opportunity for patient education and the implementation of preventive practices.
- The practice of the preoperative medical evaluation remains an unproven medical intervention.

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Perioperative Risk Models

2

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Objectives

- To provide an overview of general and system-specific perioperative risk assessment models
- To summarize the strengths and weakness of the most commonly used risk assessment models
- To provide a case example of how to apply the reviewed risk models practically

Key Points

- Many perioperative risk models have been developed over time; these include both general and organ-system-specific models.
- Models that are not efficient or cumbersome are generally not well adopted for clinical use.
- The ideal risk assessment model should be efficient, easy-to-use, well-validated, and clinically applicable to a range of patients and clinical scenarios.

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Introduction

Perioperative risk models hold promise for aiding clinical decision-making in the surgical setting. A variety of models and classification tools have been published over time, with the primary goal to objectively classify risks numerically or into categories that can be readily understood by clinicians and patients. Some models have been extrapolated from nonsurgical patient populations, whereas others have been derived and validated solely in surgical cohorts. The scope of perioperative medicine is broad, and a discussion of risks surrounding the surgical period can vary from general statements noting whether patients are acceptable candidates to detailed problem-specific discussions.

We present here a review of these models and include both risk models and preoperative classification systems, which have overlapping clinical use. Our aim is to summarize the strengths and weaknesses of existing models and highlight how they can be utilized effectively to aid clinical decision-making. Risk models studied exclusively in nonsurgical patient populations will not be reviewed here in detail, although we acknowledge that at times such models can be helpful for clinical decision-making. Studies examining multiple rather than single-variable predictors of risk are discussed here, and we specifically excluded single-variable models.

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Few models have been well-studied and validated in different orthopedic surgery cohorts specifically; thus we draw on literature examining other surgical populations at times. Discussions below have been grouped into several broad areas: general risk models and cardiac, pulmonary, hepatic, hematologic, and renal/genitourinary risk models.

General Risk Assessment Models

Table 2.1 provides a timeline of the major perioperative models reviewed here. The development of general models that capture an overall assessment of patients' health holds value to providers, who often need an efficient tool to assess broadly how patients can be expected to fair during surgery. This can be helpful for patients with multiple interacting medical comorbidities, in whom gestalt assessments can be challenging.

Table 2.1 Risk assessment tools studied in surgical patients

General	Year
American Society of Anesthesiologists (ASA) Physical Status Classification Dripps-ASA classification	1941[a] 1961
Physiologic and Operative Severity Score for the enUmeration of Mortality and Morbidity (POSSUM)	1991
Hilditch Pre-Anesthesia Screening Questionnaire	2003
Holt-Silverman Resilience Index	2006
Surgical Mortality Probability Model (S-MPM)	2012
American College of Surgeons' National Surgical Quality Improvement Program (NSQIP) Risk Calculator	2013
Surgical Outcome Risk Tool (SORT)	2014
Combined Assessment of Risk Encountered in Surgery (CARES)	2018
Cardiac	
Goldman Cardiac Risk Index	1977
Detsky Modified Risk Index	1986
Eagle Criteria	1989
American College of Cardiology/American Heart Association Guidelines	1996[b]
American College of Physicians' Algorithm	1997
Revised Cardiac Risk Index (RCRI)	1999
Fleisher-Eagle Criteria	2001
Fleischer-Eagle Algorithm	2001
Auerback & Goldman Algorithm	2006
NSQIP-Gupta Calculator	2011
Pulmonary	
Epstein Cardiopulmonary Risk Index	1993
Melendez Cardiopulmonary Risk Index	1998
Arozullah Post-Op Respiratory Failure Risk Index	2000
Arozullah Post-Op Pneumonia Risk Index	2001
Canet Prediction of Postoperative Pulmonary Complications	2010
Gupta Postoperative Respiratory Failure Risk Model	2011
Gupta Postoperative Pneumonia Risk Model	2013
OSA Specific Models:	
Berlin Questionnaire for OSA	1999
STOP Questionnaire for OSA	2008
Validation of the Berlin Questionnaire and ASA OSA Checklist	2008
American College of Chest Physicians Perioperative Management of OSA	2010
ASA Practice Guidelines for Perioperative OSA Management, ASA Screening Questionnaire for OSA	2014
Hepatology	Year
Child-Turcotte-Pugh	1984 1987
Model for End-stage Liver Disease (MELD)	2000
ASA Class	2007
Hematologic	
Caprini Model for Venous Thromboembolism (VTE)	1991
Kucher Model for VTE	2005
Patient Safety in Surgery Study/Rogers et al. VTE model [105]	2007
Padua Prediction Score for VTE	2010
Michigan Surgical Quality Collaborative/Pannucci CJ et al. VTE model [94]	2014
Renal/Genitourinary	
International Prostate Symptoms Score – Model for Postoperative Urinary Retention	1992
Risk, Injury, Failure, Loss, and End-stage Kidney (RIFLE) model for AKI	2004
ACS-NSQIP data/ Kheterpal et al. model for AKI	2009
Kidney Disease: Improving Global Outcomes (KDIGO) model for AKI	2012

[a]The ASA Physical Status Classification System was first developed in 1941, modified to include the Dripps classification in 1961, and then most recently updated in 2014

[b]The ACC/AHA joint guidelines were first published in 1996, and have been revised most recently in 2014

The first general model that garnered widespread use is the American Society of Anesthesiologists (ASA) Physical Status Classification System, first published in 1941 [1] and subsequently modified several times [2]. This tool was initially designed to categorize patients for statistical studies and importantly created a focus on patients' physical state alone, separating out the operative procedures and the ability of the surgeon or anesthesiologist. Its initial use was instrumental in helping clinicians begin to use a common language for describing patients' health preoperatively. While subsequent studies have correlated different grades of the physical status classification with mortality and other outcomes, the original and subsequent authors have been keen to highlight that it was not initially developed as a risk stratification system per se [1, 3].

The most recent update of the ASA Physical Status Classification System groups patients into one of six categories and allows for an additional "E" designation to denote emergency surgery [2]. Strengths of this tool are that it has been widely studied and used [4–9] and is readily familiar to most clinicians caring for patients perioperatively. Despite not being designed as a risk stratification tool, the classification system has been correlated with operative times, blood loss, delirium, hospital length of stay, postoperative infection

rates, and mortality in a wide range of surgical populations [10–14]. The main criticism of the model is the subjective nature of classifying patients into each group. Descriptions used, including "normal healthy patient" or "a patient with mild systemic disease," are subjectively vague, and their variable use can result in different courses of management. Examples of suggested classifications for common conditions exist in the original publication [1], and subsequently [2], but are not commonly utilized, and still allow for subjective interpretation. Assessments of interrater reliability of the model have produced mixed results, ranging from fair to moderate agreement among providers [15–17]. Nonetheless, it remains a widely used tool, and several authors have advocated it is a simple way to help predict postoperative outcomes [5, 7, 14].

Dripps and colleagues later devised their own physical status classification in 1961, with physical statuses one through five, and it is essentially identical to the original ASA model but paired down in wording. In a retrospective study of over 30,000 patients, these authors examined the contribution of anesthesia toward surgical mortality and how this related to preoperative physical status classification [18]. They addressed both the degree and nature of how anesthesia may contribute to perioperative deaths in patients undergoing spinal and general anesthesia. A clear, positive correlation between the number of deaths related to anesthesia and higher preoperative physical status classification was found. The simplified Dripps model became known as the Dripps-ASA classification, and popularly caught on for clinical use, replacing the verbose original ASA model. In 1963 the American Society of Anesthesiologists formally adopted the simplified Dripps-ASA model [19], which is the classification system that most clinicians are now familiar with as the ASA Physical Status Classification. This has been most recently updated in 2014 (Table 2.2).

Table 2.2 American Society of Anesthesiologists (ASA) Physical Status Classification System

ASA PS classification[a]	Definition
ASA I	A normal healthy patient
ASA II	A patient with mild systemic disease
ASA III	A patient with severe systemic disease
ASA IV	A patient with severe systemic disease that is a constant threat to life
ASA V	A moribund patient who is not expected to survive without the operation
ASA VI	A declared brain-dead patient whose organs are being removed for donor purposes

Data from: ASA Physical Status Classification System [2]
[a]The addition of "E" to any of the classes denotes emergency surgery, with emergency defined as existing when delay in treatment of the patient would lead to a significant increase in the threat to life or body part

Another modification of the ASA tool has been developed by Holt and colleagues who proposed a *resilience* score specific to organ systems [20]. This score is derived by adding the ASA class to a surgical complexity score (rated 1 through 5). The maximum score possible is 10, and higher scores correlate with higher rates of end-organ injury. Individual scores for each organ system can be added together to provide a comprehensive assessment. While helpful for focusing on specific organ systems, the tool is not simple or efficient and has not caught on for popular clinical use.

Recognizing the need to improve upon the Dripps-ASA model to further predict morbidity, Copeland and colleagues described a scoring system to be used for auditing purposes in patients undergoing a variety of surgical procedures [21]. The resulting Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity (POSSUM) was developed utilizing retrospective and prospective data and utilizes 12 physiologic variables and 6 operative parameters. The tool has been studied primarily at the population level. An online calculator of the model is available [22]. Some authors have observed that the POSSUM tool overpredicts both morbidity and mortality and variable results have been demonstrated when applying the model to orthopedic surgery [23–26]. To correct for this, one study added serum albumin and serum protein levels to the POSSUM score and found it an accurate predictor of mortality in patients undergoing surgery for proximal femur fractures [27]. The POSSUM tool has been extrapolated for use in several surgery-specific models (including V-POSSUM for use in vascular surgery and O-POSSUM for use in patients undergoing esophagectomy surgery), and several authors have noted it to be one of the more validated risk tools [28–32]. The downside to the tool is that it requires the input of many variables, including several variables that are not known until postoperatively, which limits its use as a preoperative assessment tool.

Determining which patients will benefit most from formal preoperative consultations and testing can be challenging. Hilditch and colleagues recognized this and devised a screening questionnaire for nursing use. It helps determine appropriate referral of patients that need to be seen prior to the day of surgery [33, 34]. Their methodology for selecting questions was robust, and the resulting 17 selected questions address general health, exercise tolerance, and risk factors for anesthesia. The authors validated their screening questionnaire in a small cohort of 100 patients undergoing inpatient orthopedic and urologic surgery. Patient responses were compared against separate anesthesiologist assessments as a method of determining validity, which was ultimately scored in the "good" or "excellent" range for most of the included questions. Such a tool may be of use in orthopedic and urology surgeries, which are both typically considered intermediate-risk surgical procedures from a cardiac

risk standpoint. Use in patients undergoing low-risk or high-risk surgical procedures would require additional study. The tool was specifically designed to determine the need for pre-surgical anesthesiology consultations, with a focus on detecting potential life-threatening complications. Other specialties may find the questions less useful for their screening purposes.

Recognizing changes in the surgical population over time, and examining a more recent surgical cohort, Glance and colleagues published their Surgical Mortality Probability Model (S-MPM) in 2012 [35]. At the time, they noted clinicians relying largely on the Revised Cardiac Risk Index for predicting cardiovascular complications and accurately observed that this later tool was not designed to predict all-cause mortality [36]. In addition, a significant portion of perioperative deaths are accounted for by non-cardiac causes [37]. Having recognized that the POSSUM [21] and Holt and colleagues [20] models were not efficient models to use at the bedside, they sought to find a more practical model. Drawing on the American College of Surgeons' National Surgical Quality Improvement Program (NSQIP) clinical dataset and examining retrospective data of over 290,000 patients, they identified three simple variables to predict 30-day mortality: ASA Physical Status, surgery-specific risk (low, intermediate, high), and emergent versus nonemergent operation. Half of the dataset was utilized for derivation of the risk calculator and the other half for validation. They developed a point system based on these three variables, ranging from zero to nine. The corresponding scoring system, class, and 30-day mortality rates are listed in Tables 2.3 and 2.4 [35]. The strength of this study rests in the large size of its surgical cohort and variety of surgery types included in the NSQIP dataset. Previous trials looked at similar variables as predictors of mortality, including one by Tiret and colleagues [4] estimating 24-hour postoperative complications, as well as the Surgical Risk Scale [38] examining the data of three surgeons, but were both based on much smaller patient groups. In considering drawbacks of the S-MPM, one might criticize the multiple steps necessary to determine a classification and associated mortality, as well as the subjective flaws of the ASA classification system. However, an important theme to highlight with S-MPM and several of the models discussed thus far is the incorporation of the ASA classification system into other tools, as it appears to be a robust predictor of perioperative outcomes.

More recently the American College of Surgeons has used the NSQIP dataset to develop and validate a tool providing preoperative estimates of eleven different outcomes, as well as a length of stay estimator [39]. This same dataset has also been analyzed on a smaller scale to develop pulmonary and cardiac risk assessment tools [40, 41]. The more comprehensive ACS-developed tool [39] is based on a robust dataset of over one million patients, drawn from over 200 hospitals at the time of its development. It is a free tool that is available online. The ACS NSQIP model has helped appropriately shift the focus toward a more comprehensive risk assessment, including estimates of infectious risks (pneumonia, urinary tract infection, surgical site infection), thromboembolic events, kidney injury, cardiac complications, death, need of returning to operating room, hospital length of stay, and even the chance a patient will need to be discharged to a rehabilitation or nursing facility. They have importantly recognized the changing healthcare environment, where in addition to emphasizing high-quality patient care there is a need to recognize costs and systems issues. The calculator is particularly useful for providing a printable color-coded bar graph for patients to understand their risks as they compare to average-risk patients. This engages patients in an unprecedented way in the informed decision-making process. The tool can be enormously helpful aiding clinicians in the otherwise challenging task of providing perspective for patients to understand risk estimates. As of 2008, only 3% of US hospitals had contributed to the ACS NSQIP dataset, which some have attributed to data collection burden and costs [42]. Notably, the dataset is based on hospitals performing a range of surgical procedures and does not include data from hospitals focusing on one surgical specialty (e.g., orthopedic-specific hospitals are excluded). Additional research is being conducted to help validate this tool in other surgical patient populations outside of the NSQIP dataset. It

Table 2.3 Surgical Mortality Probability Model (S-MPM) risk factors and points assigned

Risk factor	Points assigned
ASA physical status	
I	0
II	2
III	4
IV	5
V	6
Procedure risk	–
Low risk	0
Intermediate risk	1
High risk	2
Emergency	–
Nonemergent	0
Emergency surgery	1

Data from: Glance et al. [35]

Table 2.4 Surgical Mortality Probability Model (S-MPM) class, point total, and 30-day mortality

Class	Point total	Mortality
I	0–4	<0.50%
II	5–6	1.5–4.0%
III	7–9	>10%

Data from: Glance et al. [35]

is anticipated that the tool will become increasingly utilized as clinicians, patients, and institutions recognize its value.

After the release of the ACS NSQIP tool, the Development and Validation of the Surgical Outcome Risk Tool (SORT) was published. It is based upon a large dataset from the United Kingdom and serves as a useful comparative tool to data collected in the United States [43]. The SORT was derived from post hoc analysis of previously prospectively collected data on over 16,000 inpatient surgical procedures of various types. Two-thirds of the data were used for derivation and one-third for validation of the tool. Six variables were identified as significant predictors of 30-day mortality: ASA Physical Status, urgency of surgery, surgical specialty, severity of surgery, presence of cancer, and age. The authors note their risk score is a better predictor of 30-day mortality than some older models, such as the ASA Physical Status score or the Surgical Risk Scale [38, 43], but unfortunately the SORT has not yet been compared to the robust ACS NSQIP tool, nor does it provide outcome data beyond mortality estimates. The SORT is similarly available as a free online calculator [44].

More recently, the Combined Assessment of Risk Encountered in Surgery (CARES) model was published [45]. This tool is based on a retrospective analysis of over 79,000 patients undergoing noncardiac and non-neurological surgery at a single center in Singapore. The analysis was conducted with the aim of developing a tool for predicting both 30-day postsurgical mortality and need for intensive care unit (ICU) stay. The patients were divided randomly into derivation (70%) and validation (30%) cohorts, and the authors formulated a combined assessment using nine variables that contributed to risk across both mortality and ICU admission: age, surgical risk (moderate/severe), ischemic heart disease, ASA classification, emergency surgery, male gender, congestive heart failure, anemia, and – uniquely – red cell distribution width (RDW). Cumulative rank scores were then used to categorize risk as low, low-moderate, moderate-high, and high. The authors note the novelty of using RDW as a predictor of surgical risk, and of predicting need for ICU admission, which could aid in postoperative patient disposition. This model, while promising, is based on single-center data and ideally would benefit from prospective study in a different setting.

Finally, it is also worth briefly noting that several models have studied intraoperative and immediate postoperative variables to predict the postoperative course. Such tools can be particularly helpful for patients who have undergone urgent or emergent procedures and utilize immediate postoperative variables to provide outcome estimates. These include the APACHE II score and the Apgar score for surgery, which have been discussed in detail elsewhere [30, 46–48].

Cardiac Risk Assessment Tools

There are over two hundred million individuals undergoing noncardiac surgery each year worldwide [49], and cardiac complications during or following surgery are among the most feared perioperative events [50]. In one study, among unselected patients over age 40 undergoing elective noncardiac surgery, acute coronary syndrome occurred in 1.4% of patients and cardiac death in almost 1% [51]. Perioperative myocardial infarction affects approximately 60,000 people each year in the United States [52], and there exists a clear need to help predict and prevent such events. Multiple risk models have been developed with this aim [53].

Goldman and colleagues were the first to develop a perioperative Cardiac Risk Index for noncardiac surgery [54]. Goldman recognized that the existing Dripps-ASA screening tool, popularly utilized at the time, was not useful for predicting cardiac events and designed a study to identify risk factors for perioperative fatal and nonfatal cardiac events. The study evaluated 1001 patients undergoing noncardiac surgery over the age of 40 years. Nine independent variables were identified: auscultated S3 or observed jugular venous distention, myocardial infarction in previous 6 months, >5 premature ventricular contractions in 1 minute, rhythm other than sinus, age > 70, intraperitoneal or intrathoracic operation, emergent operation, aortic stenosis, or poor general medical condition. Each variable was given a point value, depending on its impact, and patients were divided into quartiles based on point total. Of the 19 cardiac fatalities in this study, 10 occurred in the 18 patients at highest risk. The risk of postoperative events was 1% in the lowest quartile. The study was a useful start to help predict perioperative outcomes but did not validate the predictive variables in a separate cohort of patients at the time. Limitations of the risk model also include the need to rely on physical examination skills (auscultated S3 or jugular venous distention), and the study did not include many patients undergoing vascular surgery (a group known to be at particularly high risk for cardiac events).

The Eagle Cardiac Risk Index [50] was developed in part to address the limitation of the Goldman model, having not represented vascular surgery patients well. In this retrospective observational study, multivariable analysis showed that the following factors were predictive of adverse events after vascular surgery: Q waves on ECG, history of angina, history of ventricular ectopy requiring treatment, diabetes mellitus, age older than 70 years, thallium redistribution (most sensitive), and ischemic EKG changes during or after dipyridamole infusion. This study provided clinicians a way to improve their risk stratification of patients planning to undergo vascular surgery; however, it incorporated the extra necessity of thallium imaging. This addition may be impractical to routinely perform across many patients undergoing perioperative evaluation and increases costs and exposure to radiation.

In 1986, Detsky and colleagues [55] attempted to validate the Goldman Cardiac Risk Index in a new surgical population and clarified several terms they thought were poorly defined in Goldman's original index. These included a modification of how congestive heart failure was defined (alveolar pulmonary edema in new model), defining aortic stenosis more strictly as suspected critical aortic stenosis, inclusion of more distant cardiac ischemic events, and reporting of angina pectoris. The study involved 455 patients, more vascular surgeries than Goldman's original study, and yielded predictive information separating major and minor surgeries. The study authors observed that they demonstrated a significant amount of predictive information over Goldman's original index; however, this model did not become widespread for common clinical use. Certain aspects, including its definitions of angina and heart failure, do not make it an easy-to-use tool.

In 1997, the American College of Physicians created their own guideline for patients undergoing major noncardiac surgery [56]. They felt that prior data for major noncardiac surgery were focused on patients undergoing vascular surgery, and this patient population was already at a higher risk for perioperative cardiac events. They created an algorithm for perioperative management based on the variables from the Detsky model[56] and the type of surgical procedure (vascular or nonvascular). The algorithm itself was bulky and similarly did not become popular for common clinical use.

The widely known Revised Cardiac Risk Index was published in 1999 by Lee and colleagues [51]. This index was modified from Goldman's original index [54] and devised a six-point index score for assessing the risks of cardiovascular complications with noncardiac surgery. The study evaluated 2893 patients aged >50 years who underwent nonelective noncardiac procedures with an expected length of stay at least 2 days. The six factors identified had approximately equal prognostic importance and were subsequently validated in a similar patient population. The factors include high-risk type of surgery, history of ischemic heart disease, history of heart failure, history of cerebrovascular disease, diabetes mellitus requiring treatment with insulin, and preoperative serum creatinine >2.0 mg/dL. Patients are given one point for each risk factor and then divided into low, moderate, and high risk based on their point total. This tool remains in common clinical use today, in part because the risk factors are easy for clinicians to recall. See Box 2.1, adapted from data from Cohn and colleagues [57]. Limitations of the study and model are that they do not adequately represent patients undergoing low-risk or emergent-risk surgeries. It also does not factor in functional capacity, which is an important determinant of outcomes [58–60]. The RCRI generally can categorize patients at low versus high risk for cardiac events following nonvascular noncardiac surgery; however, it is not a good predictor of overall mortality or cardiac events after vascular surgery [61].

Box 2.1 Revised Cardiac Risk Index (RCRI) and Estimates of Perioperative Cardiac Risk

- RCRI criteria [51]
  - High-risk type of surgery (vascular surgery, any open intraperitoneal or intrathoracic surgery)
  - History of ischemic heart disease (history of myocardial infarction or positive exercise test, current complaint of chest pain considered to be secondary to myocardial ischemia, use of nitrate therapy, or electrocardiogram with pathological Q waves; do not count prior coronary revascularization procedure unless one of the other criteria for ischemic heart disease is present)
  - History of heart failure
  - History of cerebrovascular disease
  - Diabetes mellitus requiring treatment with insulin
  - Preoperative serum creatinine >2.0 mg/dl
- Rate of cardiac death, nonfatal myocardial infarction, and nonfatal cardiac arrest according to number of predictors [52]
  - No risk factors – 0.4% (95% CI: 0.1–0.8)
  - One risk factor – 1.0% (95% CI 0.5–1.4)
  - Two risk factors – 2.4% (95% CI 1.3–3.5)
  - Three or more risk factors – 5.4% (95% CI 2.8–7.9)

Data from: Cohn and Fleisher [57].

Ongoing efforts at algorithm development continued with Fleisher and associates in 2001 [62]. At the time, the only other notable algorithms were the 1996 American College of Cardiology/American Heart Association (ACC/AHA) guidelines [63] and the American College of Physicians guidelines [56]. Fleisher and associates incorporated beta-blocker usage for higher-risk patients and updated information regarding preoperative coronary revascularization. In 2006, Auerbach and Goldman [64] performed a comprehensive review of measures aimed at reducing the cardiac risk of patients undergoing noncardiac surgery. They also developed an algorithm, of which portions were later adapted into the ACC/AHA guidelines. This algorithm incorporated the RCRI criteria and notably the increasingly recognized importance of functional status, as assessed through estimated metabolic equivalents of task (METs).

In 2001, Gupta and associates [40] published data based on the ACS NSQIP dataset to formulate an updated risk scoring system reflective of the modern surgical population and techniques. The authors studied over 200,000 patients who had data submitted to the NSQIP, representing over 200 hospitals. They derived and validated a model to predict cardio-

vascular events up until 30 days postoperatively. This contrasts with prior models, such as the RCRI, that examined outcomes for much shorter postoperative time frames. An online calculator and handheld phone application are available for this model [65]. As the authors themselves note, known or remote coronary artery disease (except prior percutaneous intervention and cardiac surgery) were not controlled for in the analysis. However, they observe that the predictive ability for their model is higher than that of the RCRI (c-statistic of 0.87 vs. 0.75) [40].

While not a risk model, the ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery warrant review [66]. They have functioned as standard guidelines for many years and have incorporated many of the above-noted studies and models into their recommendations, including the RCRI criteria and the ACS NSQIP model. Since 1996, the American College of Cardiology and the American Heart Association have jointly published these guidelines. They are robust, reflect a thorough assessment of the literature, and are endorsed by many different professional societies. They contain a step-by-step algorithm which incorporates key assessments of urgency of surgery, patient clinical risk factors, surgery-specific risk factors, and functional status. The guidelines have been most recently updated in 2014. Over the years, there has been a gradual trend toward emphasizing that patients undergoing low-risk surgical interventions, who are low risk from a patient-risk-factor standpoint, tend to fair well with surgery. An additional prominent theme in the guidelines is if cardiovascular testing (e.g., stress testing) is not going to impact management or perioperative care, then it is usually not necessary. In addition to the perioperative risk assessment, the 2014 guidelines discuss cardiovascular disease-specific management, as well as perioperative management of biochemical markers, medications, valve disease, and implanted cardiac devices. These guidelines currently serve as the standard of care for perioperative cardiovascular assessments and should be the first tool utilized for clinicians performing such assessments.

Pulmonary Risk Assessment Tools

Postoperative respiratory complications account for a significant cause of morbidity, mortality, and increased length of stay during the perioperative period [67]. In recent studies, death within 30 days was significantly higher in patients with postoperative respiratory failure (25.6% vs. 0.9%) or postoperative pneumonia (17% vs. 1.5%), when compared to patients without these complications [41, 68]. Thus, multiple risk models have been developed to predict respiratory complications. Epstein and colleagues developed one of the earliest pulmonary risk models based on a small prospective study looking at 42 patients undergoing lung resection for cancer [69]. At the time, there were conflicting data regarding the predictive ability of cardiopulmonary testing and peak oxygen uptake (VO2); therefore, one of their main objectives was to assess whether VO2 could predict postoperative cardiopulmonary complications compared to other methods of risk stratification. The authors used a Cardiac Risk Index (CRI) and a Pulmonary Risk Index (PRI) and combined the scores to create a Cardiopulmonary Risk Index (CPRI). The CRI was adapted and modified from Goldman and associates [54] but included left ventricular systolic function and excluded the type of surgery. The PRI included the presence or absence of obesity, current or recent tobacco use, productive cough, diffuse wheezing, ratio of forced expiratory volume in 1 second over the forced vital capacity (FEV1/FVC) of less than 70 percent, and hypercapnia. Patients with a CPRI score of four or greater had a 22 times higher risk of cardiopulmonary complications ($p < 0.0001$) than a score less than four. However, the study was small and not generalizable due to the male predominant population. In addition, subsequent studies attempting to validate the CPRI demonstrated inadequate predictive value [70].

A large prospective cohort study performed by Arozullah and colleagues selected patients who had surgery over a two-year period from the National Veterans Affairs Surgical Quality Improvement Program (VA NSQIP) and created a risk index for postoperative respiratory failure (PRF) after major noncardiac surgery [71]. Initially starting as a mandate in the mid-1980s by the US Government to improve surgical outcomes in the Veterans Administration hospitals, the VA NSQIP has expanded nationally and internationally and been adopted by the American College of Surgeons to form the NSQIP model noted above in the general and cardiology risk assessment sections. In the study by Arozullah, PRF was defined as the inability to be extubated 48 hours after surgery or any unplanned endotracheal intubation. Two cohorts of patients were evaluated from VA NSQIP with the first 81,719 cases used to develop the risk model and the second cohort of 99,390 used to validate the index. 2746 (3.4%) developed PRF. The preoperative predictors selected for the risk index included type of surgery (abdominal aortic aneurysm, thoracic, neurosurgery, upper abdominal, peripheral vascular, neck, or emergency), albumin, blood urea nitrogen, functional status, history of chronic obstructive pulmonary disease, and age 60 years or older. The predictors were assigned weighted point values. Based on the total points, the patients were assigned a class 1–5 risk category ranging from 0.5% to 30.5% risk of PRF, respectively. The 30-day mortality rate was 27% for those with PRF compared to 1% in patients without PRF. The PRF index appeared to more accurately predict the incidence of PRF for risk classes 1 and 2; however, it tended to overestimate the risk for classes 3–5. This risk index has limitations, as women were underrepresented due

to the patient population of predominately male veterans. In addition, the veteran population has a higher level of comorbid medical conditions; thus, this risk index may not be as generalizable to a younger and healthier population. Overall, however, the discriminatory ability of the risk index is good.

Since some of the previously mentioned studies had limitations, such as narrow study populations and types of surgeries, Canet and colleagues sought to study a wider range of patients and surgeries [72]. They conducted a prospective, multicenter, observational study looking at postoperative pulmonary complications (PPCs), defined as respiratory infection, respiratory failure, bronchospasm, atelectasis, pleural effusion, pneumothorax, or aspiration pneumonitis. The selected patients who were undergoing non-obstetric, in-hospital surgical procedures with general, neuraxial, or regional anesthesia were divided into two groups: one used to develop the PPC risk index and the other for validation. The resulting PPC index had seven independent risk factors (age, preoperative oxygen saturation, respiratory infection requiring antibiotics within the past month, preoperative anemia <10 g/dl, upper abdominal or intrathoracic surgery, surgery over 2 hours, and emergency procedure), which were assigned point values and then stratified to low, intermediate, or high risk for PPCs: 1.6%, 13.3%, and 42.2%, respectively. The risk factors are relatively easy to obtain and the score easy to calculate if there is access to the weighted points and equivalent stratification. However, there was inclusion of PPCs that are not typically considered severe complications or complications that can be avoided, such as new expiratory wheezing, development of pleural effusion, or atelectasis.

More recently, Gupta and colleagues utilized the NSQIP database to study PRF [41]. This dataset has grown in recent years to now include over 350 hospitals. In this study the primary endpoint evaluated was PRF through 30 days after surgery, including unplanned intubation during surgery or postoperatively, the requirement for reintubation, and mechanical ventilation for >48 hours postoperatively. Using the 2007 dataset of 211,410 patients, a risk model was developed, and subsequently, the 2008 dataset of 257,385 patients was used to validate the model. 6531 (3.1%) of the derivation cohort and 6590 (2.6%) of the validation cohort patients developed PRF. Patients with PRF had more complications in general than patients without PRF, and death within 30 days was significantly higher in those with PRF (25.62% vs. 0.98%; p <0.0001). Although PRF was associated with 21 statistically significant variables, five preoperative risk factors were selected by the authors: type of surgery, emergency case, dependent functional status, preoperative sepsis, and high ASA class. Narrowing the variables to these five factors reduced the complexity and improved the usability of the model for the development of the calculator. In addition, analysis using an increased number of variables did not result in improved discriminatory ability. The c-statistic was 0.894 and 0.897 for datasets 2007 and 2008, respectively, suggesting strong predictive ability. This risk calculator is easy to use and has excellent generalizability, having included a broad study population of academic and private hospitals, a wide age range, both genders, and multiple surgical specialties.

A specific postoperative complication worth noting is postoperative pneumonia, since it is a significant cause of postoperative increased length of stay and mortality. There have been two notable risk models developed by the authors Arozullah and Gupta [68, 73]. Both models have strong predictive ability (Arozullah Postoperative Pneumonia Risk Index c-statistic 0.805–0.817 and Gupta Postoperative Pneumonia Risk Model c-statistic 0.855–0.860). Notably, the Arozullah model was derived from male veteran patients, again, limiting its generalizability. In examining these models, the risk factors most closely associated with postoperative pneumonia were age, ASA class, chronic obstructive pulmonary disease, functional status, preoperative sepsis, smoking within 1 year of surgery, and type of surgery.

There is increasing recognition of obstructive sleep apnea (OSA) as a significant risk factor for postoperative hypoxemia, ICU transfers, longer lengths of stay, respiratory failure, and postoperative cardiac events [74, 75]. In studies evaluating the prevalence of OSA in the general surgical population, almost a quarter were identified to be at high risk for OSA, and over 80 percent of these patients did not have a diagnosis of OSA prior to surgery [76]. Thus, there are tools that have been developed to screen for OSA preoperatively. The Berlin Questionnaire, one of the first questionnaires created, was initially used to identify patients with possible OSA in the primary care population [77]. At a conference in 1996, US and German pulmonary and primary care physicians discussed and selected questions after a literature review and came to a consensus with a series of questions focused on known risk factors for sleep apnea. These 11 questions focused on snoring, daytime sleepiness, high blood pressure, and patient self-reported height and weight. This questionnaire, an early form of the American Society of Anesthesiologists (ASA) Checklist, has subsequently been validated in surgical populations, with sensitivities ranging from 69% to 87% depending on the severity of disease [78].

Chung and colleagues aimed to develop and validate a simple questionnaire to screen surgical patients for OSA [79]. Based on their previous work on the Berlin Questionnaire and a literature review, four self-administered yes/no questions were developed, utilizing the mnemonic STOP (snoring, tiredness during the daytime, observed stop breathing, high blood pressure). The STOP questionnaire was initially given as a pilot study to 592 preoperative clinic patients. Subsequently, it was given to 2467 preoperative patients without a prior diagnosis of OSA, and of these patients, 27.5% were classified as being at high risk of OSA. After polysomnography was obtained in 211 patients, the apnea-

hypopnea index (AHI) scores were stratified, and the sensitivities of the STOP score were 74.3% and 79.5% for AHI scores of greater than 15 and greater than 30, respectively. On further examination of the demographics and predictive results of the study it was determined that with the addition of four more factors of "Bang" to STOP-Bang (BMI, age >50 years, neck circumference, gender), the sensitivity was improved to 92.9% and 100% for AHI scores greater than 15 and greater than 30, respectively. To predict the risk of OSA using STOP, if two or more of the questions are answered "yes," then the risk is considered high. Utilizing STOP-Bang, a total of five "yes" responses indicate a high risk of having OSA. This tool is ideal in the preoperative setting due to its ease of administration and brevity. All three of these tools, the Berlin Questionnaire, ASA Checklist, and Stop Questionnaire, were compared and validated in a surgical population by Chung and associates [79]. The Berlin and ASA checklist, like the STOP Questionnaire, were demonstrated to have a moderately high level of sensitivity for detecting OSA in the preoperative population. They also found that if the preoperative patients had a high risk of OSA by either the STOP questionnaire or ASA checklist, or had an AHI score greater than 5, the patients were more likely to develop postoperative complications. An additional modification of the STOP-Bang model has been to look at preoperative serum bicarbonate levels in addition to the questionnaire, and some authors have suggested this increases the specificity of the questionnaire [80].

The ASA Task Force on Perioperative Management of Patients with Obstructive Sleep Apnea published guidelines in 2006 with a subsequent update in 2014 [81]. Included in the guidelines is a 12-question checklist assessing for OSA preoperatively focusing on invasiveness of surgery, type of anesthesia, and requirement of postoperative opioids. In the study by Chung and associates discussed above [79], the sensitivity of the ASA OSA checklist was 72–87%, depending on the AHI score. The ASA guidelines and the CHEST Perioperative Management of Obstructive Sleep Apnea 2010 Guidelines recommend considering the use of a preoperative screening tool for OSA; however, they acknowledge a wide variance in sensitivity, specificity, and predictive values of the models [82]. It is important to note that identification of OSA preoperatively, and subsequent interventions targeting the prevention of OSA-related complications, has not clearly been demonstrated to improve morbidity or mortality perioperatively.

Hepatic Risk Assessment Tools

It has long been appreciated that patients with liver disease have increased perioperative morbidity and mortality. While this has been demonstrated for patients with many different types of liver dysfunction (including acute hepatitis, alcoholic hepatitis, and fulminant liver failure), most of the evidence comes from patients with cirrhosis. This is of relevance as the number of patients with cirrhosis has increased due to improved long-term survival, shifting practice patterns in the era of liver transplantation, increased incidence during the hepatitis C epidemic, and newer treatment options for hepatitis C virus [5, 83]. Furthermore, many patients with cirrhosis are referred for surgical evaluation at one point during their chronic illness. An oft-cited previous estimation was that 10% of patients with liver disease underwent surgery during their final 2 years of life, when their liver disease was least compensated [84].

Much of evidence utilizing risk models to predict surgical risk in patients with cirrhosis comes from single-center retrospective series, which is true of all the studies cited in this section. Nevertheless, the data are strengthened due to the consistency of some of the published literature. The Child-Turcotte score was the first model used for this purpose. Initially described in 1964 to estimate risk of patients undergoing portosystemic shunt placement [85], the model has subsequently been applied to other surgical groups. Points are assigned for ascites, encephalopathy, bilirubin, albumin, and nutritional status and then added into a total score to stratify patients into Child-Turcotte class A, B, or C. Pugh modified this classification with the replacement of prothrombin time for nutritional status in a 1973 publication detailing a series of patients undergoing esophageal transection for varices, and this modified system is the one currently in use (Table 2.5) [86].

Among the retrospective series demonstrating a correlation between Child-Turcotte-Pugh (CTP) class and postoperative outcomes, one of the most important is a 1984 series of 100 consecutive patients with cirrhosis (predominantly alcoholic) undergoing non-shunt open abdominal surgery [87]. Mortality during the postoperative period was 10%, 31%, and 76%, respectively, for CTP class A, B, and C patients. Similarly, postoperative mortality was 10%, 30%, and 82%, respectively, for CTP class A, B, and C patients

Table 2.5 Child-Turcotte-Pugh scoring system

Child-Turcotte-Pugh scoring system			
–	Points		
	1	2	3
Ascites	None	Easily controlled	Poorly controlled
Encephalopathy	None	Grade I or II	Grade III or IV
Bilirubin (mg/dL)	<2	2–3	>3
Albumin (g/dL)	>3.5	2.8–3.5	<2.8
PT (sec > control) or INR	<4 <1.7	4–6 1.7–2.3	>6 >2.3
–	Classification		
–	A	B	C
Total points	5–6	7–9	10–15

Data from: Pugh et al. [86]

undergoing non-shunt abdominal surgery in another series of 92 patients (48% of whom had alcoholic cirrhosis) in 1997 [88]. While these were both smaller cohort studies, the nearly identical findings of the two studies done more than 10 years apart are striking.

While CTP classification has proven useful for predicting surgical risk, a variety of criticisms have been applied to the classification [89]. The score and its chosen variables were empirically derived and do not factor data such as serum creatinine and sodium values that have subsequently been found to have a strong association with mortality in patients with cirrhosis. Two of the variables – ascites and hepatic encephalopathy – involve subjective interpretation with limited inter-operator reliability. These clinical variables specifically limit the accuracy of classifications assigned in retrospective series, including those used to link CTP class to surgical risk.

Another model that predicts perioperative mortality is the Model for End-Stage Liver Disease (MELD) score. The MELD score was first developed in 2000 to predict mortality following elective transjugular intrahepatic portosystemic shunts (TIPS) for refractory ascites or recurrent variceal bleeds [90]. In addition to the limits of the CTP classification listed above, a specific limitation in the setting of TIPS is that many patients are class C and the CTP classification cannot discriminate among them. The MELD score accurately predicted mortality following TIPS, and the authors hypothesized it may have prognostic utility in other clinical scenarios in patients with cirrhosis. A 2001 publication demonstrated that the MELD score accurately predicted 3-month mortality of patients hospitalized for hepatic decompensation, outpatients with noncholestatic cirrhosis, patients with primary biliary cirrhosis, and unselected "historical" patients from the 1980s [91]. Given its wide applicability, the MELD score was felt to meet the need of an improved means to prioritize cadaveric liver transplantation, and in February 2002, the United Network for Organ Sharing (UNOS) implemented the score as the predominant criterion for allocation [92]. This replaced the prior system that was based largely on waiting time. The standard formula now in use is as follows:[1]

$$\begin{aligned}\text{MELD score} = {} & 3.78 \times \log_e(\text{bilirubin in mg/dL}) \\ & + 11.2 \times \log_e(\text{INR}) + 9.57 \\ & \times \log_e(\text{creatinine in mg/dL}) + 6.43\end{aligned}$$

In this setting of widespread use, the MELD score was subsequently studied to predict risk in nontransplant nonshunt surgery. In 2005, Northup and coworkers studied 140 patients and developed a rule of thumb that held true for both abdominal surgeries and for the total surgical population (which included patients undergoing orthopedic, spinal, cardiac, vascular, and urologic surgery): 30-day postoperative mortality increased by approximately 1% per increase in MELD point for MELD scores 5% to 20% and 2% per increase in MELD point beyond 20, beginning with a 5% risk at a MELD score of 5 [93].

A subsequent study of 772 patients with cirrhosis undergoing orthopedic, cardiac, and abdominal surgery (other than laparoscopic cholecystectomy) also found the MELD score to effectively predict surgical risk. 30-day postoperative mortality was 5.7%, 10.3%, and 25.4%, respectively, for MELD scores of 7 or less, 8 to 11, and 12 to 15 [5]. This study is also one of the studies that have recently evaluated the use of ASA class to predict surgical risk in patients with cirrhosis. In multivariable analysis, the increase in mortality for patients with ASA class IV versus lower classes was equivalent to the same increase in mortality that would be predicted had the patient held a MELD score 5.5 points higher. The median survival of the ten patients with ASA class V (all of whom underwent emergency surgery) was only 2 days.

In considering surgical risk in a patient with cirrhosis, it is important to realize that other variables not addressed by the above risk models are predictive of operative risk. Type of surgery significantly impacts risk. In particular, portosystemic shunt placement and orthotopic liver transplantation are better tolerated than other abdominal procedures [88]. Regarding patient-specific factors, preoperative sepsis and emergency surgery have been identified as independent risk factors in several studies [87, 88].

Venous Thromboembolism Risk Assessment Tools

The term venous thromboembolism (VTE) comprises both in situ deep venous thrombosis (DVT) and pulmonary embolism (PE). The annual incidence of VTE in the United States is nearly 600,000, and PE is thought to cause more than 100,000 deaths per year in the United States [94]. The increased risk of VTE in surgical patients is well documented. Randomized controlled trial data comparing different types of pharmacologic VTE prophylaxis to placebo in general surgery patients suggest that patients receiving placebo have a DVT rate of about 20%, a PE rate of 1.6%, and a fatal PE rate of 0.9% [95]. The rates of confirmed DVT are even higher in patients undergoing general surgery for cancer and in patients undergoing major orthopedic surgery [95]. Patients undergoing orthopedic surgery as a group are often considered to be at *high risk* for VTE events, and it is worth asking if risk stratification is even necessary in this

[1]Bilirubin and creatinine values less than 1.0 mg/dL are rounded to 1.0 mg/dL. Patients with a creatinine greater than 4.0 mg/dL or who have received dialysis twice in the past week receive a creatinine value of 4.0 mg/dL. The score is rounded to the nearest integer.

surgical population. However, orthopedic surgeries comprise a wide range of procedure complexity, length of surgery, length of immobility, and length of hospital stay. Additionally, the consequences of potential bleeding when pharmacologic VTE prophylaxis is used are different in, for example, spinal surgery and total knee replacement surgery. Consideration of both the type of surgery and patient risk factors holds value in assessing patient risk for VTE. Beyond categorizing orthopedic surgery patients as *high risk* for VTE, we hope the below models studied in a variety of surgical populations may be helpful for better understanding additional risk factors and predictors of VTE risk. Clearly, effective strategies to assess which patients might be at highest risk for VTE are of strong interest to patients and practitioners alike.

Understanding of the risk factors involved in VTE development dates to Rudolf Virchow [96], who proposed that thrombosis was linked to three underlying etiologies: vascular endothelial damage, stasis of blood flow, and hypercoagulability of blood. Further attempts to identify specific risk factors were made in the 1970s and 1980s with Nicolaides and Irving [97] proposing a multivariable model to predict development of DVT and Janssen and coworkers [98] expanding on this model to determine the relative risk of DVT compared to a healthy control population. Salzman and Hirsh [99] subsequently sought to risk stratify patients as low, moderate, or high risk, based on the expected frequency of VTE in the absence of thromboprophylaxis.

However, the first widely accepted predictive tool was developed by Joseph Caprini and colleagues in the 1980s and 1990s [100]. These authors interviewed 538 patients undergoing surgery upon admission to a hospital. A worksheet with 20 risk factors was used to compute a total risk score. Most risk factors were assigned a weighting factor of one; however, select risk factors were weighted higher (age 61–70 years old = 2 points, age over 70 years = 3 points, and previous history of DVT or PE = 3 points). Patients were then categorized by their total point score, as either low risk (1 point or less), moderate risk (2–4 points), or high risk (5 or more points). The authors found 34.5% of patients to be at low risk, 48.5% at moderate risk, and 17% at high risk. They identified significant positive correlations with the previously noted risk factors and models, although less so with the Janssen model [98], which had used a very large number of risk factors with variable weights.

Caprini continued to refine this model further, adding a fourth "highest-risk" category [101], and over time health systems adopted the model for patient management. One of the first large health systems to apply the Caprini tool clinically was the University of Michigan Health System (UMHS). In 2010, Bahl and coworkers analyzed UMHS data, with a total of 8216 general, vascular, and urologic surgery inpatients from the UMHS National Surgical Quality Improvement Program discharged between 2001 and 2008. Patients were analyzed using 30-day postoperative mortality and morbidity outcomes, including VTE. A cumulative VTE risk score and risk level was assigned to each patient by using an internally developed, previously validated retrospective risk scoring method based on the Caprini model, using data from various electronic sources. Most (52.1%) of the study population was characterized as highest risk (risk score 5 or more); 36.5% were categorized as high risk (risk score 3–4), 10.4% as moderate risk (risk score 2), and 0.9% as low risk (risk score 0–1). The rates of VTE in those groups, respectively, were 1.94%, 0.97%, 0.70%, and 0%. Only the difference between highest- and high-risk groups rose to the level of statistical significance. Within the highest risk group, the authors found accelerated growth in the rates of VTE development with higher cumulative risk scores, noting a statistically significant difference between risk scores of 7 or 8 when compared to scores greater than 8. Through logistic regression analysis, the authors identified recent pregnancy, recent sepsis, malignancy, history of VTE, and central venous access as individual factors with a statistically significant association with VTE and age, varicose veins, and positive Factor V Leiden as factors with marginally significant associations. Based on these findings, the authors concluded that their risk scoring system, based on the Caprini risk assessment model, was a valid method for identifying patients at risk for VTE 30 days after surgery. The study was limited by the fact that it used a retrospective risk scoring method that was unable to identify all potential risk factors. Another limitation was the single institution nature of the analysis, perhaps limiting its generalizability. Finally, the 30-day cutoff for analysis potentially underestimated VTE prevalence, and the authors observe studies demonstrating VTE risk beyond 30 days following hospitalization [102].

Several other models aimed at assessing risk for VTE were developed concurrently with the Caprini model. The "Kucher method" was borne out of a study of 2506 medical and surgical patients hospitalized between 2000 and 2004 and examined the impact of an electronic medical record alert on VTE prophylaxis and VTE rates. Eight common risk factors (cancer, prior VTE, hypercoagulability, major surgery, advanced age, obesity, bed rest, and use of hormone replacement therapy or oral contraceptives) were used to formulate a risk profile for venous thromboembolism; each factor was weighted according to a point scale. The first three factors listed were given a score of 3, the risk factor of major surgery was given a score of 2, and the others were given a score of 1. Patients were randomized into two groups: (1) those who had an electronic alert to physicians noting a given patient's VTE risk and (2) a control group where no alert was issued. Following required acknowledgment of the electronic alert, the physician had to choose whether to withhold prophylaxis or order mechanical and/or pharmacologic pro-

phylaxis. The computer alerts significantly increased the rates of prophylaxis orders (14.5% in the control group versus 33.5% in the intervention group). The primary endpoint of DVT or PE at 90 days occurred in 4.9% of patients in the intervention group and 8.2% of patients in the control group – a relative reduction of 41%. Limitations of this study include an overrepresentation of medical patients (82.7% of the study population) and a high prevalence of cancer (79.7% of the study population) [103].

The Padua Prediction Score is a model that built upon the Kucher method. This model was developed by incorporating some additional risk factors for VTE and modifying the assigned scores of select factors, with the goal of including all conditions for which thromboprophylaxis would be recommended. Factors assigned a score of 3 were active cancer, previous VTE, reduced mobility, and known thrombophilic condition. Recent trauma/surgery was assigned a score of 2. Heart/respiratory failure, acute myocardial infarction/ischemic stroke, acute infection and/or rheumatologic disorder, obesity, and ongoing hormonal treatment were all assigned a score of 1. The authors used this model in a prospective cohort study of 1180 patients who were sorted based on whether they were low risk (risk score < 4, which included 711 patients) or high risk (risk score ≥ 4, which included 469 patients). Attending physicians were not aware of their patients' risk categories; the patients in the high-risk group were analyzed as to whether adequate VTE prophylaxis was administered, which was defined as administered within 48 hours of admission and covering 80% of the hospital stay, with daily administration of predetermined doses of heparin, enoxaparin, dalteparin, nadroparin, or fondaparinux. Of patients in the high-risk group, 186 (39.7%) received adequate thromboprophylaxis per the authors' definition. In the high-risk group, 4 of the 186 patients receiving adequate prophylaxis (2.2%) developed VTE in a period of 90 days following admission, compared with 31 of the 283 patients (11.0%) not receiving adequate prophylaxis (HR 0.13, 95% CI 0.04–0.40, $p < 0.001$, following adjustment for differences in risk factor prevalence between the groups). In the low-risk group, only two patients (0.3%) developed VTE – one of whom received prophylaxis (out of the 52 low-risk patients receiving prophylaxis) and one of whom did not (out of 659 in the low-risk group who were not prophylaxed) – yielding a HR of 32.0 for VTE in high-risk patients without prophylaxis versus low risk (95% CI 4.1–251.0, $p = 0.001$). The authors noted that the Padua Prediction Score categorized twice as many patients as high risk compared with the Kucher score: 9 of the 37 VTE events occurred in high-risk patients that, using the Kucher score, would have been categorized as low risk. The authors acknowledge that their study was limited by a few factors, including the lack of randomization of whether high-risk patients received thromboprophylaxis (though such randomization would have ethical implications) and the lack of testing for VTE unless signs or symptoms of VTE were present [104].

Rogers and coworkers used data from the Patient Safety in Surgery Study (PSS) to develop and test a risk model for VTE, with the goal of having a method to assess preoperative risk of VTE in patients undergoing general and vascular surgery. Data were taken from the PSS study, which involved over 180,000 patients from 142 Veterans Affairs and private-sector hospitals. These patients were randomly divided in half for derivation and validation cohorts. The authors collected information about patient risk factors and postoperative adverse events. VTE was used as the primary dependent variable, with patient characteristics, risk factors, laboratory values, and relative value unit (RVU) of the procedure – a surrogate for surgical complexity – as potential independent variables. Using bivariate analysis, the authors were able to identify 31 preoperative risk factors and 13 preoperative test results associated with VTE; with logistic regression, they narrowed this list down to 15 factors having independent association with VTE. Risk score points were assigned to each risk factor based on odds ratios. A score of less than 7 conferred "low risk," a score of 7–10 was considered "medium risk," and a score of greater than 10 was considered "high risk." These scores were tested in the validation arm and were found to be highly predictive of VTE risk [105].

Another model used to assess 90-day risk of VTE events in postsurgical patients was published by Pannucci and coworkers in 2014. This study was part of the Michigan Surgical Quality Collaborative (MSQC), a partnership among 52 Michigan hospitals, Blue Cross Blue Shield of Michigan, and the Blue Care Network; it was limited to analysis of inpatient surgeries of a nonemergent nature. Like the Rogers [105] study, a large group of over 10,000 patients were randomized to derivation and validation cohorts, this time in a 2:1 ratio. Through multivariate regression-based analysis, the authors identified seven variables – age ≥ 60, BMI ≥ 40 (each 1 point), male gender (2 points), sepsis/septic shock/SIRS, personal history of VTE (each 3 points), family history of VTE (4 points), and current cancer (5 points). The risk model was found to predict 90-day VTE rates well in the validation cohort [94].

There is no clear consensus on which risk model may be the preferred model to use for patients undergoing surgery. One study compared the Caprini and Pauda risk assessment models and suggested that the Caprini model was more accurate for identification of patients at risk for VTE, but this study was limited to medical patients only [106]. While the American College of Chest Physicians guidelines on VTE prevention acknowledge the importance of individualized risk stratification, more rigorous work needs to be done to identify the best method to do so [107].

Renal/Genitourinary Risk Assessment Tools

The potential risk of surgery to precipitate a decline in renal function, or acute kidney injury (AKI), is well documented. Many studies have focused on the risks associated with cardiac and vascular surgery. Up to 30% of patients undergoing cardiac surgery experience AKI, with approximately 1% of such patients requiring hemodialysis [108]. Evidence shows smaller, but still significant, risks for patients undergoing major noncardiac surgery to develop AKI, defined here as a significant reduction in calculated creatinine clearance to less than 50 mL/min. Such AKI occurs in about 1% of patients undergoing noncardiac surgery, based on a study of 15,000 patients with no baseline renal dysfunction [109]. Due to the high costs and morbidity associated with AKI, it is crucial to identify which patients might be most vulnerable.

A major study in this area was published in 2009, using data from the previously discussed ACS-NSQIP dataset. Using year 2005–2006 data of over 150,000 cases, Kheterpal and coworkers sought to identify the incidence of AKI following general surgery and the risk factors involved in its development. They developed a risk index based on these factors. Patients undergoing vascular, cardiac, urologic, ophthalmologic, podiatric, and obstetric procedures were excluded, as were patients undergoing outpatient surgeries and patients with preexisting AKI. In all, over 75,000 patients met inclusion criteria; randomization of this group was distributed to 75% in a derivation cohort and 25% in a validation cohort. About 1% of these patients developed postoperative AKI (defined by ACS-NSQIP as an increase in creatinine >2 mg/dL from baseline or a change in renal function requiring renal replacement therapy). Using multivariate logistic regression, the authors found the following to be independent predictors of AKI: age ≥ 56, male sex, emergency surgery, intraperitoneal surgery, diabetes mellitus requiring oral or insulin therapy, active congestive heart failure, ascites, hypertension, and mild or moderate preoperative renal insufficiency (creatinine >1.2 mg/dL). A risk index was developed with classes based on the number of risk factors present – class I (0–2 risk factors), class II (3 risk factors), class III (4 risk factors), class IV (5 risk factors), and class V (≥6 risk factors) – and was formulated using score groupings based on statistically significant ($p < 0.001$) differences in AKI development between consecutive classes (class I vs. class II, class II vs. class III, etc). There was excellent concordance when the risk assessment model was applied to the validation cohort. Some potential factors that might precipitate AKI were not accounted for this risk index, including hydration preoperatively and intraoperatively, use of nephrotoxic agents, variations in postoperative medical management, and facility type or region. However, the eightfold increase in 30-day all-cause mortality makes this a useful model for predicting AKI perioperatively. Kheterpal's Acute Kidney Injury Risk Factors and Association Preoperative Classification are listed in Box 2.2 and Table 2.6 [110].

Box 2.2 Perioperative Acute Kidney Injury Risk Factors

- *Acute kidney injury risk factors*
  - Age ≥56 year
  - Male sex
  - Active congestive heart failure
  - Ascites
  - Hypertension
  - Emergency surgery
  - Intraperitoneal surgery
  - Renal insufficiency – mild or moderate[a]
  - Diabetes mellitus – oral or insulin therapy

Data from: Bellomo et al. [111].
[a]Preoperative serum creatinine value >1.2 mg/dl.

Of note, recent analysis suggests that the ACS-NSQIP criteria for AKI potentially exclude many patients with postoperative renal decline, thereby underestimating the prevalence of AKI as a complication of surgery. Two current consensus definitions for AKI are RIFLE and KDIGO. The RIFLE (Risk, Injury, Failure, Loss, and End-stage kidney) model stratifies patients into multiple grades of potential and actual AKI, with a doubling of baseline creatinine or GFR decrease >50% defining AKI [111]. The KDIGO (Kidney Disease: Improving Global Outcomes) guidelines expands AKI criteria to changes in serum creatinine as small as 0.3 mg/dL [112]. When applied to a group of over 47,000 patients in the University of Florida Data Repository, 37% of patients met RIFLE criteria for AKI, whereas only 3% were classified with AKI using ACS-NSQIP criteria. Hospital and 90-day mortality rates were significantly increased in patients meet-

Table 2.6 Acute kidney injury preoperative risk classification

Preoperative risk class	Acute kidney injury incidence % (*n*)[a]	Hazard ratio (95% confidence interval)[a]
Class I (0–2 risk factors)	0.2 (66)	
Class II (3 risk factors)	0.8 (104)	4.0 (2.9–5.4)
Class III (4 risk factors)	1.8 (144)	8.8 (6.6–11.8)
Class IV (5 risk factors)	3.3 (118)	16.1 (11.9–21.8)
Class V (6+ risk factors)	8.9 (129)	46.3 (34.2–62.6)

Data from: Bellomo et al. [111]
[a]Based on data from derivation Cohort, $N = 57{,}080$ patients

ing criteria for AKI regardless of the predictive model used, suggesting clinically significant AKI may be a more prevalent problem than the ACS-NSQIP model suggests [113].

Another common postoperative problem is acute urinary retention. Postoperative urinary retention (POUR) often necessitates urinary catheterization for bladder decompression [114], which in turn has the potential to lead to infectious complications, sepsis, and prosthesis failure [115]. Past studies of patients undergoing orthopedic surgery have found variable rates of POUR – ranging from 8% to 53% [116–118]. However, these studies tended to have high numbers of elderly patients and were restricted to arthroplasty procedures, so the rates of POUR may have been overestimated. In one retrospective study of a large unselected cohort, the overall rate of POUR following orthopedic surgery was found to be much lower – about 2.3%. These results were based on a need for postoperative catheterization and urologic consultation as opposed to objective data such as sonography – so the rates of POUR in this study may have, conversely, been underestimated. The authors identified age, male sex, joint replacement surgery, hypertension, and diabetes as risk factors for POUR [119]. While the actual rates of POUR may be difficult to quantify, AKI is often associated with a cascade of additional complications, and an effective tool to predict which patients might be at greatest risk is important.

In male patients, the International Prostate Symptom Score (IPSS) was developed by the American Urological Association (AUA) to characterize the severity of lower urinary tract symptoms in men. It asks men to rate, on a scale of 0–5, the severity of seven symptoms (incomplete emptying, frequency, intermittency, urgency, weak stream, straining, and nocturia) [120]. Several studies have highlighted the utility of IPSS as a predictive tool for postoperative urinary retention in orthopedic patients. One study analyzed the IPSS scores and prevalence of POUR in 95 male patients undergoing total knee or hip arthroplasty. The patients were categorized based on the severity of their baseline urinary symptoms – mild (IPSS 0–7), moderate (IPSS 8–18), and severe (IPSS >18). A total of 32 patients (33.68%) developed POUR. Only 11 of 62 (17.7%) of patients with mild symptoms developed POUR, but 15 of 27 (55.5%) of those with moderate symptoms and 6 of 6 (100%) of those with severe symptoms experienced it; these differences were statistically significant [121]. Another study of 118 male patients undergoing total hip and knee replacements, using slightly different categorizations based on IPSS (mild = 0–7, moderate = 8–19, severe = 20–35), showed similar findings. The mean IPSS score in the 45 patients who developed POUR (8.73) was more than double that of the 73 patients who did not (4.315, $p < 0.01$). While only 27.7% of patients with mild symptoms developed POUR, 100% of patients with severe symptoms did [122]. While the absolute number of patients included in these studies is small, the scoring system seems particularly adept at predicting POUR in patients with baseline severe IPSS scores. An obvious limitation of both studies is the restriction to male patients. While studies do demonstrate male sex as a significant risk factor for the development of POUR [119], it is not a complication exclusively limited to male patients, and model development to predict POUR in female patients is needed.

Additional Models

Several other models have been studied in nonsurgical patient populations, or cardiac surgery patient cohorts only, and have been used by clinicians to further estimate patient-specific surgical risks. While potentially useful, it is important to note these have not been well validated prospectively in noncardiac surgical populations. The Papworth Bleeding Risk Score has shown some promise as a useful tool for predicting bleeding in patients undergoing cardiac surgery, specifically in patients who are deemed low risk for perioperative bleeding [123–126]. The HAS-BLED score has also been shown to be a useful tool in patients undergoing cardiac surgery [127]. The APACHE II score, as noted above, has been particularly useful for estimating risks in acutely ill patients, especially those in ICU settings. While this latter model has not been studied prospectively for perioperative outcomes, this score may still be of use in perioperative decision-making [128].

Discussion and Summary

The ideal preoperative screening tool should be efficient, easy to use, and applicable to a variety of surgical procedures and patient types and utilized in both elective and urgent surgeries. It is neither practical nor necessary for all patients undergoing surgery to be evaluated with every one of the above risk assessment tools. In deciding how to best select the appropriate screening tools to utilize, one must keep in mind the system in which patients are receiving care, incidences of common medical complications of planned surgical interventions, and the patients' most active medical conditions predisposing to such complications.

For centers where resources for primary care or anesthetic consultations may be limited, a validated nursing-conducted screening questionnaire may be a useful tool to help prioritize which patients necessitate a formal preoperative consultation prior to the day of surgery [34]. For patients for whom quick bedside assessments are needed prior to urgent surgery, models such as the RCRI, ASA Physical Status, and S-MPM may be particularly useful. For patients undergoing elective surgery who have multiple comorbidities and

patients aiming to be more involved in the decision-making process, models like the ACS NSQIP tool may prove more appropriate. Different clinical care systems will find the various models useful at different screening points preoperatively. Ideally, the tool(s) selected for use will be implemented with sufficient time for a well-formulated multidisciplinary treatment plan to be formulated before surgery. It is important to share the knowledge gathered through these tools preoperatively with the rest of the treatment team caring for patients throughout the perioperative phase. In the experience of the authors, anecdotally we find that the mere sharing of knowledge of increased risks for potential complications leads team members to demonstrate heightened vigilance and improved communication for appropriate care.

Some additional principles are important to follow. Risk scores should not be used in isolation for clinical decision-making, but rather to complement it. Universal screening with any one specific test (laboratory tests, electrocardiograms, etc.) is also not advisable, and multiple professional societies support this contention [66, 129–131]. Strict cut-off risk scores or particular laboratory values are also not generally advised and should always be used in clinical context. Several key themes can be seen in the above models, including the importance of functional status. Functional status assessed preoperatively, through, for example, the Duke Activity Status Index, is particularly predictive of a variety of complications [132]. Conversely, patients with excellent functional status, even those with multiple comorbidities or those undergoing higher-risk surgeries, often fair quite well with surgery. An additional theme noted in the above risk models is the common incorporation of the ASA Physical Status Classification System into many models. Anesthesiologists have long recognized the value of this tool, and it may serve as an efficient bedside tool for quickly gauging risk.

Cardiac risk assessments have traditionally been a cornerstone of perioperative risk assessments, and generally, some comment about cardiac risks is expected. However, depending on an individual's risk factors, cardiac complications might not be the most common or even most worrisome complications to anticipate. There will be no *one-size-fits-all* approach in utilizing the above risk models but rather an assessment by the clinician of the most active medical conditions, as well as the most concerning medical complications that one does not want to miss.

Underlying the use of risk models is the implication that their use will alter management, either by addressing modifiable risk factors or, for factors that may not be modifiable, by helping to determine if surgery itself carries too high of a risk for a given patient. While limited, there is some evidence that goal-directed interventions can reduce morbidity, mortality, and length of stay [133–136]. It is clear, however, that more studies are needed in this area.

In summary, risk assessment tools utilized preoperatively can be useful adjuncts to a comprehensive care plan for patients undergoing surgery. Utilized appropriately, they can help patients make informed decisions and clinicians better anticipate postoperative outcomes. Risk assessment tools most commonly include patient-specific medical comorbidities as risk factors. Other important variables that influence perioperative outcomes include the type of surgery and anesthesia, functional status, and important systems and quality issues.

Summary Bullet Points

- Risk assessment models can be used to predict the likelihood of perioperative complications and the potential sources of risk in patients undergoing orthopedic surgery.
- Risk assessment models most commonly use patient-specific medical comorbidities as risk factors.
- Clinical decision-making can be guided by, but should not rely solely upon, risk modeling.
- The American Society of Anesthesiologists Physical Status Classification, while partly subjective, is a consistently strong predictor of perioperative outcomes in several models.
- The ACS-NSQIP model offers the unique ability to engage patients directly by providing a color-coded risk assessment profile to share with patients.

Case Study

A 72-year-old woman with long-standing rheumatoid arthritis (RA) is seen for preoperative consultation 14 days prior to planned revision total knee replacement. The diagnosis of RA was made 30 years ago and followed an early aggressive course necessitating trials of numerous medications, chronic steroid dependence, and multiple joint replacements. Indeed, over the years, she has undergone total knee, hip, shoulder, and elbow replacements as well as arthroplasty of several metacarpal phalangeal joints. Relative quiescence of the disease process has been achieved over the last 15 years with methotrexate, etanercept, and moderate dosages of prednisone. Recently, pain in her left knee, replaced 17 years earlier, has increased due to prosthetic loosening. Consequently, she has become more functionally impaired requiring a walker to ambulate, hence the proposed revision surgery.

Her past history has not been limited to her rheumatic disease with the development of progressive mitral insufficiency and congestive heart failure for which she underwent mitral valve replacement 4 years previously. In association with her

valvular disease, she has experienced episodes of atrial fibrillation with intermittent episodes of bradycardia; the diagnosis of sick sinus syndrome was made, and a cardiac pacemaker implanted 2 years ago. On echocardiography, her left ventricular function is mildly impaired with an ejection fraction of 45%. Cardiac stress testing done 1 year ago did not suggest ischemia. Additional comorbidities include hypertension, hyperlipidemia, and stage three chronic kidney disease (creatinine 1.8 mg/dL, GFR 48). Further, she has suffered a mild stroke in association with the atrial fibrillation, though recovered fully. Pulmonary function studies demonstrate moderate restrictive lung disease. Pulmonary nodules with interstitial changes have been present for several years, likely related to her RA and possible amiodarone therapy taken earlier in her course. In addition to her medication for RA, she is on multiple other medications including metoprolol, diltiazem, atorvastatin, and rivaroxaban.

On physical examination she looks chronically ill and demonstrates the joint stigmata of severe RA. Her blood pressure is normal (119/69), her pulse irregularly irregular at a rate of 66, and there is no jugular venous distension; mild dry bibasilar crackles are noted on pulmonary examination and prosthetic heart sounds emanating from her mitral valve are audible. There is no pedal edema. An EKG reveals atrial fibrillation and a left bundle branch block which is unchanged from a tracing dating back over 5 years.

How Does One Approach the Perioperative Risk Assessment of Such a Patient?

The multifactorial nature of this patient's risk for surgery is self-evident and can be approached in several ways. With her multiple comorbidities, the perioperative risk calculus is complex; however given her underlying cardiac disease, the heart seems a logical place to start. With problems in multiple (valvular, conduction, myocardial) domains of cardiac function, the evaluation of her cardiac risk must first include a consideration of her potential for coronary artery disease. The perceived risk is premised not only on the presence of traditional risk factors (hypertension, hyperlipidemia) but also the patient's long-standing RA, its associated inflammatory nature significantly augmenting the risk of atherosclerosis [137]. Despite her cardiac problems, when the RCRI criteria are applied, this patient's risk for postoperative cardiac complications appears surprisingly favorable (2.4%), a judgment premised on the presence of only two RCRI risk factors (heart failure, prior stroke), the other four (high risk surgery, ischemic heart disease, diabetes mellitus, serum creatinine >2.0) being absent or not established. Yet clinical experience and judgment suggest this risk to be an underestimate, an unease arising from concerns about her potential for coronary disease.

The ACS-NSQIP assessment tool seems ideally suited for such a patient. NSQIP, which views perioperative risk through a wide-angled lens, provides a much more robust construction of a patient's vulnerabilities. Inputting this patient's variables into this risk calculator [39] demonstrates an increased risk across a span of common complications, predicting a 10% probability of a serious postoperative event, and an above average risk in all categories. Broad-based models such as the NSQIP methodology are therefore useful not only to physicians but also to the patient providing risk estimates for a range of possible adverse outcomes. Employed in this fashion, the preoperative physician or surgeon might highlight to this patient her elevated risks for noncardiac complications including the need to return to the operating room, thromboembolic events, wound infection, or pneumonia. For comparison to other predictive models, the patient's overall 30-day NSQIP mortality is estimated at approximately 1%; by comparison the SORT model predicts 0.85% 30-day mortality in this patient. Further her NSQIP risk for the development of AKI is 1%, and 1.8% by Kheterpal's Acute Kidney Injury model. Her risk of developing pneumonia by NSQIP is estimated at above average, specifically 1%. By comparison the Gupta Postoperative Pneumonia Risk Model predicts a rate of 2.23%. So it can be readily seen that such assessments could be setting a patient's expectations for surgery and aid in their preoperative decision-making.

Several other important issues are not directly addressed by the above risk models. For instance, issues pertaining to anticoagulation are relevant: how to manage factor Xa inhibitors in relation to surgery, how to best prevent surgery-related venous thromboembolic events in this patient, and how to prevent those related to her mitral valve replacement. In addition she is on several immunosuppressant medications. While methotrexate can be continued preoperatively [138], prednisone and etanercept do increase the risk of perioperative infections, and a recommendation to hold versus continue these medications requires a balance of such risks against managing her disease activity. Etanercept should be held for one full dosing interval (1 week) prior to surgery, based upon the estimated half-life of this medication. While "stress-dose" steroids have been historically overutilized, depending on her daily prednisone dosing, she may also require supplemental steroid dosing perioperatively, due to possible suppression of her endogenous adrenal function. Perioperative beta-blocker therapy is a discussion unto itself; note that the strongest recommendation for administering beta-blocker therapy perioperatively exists for those patients already on beta-blocker therapy [66]; thus in this case the continuation of metoprolol is indicated. Limited data also exist for beneficial effects of continuing statin therapy in the perioperative period [139–141], notably in patients undergoing vascular surgery. Extrapolating this potential benefit, the continuation of atorvastatin is also recommended.

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3 The Prevalence of Disabling Musculoskeletal Conditions and the Demand for Orthopedic Surgery in the Twenty-First Century

Anas Saleh and Charles N. Cornell

Objectives

- To document the prevalence of musculoskeletal diseases which require hospitalization and often surgical treatment
- To present the typical outcomes of surgical treatment of musculoskeletal conditions
- To present the risk and incidence of complications associated with surgical care of musculoskeletal conditions

Key Points

- The majority of hospitalizations and indications for surgery for musculoskeletal conditions result from degenerative diseases of the spine and major lower extremity joints.
- Spinal surgery, which follows careful selection criteria, typically results in pain relief, improved function, and improved quality of life which is maintained over long-term periods of observation.
- Complications following spinal surgery are affected by the age of the patient, anatomic location of disease, and the surgical approach. Older patients with preexisting comorbidities, posterior approaches to the cervical spine, and anterior approaches to the thoracolumbar spine are associated with higher risks of postoperative complications.
- Rapid growth in the demand for total hip and total knee arthroplasty has occurred over the past decade reflecting aging of the population as well as the success and safety of these procedures.
- Morbidity and mortality following total hip replacement (THR) and total knee replacement (TKR) are rare, and the incidence of complications and death has decreased over time. Thromboembolic events have been reduced with adoption of routine prophylaxis protocols.
- Myocardial infarction occurs in approximately 3% of patients, and stroke in 0.5% and patients over 70 years of age appear to be at greater risk.

Introduction

Musculoskeletal conditions are among the most disabling and costly conditions affecting the American population. As the US population rapidly ages, musculoskeletal impairments will increase. By the year 2030, the number of individuals in America over the age of 65 will double, with people above 85 years of age constituting the fastest-growing segment of our society [1]. Similar demographic changes are predicted for Europe. Bone and joint disorders account for more than one half of reported conditions in people over the age of 50 and are the most common cause of pain and disability. In 2011 53% of the US population was considered to have musculoskeletal disorders or diseases [1].

The economic impact of musculoskeletal disease is enormous. The projection of direct costs of the medical care required to treat musculoskeletal conditions from 2002 to 2004 was $510 billion, or 4.6% of our nation's gross domestic product (GDP). Indirect costs resulting from lost wages due to inability to perform one's job added another $331 billion, or 3.1% of GDP [1]. From 1998 to 2011, these costs were estimated to have increased 105%. Advances in the care

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of patients with musculoskeletal diseases that mitigate the long-term suffering and economic impact of these conditions and help these patients return to full and active lives are clearly the goal for all physicians involved in their care.

The majority of hospitalizations and indications for surgery for musculoskeletal conditions result from degenerative diseases of the spine and major lower extremity joints. The aims of this chapter are to review the current incidence of degenerative disorders of the spine that lead to reconstructive spine surgery and to review the incidence of complications resulting from spine surgery as well as the incidence and prevalence of osteoarthritis of the hip and knee leading to the frequency of total hip and total knee arthroplasty procedures. The frequency of complications following these procedures will also be reviewed.

Incidence of Degenerative Disorders of the Spine

Lumbar spine disorders are more common than cervical spine disorders, but combined they represent one of the most frequent reasons for physician visits and hospitalization. The majority of patients presenting with back pain are in the age group between 18 and 64 years of age [1]. In many of these cases, patients lose work days compounding the financial and societal impacts of the problem.

Lower back pain is the most frequently reported single site of pain in the back. In 2004, between 30% and 40% of people in the USA report experiencing low back pain in a previous 3-month period [2, 3]. Overall, about one in two persons report experiencing back pain at least once a year, which is a greater rate of pain than that reported for hips, knees, or upper limbs (Fig. 3.1). Degenerative disk disorder of the spine is the most common disease entity associated with lower back pain. In 2004, lumbar disk disorders, including disk degeneration and herniation, comprised 27% of hospitalizations and were seen most frequently among persons aged 45–74. In 2011 52 million US citizens visited a physician for evaluation and treatment of low back pain [1]. Although cervical/neck pain is less common than lower back pain, it is still a very common reason for physician visits, accounting for 1.5% of all health-care visits. Both low back pain and neck pain are found more commonly among females.

Incidence of Spine Procedures

Nonsurgical intervention is usually the preferred initial treatment for back pain. Spine surgery may be indicated in cases of severe intractable pain that causes significant disability.

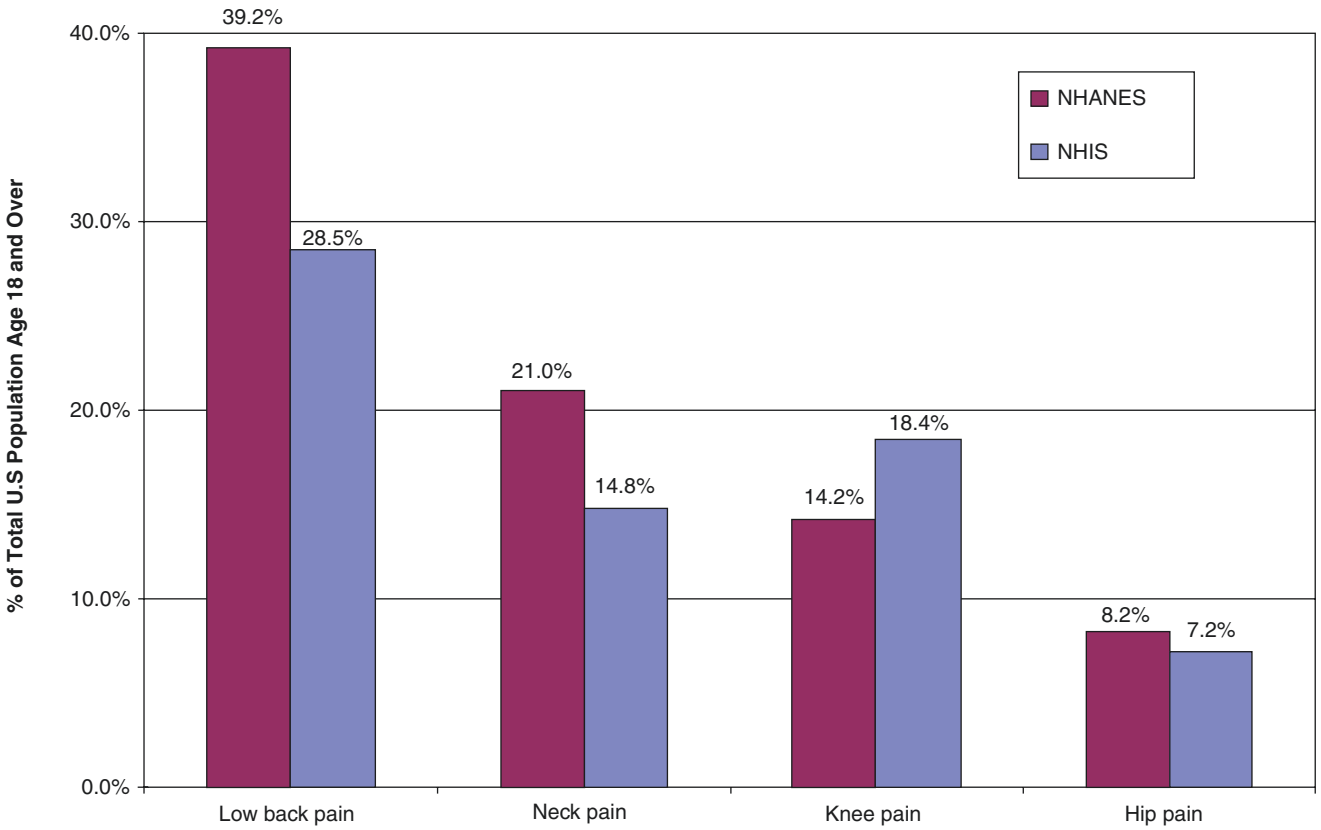

Fig. 3.1 Prevalence of self-reported joint pain by site for persons aged 18 and over in two national health surveys, USA 1999–2005. *NHANES* National Health and Nutrition Examination Survey, *NHIS* National Health Interview Survey. (Used with permission of AAOS from Jacobs [91])

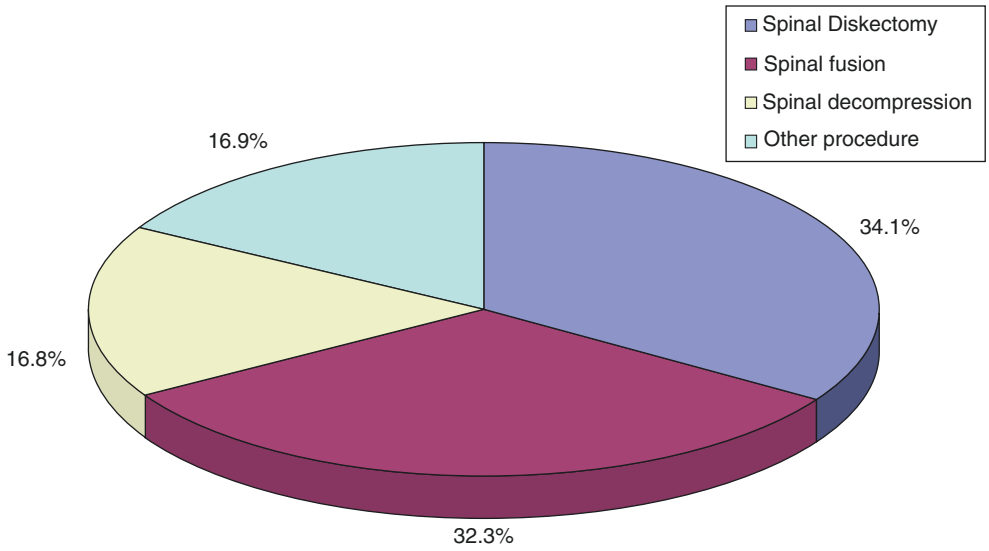

Fig. 3.2 Select spine procedures as a proportion of all spine procedures, USA 2004. (Used with permission of AAOS from Jacobs [91])

The three most frequently performed spine procedures in 2004 were diskectomy, spinal fusion, and spinal decompression (Fig. 3.2).

Spinal diskectomy was the most common spine procedure in 2004, performed in 325,300 cases accounting for 34% of all spine procedures. As of 2011 this figure has risen to 370,000 cases [4]. Approximately 60% of these diskectomies were performed for degenerative disease of the lumbar spine (disk degeneration, spondylosis, spinal stenosis) and around 30% for cervical indications. The most common primary diagnosis in cervical spine fusion cases is cervical disk displacement (19%).

Spinal fusion, the second most common spine procedure performed in 2004, may be done in conjunction with spinal decompression. In 2004, over 307,800 spine fusion procedures were performed (32% of all spine procedures). That number has risen to 450,000 for 2011. Lumbar spinal fusion rates have increased more rapidly than the rates of cervical or thoracic fusion [5, 6], and in 2004, the number of lumbar fusion procedures was higher than cervical procedures, accounting for 46% versus 41% of all fusion procedures. It should be noted, however, that rates of lumbar fusion vary dramatically among geographic regions, hospitals, and even between surgeons in the same hospital, probably due to the variation in consensus regarding the indications for and the outcomes of lumbar fusion [7]. Decompression procedures that are presumably performed for spinal stenosis were performed in 160,000 cases during 2004 and 170,000 by 2011 representing 17% of spine procedures.

The population of lumbar spine stenosis represents a growing public health challenge for spine surgeons around the world. The literature showed good outcomes after elective surgical management of lumbar stenosis and stable pain relief up to 10 years [8–10]. A recent observational cohort study sought to compare the improvement in patient self-reported quality of life after lumbar spine surgery (decompression alone or decompression and fusion) with the benchmark set by total joint arthroplasty [11]. With strict patient selection criteria and appropriate nonsurgical management, the results of this study showed excellent improvement in patient-reported quality of life after both decompression alone and decompression and fusion for lumbar stenosis. At 2 years after surgery, 85% and 80% of patients reported improved physical and mental quality of life questionnaires, respectively, which is comparable to that of total hip and total knee arthroplasties. Several studies have shown that the initial results of surgery, particularly regarding relief of leg symptoms, can be reasonably maintained (60–80%) in the long term with an approximate reoperation rate of 1–2% per year [10, 12–16].

The incidence of spinal fusion expressed as the number of procedures performed per 100,000 persons in the population has increased dramatically over the past 15 years. In 1998 the incidence was 85 per 100,000, which has risen to 122 per 100,000 in 2004. The likely explanations for this increase are advances in spinal instrumentation technology, improvements in the resolution of diagnostic imaging, and the broadening of indications for spine surgery. However, some of the increase must be attributed to the aging of the population with an accompanying increased incidence of spinal disorders as well as increased training in spinal surgery.

Incidence of Complications After Spine Surgery

Before reviewing the literature for incidence of complications in spine surgery, it is crucial to realize that reported incidence rates vary significantly due to several factors,

including: (1) definition and classification of complications, (2) study methodology, (3) surgeon-related factors, (4) procedure-related factors, and (5) patient-related factors.

Definition and Classification of Complications

Efforts to understand, report, and reduce complications in spine surgery have been hampered as a result of the lack of a meaningful and universally acceptable definition. The complex field of spine surgery has been a particularly challenging area for the development of a consensus to constructively define and classify complications. The term "complication" is typically used with an emphasis on events that occur intraoperatively or immediately after surgery. Some authors developed severity scores to better measure the severity of adverse events [17], whereas others used spine surgeon surveys that are validated through parallel assessment of patients undergoing spine surgery [18]. Several studies have graded complications as minor, moderate, or major [19–21].

Rampersaud and colleagues used the term "adverse events" to describe "any unexpected or undesirable event(s) occurring as a direct or indirect result of surgery" and defined a complication as a disease or disorder resulting from surgery that will change the expected outcome of the patient [22]. According to these definitions, 98 intraoperative adverse events out of 700 surgeries (14%) were reported, but only 23 of them resulted in acute postoperative clinical complications (3%). For example, a dural tear was reported in 58 cases, but after primary repair, only 8 patients continued to have CSF leak and headache. Therefore, a study investigating the incidence of CSF leaks may underestimate the incidence of dural tears, leading to conflicting incidence reports, and a false sense of security that overlooks protocols that could easily minimize or prevent these typically "inconsequential" adverse events. Unfortunately, the overall strength of the evidence to establish a standardized system for grading and defining complications in spine surgery is low indicating that further exploration and standardization are needed [23].

Study Methodology

Retrospective studies may underestimate actual complication incidence through the introduction of investigator recall bias [24, 25]. A disproportionate reliance on the memory of investigators and accuracy of medical records may lead to falsely low or high reported rates of complication. Also, the reliance on the International Classification of Diseases (ICD-9) codes to search complications and procedures compromises the quality of data. This method inherently limits the scope and therefore the incidence of complications. In addition, ICD-9 codes do not address the severity of complication. For example, Deyo and colleagues [26] retrospectively analyzed a statewide hospital discharge registry and compiled data on more than 18,000 hospitalizations over a 2-year period. The authors reported an overall complication rate of 10.3% for the surgical treatment of degenerative lumbar spine disease. However, since they used ICD-9 codes for identifying complications, the most frequently listed complications were unspecified or unclassified (2.5%); thus, it was impossible to gauge their severity. Moreover, ICD-9-CM codes were used to describe the surgical procedure, which do not provide more details about the procedures such as the number of levels, use of microsurgical techniques, or methods of arthrodesis.

One systematic review of spine surgery articles assessing complications of surgery indicated that retrospective reviews underestimate the incidence of complications. Overall, prospective studies reported a higher incidence of complications (19.9%) than did retrospective studies (16.1%, $p < 0.001$, OR 1.3) [19]. Moreover, duration of follow-up correlated with complication incidence, with longer periods of follow-up associated with an increased incidence of operative complications.

Surgeon-Related Factors

Due to the wide range of complication rates of spine surgery, some authors have questioned the effect of the surgeon's experience on complication rates. Wiese and colleagues compared the incidence of durotomy between surgeons who had performed 50–100 and those who performed >500 microdiskectomies and demonstrated a higher incidence of overall complications rate in the former group (10.7% versus 2.2%, $p < 0.001$) [27]. However, another recent retrospective study of more than 108,000 cases performed by members of the Scoliosis Research Society (SRS) did not find a difference in the incidence of durotomy depending on surgeon experience, with active members presumably having more and candidate members presumably having less experience [28]. Although not specifically assessed, the vast majority of candidate members of the SRS are fellowship-trained spine surgeons dedicated to the treatment of complex spinal conditions. This may contrast with the less experienced group described in the study of Wiese and coauthors.

Procedure-Related Factors

Complications also vary in severity and incidence among the different surgical approaches and anatomical regions. For example, in cervical spine surgery, the posterior

approach-related complications include pain from injury to paraspinal muscles, epidural hematoma, and neurological injury, whereas dysphagia, recurrent laryngeal nerve damage, and rarely tracheal or esophageal perforation can occur with an anterior approach [29, 30]. As for the different anatomical regions of the spine, one meta-analysis indicates that thoracolumbar procedures have significantly more complications than in cervical procedures (17.8% versus 8.9%, $p < 0.001$) [19].

Overall complication rates in cervical spine surgery range from 0.1% to 19.3% and the mortality rates from 0.1% to 0.8% [23]. Although an anterior approach is associated with a greater incidence of dysphagia and hoarseness, the posterior approach, particularly posterior fusion procedures, has been consistently associated with greater incidence of complications and perioperative morbidity and nearly double resource utilization including hospital length of stay, inflation adjusted cost, and likelihood of discharge to an assisted-living facility [31–33]. A population-based analysis of 771,932 anterior cervical spine fusions from the National Hospital Discharge Survey (NHDS) showed an overall procedure-related complication rate of 7.23% in the period 1990–1994, 5.05% in 1995–1999, and 4.82% in 2000–2004 [34]. See Fig. 3.3. A reduction was seen for all organ-specific complications between 1990 and 2004, except for cardiac and respiratory. In-hospital mortality decreased from 0.93 to 0.2 and 0.18% in the time periods 1990–1994, 1995–1999, and 2000–2004.

In lumbar procedures, the overall complication rates range from 3.7% to 12.8% [23]. Reoperation rates range from 0.5% to 19% and are highest in fusion procedures. In general, fusion procedures appear to be associated with a higher overall rate of complication [26, 35]. The introduction of minimally invasive approaches and techniques does not appear to have reduced this higher complication risk when fusion accompanies decompression [36]. In a recent study, data collected between 1998 and 2006 from the National Inpatient Sample were analyzed to assess the incidence of perioperative morbidity and mortality in anterior, posterior, and anterior/posterior non-cervical spine fusion [37]. 261,356 admissions were identified during which a primary spine fusion procedure was performed. Of those, 77% were anterior, 14% were posterior, and 9% were anterior/posterior fusions. Procedure-related complications were more frequent among anterior/posterior spine fusions (23.8%) as compared to anterior (18.7%) and posterior (15%) spine fusion (Table 3.1). Also, the incidence of thromboembolic events was higher among anterior/posterior spine fusion patients. While anterior procedures in the cervical regions appear to be associated with fewer complications, this study indicates that this does not hold true for thoracic and lumbar regions of the spine. Procedures involving the anterior thoracolumbar spine are associated with higher morbidity and mortality, possibly due to the entry of abdominal and thoracic cavity and the proximity of vital organs. The highest rate of morbidity and mortality was seen in the anterior/posterior fusion

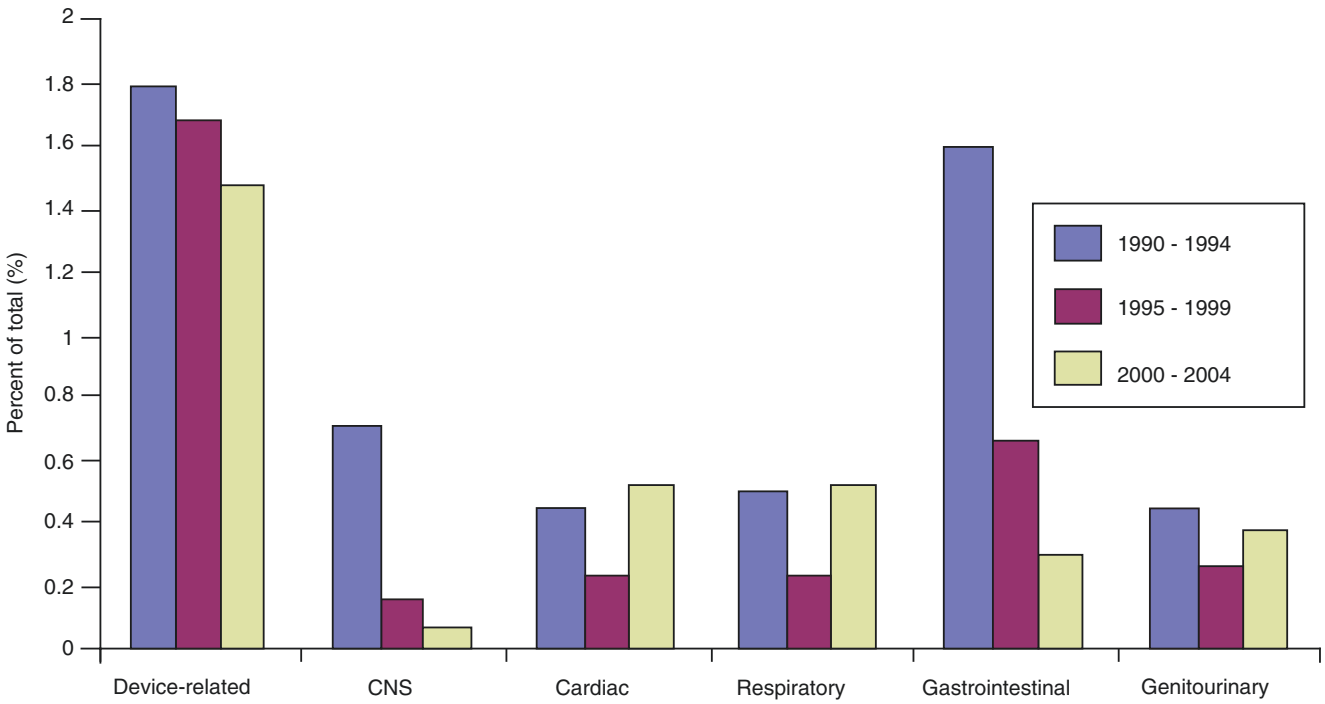

Fig. 3.3 Prevalence of procedure-related complications following anterior cervical spine fusion, United States 1990–2005. (Used with permission of Wolters Kluwer from Marwar et al. [92])

Table 3.1 Prevalence of procedure-related complications after non-cervical spine fusion, USA 1998–2006

Complication	Non-cervical spine fusion			
	Anterior, % (N = 36,224)	Posterior, % (N = 201,885)	Anterior/posterior, % (N = 113,991)	All procedures, % (N = 261,356)
Complications affecting specific body system				
Central nervous system	0.4	10.2	0.8	0.9
Cardiopulmonary	3.2	2.4	5.3	2.8
Gastrointestinal	4.8	2.1	5.6	2.8
Genitourinary	0.9	1.1	1.2	1.1
Other complications of procedure				
Postoperative shock	0.1	0.1	0.2	0.1
Hematoma	1.5	1.6	2.7	1.6
Postoperative infection	0.8	0.5	1.2	0.6
Thromboembolic events	0.9	0.7	1.3	1.2
Pulmonary embolism	0.3	0.3	0.5	0.5
Death	0.5	0.3	0.4	0.3

Used with permission of Wolters Kluwer from Memtsoudis et al. [37]
$p < 0.001$ between all approach types

patients, which can be explained by longer surgical times, more blood loss, and increased surgical complexity.

Medical complications that results from spine surgery are challenging to manage. A significant number of patients undergoing orthopedic surgery are elderly, predisposing them to several medical complications. The rates of cerebrovascular, cardiopulmonary, gastrointestinal, and genitourinary complications in the National Inpatient Sample from 1998 to 2006 were 0.9%, 2.8%, 2.8%, and 1.1%, respectively (Table 3.1) [37]. In another single-center prospective study of 248 consecutive patients undergoing spine surgery in 2008, the rates of specific medical complications were reported, including myocardial infarction (1.2%), pulmonary embolism (0.8%), cerebrovascular accident (0.4%), urinary tract infection (15.7%), pneumonia (2.0%), and death (0.8%) [21].

In the context of surgical complications after spine fusion, there has been an appreciation in the more recent spine surgery literature that frequent and occasionally catastrophic complications are associated with the use of recombinant human bone morphogenetic protein-2 (rhBMP-2). When it was first introduced in 2002, preliminary human trials for a variety of spinal fusion techniques found no adverse events associated with rhBMP-2 use [38, 39]. As the use of BMP increased, with 25% of all fusions utilizing BMP in 2006 [40], a series of studies reported serious complications associated with rhBMP-2 use, ranging from 10% to 50% depending on the approach [41]. These complications were associated with swelling of neck and throat leading to compression of airways and/or neurological compromise in the cervical region and radiculitis, ectopic bone formation, and osteolysis in the lumbar region. Epstein and Chrastil separately summarized multiple adverse events attributed to the use of BMP/Infuse in spine surgery [36].

Mortality rates among patients undergoing cervical and lumbar spine surgeries are <1%. Though death events are rare in the cervical and lumbar spine, they are more common after thoracic spine surgery with rates as high as 64% among vertebroplasty patients and 7.5% among balloon kyphoplasty patients [23].

Patient-Related Factors

Another factor leading to the increased variation in reported complications is the patient population. As would be expected in any surgical procedure, the risk of postoperative complications in spine surgery increases in older patients and patients with multiple comorbidities such as cardiac disease and diabetes [20, 31, 33, 42–44]. Patients with preoperative neurologic abnormalities are at higher risk of developing postoperative complications (OR, 2.88; CI, 1.42–5.83) [30, 31]. Complication rates are also affected by the primary diagnosis for the patient. Reoperation rates have been reported to be higher in patients diagnosed with herniated disk disease [45].

Prevalence of Osteoarthritis and Related Reconstructive Surgeries of the Hip and Knee

Osteoarthritis (OA) is the most common type of arthritis, frequently affecting knees and hips, leading to progressive damage to the cartilage and other joint tissues. In a study conducted in Johnston County, NC, the prevalence of knee and hip OA among adults aged 45 years and older was 17% and 10%, respectively [46, 47]. The prevalence is higher in older age groups and among women but lower in Hispanics (16.5% versus 22% for non-Hispanics and African Americans) [48].

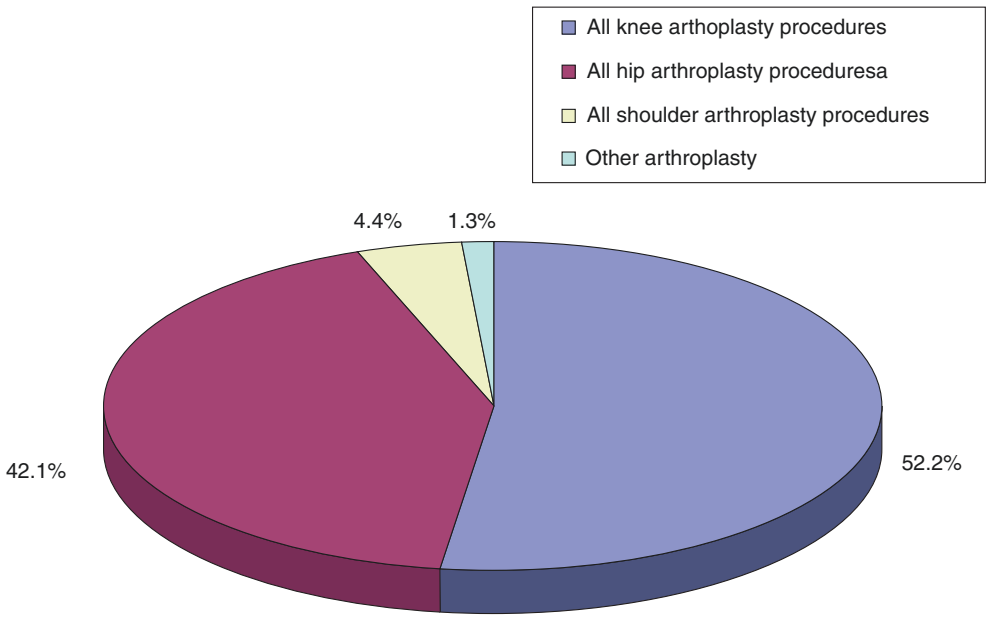

Fig. 3.4 Arthroplasty procedures by type, USA 2004. (Used with permission of AAOS from Jacobs [91])

Although a great variety of medications have been used to address the pain and disability associated with osteoarthritis, total joint arthroplasty remains the definitive treatment for advanced, symptomatic joint destruction. Total joint arthroplasty is indicated for arthritis and a variety of other rheumatic conditions, but osteoarthritis remains the principle diagnosis in 82.5% of total hip replacements and 96.8% of all total knee replacements [2]. The hip and the knee are the most frequently replaced joints. In 2004, hip and knee replacements accounted for 95% of the 1.07 million arthroplasty procedures performed (Fig. 3.4). Over 232,000 primary total hip arthroplasty procedures were performed (25% of all arthroplasty procedures), and over 454,000 primary total knee arthroplasty procedures were performed (48%). By 2011 these figures increased to 300,000 total hip arthroplasties and 650,000 total knee replacements. Females undergo 62% of all total joint replacement procedures, and they undergo total knee arthroplasty twice as frequently as men reflecting the greater prevalence of knee OA in females than in males. In terms of age distribution, 60% of primary and revision total hip and knee arthroplasty procedures are performed in patients above 65 years of age.

Data on the survival of total joint replacement implants come from several national registries. Survival rates vary depending on several factors such as patient age, implant type, and the use of cement versus cementless fixation. Analysis of the Finnish arthroplasty registry showed that for patients older than 55 years of age, the survival rates of total hip implants ranged from 92% to 98% at 10 years, 86–93% at 15 years, and 77–82% at 20 years, with the endpoint defined as revision due to aseptic loosening of the implant [49]. Revision rates represent a crude measure of implant failure, as the need for revision operation is probably the only quantifiable event that forces the patient to return to hospital. In a systematic review, national registries were analyzed to identify revision rates after total hip and knee arthroplasties [50]. After primary hip replacement, a mean of 1.29 revisions per 100 observed component years was seen. Similarly, after total knee replacement, 1.26 revisions per 100 observed component years were seen. As for the patient's subjective measure of health-related quality of life, several studies compared patients undergoing total joint replacement with a reference health group with a similar age and sex distribution [51, 52]. Patients that benefited from joint replacement had remarkably improved physical and psychosocial scores from 1 to 2 years postoperatively, and these scores were maintained up to 3–5 years.

The annual number of total joint replacement has been increasing from 1991 to 2011. There has been a threefold increase in total knee replacements, while the annual number of total hip replacements doubled. These increases in joint arthroplasty utilization outnumber the increase in incidence of OA as would be expected from an aging population. This probably represents broadening of the indications of arthroplasty procedures due to their safety and durability. There has been a parallel increase in the total estimated cost of performing total knee replacement procedures from $5.4 billion in 1998 to $14.3 billion in 2004. Projected growth model for hip and knee replacement procedures estimates that by 2030 there will be over 570,000 primary total hip replacements performed annually in the USA and nearly 3.5 million primary total knee replacements, with associated need for manpower, operating room capacity, and health care costs [1].

The Incidence of Complications After Total Knee and Total Hip Arthroplasty

General Trends

Despite the efficacy of total knee and total hip arthroplasty, complications can occur which result in poor functional outcomes for a subset of patients. In light of the prevalence and the increasing trends of these procedures, documenting and reviewing associated adverse events remains a priority to help optimize patient care. The National Hospital Discharge Survey (NHDS) was analyzed from 1990 to 2004 in order to elucidate temporal changes in demographics, hospital stay, in-hospital complications, and mortality of patients undergoing primary total knee [53] and total hip [54] arthroplasty during a 15-year study period in the USA. Frequencies of procedure-related complications over time were identified using ICD-9-CM diagnosis codes. In their analysis, the authors created three 5-year periods to simplify temporal changes (1990–1994, 1995–1999, and 2000–2004).

A total of 3,830,420 patients had undergone total knee arthroplasty from 1990 to 2004 based on the NHDS [53]. As expected, there was an increased utilization of primary total knee arthroplasty, increased proportion of younger patients, as well as an increased number of comorbidities among patients. Despite an increase in the rate of comorbidities, the procedure-related complication rate decreased from 12% during the period from 1990 to 1994 to 7% during the period from 2000 to 2004 (Table 3.2). Approximately half were categorized as organ-specific. Although mortality rate declined from 0.50% during the period from 1990 to 1994 to 0.21% during the period from 1995 to 1999, mortality increased slightly to 0.28% during the period from 2000 to 2004. Despite progressive increase in the use of thromboprophylaxis during these time periods, the authors did not find a concomitant decline in mortality or pulmonary embolism during the most recent time period (2000–2004). In fact, the rate of pulmonary embolism increased from 0.29% in the period from 1995 to 1999 to 0.52% in the period from 2000 to 2004 (Table 3.2). An increase in patient comorbidities could explain recent trends toward increasing rates of pulmonary embolism and overall mortality.

As for total hip arthroplasty, 2,288,579 patients were identified between 1990 and 2004 [54]. The trends were generally similar to those in total knee arthroplasty. The utilization of this procedure has increased, with the highest percent of increase in the group of patients aged between 45 and 64. Also, there has been an increase in the number of comorbidities, with hypertension being the most common comorbidity occurring in nearly half of all patients in the most recent time period studied (2000–2004). Nevertheless, procedure-related complications and adverse events decreased over the study period, from 15% in the period from 1990 to 1994 to 9% in the period from 2000 to 2004 (Table 3.3). In-hospital mortality rate remained low and slightly decreased (0.33% in 1990–1994 to 0.29% in 2000–2004). Fortunately, the incidence of pulmonary embolism has decreased from 0.46% to 0.26%, which is reassuring as much effort and creation of practice guidelines have been devoted to reduction of these thromboembolic events. Since 2010 after passage of the Affordable Care Act, a database of hospital readmissions has been maintained [55].

Specific Complications: Medical

As the prevalence of hip and knee osteoarthritis increases with increasing age, more of total joint replacement procedures will be performed in patients with some degree of cardiac, pulmonary, cerebral, renal, and hepatic disease.

Table 3.2 Prevalence of procedure-related complications in patients undergoing total knee arthroplasty, USA 1990–2004

	Total knee arthroplasty							
	1990–1994 (N = 807,687)		1995–1999 (N = 1,204,109)		2000–2004 (N = 1,818,624)		1990–2004 (N = 3,830,420)	
Complications	n	% of total	N	% of total	n	% of total	n	% of total
Complications affecting specific body system								
Central nervous system	143	0.02	3180	0.26	2405	0.13	5758	0.15
Cardiopulmonary	24,923	3.09	31,041	2.57	31,888	1.75	87,852	2.29
Gastrointestinal	9224	1.14	13,159	1.09	16,096	0.89	38,479	1.01
Genitourinary	12,188	1.51	13,554	1.13	11,611	0.64	37,353	0.98
Other complications of procedure								
Postoperative shock	396	0.05	71	0.01	129	0.01	596	0.02
Hematoma	11,017	1.36	18,403	1.53	14,400	0.79	43,820	1.14
Postoperative infection	2090	0.26	1748	0.15	4325	0.24	8163	0.21
Thromboembolic events	6876	0.85	6954	0.58	10,816	0.59	24,646	0.64
Pulmonary embolism	2872	0.36	3518	0.29	9546	0.52	15,936	0.42
Death	4028	0.50	2502	0.21	5094	0.28	11,624	0.30

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$p < 0.001$ between all time periods

Table 3.3 Prevalence of procedure-related complications in patients undergoing total hip arthroplasty, USA 1990–2004

	Total hip arthroplasty							
	1990–1994 (N = 603,528)		1995–1999 (N = 731,921)		2000–2004 (N = 953,130)		1990–2004 (N = 2,288,579)	
Complications	n	% of total	N	% of total	n	% of total	n	% of total
Complications affecting specific body system								
Central nervous system	140	0.02	1752	0.24	2025	0.21	3917	0.17
Cardiopulmonary	13,760	2.28	16,083	2.19	18,310	1.92	48,153	2.11
Gastrointestinal	7107	1.18	7521	1.03	7157	0.75	21,785	0.95
Genitourinary	9612	1.59	6345	0.87	8877	0.93	24,834	1.09
Other complications of procedure								
Postoperative shock	449	0.07	49	0.01	524	0.06	1022	0.05
Hematoma	8304	1.38	12,494	1.71	13,700	1.44	34,498	1.51
Postoperative infection	4160	0.69	4738	0.65	1884	0.20	10,783	0.47
Thromboembolic events	3588	0.60	1941	0.27	3082	0.32	8611	0.38
Pulmonary embolism	2787	0.46	2193	0.30	2481	0.26	7461	0.33
Death	1977	0.33	2446	0.33	2839	29.00	7262	0.32

Used with permission of Springer Nature from Liu et al. [54]
$p \leq 0.001$ between all time periods

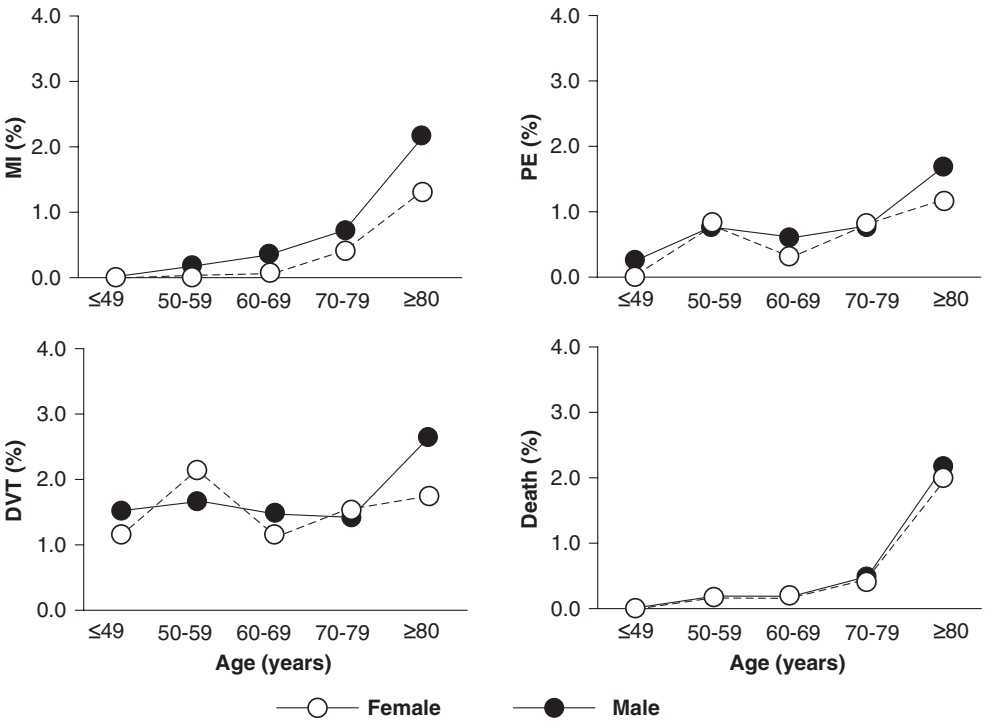

Fig. 3.5 Frequency of myocardial infarction (MI), pulmonary embolism (PE), deep venous thrombosis (DVT), or death within 30 days after primary total hip or knee arthroplasty according to age and gender. (Used with permission of Wolters Kluwer from Mantilla et al. [56])

Therefore, accurate knowledge of rates of perioperative medical complications in elderly population is valuable for the decision-making process when considering elective surgeries. Prospectively collected data from the total joint registry at the Mayo Clinic during a 10-year period (1986–1995) were used to identify patients with postoperative myocardial infarction, pulmonary embolism, deep venous thrombosis, or death within 30 days after total hip or knee arthroplasties [56]. Out of 10,244 patients, the overall rate of myocardial infarction, pulmonary embolism, deep venous thrombosis, and death were 2.2%, 0.4%, 0.7%, 1.5%, and 0.5%, respectively (Fig. 3.5). Eighty-three percent of myocardial infarction occurred within 3 days and were more frequent among males and patients aged 70 years or older. There was no difference in the overall adverse event frequency between total knee and total hip procedures, except for pulmonary embolism, which was highest in patients undergoing bilateral knee operations. A separate study investigated the incidence of perioperative stroke and found that 36 of 18,745 patients (0.2%) undergoing total hip and knee arthroplasties between 2000 and 2007 suffered a perioperative stroke [57]. Nine of the 36 patients died within the first year (25%). This study indicates that perioperative stroke is a rare but devastating complication of total joint arthroplasty.

Infection

Deep periprosthetic joint infection remains the most complex and costly complication. Even with a two-stage exchange implant-exchange protocol, failure rates in hips infected with methicillin-resistant organisms can reach as high as 21% [58]. A retrospective review of 8494 primary knee and hip arthroplasties reported a 0.5% overall rate of infection (30 of 5719 knees and 13 of 2775 hips) [59]. Obesity, diabetes, and younger age were identified as risk factors for infection in total joint arthroplasty. The rate of infection following total hip arthroplasty in the medicare beneficiary population from 1995 to 1996 was around 0.2% (137 of 58,521) for primary arthroplasty and 0.96% (124 of 12,956) for revision surgery [60]. A more recent review of discharge data from over 139,000 patients undergoing primary total hip arthroplasty between 1995 and 2005 reported a higher wound infection rate of 0.7% [61]. Total knee arthroplasty appears to have a slightly higher infection rate than total hip arthroplasty [59, 62, 63]. The exact reason for knees having higher infection rates remains subject to debate. Possible explanations include differences in vascular supply, skin thickness, joint motion, the use of tourniquet, and surgical approach.

Antibiotic prophylaxis is fundamental to the reduction of primary periprosthetic infection and has been shown by meta-analysis to reduce the relative risk of wound infection by 81% [64]. As *clostridium difficile* infections are thought to be an iatrogenic complication of antimicrobial prophylaxis [65], particularly third-generation cephalosporins, clindamycin, and ciprofloxacin, several investigators sought to identify the incidence of *Clostridium difficile* infections in patients undergoing total joint arthroplasty [66, 67]. These studies showed a very low incidence of 0.17%.

Although the risk of infection after total joint arthroplasty is small (<1%), considering the large number of arthroplasty procedures performed every year, and considering the mean cost of $68,053–$107,264 to treat each infection [68], this risk poses a significant economic burden.

Dislocation

Dislocation is one of the most common complications after total hip arthroplasty [69]. Reported rates of dislocation (≤90 days postoperatively) vary and range between 1.39 [61] and 3.2% [70] for primary arthroplasties. A comprehensive review published by Morrey in 1992 concluded that the long-term dislocation rate averaged 2.25% in the primary total hip arthroplasty setting [71]. As in infections, rates were higher after revision surgery reaching 8% [60]. Dislocations are also seen following total knee arthroplasties but to a lesser extent. A study of 2033 total knee arthroplasties in medicare beneficiaries from 2002 to 2004 reported only four cases of dislocation (0.2%) [72].

Venous Thromboembolism

Venous thromboembolism is a serious complication that is used by the government and insurance payers as a performance measure of hospitals as well as surgeons. Prior research showed that 35% of patients die within 1 year after the onset of venous thromboembolism [73]. In the Danish total hip registry from 1995 to 2006, 686 of 67,469 (1.02%) patients were rehospitalized due to venous thromboembolism at a median of 22 days following surgery. Ninety-three percent of the 67,469 patients received pharmacological prophylaxis with use of a low-molecular-weight heparin. The prevalence of symptomatic deep vein thrombosis was 0.7% (499 patients), and the prevalence of nonfatal pulmonary embolism was 0.3% (205 patients). The rate of mortality due to venous thromboembolism was 0.05% (38 patients). However, these rates are lower than previous reports as there are differences in study populations, study design, proportion of patients receiving pharmacological prophylaxis, and type and duration of treatment [74–77].

Periprosthetic Fractures

Periprosthetic fractures are fractures that occur in association with an orthopedic implant. These fractures are of great importance as one study has documented a higher risk of death after periprosthetic fracture as compared with a similar population of patients undergoing uncomplicated total hip arthroplasty [78]. Incidence of periprosthetic fractures about a total hip arthroplasty is variable, with multiple studies noting an incidence of 0.1–18% [79–82]. The incidence is greater after revision arthroplasty as revision surgery is associated with problems with bone stock about the components resulting from stress shielding, osteolysis, and other factors. Data from the Mayo Clinic joint registry revealed fracture rates of 1% after primary total hip arthroplasty and 4% after revision total hip arthroplasty [83]. The prevalence of periprosthetic fracture about total hip arthroplasty continues to increase with time as more and more patients are undergoing total hip arthroplasty, with more surgeries being performed on older patients who may be at an increased risk of falls [78, 83, 84]. Similarly, rates of periprosthetic fractures about total knee arthroplasty are increasing as the population ages [85, 86]. The incidence is 0.3–2.5% for primary total knee arthroplasty and up to 38% for revision [87–89].

Summary

As our population continues to age with a growing incidence of degenerative musculoskeletal disease, a large number of surgical procedures will be performed every year. Spine and total joint replacement procedures gained popularity with the increasing evidence of their long-term efficacy. Advances in the surgical techniques and perioperative care broadened sur-

gical indications, which paralleled the rapid growth of the elderly population suffering from degenerative diseases. Therefore, the increasing number of older individuals with multiple comorbidities opting for surgery is not necessarily accompanied by an increase in complication rates. Nevertheless, these complications constitute a large economic burden and a major challenge for orthopedic surgeons and physicians [90]. As such, accurate reporting of these complications and more cautious analysis of epidemiological studies are crucial to implement optimal medical and surgical management.

Summary Bullet Points

- As the population of the USA ages, the demand for orthopedic surgery for degenerative conditions has risen. Total joint replacement and spinal reconstructive procedures are highly successful, but success depends on proper surgical indications and technique.
- Complications following total joint replacement are rare. Thromboembolic events resulting in myocardial infarction, stroke, and pulmonary embolism are among the most common complications, but the incidence of these has fallen with adoption of routine prophylaxis.
- Patients of advanced age and/or with poorly controlled diabetes are at the highest risk of complications following elective orthopedic surgery.

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The Rheumatic Diseases: A Primer

4

Bella Mehta, C. Ronald MacKenzie, and Stephen Paget

Objectives

- To understand the importance and impact of these conditions on society and the health-care system
- To appreciate that such patients make up a significant proportion of an orthopedic practice
- To appreciate the protean nature of these disorders and their varied pathophysiology
- To understand the systematic approach to the differential diagnosis of these conditions presented
- To overview the diagnostic evaluation of systemic rheumatic diseases

Key Points

- Chronic rheumatic diseases represent a broad category of conditions that share a common feature: the destruction of cartilage and its consequences.
- While these conditions differ in their pathophysiology, the final common target is often the joint; hence, such patients frequently require orthopedic surgery.
- Classification of rheumatic diseases follows this organization: osteoarthritis; disorders of the synovium (rheumatoid arthritis), connective tissue diseases (systemic lupus erythematosus, antiphospholipid syndrome, systemic sclerosis, inflammatory disease of the muscle), spondyloarthritis (ankylosing spondylitis, psoriatic arthritis, enteropathic arthropathies, reactive arthritis, etc.), vasculitides (polymyalgia rheumatica/temporal arteritis, polyarteritis nodosa, microscopic polyangiitis, granulomatosis with polyangiitis, eosinophilic granulomatosis with polyangiitis, cryoglobulinemic vasculitis), metabolic bone disease (osteoporosis), crystal-induced arthropathies (gout, calcium pyrophosphate-associated arthropathy), infectious arthritis, sarcoidosis

Introduction

Estimates of the prevalence of arthritis and the rheumatic diseases in general make evident the enormous impact that these conditions have on the US populace and the health-care system in general. More than 21% of US adults (46 million people) currently report physician-diagnosed arthritis. The National Arthritis Data Workgroup, an impressive collaborative effort from the Centers for Disease Control and Prevention, the National Institutes of Health, the American College of Rheumatology, and the Arthritis Foundation, has published analyses that project an increase of physician-diagnosed arthritis to nearly 67 million people (an increase of 40%) by the year 2030 [1]. While the majority of this health burden arises as a consequence of osteoarthritis, the entire span of the rheumatic diseases, such as rheumatoid arthritis, psoriatic arthritis, juvenile arthritis, spondyloarthropathies, enteropathic arthritis, systemic lupus erythematosus, systemic sclerosis, and primary Sjogren's syndrome, contributes to the impact of this class of conditions. Already the leading cause of disability in the nation, the number of people with arthritis and arthritis-attributable limitation in activity is a serious public health issue. Such observa-

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tions highlight the importance of effective interventions and programs to reduce the impact (loss of productivity, costs of therapy) of these chronic diseases. Ultimately, orthopedic intervention is required in many of these individuals to address the main issues of palliation of pain, inflammation, and further structural damage and disability compromising one's quality of life. Factors such as an increased patient awareness of the benefits of surgery, improvements in surgical techniques, and the desire for an active lifestyle have, in concert with the increasing prevalence of chronic arthritis, fueled the growth in utilization of orthopedic surgery. The orthopedic perspective and contemporary estimates concerning the rates of total joint replacement and spine surgery have been extensively reviewed in Chap. 5. This chapter introduces the broader spectrum of the rheumatic diseases as viewed by the rheumatologist as such patients frequently require orthopedic intervention. Beginning with a review of the relevant pathobiology, a concise primer of the essential diseases is then presented.

Pathological Considerations

The elemental pathological process leading to orthopedic surgery is damage and gradual loss of the articular cartilage. However, all structures within the joint including the bones and connective tissue are affected. Osteoarthritis involves the joint in an asymmetric, localized pattern of involvement, with focal stress across the joint. This leads to misalignment and progressive alterations in load bearing relationships of the joint, resulting in the radiographic joint space narrowing and chronic joint damage. The structural changes occur in concert with biochemical abnormalities that ensue within the cartilage component, the underlying subchondral bone, joint capsule, and synovial membrane. Microscopically, biomechanical properties of the normal cartilage contain two main components: extracellular matrix (rich in type II, IX, and XI collagens and proteoglycans) and the chondrocytes lying within the matrix, responsible for maintaining homeostatic synthesis of the extracellular matrix components. The abnormal mechanical stress that occurs in OA causes alterations in chondrocyte metabolism and incites local inflammation by inducing synthesis of proteases, such as matrix metalloproteinase (MMP)-1, MMP-8, and MMP-13, and inflammatory mediators, such as interleukin (IL)-8, IL-6, prostaglandin E2, and nitric oxide [2]. The joint damage results from the metabolic imbalance due to accelerated cartilage degradation coupled with an insufficient reparative response. These processes incite localized tissue response consisting of inflammation of the joint lining and further loss of mechanical properties of the affected joint. Owing to the synthesis of metalloproteinases, there is gradual loss of the matrix components. Alterations of the proteoglycan content and structure then follow, and with continued deterioration in the cartilage and its load bearing capacity, stiffness and pain ensue, as nociceptive and proprioceptive receptors in the periosteum are activated due to the loss of the protective layer of the articular cartilage. Bone remodeling occurs in the underlying subchondral bone, causing sclerosis of the bone, formation of bone cysts, increased subchondral plate thickness, and reactive osteophyte formation at joint margins as a result of abnormal reparative process [3, 4].

Osteoarthritis is the most common cause of end-stage arthritis. Osteoarthritis may be primary, due to biochemical changes in the cartilage, or secondary to systemic disease affecting the cartilage, joint damage from pre-existing inflammatory joint disease, or trauma. It is a heterogeneous disease with various etiologies. Mechanical overload and imbalances lead to further cartilage degradation, processes that culminate in a failure of the mechanical functioning of the surrounding normal structures. Important adaptive responses such as subchondral sclerosis and osteophyte formation occur in response to joint overload, and, if chronically present, cyst formation in the sub-articular bone may also result. Over time the osteophytes or bone spurs will lead to restricted range of motion.

Inflammatory arthritis, by contrast, is a constellation of diseases that target the synovium. Included in this class of disorders are such conditions as rheumatoid arthritis (RA), psoriatic arthritis (PsA), and the spondyloarthritis (SpA). Common to all is the release of inflammatory mediators by the synovium leading to cartilage destruction. In contrast to osteoarthritis, mechanical overload is not a primary mechanism; as such, bone sclerosis or osteophyte formation is not seen. Rather, the inflammatory synovitis leads to a loss of cartilage matrix, marginal bony erosions, destruction of the joint capsule, and osteopenia.

Trauma is also an important cause of joint destruction. Post-traumatic arthritis is initiated by cartilage damage at the time of injury or by secondary mechanical imbalances that result from fractures of juxta-articular bone. Abnormal loading conditions will subsequently lead to a wear-and-tear form of cartilage damage.

Osteonecrosis, also termed avascular necrosis, is another entity that may lead to joint arthritis. In this process the blood supply to the bone is compromised leading to necrosis of the bone supporting the articular surface. The most commonly affected joints are the hip, shoulder, and knee. As the disease progresses, the necrotic bone may collapse leading to the loss of articular integrity and progressive cartilage deterioration. Avascular necrosis of the bone is frequently seen in patients with rheumatic disease who have been exposed to glucocorticoids.

Other conditions that may lead to joint damage include storage and deposition disorders (hemochromatosis, alkaptonuria, Wilson's disease, Gaucher's disease), crystal deposition diseases (chondrocalcinosis, gout), tumor (synovial chondromatosis), and infectious (post-septic) and bleeding disorders (hemophilia).

Owing to the prominent involvement of joints and the musculoskeletal system, patients who acquire these often multi-systemic conditions frequently require orthopedic intervention. The protean clinical manifestations of these diseases, coupled with important medication-related management considerations, present challenges encompassing the span of perioperative medical practice. Indeed such patients are amongst the most challenging encountered in the perioperative setting [5, 6].

Laboratory Considerations

The clinical laboratory can be of great help in the diagnosis of rheumatic conditions. Although laboratory tests are often informative, they are rarely definitive or diagnostic. Laboratory examinations must be used in conjunction with a complete history and physical and radiographic examinations. When diagnosing a disorder, one of the most important considerations is to determine whether the cause is inflammatory (and frequently systemic) or noninflammatory. Inflammatory rheumatic conditions often have an acute phase response. The acute phase response occurs after many other events, including infections, trauma, immune diseases, crystalline deposition, and malignancy. Acute phase reactants such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are often elevated in systemic rheumatic diseases. Moderate elevations of CRP occur in most connective tissue diseases (1–10 mg/dL). Very high levels are seen in bacterial infections and systemic vasculitis (15–20 mg/dL). Diabetes, obesity, and cigarette smoking can increase CRP levels in variable amounts. CRP levels fall when inflammation subsides. Since a substantial stimulus is required for CRP elevation, a normal value does not exclude an inflammatory process; thus, some clinicians prefer sending ESR concomitantly with CRP. Normal ESR is considered 0–15 for males and 0–20 for females. ESR increases with age; thus, "normal" levels are variable with levels up to 40 mm/hour common in healthy elderly people. Thus, ESR and CRP are neither diagnostic nor specific though are often helpful in evaluating patients with systemic inflammatory/rheumatic conditions. Table 4.1 summarizes useful laboratory tests for the diagnoses of rheumatic diseases. These may be used in conjunction with the signs and symptoms to diagnose rheumatic conditions. Each of these is explained in detail along with the description of the individual diseases.

Table 4.1 Useful laboratory tests for rheumatic diseases

Tests/autoantibodies	Comments
Erythrocyte sedimentation rate (ESR)	Acute phase reactant often elevated in systemic inflammatory diseases
C-reactive protein (CRP)	Acute phase reactant often elevated in systemic inflammatory diseases
Rheumatoid factor (RF)	Rheumatoid arthritis and sometimes detected in Sjogren's syndrome
Anti-cyclic citrullinated peptide (anti-CCP)	Rheumatoid arthritis
Anti-double-stranded DNA (ds-DNA)	Systemic lupus erythematosus (SLE)
Antinuclear antibodies (ANA)	Nearly 100% of SLE patients are positive Also seen in other connective tissue diseases
Complements – C3 and C4	Decreases in C3 and C4 levels precede SLE flares
Anti-Ro (SS-A)	Sjogren's syndrome
Anti-La (SS-B)	Sjogren's syndrome
Anti-Smith	SLE
Anti-RNP	SLE, mixed connective tissue disease (MCTD)
Lupus anticoagulant	Antiphospholipid syndrome
Anti-cardiolipin antibodies IgG, A, and M	Antiphospholipid syndrome
Beta-2 glycoprotein IgG, A, and M	Antiphospholipid syndrome
Anti-DNA topoisomerase I (Scl-70)	Scleroderma
Anti-centromere antibodies	Scleroderma
Anti-RNA polymerase III	Scleroderma
Anti-Jo 1, Anti-Mi2, Anti-SRP, etc.	Dermatomyositis/polymyositis
HLA–B 27	Spondyloarthritis
Anti- neutrophil cytoplasmic antibodies (ANCA)	Vasculitides
Angiotensin-converting enzyme (ACE)	Elevated levels detected in sarcoidosis

The Rheumatic Diseases

Box 4.1 presents a general classification of the rheumatic diseases.

Osteoarthritis (OA)

The most common form of arthritis, osteoarthritis, is a heterogeneous group of common conditions that share similar pathological and radiographic features, specifically loss of articular cartilage. It should be considered, furthermore, as an organ failure of the synovial joint, driven by a primary defect in any of its supporting tissues (ligaments, meniscus, subchondral bone, periarticular muscles, synovium, nerves, or articular cartilage) [7]. There are many pathophysiological mechanisms that alter

Box 4.1 Classification of the Rheumatic Diseases

- Osteoarthritis
- Disorders of the synovium
  - Rheumatoid arthritis
- Connective tissue diseases
  - Systemic lupus erythematosus
  - Antiphospholipid syndrome
  - Systemic sclerosis
  - Inflammatory disease of the muscle
- Spondyloarthritis
  - Axial spondyloarthritis
    - Ankylosing spondylitis
    - Nonradiographic axial spondyloarthritis
  - Peripheral spondyloarthritis
  - Psoriatic arthritis
  - Enteropathic arthropathies
  - Reactive arthritis
- Vasculitides
  - Polymyalgia rheumatica/temporal arteritis
  - Polyarteritis nodosa
  - Microscopic polyangiitis
  - Eosinophilic granulomatosis with polyangiitis (Churg-Strauss)
  - Granulomatosis with polyangiitis (Wegener's granulomatosis)
  - Cryoglobulinemic vasculitis
- Metabolic bone disease
  - Osteoporosis
- Crystal-induced arthropathies
  - Gout
  - Calcium pyrophosphate-associated arthropathy
- Infectious arthritis
- Other
  - Sarcoidosis

the relationship between mechanical factors and tissue response of the synovial joint; however, in the end stage of the disease, all components of the joint fail. An age-related disorder, OA, is uncommon before age 40 but increases in prevalence thereafter; by age 70 most people have pathological changes of OA though they may not be symptomatic. Other risk factors include female gender, ethnicity (>blacks), genetic predisposition, obesity (especially for knee OA), and trauma. The causes for primary or idiopathic osteoarthritis remain unclear. Research has focused on the intra-articular alterations involving the articular cartilage and subchondral bone, and considerable interest has arisen in the role of the neuromuscular unit involved in joint motion, stability, and proprioception as contributing to the progression and/or predisposition to the development of OA [8, 9].

Osteoarthritis is a focal disease not affecting all joints equally; even within a given joint, the involvement may be patchy and asymmetric. Its pathogenesis involves an incongruence between normal cartilaginous degradative and repair mechanisms, which results in a net loss of cartilage, bony hypertrophy, and osseous outgrowths (osteophytes). Its primary symptoms are use-related joint pain and stiffness (gelling). On physical examination, some combination of joint tenderness, crepitus, bony enlargement, malalignment, decreased range of motion, and joint effusion are usually noted. Treatment is mainly symptomatic (NSAIDs, analgesics, intra-articular injections). In those with severe disease, total joint arthroplasty is the only definitive therapy. Radiographic findings include asymmetric joint space narrowing, subchondral sclerosis and cystic change, and marginal osteophytes (bony spurs) (Figs. 4.1 and 4.2). When the

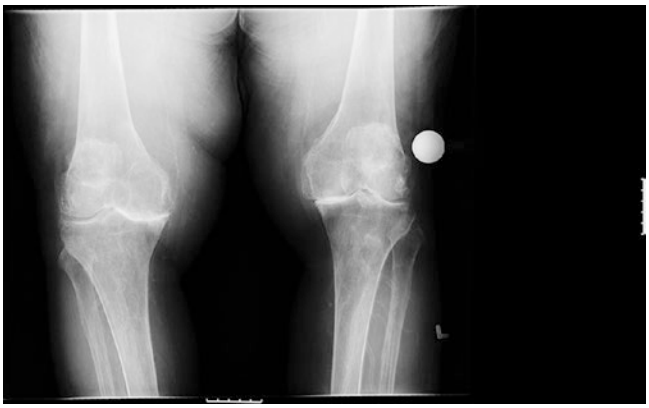

Fig. 4.1 Radiograph of osteoarthritis in knees: varus deformity. X-ray of bilateral knees showing advanced, severe bilateral degenerative arthrosis most marked in the medial compartments bilaterally where there is bone on bone apposition. Tricompartmental osteophytosis is present. Bilateral varus deformity is noted

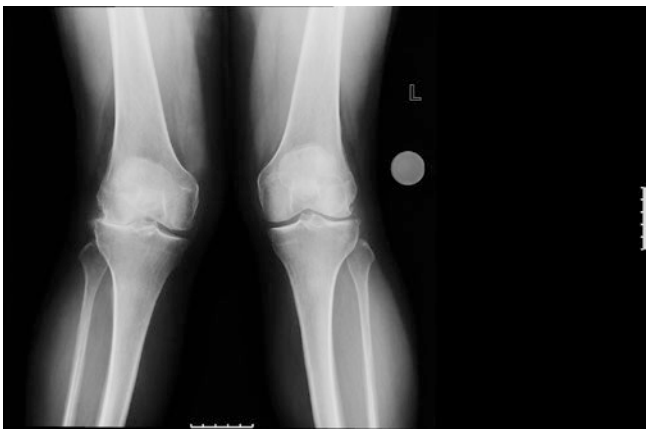

Fig. 4.2 Radiograph of osteoarthritis in knees: valgus deformity. *Right knee* shows severe degenerative arthrosis with tricompartmental osteophytes and lateral bone-on-bone apposition with marked valgus deformity. *Left knee* shows moderate degenerative arthrosis with small joint line osteophytes and moderate lateral compartment narrowing with valgus deformity

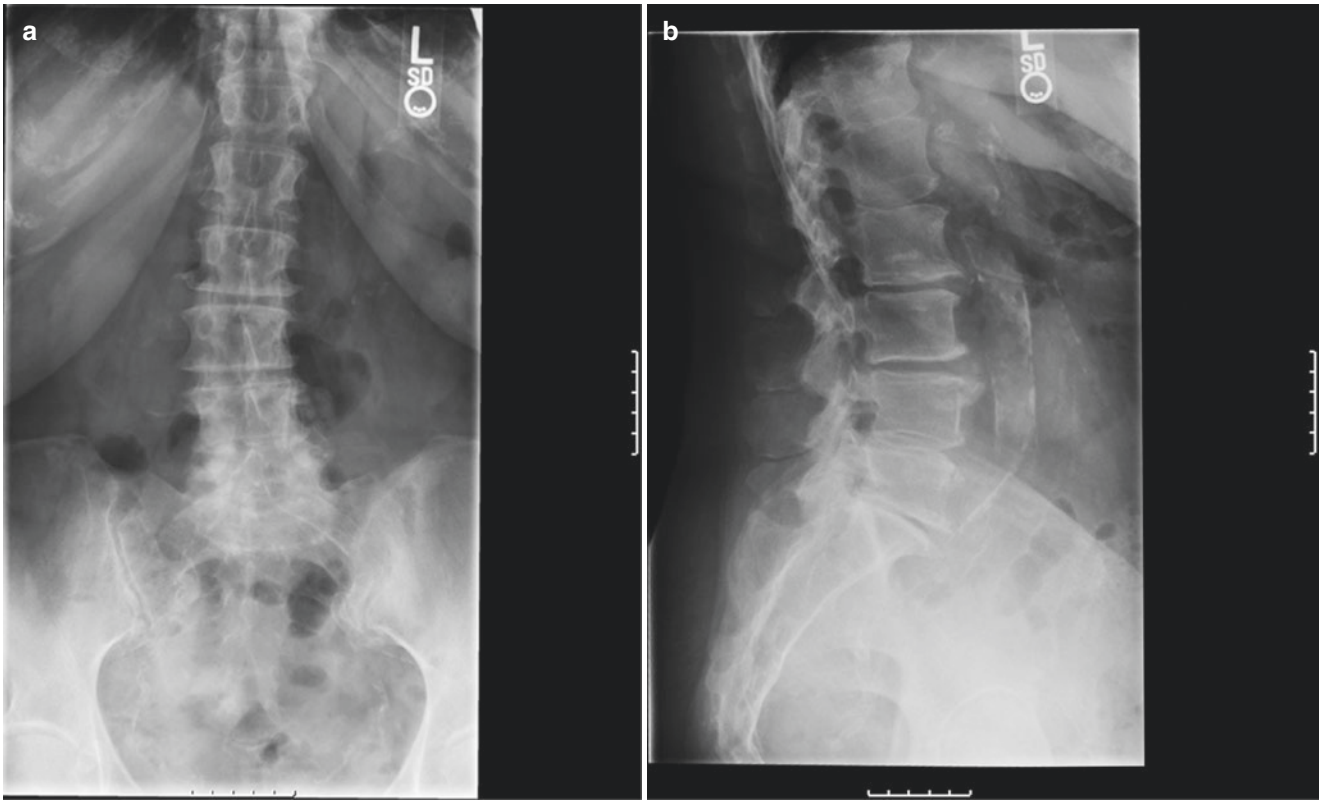

Fig. 4.3 (**a**, **b**) Radiograph of osteoarthritis of lumbar spine. There is a mild curvature of the lumbar spine convex right with multilevel degenerative disk disease with disk space narrowing, endplate sclerosis, and osteophytes at L4–L5 and L5–S1

spine is predominantly involved, disk degeneration and facet joint arthritis result in symptomatic stenosis, necessitating decompression (and fusion) surgery in order to alleviate symptoms and restore a functional activity (Fig. 4.3a, b).

Disorders of the Synovium

Rheumatoid arthritis (RA) is the prototypical disorder primarily affecting the synovium. Whereas the normal synovium consists of a thin intimal lining layer, one to three cell layers thick, comprised of roughly equal proportions of different cell types (macrophage-like synoviocytes or type A synoviocytes and fibroblast-like synoviocytes or type B synoviocytes), in contrast the synovial tissue in RA is greatly hypertrophied (up to 8–10 cell layers thick) displaying increased numbers of both type A and B synoviocytes accompanied by mononuclear cell infiltration of the sublining below the intima transforming the milieu as the pot of inflammatory cytokines and proteases (Fig. 4.4a, b) [10, 11]. The subintimal region where the blood vessels are located becomes heavily infiltrated with inflammatory cells, including T and B lymphocytes, plasma cells, natural killer cells, macrophages, and mast cells. The hypertrophied synovium transforms into villous-like projections, also called pannus, which protrude into the joint cavity and invade the juxtaposed articular cartilage and underlying bone, resulting in cartilage destruction bone erosions and ultimately compromising the integrity of each component of the joint (Fig. 4.5a, b). The destructive properties of the pannus are a result of (1) increased synthesis of metalloproteinases and other proteinases by synovial fibroblasts and monocytes; (2) chondrocyte activation by key cytokines (IL-1, TNF-α, and TGF-ß), resulting in decrease in collagen and proteoglycan synthesis; and (3) recruitment and differentiation of cells that express an osteoclast phenotype leading to focal bone erosions. It is hypothesized that the osteoclast differentiation from the macrophage lineage results in response to inflammatory mediators and cytokines (L-1, TNF-α, IL-17) produced by fibroblast-like synoviocytes in the rheumatoid synovium [12].

Rheumatoid arthritis is a chronic systemic inflammatory disease, driven by autoantibodies and immunologically overactive cells that primarily target the synovium as well as extra-articular tissues and organs. The etiopathogenesis of RA involves a complex interplay of genetic predisposition and probable environmental factors that trigger a cascade of intra-synovial immune response that perpetuates a pro-inflammatory milieu of cellular and molecular phenomena that lead to erosions of the cartilage and bone. Rheumatoid

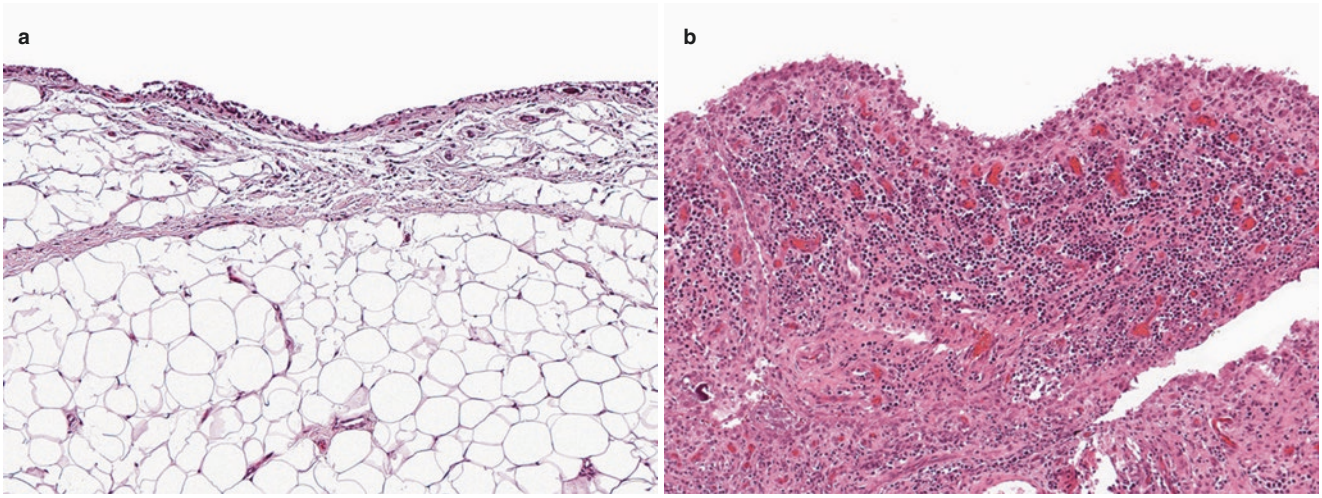

Fig. 4.4 (**a**) Normal synovium: This layer is usually only 1–3 cells thick, comprised of type A macrophage-like synoviocytes and type B fibroblast-like synoviocytes. (**b**) Synovial lining in rheumatoid arthritis: This lining is greatly hypertrophied (8–10 cells thick)

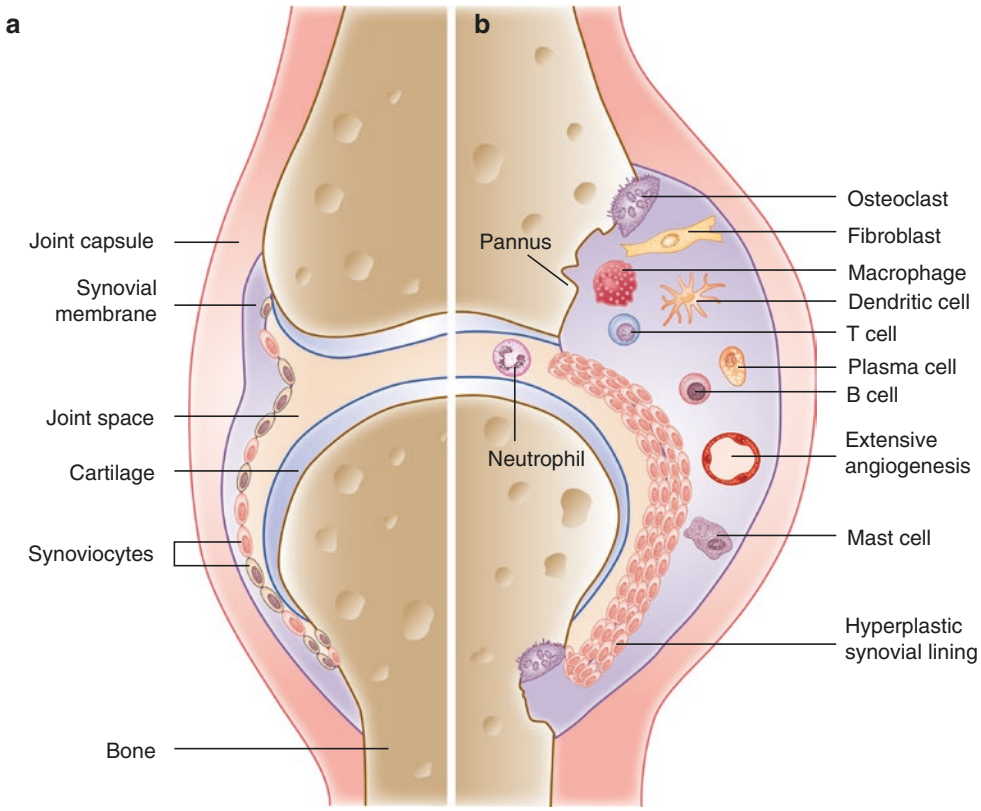

Fig. 4.5 Pannus formation in rheumatoid arthritis. (**a**) Normal synovium with thin intimal layer. (**b**) Synovium in RA showing hypertrophied synovial layer, increased infiltration by inflammatory cells, and angiogenesis. The pannus that develops invades into the joint cavity, articular cartilage, and subchondral bone. (Used with permission of Springer Nature from Strand et al. [37])

arthritis affects females more often than males (RR 3:1). Its peak onset is in the fourth to fifth decade. Usually RA presents insidiously over several weeks to months, with the initial pattern localized to inflammation of the smaller peripheral joints, typically symmetric in distribution, and often with concurrent systemic features of fatigue and generalized malaise. Uncontrolled joint inflammation, characterized by tenderness, swelling, and dysfunction, may lead to larger joint involvement and destruction of synovial joints, followed by deformities and loss of joint function (Fig. 4.6a, b). Extra-articular manifestations may arise but have become less common in the modern therapeutic era.

Products of the human leukocyte antigen (HLA) region of Class II genes of the major histocompatibility complex (MHC) play an important role in the susceptibility and pathogenesis of RA. Individuals who are HLA-DRB4 posi-

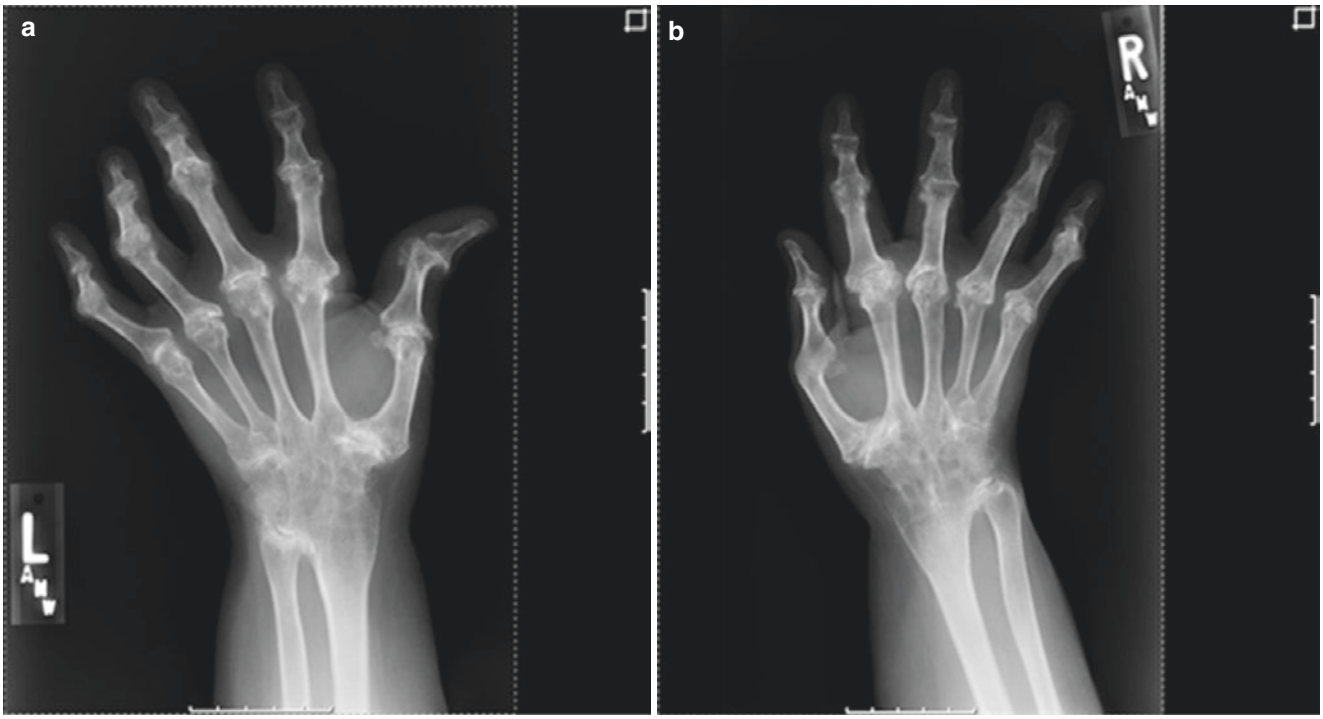

Fig. 4.6 (**a**) Radiographic changes of advanced rheumatoid arthritis. (**b**) Rheumatoid involvement of the metacarpal and proximal interphalangeal joints bilaterally. There is fusion of the carpal joints bilaterally. The radiocarpal joints are fused. The carpal metacarpal joints are fused. Joint space narrowing, mild proliferative changes, and erosions are noted in the MP and PIP joints. There is relative sparing of the DIP joints

tive are more likely to develop severe disease, marked by erosions of the joints, deformity, and disability. The concept of "shared epitope" refers to a common structural domain that consists of 5-amino acid sequence (QKRAA) found on several HLA-DR4 alleles, which has been shown to confer susceptibility to RA [13]. Early in the development of disease, T-lymphocyte infiltration occurs in the synovial tissue, followed by proliferation of the synovial lining; over time synovial infiltration by B cells, macrophages, and fibroblasts follows, and, in response to the production of various chemotactic factors, granulocytes migrate into the joint space discharging pro-inflammatory substances increasing vascular permeability and perpetuating the inflammatory response.

Relevant laboratory studies include markers of the inflammatory response of acute phase reactants (ESR, CRP), rheumatoid factor (RF), and anti-cyclic citrullinated peptide (anti-CCP) antibodies. Rheumatoid factors are autoantibodies directed against the Fc portion of immunoglobulin G (IgG) and are found in 75–80% of RA patients during the course of their illness. The immune complexes deposit into joints and tissues, exacting inflammation and damage. RF lacks specificity as levels may be elevated in certain infectious states (hepatitis, human immunodeficiency virus (HIV), endocarditis), malignancy (multiple myeloma), and also other connective tissue diseases (systemic lupus erythematosus (SLE), primary Sjogren's syndrome, scleroderma, myositis) [14]. Detection of anti-CCP antibodies has been shown to have greater specificity (95–97%), with similar sensitivity to RF for the diagnosis of RA [15, 16]. More recently, anti-citrullinated protein antibodies (ACPA) have emerged as a distinctive subset of patients with RA [17]. It has been shown to be both a strong prognostic indicator for the development of RA in the preclinical stage and a predictor of the extent of joint destruction [18–20]. Seropositivity for ACPA at baseline has been associated with subsequent structural damage in the setting of more persistent synovitis. ACPA status has become an important autoantibody biomarker with both diagnostic and prognostic value.

The therapeutic armamentarium of RA includes combinations of symptomatic therapies such as nonsteroidal inflammatory drugs (NSAIDs) and corticosteroids, non-biologic disease-modifying anti-rheumatic drugs (DMARDs) including methotrexate, leflunomide, sulfasalazine, hydroxychloroquine and biological DMARDs such as tumor necrosis factor (TNF) blockers (infliximab, etanercept, adalimumab, golimumab, and certolizumab), interleukin-1 (IL-1) blockade (anakinra), IL-6 receptor blockade (tocilizumab), T cell co-stimulation blockade (abatacept), and B cell depletion (rituximab) with more in development. JAK inhibitors (tofacitinib, baricitinib) are newer small molecules used in the treatment of RA. Non-biologic and biologic DMARDs have demonstrated major effects on inflammation as well as tempering the pace of structural damage in the chronic

course of this illness. Thus patients require surgical interventions at a much later age than before these medications were introduced. Medications are, however, an important consideration in the perioperative setting, as they can complicate surgical interventions increasing the risk of postoperative infection and impairing wound healing (Chap. 27).

Connective Tissue Diseases

The most common of these conditions is systemic lupus erythematosus (SLE), a prototypical autoimmune disease driven by autoantibodies which target multiple organ systems including joints, skin, and kidneys. This condition occurs mainly in woman during their reproductive years (female to male ratio of 10:1) and disproportionately affects minorities, more commonly affecting African Americans, Asians, and Latinos (prevalence of 1:250–1:500), compared to Caucasians (1:2000) [21, 22]. A hallmark is the diverse clinical expression and undulating course of this condition. The relapsing-remitting pattern of disease, along with the clinical heterogeneity, makes SLE one of the challenging autoimmune disorders not only to diagnose but also to treat. The most prevalent and severe manifestation of systemic involvement is renal disease (lupus nephritis), though other important manifestations involving the musculoskeletal, cutaneous, and neurologic systems frequently arise in the course of this illness. Constitutional symptoms (fever, fatigue, malaise) are the most common presenting complaints and herald the onset of disease flares. Often, the temporal sequence of organ involvement and the severity of its course are unpredictable. While its cause remains unknown, autoantibodies directed at cell nuclei and their constituents are hallmarks of this condition and are believed important to the pathogenesis of the disease. Deposition of immune complexes on a variety of target organs results in tissue injury from inflammation, thrombosis from premature infarction of blood vessels, and/or vasculitis. Multiple mechanisms are at play, and lupus pathogenesis is complex due to nonlinear immune pathways. However, the formation of pathogenic autoantibodies as well as its defective clearance signals a dysregulated immune response with activation of the complement cascade, immune cell types (B cells, T cells), cytokines (type I interferon-α), and proteins involved in the inflammatory response. While hereditary and environmental susceptibility factors are believed important in the pathogenesis, pregnancy and certain drugs are also known disease precipitants.

Beyond the clinical complexity of diagnosis and tracking the course of illness, the challenge often becomes offering treatment modalities that strike the fine balance between immunosuppression and immune dysregulation. Corticosteroids and immunosuppressants remain the mainstay of therapy. Since their introduction in the 1950s, corticosteroids have altered the management of most rheumatic diseases and have led to gradual improvements in the morbidity and mortality of lupus patients. However, major toxicities are associated with long-term corticosteroid use, including infection, deleterious effects on bone health, and disturbances to glucose homeostasis. Thus, antimalarials (Plaquenil or hydroxychloroquine), nonsteroidal anti-inflammatory drugs (NSAIDs), azathioprine (Imuran®), methotrexate, cyclosporine, mycophenolate mofetil (CellCept®, Genentech, San Francisco, USA), and cyclophosphamide (Cytoxan®) have been utilized for their steroid-sparing and immunosuppressive effects. In addition belimumab (Benlysta®, GlaxoSmithKline, Brentford, UK), a monoclonal antibody to a soluble B-lymphocyte stimulator, is an FDA-approved medication for the treatment of autoantibody (ANA and/or dsDNA)-positive SLE patients with mild to moderate disease despite standard therapy.

As will be discussed, avascular necrosis or osteonecrosis is seen relatively commonly (4–15%) in SLE patients who have received high doses of corticosteroid therapy for serious organ involvement. Although the pathogenesis of osteonecrosis remains unclear, the final common pathway of subchondral bone destruction involves a compromise of blood flow preventing essential nutrients and normal reparative processes, leading to further osteocyte death [23]. AVN accounts for a numerically small but important indication for total joint replacement, particularly of the hip, knee, and shoulder in SLE patients (Fig. 4.7). Owing to an inherent and

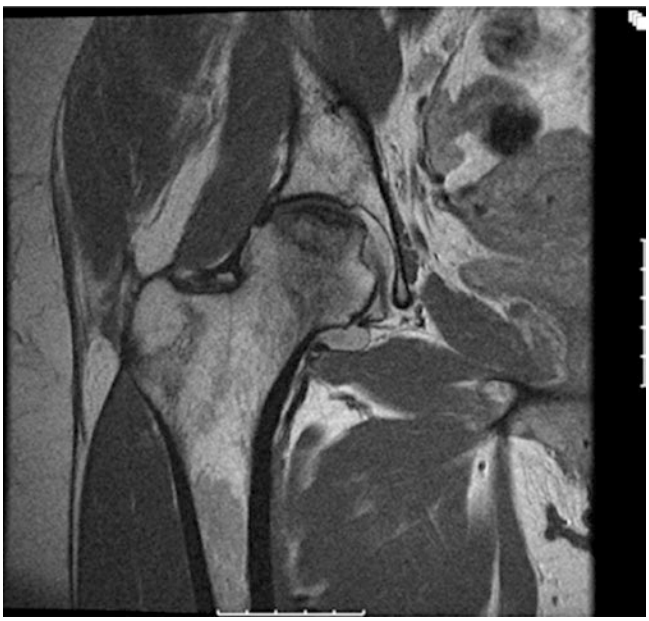

Fig. 4.7 Avascular necrosis of the hip in systemic lupus erythematosus. The R hip reveals extensive avascular necrosis involving almost the entire articular portion of the femoral head, with mild collapse of the superior femoral head. This has elicited a moderate degree of edema within the proximal right femur as well as a joint effusion of the right hip joint. Avascular necrosis also affects the greater trochanter

drug-induced immunosuppression, patients with SLE are also at increased risk for the development of septic arthritis, the acute therapy of which may require input from the orthopedic surgeon.

Autoantibodies are typically found in SLE patients and may be important for the diagnosis. Antinuclear antibodies (ANA) are a hallmark of SLE. These are antibodies directed against the cell nucleus. The ANA is positive in 95–99% of patients. Values of 2+ or greater or titers of 1:40 or greater are considered abnormal. The pattern of the ANA (e.g., speckled, diffuse, rim, centromere) can provide differential diagnostic information. Homogenous patterns are least specific, whereas rim pattern is characteristic of SLE. SLE patients may have high-titer anti-double-stranded anti-DNA antibodies. A decrease in complement level (C3 and C4) may precede the disease flare in SLE. Antibodies to extractable nuclear antigens (ENA) include Anti-Ro, Anti-La, Anti-Smith, and Anti-RNP which are often seen in SLE patients and other related disorders. For example, Anti-Ro and Anti-La are specifically seen in Sjogren's syndrome, whereas Anti-RNP is seen in mixed connective tissue disease. Many other laboratory tests may be abnormal in SLE and can be used in conjunction with the more specific tests for assessing disease. These include a low white blood count (usually with neutropenia and lymphopenia), anemia (sometimes an autoimmune hemolytic anemia with positive Coombs), thrombocytopenia, and elevated partial thromboplastin time (PTT).

Antiphospholipid syndrome is a systemic connective tissue disorder characterized by venous or arterial thrombosis and/or pregnancy morbidity. It can occur as a primary condition or in the presence of SLE or other systemic autoimmune disease. It is characterized by antiphospholipid antibodies and thrombocytopenia. Patients with these syndromes may present with ischemia, necrosis, and gangrene of the toes. Many patients with antiphospholipid syndrome present with avascular necrosis of joints. Standard antiphospholipid antibodies include the lupus anticoagulant, anti-cardiolipin antibodies, beta-2 glycoprotein. Treatment with anticoagulation is usually indicated. In the perioperative setting, patients with antiphospholipid syndrome need to be carefully monitored as the risk of thrombosis can be extremely high during these times.

Another important condition of the connective tissue is that commonly known as systemic sclerosis (scleroderma). Scleroderma exits in two major and distinct forms: localized scleroderma (LSc), which is confined to the skin and subcutaneous tissues, and systemic sclerosis (SSc), which almost always has internal organ involvement but may be limited or diffuse in its cutaneous distribution. Limited disease is defined as skin thickening that affects the distal extremities below the elbows and/or below the knees and to a lesser extent involves the face and neck, whereas diffuse cutaneous disease refers to extensive skin sclerosis affecting the proximal limbs, trunk, face, and neck regions. Rarely, systemic sclerosis can also present as *SSc sine scleroderma* with the typical vascular and fibrotic features of systemic disease but without cutaneous involvement.

Localized scleroderma, an entity that is distinct from *limited* scleroderma, includes dermatologic conditions such as morphea (circumscribed patches of thickened skin), linear scleroderma, pansclerotic morphea, or mixed scleroderma; rarely are there extracutaneous manifestations. Localized and limited scleroderma should be thought of as two distinct diseases with different clinical manifestations and prognosis (Fig. 4.8). In limited cutaneous sclerosis, formerly termed as CREST syndrome (*c*alcinosis of the digits, *R*aynaud's phenomenon, *e*sophageal dysmotility, *s*clerodactyly, and *t*elangiectasia), patients generally have prominent vasculopathic phenotype. One of the most characteristic clinical manifestations of vascular dysfunction is Raynaud's phenomenon, which is due to arterial vasoconstriction in the digits precipitated by cold or stress, manifested by the triphasic color

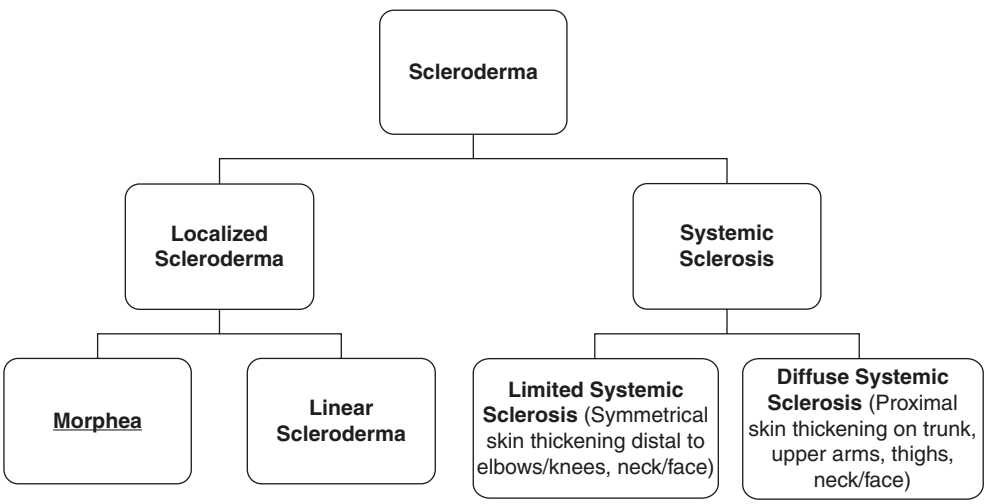

Fig. 4.8 Schematic diagram for classification of scleroderma

changes (white (pallor) → blue (acrocyanosis) → red (reperfusion hyperemia)). Abnormal nailfold capillaroscopy with scleroderma pattern is common. Pulmonary vascular disease, primarily pulmonary arterial hypertension, is more commonly seen in limited cutaneous disease, affecting up to 40% of patients. In systemic sclerosis, clinical manifestations arise as a consequence of an obstructive vasculopathy involving the small vessels, the pathological accumulation of collagen in the skin and other organ systems resulting in fibrosis, and autoimmunity as evidenced by a number of associated autoantibodies. Often a severely debilitating disease, pulmonary parenchymal disease (interstitial fibrosis) has become the most common form of death for such patients [24]. Laboratory tests often help in the diagnosis. Nucleolar and speckled pattern ANA is common in scleroderma and CREST. Anti-DNA topoisomerase I (Scl-70) antibodies, anticentromere antibody, and antibodies to RNA polymerase III may be found in patients with scleroderma. There is no effective treatment for this disorder. An important complication of this condition is the ischemic digit, usually the finger, due to an obliterative vasculopathy and vasospasm in which the caliber of blood vessels narrows and irreversible tissue loss may ensue. Chronic ischemia may lead to digital ulcers, gangrene, tapering of fingers due atrophy of underlying soft tissue, and skin changes referred to as sclerodactyly (localized thickening and tightness of the digit). A consequence of the vascular obstructive and vasospastic elements of this disease, SSc manifestations in the hand may require the participation of a hand surgeon experienced in microsurgical revascularization, digital arterial reconstruction to improve digital vascular perfusion, and peripheral sympathectomy to relieve pain. There also may be a role of surgery for advanced SSc affecting the hand, in which chronic ischemia and fibrosis may lead to atrophy and contractures of the digits, nail deformities, and calcinosis (Fig. 4.9a, b); however, surgical benefits should be balanced with risks of impaired wound

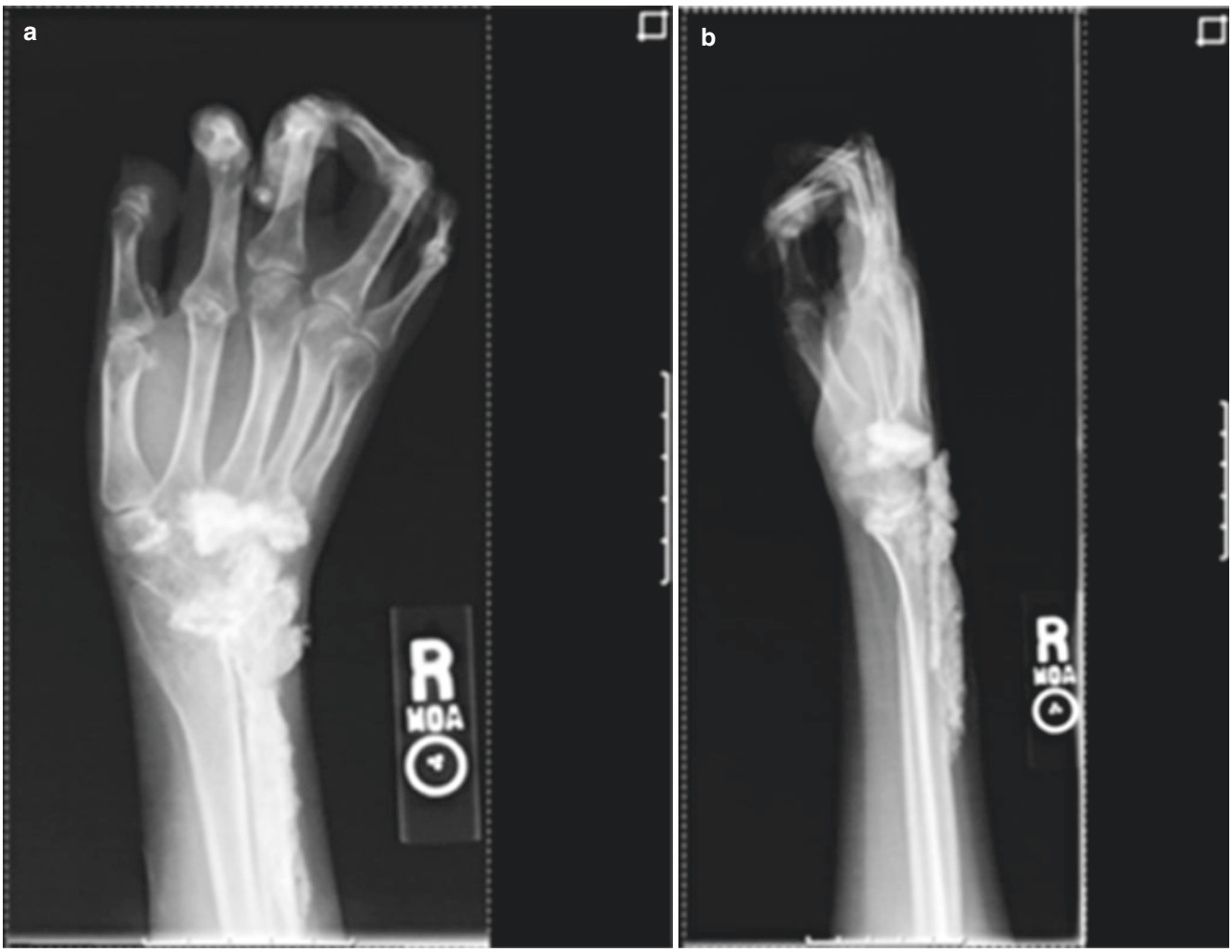

Fig. 4.9 (**a**) Calcinosis and contracture in scleroderma. (**b**) There are flexion contractures of the PIP joints bilaterally. There are soft tissue calcifications around the wrists, hands, and distal forearms bilaterally. There is acroosteolysis with loss of the terminal tufts of distal phalanges at multiple fingers

healing and the progressive course of SSc [25]. Important perioperative surveillance/screening of pulmonary disease (pulmonary arterial hypertension and/or pulmonary fibrosis) is imperative in SSc patients, especially if dyspnea is present.

A less common but important form of the connective tissue disease includes the inflammatory diseases of the muscle—dermatomyositis (DM) and polymyositis (PM). These represent another heterogeneous group of disorders, and they share the clinical features of a progressive skeletal muscle weakness and fatigue and a decrease in endurance. Disease-specific autoantibodies are also frequently found, but ultimately the diagnosis is made by muscle biopsy that demonstrates an inflammatory infiltrate. Treatment includes corticosteroids, IVIG, and immunosuppressive therapy with medication such as methotrexate and azathioprine. These diseases rarely require orthopedic intervention.

Spondyloarthritis

Spondyloarthritis (SpA) comprises a group of inflammatory disorders with overlapping clinical manifestations and a shared genetic marker (HLA-B27). The most distinguished clinical features are inflammation of axial joints (especially sacroiliac joints), asymmetric oligoarthritis, dactylitis, and enthesitis. Axial spondyloarthritis (axSpA) is a potentially disabling inflammatory arthritis of the spine, usually presenting as chronic back pain, typically before the age of 45. Patients with axSpA can be classified as having either of two subtypes of axSpA: ankylosing spondylitis (AS) or nonradiographic axSpA (nr-axSpA). AS is the prototypical SpA, but other disorders such as nr-axSpA, peripheral SpA, psoriatic arthritis (PsA), the enteropathic arthropathies, and reactive arthritis are now categorized as SpA [26]. Patients who present with clinical features suggestive, but not diagnostic, of SpA are labeled as "undifferentiated" spondyloarthritis. In contrast, those with well-defined clinical features have been referred to in the past as "seronegative" spondyloarthropathy. This designation implies the genetic, clinical, and pathophysiologic characteristics of these conditions while making reference to the absence of rheumatoid factor.

The first distinguishing feature of SpA is the presence of enthesitis, an inflammation of the bony insertion points of tendons, ligaments, or the joint capsule. Enthesitis is responsible for the multiple spinal and peripheral manifestations characteristic of this class of rheumatic conditions in which pain, stiffness, and restriction develop at sacroiliac and other spinal joints. Extraspinal enthesitis commonly affects the Achilles tendon insertions to the calcaneus and plantar fascia. A second trademark of these conditions is the presence of axial arthritis (i.e., sacroiliitis and spondylitis). Inflammatory synovitis and capsular enthesitis at the sacroiliac joints result in sacroiliitis; similarly inflammation of the entheses associated with paraspinal ligaments ultimately leads to spondylitis. Such involvement also accounts for the involvement of the intervertebral disks, symphysis pubis, and manubrioclavicular and sternoclavicular joints. These conditions are brought to their fullest expression with the addition of peripheral joint involvement, an uncommon feature in AS but commonly seen in PsA or reactive arthritis. Various patterns are commonly seen and vary according to the associated disease process. For instance, in AS, the shoulder and hips are most frequently involved. In contrast, an asymmetric lower extremity oligoarthritis (knee, ankle) is more commonly seen in reactive arthritis, while distal interphalangeal joint disease usually denotes PsA. An important feature of the SpAs is the "sausage" digit or dactylitis, an inflammatory process involving a small joint synovitis combined with an enthesitis of the tendon sheaths, insertions, and various other supporting tissues of the digit (fingers or toes). Combined, these processes produce the sausage-like swelling, a finding virtually pathognomonic of SpA. More than 90% of patients with ankylosing spondylitis (AS) and 50–70% of patients with other forms of SpA are positive for human leukocyte antigen (HLA)-B27. Acute phase reactants may also be elevated in these patients. The background prevalence of HLA-B27 is 6–10% in Caucasians, and only a small minority of HLA-B27 patients ever experience clinical manifestations, which makes the test of limited use.

As the prototypical disease among SpA, the symptoms of AS usually begin in the third or fourth decade of life with the gradual onset of inflammatory back pain. It predominantly affects men at much higher frequency than women (ratio of 9:1). Signs and symptoms of spinal involvement predominate, and the inflammatory (as opposed to mechanical) nature of the condition is suggested by a number of features: age <40 years, insidious onset, duration of <3 months, marked morning stiffness, and improvement with activity. Patients often complain of back pain at nighttime. Sacroiliitis, a common initial feature, presents as pain in buttocks which may radiate down the legs and/or hip pain. In a minority of patients, peripheral oligoarthritis and enthesitis accompany the axial involvement. Concurrent constitutional features of fatigue, weight loss, and depression often may be present. Progressive involvement of the entire spine occurs over years, resulting in spinal pain, stiffness, and severe restriction of the spine (Fig. 4.10). Family history often reveals others with early-onset back pain or inflammatory problems in the eye (uveitis, iritis). Diagnosis of AS should be predominately based on the clinical presentation of usually a young man (before the age of 40 years) who presents with chronic inflammatory back pain.

While the magnetic resonance imaging (MRI) has greatly facilitated diagnosis in SpA, various criteria have been devel-

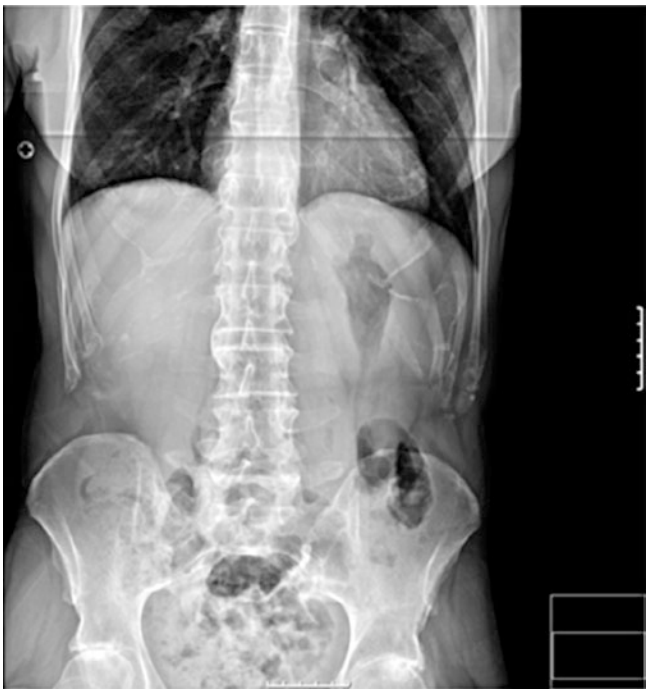

Fig. 4.10 Spinal radiograph in severe ankylosing spondylitis. There is complete fusion of the sacroiliac joints bilaterally and axial joint space narrowing of both hip joints. In the spine, bridging syndesmophytes are noted focally at L2–L3 on the *right* as well as T10–T11 on the *right* and T9–T10 on the *left*

oped both for diagnosis and for classification purposes in research and clinical trials. The New York criteria of 1968, later modified (1984), were the first such systems though have been largely replaced by the criteria described by newer criteria like the Assessment of SpondyloArthritis international Society (ASAS) that outline important clinical and radiographic features; further classifications for the peripheral forms of these diseases have also been developed (Fig. 4.11a, b) [26–31]. However, all of these classifications have low sensitivity in detecting early disease.

Patients with AS exhibit radiographic abnormalities consistent with sacroiliitis, but such findings are absent or minimal on plain radiography in nonradiographic axial spondyloarthritis (nr-axSpA). The diagnosis is supported by evidence of active inflammation of the sacroiliac joints on MRI, by a combination of other clinical findings, or both. Peripheral spondyloarthritis is the term used to describe patients with features of SpA whose symptoms and findings are predominantly peripheral.

In contrast, patients with psoriatic arthritis are also often young, but rather than spinal disease, the more typical presentation is that of an asymmetric oligoarthritis in conjunction with other characteristic features such as destructive DIP involvement, nail changes, sausage digits, arthritis mutilans, and the aforementioned peripheral enthesopathy (often the Achilles tendon or plantar fasciitis). For those that do have spondyloarthritis of PsA, the asymmetric involvement of sacroiliitis can distinguish that from the spondyloarthritis of AS, which classically affects both sacroiliac joints. Also, approximately a third of patients with psoriasis will develop PsA; the majority of patients develop psoriasis years prior to inflammatory musculoskeletal features; however, there is a group of patients (15–20%) in whom the joint disease precedes the skin disease [32]. PsA can develop in people who have any level severity of psoriatic skin disease from mild to very severe. With respect to the enteropathic disease entities, this form of inflammatory arthritis develops in patients with Crohn's disease, ulcerative colitis, or microscopic colitis. Sacroiliitis is common, and the peripheral joint arthritis tends to take the form of a large joint inflammatory process that follows the clinical activity of the underlying gastrointestinal disease. The pattern of arthritis is variable; it is commonly asymmetric but can present in a migratory or additive fashion and tends to be non-erosive. Arthritis associated with Crohn's disease and with ulcerative colitis will have negative stool and synovial fluid cultures. Intestinal biopsy and histopathology are helpful in confirming clinical suspicions. Anti-*Saccharomyces cerevisiae* antibodies (ASCAs) may be positive in ulcerative and microscopic colitis.

Lastly, there is reactive arthritis formerly known as "Reiter's syndrome." This is the clinical presentation of inflammatory arthritis coupled with extra-articular features seen in susceptible individuals following a genitourinary or gastrointestinal infection. Such individuals develop a seronegative, inflammatory arthritis arising weeks after the antecedent infection accompanied by ocular (conjunctivitis, uveitis), mucocutaneous (oral ulcers, balanitis, keratoderma blennorrhagicum), gastrointestinal (dysenteric), and genitourinary manifestations (urethritis, cervicitis). Infectious agents most often implicated include *Chlamydia*, *Salmonella*, *Campylobacter*, *Yersinia*, and *Shigella* species. These organisms are rarely cultured from the joint fluid or synovial tissue, hence the designation *reactive*. The peripheral joint involvement is usually an asymmetric lower extremity oligoarthritis, though, as with the other spondyloarthritis, sausage digits (dactylitis) are also a common feature. Axial involvement is uncommon and distinguishable from AS by its predominate asymmetric pattern of sacroiliitis and paramarginal syndesmophytes. Lastly, patients may present with features suggestive (seronegative oligoarthritis and enthesitis) but not diagnostic of these conditions. In such patients the diagnostic designation is that of an undifferentiated spondyloarthritis.

Once difficult to treat with nonsteroidal anti-inflammatory drugs, new biologic therapies such as tumor necrosis factor (TNF) inhibitors have markedly improved the clinical course and symptomatic experience of patients suffering with these conditions. Nonetheless, given the peripheral joint involvement seen in these conditions, patients who suffer from these conditions ultimately may require total joint arthroplasty.

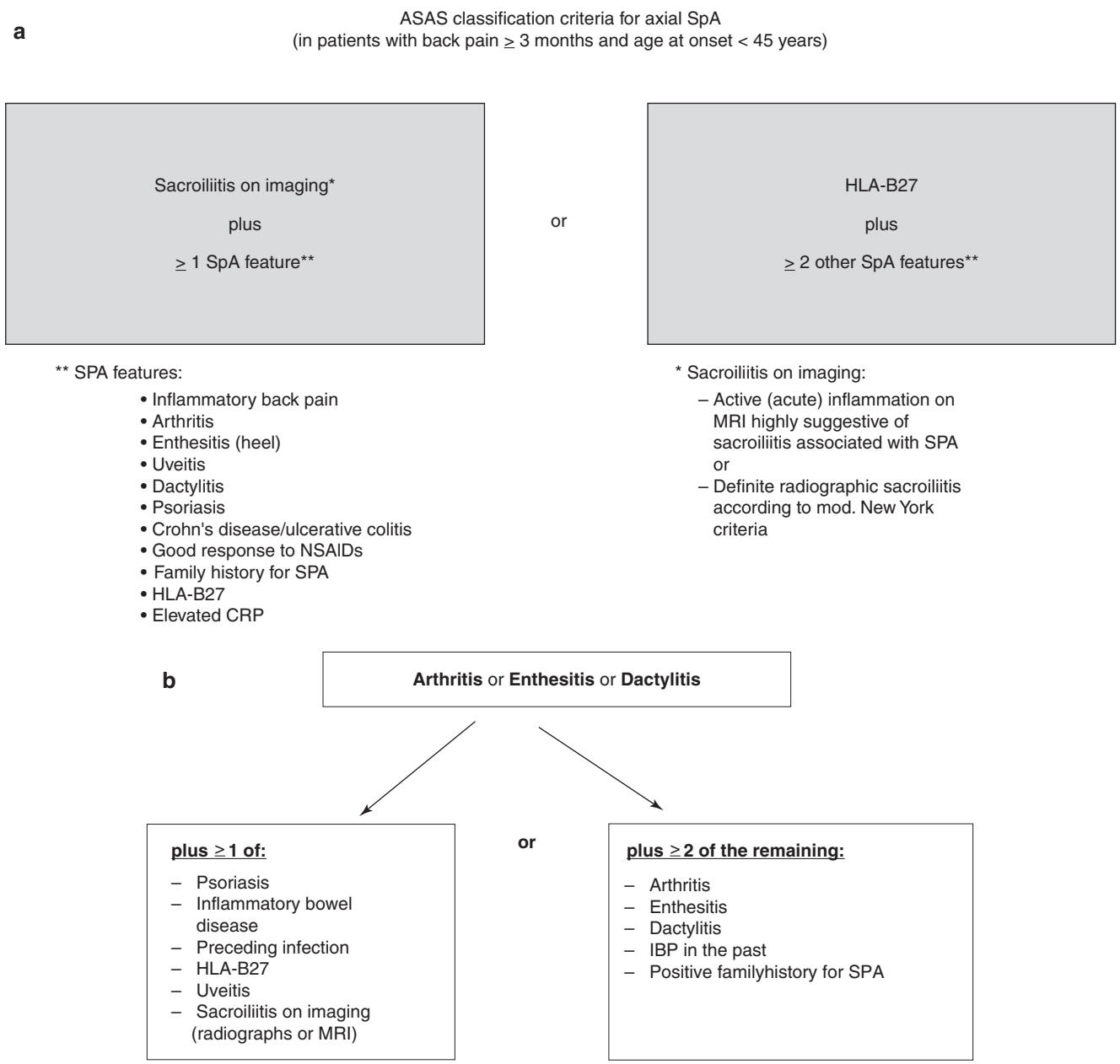

Fig. 4.11 (**a**, **b**) Criteria for diagnosing ankylosing spondylitis. Sensitivity 82.9%, specificity 84.4%; n = 649 patients with chronic back pain and age at onset <45 years. Imaging arm (sacroiliitis) alone has a sensitivity of 66.2% and a specificity of 97.3%. ∗∗Note: Elevated CRP is considered a SpA feature in the context of chronic back pain. (**a** Used with permission of BMJ Publishing Group LTD from Rudwaleit et al. [31]; **b** Used with permission of BMJ Publishing Group LTD from Rudwaleit et al. [26])

Vasculitides

The term vasculitis refers to disease conditions that involve inflammation of the blood vessels with resultant tissue necrosis and organ failure. The spectrum of disease is broad with overlapping features. While its classification systems had historically relied on eponyms, it is now categorized according to the size of the involved blood vessels. Polymyalgia rheumatica and temporal arteritis are amongst the best known examples, but also included are such conditions as polyarteritis nodosa, granulomatosis with polyangiitis (formerly known as Wegener's granulomatosis), microscopic polyangiitis, eosinophilic granulomatosis with polyangiitis (formerly known as Churg-Strauss syndrome), and cryoglobulinemic vasculitis to name a few. Often, small-vessel vasculitis will present as a rash or palpable purpura on the lower extremities and is often referred to as leukocytoclastic vasculitis. Patients often present with foot drop.

Immunologic causes of vasculitis often have characteristic laboratory findings, e.g., antineutrophil cytoplasmic antibodies (ANCA) or the presence of cryoglobulins. Acute phase reactants are usually high in these conditions. Treatment paradigms rely on corticosteroids and immunosuppressants. Orthopedic intervention is rarely needed in the course of these conditions.

Metabolic Bone Disease

Osteoporosis is a widely recognized disorder of skeletal muscle characterized by low bone mass and microarchitectural deterioration of bone, increasing its fragility and susceptibility to fracture. Pathophysiologically comprised of a heterogeneous group of disorders, osteoporosis is characterized by a net loss of bone (bone resorption activity dominating over bone formation activity) resulting in a decrease in the overall density of mineralized bone (Fig. 4.12). Osteoporotic fractures, which result from the inability of the bone to absorb a traumatic load, may have devastating consequences for patients and with an aging population have become so common as to constitute a threat to public health. Owing to the causal association between this condition and fracture (wrist, hip, spine) and the importance of bone quality in osseous healing, it is one of the most important rheumatic diseases now encountered on orthopedic services. It is important to analyze the laboratory markers like serum calcium, phosphate, magnesium, vitamin D, serum potassium, creatinine, and parathyroid and thyroid hormones when making the diagnosis and treating osteoporosis.

The aim of osteoporotic screening and treatment is to prevent fractures. Dual X-ray absorptiometry (DXA) is the primary diagnostic tool for the detection of osteoporosis. Using population standards, the World Health Organization (WHO) defines osteoporosis as a bone density measurement of the spine that is >2.5 standard deviations below the mean of the standard for a 35-year-old population in the appropriate gender. Osteopenia is defined as a T score between 1.0 and 2.5 standard deviations the bone density of a standard 35-year-old population. Additionally, the Z score provides an evaluation of bone density as it relates to age-matched controls. While bone density is a primary indicator of bone quality, there are other structural and material factors, such as bone macro- and microarchitecture, degree of mineralization and micro-damage accumulation, and bone turnover that influence overall bone quality [33]. Indeed in the orthopedic surgical setting, its implications extend to such considerations as the achievement of bony fusion after spinal surgery as well as the anticipated longevity of total joint replacement, subjects addressed in Chap. 31.

Crystal-Induced Arthropathies

Owing to fluid shifts and dehydration, gout (uric acid) and pseudo-gout (Ca^{2+} pyrophosphate) deposition in peripheral joints occurs frequently after surgery. As such, they are com-

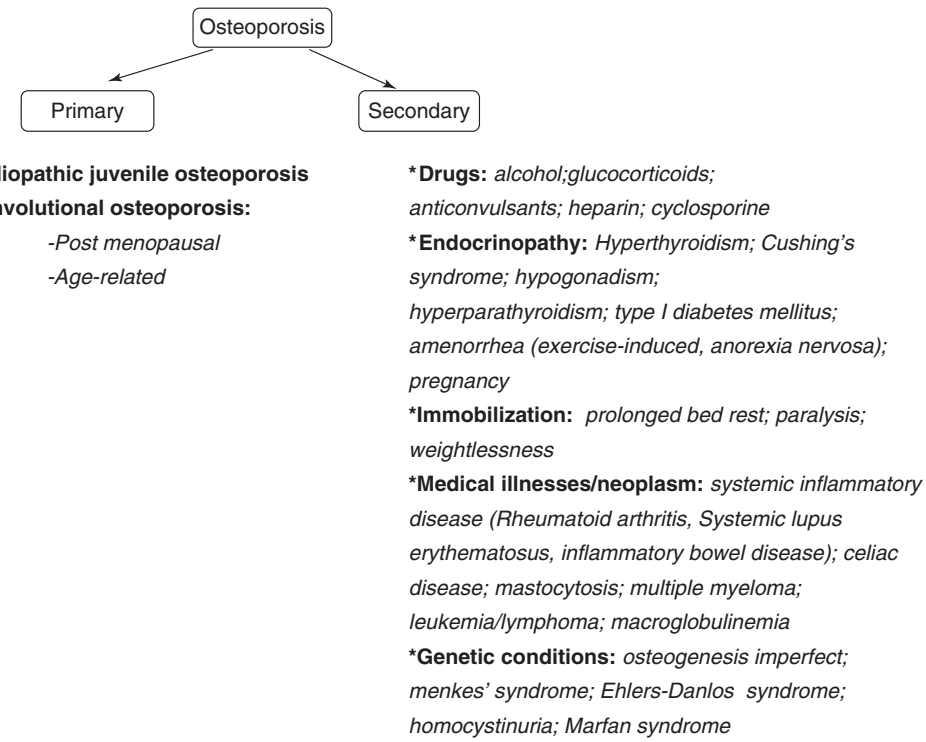

Fig. 4.12 Common causes of osteoporosis

mon management problems in the postoperative period. The archetypal presentation of these conditions is well known to clinicians taking the form of the sudden onset of severe pain, swelling, and erythema, usually of a single joint, and in approximately 50% of cases, it affects the first metatarsophalangeal joint (podagra) [34]. Other joints are not uncommon; however, the tarsometatarsal joint and ankle are frequent sites as are the knee and wrist. The latter are frequently seen in Ca^{2+} pyrophosphate crystal deposition (CPPD). Diagnosis is premised on the demonstration of pathognomonic crystals within the synovial fluid as seen via polarized light microscopy; that is, the negatively strongly birefringent, needle-shaped monosodium urate crystal in the case of gout versus the positively weakly birefringent, rhomboid crystal of CPPD (Fig. 4.13a, b). Patients with gout often have an increased uric acid level in the serum. In the postoperative setting, treatment involves the oral administration of nonsteroidal anti-inflammatory drugs, short courses of corticosteroids (or ACTH), or intra-articular injections of such steroids. Because of the potential for gastrointestinal side effects, oral colchicine is a less favored medication after surgery. The management of gout arising in the perioperative setting is fully reviewed in Chap. 22.

Another form of crystalline disease is calcium hydroxyapatite crystal deposition disease, a common entity best characterized as "calcific tendinitis" most frequently affecting the shoulder but also affecting other sites such as the hips, wrists, and feet. This syndrome is typically recognized by recurrent pain due to the pathologic peri- and/or intra-articular buildup of calcific material around the tendons/joints, which occurs as primary (or idiopathic) or as a secondary process due to various disease processes including renal disease, collagen vascular disease, metabolic disorders, or trauma. Hydroxyapatite crystals are small, amorphous, and nonbirefringent in polarized light, thereby making it difficult to diagnose with light microscopy; diagnosis is made on the basis of radiographic findings of calcium deposits in the typical periarticular and tendinous sites and concomitant clinical symptoms (Fig. 4.14). Rarely requiring surgical intervention, treatment of hydroxyapatite deposition disease involves conservative measures, such as nonsteroidal anti-inflammatory medications (NSAIDs), intra-articular steroid injections, and physical therapy.

Infectious Arthritis

Invasion of a joint by pyogenic bacteria is responsible for rapidly progressive joint destruction, osteomyelitis, and potentially systemic spread of the infection. The majority of such infections arise from hematogenous spread of offending bacteria to the affected joint(s). Predisposing factors include IV drug use, indwelling catheters, the use of immunosuppressive medication, and a host of disease processes that suppress immunity. Important examples of the latter include diabetes mellitus, chronic inflammatory arthritis, HIV infection, and alcoholism, to name a few.

The major pathogens are the gram-positive cocci (usually staphylococcal species) accounting for >75% of cases. *Staphylococcus aureus* is the most common offending agent, followed by streptococci and pneumococci; *Staphylococcus epidermidis* is often seen in the setting of prosthetic joint infection, rarely arising in the native joint. Gram-negative organisms, though a much less common cause of septic arthritis, are more often encountered in intravenous drug abusers. Associated

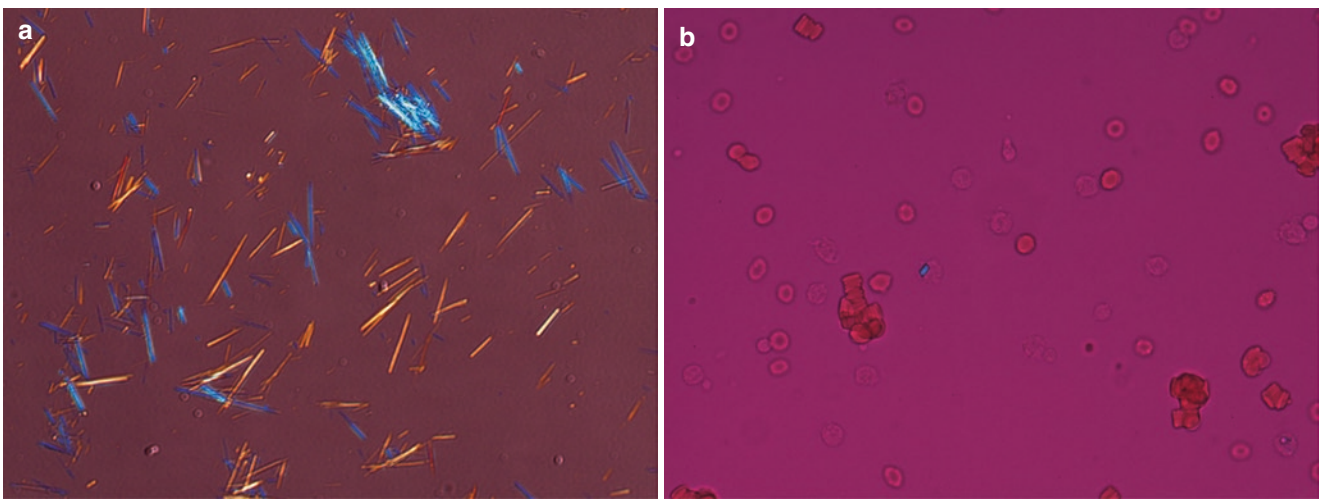

Fig. 4.13 (**a**) Gout: monosodium urate crystals. Strongly negative birefringent, needle-shaped crystals aspirate from tophaceous deposit. Crystals are *yellow* when parallel (*blue* when perpendicular) to the long axis of the first-order red compensator on polarized light microscopy consistent with gout. (**b**) Pseudo-gout: calcium pyrophosphate dehydrate (CPPD) crystals. Weakly positive birefringent, rhomboid-shaped or polymorphic crystals aspirated from joint of a patient with pseudo-gout. Crystals are typically *blue* when parallel (*yellow* when perpendicular) to the long axis of the first-order red compensator on polarized light microscopy consistent with pseudo-gout

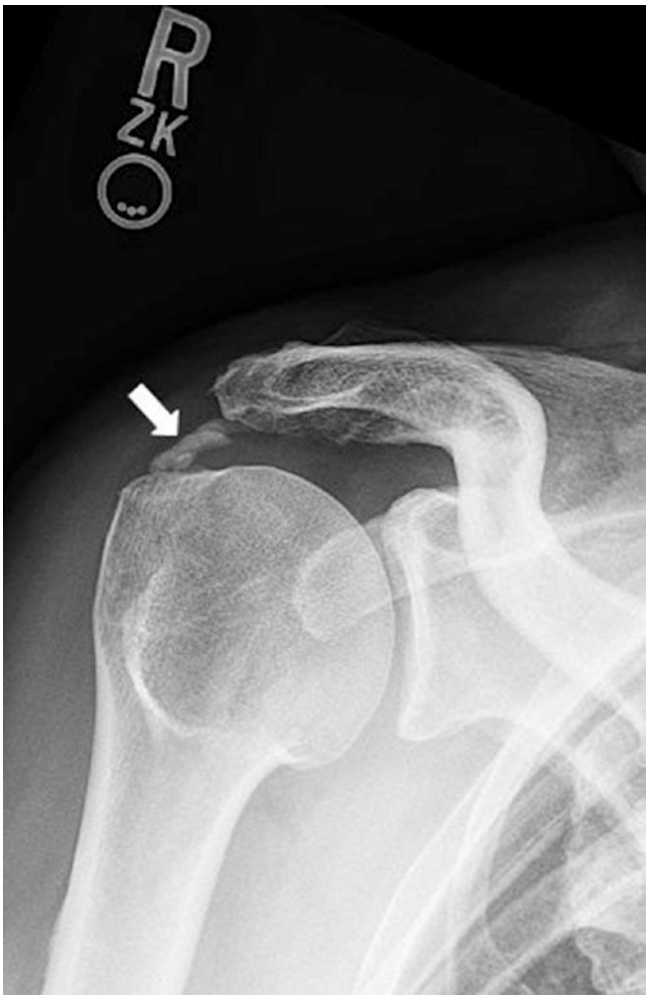

Fig. 4.14 Calcific tendonitis of shoulder. Amorphous calcific deposit on supraspinatus tendon near its insertion site at the greater tuberosity

with a purulent joint fluid (WBC >50,000, predominately granulocytes), a definitive diagnosis requires the demonstration of bacteria in the joint fluid. Antibiotic therapy logically follows from culture of the synovial fluid. Prompt diagnosis and treatment is vital in order to achieve optimal recovery. Tuberculosis has extrapulmonary manifestations which may affect joints and is common in endemic countries as well as in immunosuppressed population [35]. Removal of the prosthesis is often required followed by a course (6 weeks) of intravenous antibiotic therapy and ultimately reimplantation.

Another important infectious agent affecting the joints is the spirochete *Borreliella* causing Lyme disease. Lyme disease is caused by a tick-borne virus which often affects the knee joints. The diagnosis of Lyme disease is based primarily on the clinical history (e.g., erythema migrans, cardiac, neurologic joint), exposure to the tick vector in an endemic area, and confirmation with lab testing. If Lyme disease is suspected, a screening test is performed with ELISA followed by a confirmatory Western blot test. Patients need to be treated with appropriate antibiotics like doxycycline once diagnosed. These patients rarely require surgical intervention.

Sarcoidosis

Sarcoidosis is a disorder of unknown etiology, characterized pathologically by presence of non-caseating granulomas in affected organs. It typically affects younger adults with manifestations like bilateral hilar adenopathy, pulmonary radicular opacities, skin or eye lesions, as well as bone and joint manifestations. Articular manifestations of sarcoid may be the presenting feature of the disease and may present in isolation or combined with the other clinical manifestations. Clinically joint involvement is found in 14% of patients at presentation and may be seen up to 38% on follow-up [36]. Elevated levels of serum angiotensin-converting enzyme (ACE) can be detected. Acute sarcoid arthritis (Löfgren syndrome) commonly involves the ankle, whereas chronic arthritis mainly manifests with sarcoid bone lesions which are histologically granulomas. If these occur in weight-bearing joints, surgical intervention may be needed. The mainstay treatment for this remains corticosteroids.

Summary

The chronic rheumatic diseases represent a broad category of conditions that share a common feature, the destruction of cartilage and its consequences. While these conditions differ in their pathophysiology, the final common pathway is often the joint; hence, such patients frequently require orthopedic surgery. Presented herein is a short summary of the important conditions, presenting their broad range of clinical expression the purpose of which is the education of the readership. A second chapter (Chap. 12) in this book presents the clinical approach to the assessment of such patients prior to undergoing surgery.

Summary Bullet Points

- The chronic rheumatic diseases are prevalent conditions with a major impact on society and the healthcare system.
- Given their prevalence and the involvement of the joints, such patients may make up a significant proportion of an orthopedic patient population.
- The rheumatic diseases share one central feature: the destruction of joints.
- Although a disparate group of disorders, a systematic approach to the differential diagnosis of these conditions is presented.

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The Pathophysiologic Events of Total Joint Replacement Surgery

5

Stavros G. Memtsoudis

Objectives

- To discuss issues surrounding the role of intravasation of bone, cement, and fat into the systemic circulation and its effects on various organ systems
- To discuss the relationship of overall embolic load and end-organ reserve in the context of clinical outcomes
- To specifically review the pathophysiology of cement and fat embolism
- To elucidate additional pathophysiological components relevant to spine surgical interventions
- To review interventions targeted to reduce the impact of intraoperative insults on clinical outcomes

Key Points

- During reaming and insertion of a prosthesis, areas usually occupied by bone marrow are pressurized leading to intravasation of debris made up by fat, marrow cells, cement, and bone.
- Various organs are affected by this insult, including the cardiopulmonary system.
- The higher the embolic load and the lower the patient's end-organ reserve, the more likely clinical symptoms may develop.

Introduction

A large number of insults including tissue trauma, blood loss, and activation of various neurohumoral cascades are underlying causes for perioperative complications.

While patients undergoing orthopedic procedures are not exempt from exposure to these stresses, a number of specific events associated with the nature of orthopedic surgery make this patient population unique and thus warrant special attention and discussion.

In this context, intraoperative embolization of bone, cement, and marrow material during instrumentation and manipulation of osseous structures may explain the mechanism by which perioperative complications after total joint replacement present [1, 2]. Indeed, complications which can be traced to intraoperative debris embolization have been linked to some of the highest rates of associated mortality [3]. While embolic load influences the development of complications on one side of the equation, outcomes are affected by end-organ reserve of a particular patient on the other.

This chapter therefore reviews the nature and pathophysiology of the so-called bone cement syndrome and its effects on various organ systems. Various factors influencing the predisposition to the development of complications are presented, and approaches to ameliorate the impact are discussed.

Pathophysiology of the Bone Cement Syndrome

Orthopedic surgery is inadvertently associated with the invasion of the bone marrow canal in order to prepare the bone for the prosthetic components. During various portions of preparation, i.e., reaming and insertion of a prosthesis, areas usually occupied by bone marrow are pressurized leading to intravasation of debris made up by fat, marrow cells, cement, and bone. While studies suggest that these events occur in

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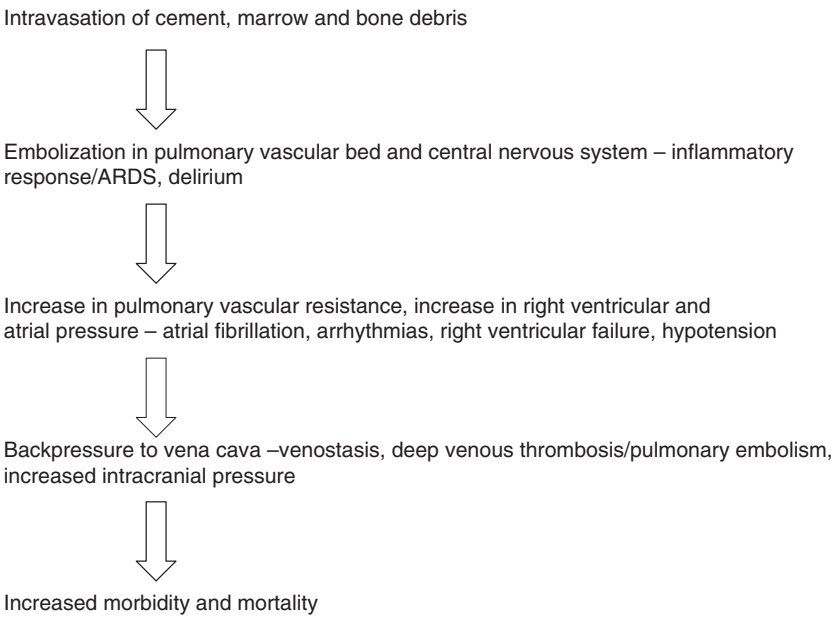

Fig. 5.1 Process and effect of embolization of cement and bone marrow debris on organ systems

the majority of patients [4–6], the effects remain clinically insignificant and transient in most of the cases [7]. However, derangements manifesting in an increase in pulmonary arterial pressures, right heart strain, cardiovascular collapse, lung injury, and death have been described [6, 8]. Mechanisms for the various degrees of presentation of these events remain speculative to date but are thought to be related to the overall load and size of particles gaining access to the pulmonary vasculature [6, 9, 10].

Some of the proposed mechanisms include mechanical embolization of debris, toxic effects of methylmethacrylate, neuromodulation during marrow canal pressurization [11], and release of vasoactive substances promoting microthrombi [6, 12, 13].

Investigations into the toxicologic effects of methylmethacrylate monomers suggest a direct negative inotropic effect in vitro [13]. However, subsequent measurements in the clinical setting suggest that plasma concentrations in vivo are too low to account for hypotensive effects encountered during the cementation process [14]. Cement fixation of hip prostheses has been linked to release of anaphylatoxins C3a and C5a. No such release was seen in uncemented prostheses in the same study [9].

While methylmethacrylate-modulated effects may play a role in the pathophysiology of the bone implantation syndrome, the impact of fat emboli has been better defined in the literature [2]. In its extreme form, it presents as the "fat embolism syndrome" and is associated with pulmonary, hematologic, central nervous, and other organ system complications secondary to the effects of fat-mediated embolization and inflammation [2, 15], the details of which are discussed next.

Physiologic Effects on Various Organ Systems

The embolization of cement and bone marrow debris is not confined to the venous and pulmonary systems. Evidence suggests that smaller particles travel through the pulmonary circulation and potentially through a patent foramen ovale, facilitated via perioperatively increased pulmonary arterial pressures [6], thus leading to microembolization of various organ systems (Fig. 5.1) [1, 16].

Cardiopulmonary Effects

Effects surrounding unilateral arthroplasty on the pulmonary vasculature have been described in the past. Most trials, however, have found little clinical significance and have described changes in pulmonary pressures and right heart function as small and relatively short-lived [17–19]. In contrast, Urban and colleagues found that 22% of patients undergoing revision total hip arthroplasty showed significant decreases in right ventricular function and increases in pulmonary vascular resistance [6]. Further, increases in pulmonary vascular resistance may be more pronounced and prolonged during bilateral procedures [10, 20] stressing the role of embolic load as discussed later in this chapter.

Decreased end-organ capacity of the cardiopulmonary system has been shown to be a major factor in the patient's ability to absorb the stresses induced by intraoperative events. Thus, patients with preexisting right heart strain, as is the case with pulmonary hypertension, are at particularly

high risk for morbidity and mortality [21]. In a study of nationally representative data, patients with pulmonary hypertension undergoing total hip arthroplasty experienced an approximately fourfold increased adjusted risk of mortality (2.4% vs. 0.6%) and those undergoing total knee arthroplasty a 4.5-fold increased adjusted risk of death (0.9% vs. 0.2%) compared with patients without pulmonary hypertension in a matched sample ($P < 0.001$ for each comparison). Further, the study found that the degree of pulmonary hypertension played a significant role in the risk for complications. Patients undergoing total hip arthroplasty and who suffered from primary pulmonary hypertension, which is associated with more severe disease, experienced the highest mortality rate (5% (95% CI, 2.3–7.7)). In support of this concept are Ramakrishna and colleagues' findings that a right ventricular systolic pressure to systemic systolic blood pressure ratio over 0.66 was a predictor for postoperative mortality [22].

Thus, it seems prudent to identify patients with potentially subclinical increases in pulmonary pressures and consider them at increased risk for complications. In this context it has been suggested that right ventricular dysfunction is more prevalent in patients with obesity and sleep apnea and patients with a history of pulmonary embolism [23, 24].

Effects in Other Organ Systems

It has been hypothesized that intraoperative embolization of debris and increases in pulmonary pressures may represent a common pathway for complications associated with a high incidence among mortalities after hip and knee arthroplasty. In an analysis of data spanning over a 15-year time period, we were able to establish that complications that can be linked to embolic phenomena (i.e., pulmonary embolism, adult respiratory distress syndrome, and central nervous system events) had a much higher incidence among fatalities compared to patients that did not die perioperatively [3]. In the context of previous findings, it has been therefore suggested that pulmonary embolization of bone and cement debris can cause pulmonary inflammation and injury [12, 25] manifesting in adult respiratory distress syndrome in its extreme form. The hemodynamic effect is that of increased pulmonary pressures which may promote increased right heart strain leading to atrial and ventricular arrhythmias. In the setting of increased right heart pressures, reduced venous return may promote venostasis and therefore contribute to the risk of deep venous thrombosis and pulmonary embolism. Increases in central venous pressure may further decrease venous return from the central nervous system, which, in the setting of not infrequently detectable microembolization [26] of the brain by debris material during the implantation process, may negatively affect central nervous system outcomes [3] (Table 5.1).

Table 5.1 Gurd's criteria for the diagnosis of fat embolism syndrome

Major criteria	Petechiae
	Respiratory insufficiency
	Cerebral signs
Minor criteria	Tachycardia (HR >120)
	Fever
	Retinal signs
	Jaundice
	Renal insufficiency
Laboratory findings	Thrombocytopenia
	Anemia
	High erythrocyte sedimentation rate
	Fat macroglobulinemia

Used with permission of the Licensor through PLSclear from Gurd and Wilson [41]
One major, four minor, and one laboratory finding is necessary for diagnosis

Supporting the hypothesis that a decrease in end-organ reserve plays a prominent role in the pathophysiology of complications are data suggesting that patients with decreased pulmonary vascular reserve are at increased risk for deep venous thrombosis, pulmonary embolism, and atrial fibrillation [21, 27]. The odds for patients with pulmonary hypertension to develop ARDS, PE, and DVT after total hip arthroplasty were 4.86 (95% CI, 3.60–6.57), 4.63 (95% CI, 3.32–6.45), and 2.35 (95% CI, 1.78–3.10), respectively [21]. In an unpublished review of individuals undergoing total joint replacement with pulmonary hypertension at our institution, 33% developed atrial fibrillation. The incidence of the latter complication among total joint arthroplasty recipients has been quoted to be 3.1% [28]. Further, the existence of dementia or cerebrovascular disease has been shown to increase the risk of perioperative mortality after hip and knee arthroplasty by 7- and 4.5-fold [3].

The Role of Embolic Load

The evaluation of the role of the overall load of embolic material on outcomes has been facilitated through the study of procedures performed on bilateral joints in which the material gaining access to the vasculature is presumably doubled. While the controversy regarding the approach to patients requiring bilateral joint replacement is ongoing, it has been accepted that simultaneously performed procedures carry a higher risk of morbidity compared to unilateral procedures [29–31]. It is likely that increased embolic load may be responsible for higher rates of ARDS and thromboembolic events seen in patients undergoing bilateral versus unilateral total knee arthroplasty [30]. Similarly, increased exposure of the central nervous system and kidneys to embolic material may at least in part explain higher rates of delirium and renal complications in bilateral versus unilateral joint arthroplasty patients [30, 31].

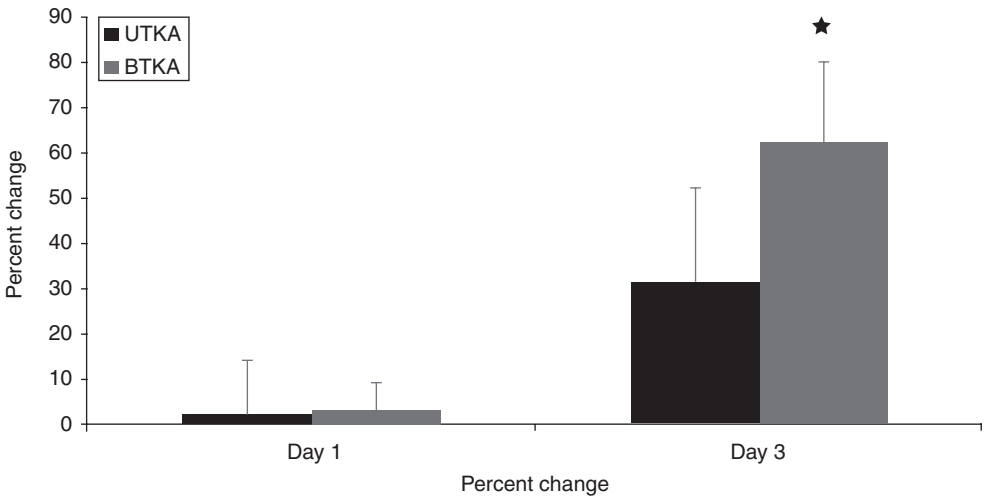

Fig. 5.2 Percent change of urine desmosine/creatinine levels compared to baseline values. Only the rise of levels on day 3 for bilateral total knee arthroplasty (*BTKA*) patients was statistically significant (see *star*). (Used with permission of Springer Nature from Memtsoudis et al. [25])

Indeed, investigations on the role of bilateral versus unilateral debris exposure on the degree of lung catabolism suggest significantly higher levels of lung injury after bilateral total knee arthroplasty. Desmosine, a breakdown product of elastin, which is found in large amounts in lung tissue, was found at significantly higher concentrations in the urine of patients undergoing two versus one knee replacement (Fig. 5.2) [25]. This finding is consistent with the higher rates of ARDS observed in patients undergoing bilateral joint replacement [30]. When evaluating pulmonary vascular parameters in patients undergoing bilateral hip arthroplasty, an increase in pulmonary vascular resistance was observed after the second but not the first hip implantation when compared with values at incision. Pulmonary vascular resistance remained elevated 1 h after surgery, and pulmonary artery pressures were significantly elevated on postoperative day 1 compared with those at baseline [10]. These findings are important in two ways: (1) they suggest that there exists a clinical injury threshold that allows individuals to absorb an insult through pulmonary capillary artery recruitment [12] and without manifesting hemodynamic changes. The exposure to an increased insult, i.e., a larger embolic load, may surpass this threshold, however, and may expose patients to increased risk of developing clinically significant complications; (2) increases in pulmonary vascular resistance and therefore right heart strain may be more prolonged than previously thought, thus exposing patients to longer periods of cardiopulmonary stress.

It may also be important to mention the at first glance "paradox" finding of decreased mortality found after revision versus primary total knee arthroplasties [3, 32]. While revision surgeries may be generally viewed as technically more difficult, the fact that the previously invaded femoral canal contains less or no medullary contents that can be forced intravascularly may explain this phenomenon. This benefit may, however, not relate to revision hip surgeries, which are usually associated with significantly longer surgical time and higher blood loss in the absence of the possibility to use a tourniquet [3, 32].

The Role of Cement

Further, reports have been published elucidating the role of methylmethacrylate on outcomes. Many investigations seem to suggest that the use of a cemented prosthesis is associated with increased risk of morbidity and mortality [32]. In a study of over 20,000 patients undergoing total knee arthroplasty, Parvizi and colleagues noted that all 47 mortalities observed in this cohort occurred in cases in which cement was used. In a multivariate regression, the use of cement was associated with an increased adjusted risk for a fatal outcome [32].

While the cause of mortality after joint arthroplasty is almost certainly multifactorial, clinical investigations comparing surgery with the use of cement versus without it found significantly less embolic material entering the pulmonary vascular tree in those in whom no cement was used [33].

The use of vacuum drainage placed in the proximal femur to reduce the increase of intramedullary pressure during insertion of the prosthesis has been shown to reduce the incidence of embolization during cemented hip arthroplasty as assessed by transesophageal echocardiography [34]. Koessler and colleagues found that embolization of material occurred in 93.3% of patients operated on with the conventional cementing technique, compared with only 13.3% of patients operated on with the modified approach ($P < 0.05$).

Although it is likely that the use of cement may play a role in the severity of intraoperative embolic events, it is important to consider that patients requiring cemented prostheses often present with poor bone quality, are older, and therefore

are burdened with comorbidities and decreased end-organ reserve. Thus, the possibility that the use of cement is a surrogate marker of demographic factors predicting adverse outcome in patients has to be kept in mind when interpreting studies of this kind.

The Role of Fat Embolization: The Fat Embolism Syndrome

Although commonly thought to occur in patients suffering from long bone fractures, the intravasation of fat globules originating from the bone marrow can occur during the reaming and instrumentation process. Embolization of fatty material results in the occlusion of small blood vessels in the lungs, central nervous system, and other organs. Subclinical levels of embolization can be detected in over 90% of patients undergoing total hip arthroplasties and between 46% and 65% in those with knee replacements [27, 35]. However, serious multi-systemic manifestations termed fat embolism syndrome (FES) occur less frequently. While the true incidence of FES is unknown, it has been reported to lie between 1% and 29%, depending on diagnostic criteria used [36–38]. Mortality associated with FES reaches 20% and depends on the severity of end-organ involvement [39] especially that of the pulmonary and central nervous system [40].

Diagnosis requires a high level of suspicion and interpretation of clinical signs. The classic triad described by Gurd and colleagues includes respiratory insufficiency, neurologic changes, and upper body petechiae [41], while other nonspecific criteria include tachycardia, fever, jaundice, renal failure, and cardiovascular collapse [42]. Right heart strain pattern on ECG, anemia and coagulopathy on laboratory testing, fat globules on pulmonary artery blood aspirates on frozen section, and pulmonary edema on chest *X-ray* may be found [43–45].

A number of scoring systems have been developed in order to aid with the diagnosis of FES (Tables 5.1 and 5.2). Gurd and colleagues originally proposed a combination of major and minor criteria and laboratory findings (Table 5.1) [41], while others have modified this approach to include further parameters (Table 5.2) [46, 47].

Table 5.2 Schonfeld's criteria for diagnosis of fat embolism syndrome

Clinical findings	Score
Petechiae	5
Chest *X-ray* changes	4
Hypoxemia	3
Fever	1
Tachycardia	1
Tachypnea	1
Confusion	1

Used with permission of the American College of Physicians from Schonfeld et al. [47]
A total score of >5 is required for diagnosis

While the pathophysiology of FES is not fully understood, two major theories prevail in the literature attempting to explain its pathogenesis. The mechanical theory suggests that lipid globules enter the bloodstream and occlude blood vessels in the lung bed and other organs, thus causing ischemia and inflammation, which in turn may lead to cerebral, renal, and other organ dysfunctions.

A biochemical theory proposes the direct effects of free fatty acids on pneumocytes, leading to hypoxia, pulmonary hypertension, and eventually cardiopulmonary compromise. The effect of free fatty acids on various organ systems explains the other clinical sequelae of FES [16, 48, 49].

The Pathophysiology of Spine Fusion Surgery

While the pathophysiologic principles discussed previously also apply in the setting of spine fusion surgery, this surgical entity is less homogeneous compared to joint arthroplasties. Surgical approaches, invasiveness, and length of operation vary widely to accommodate a plethora of pathologies, including traumatic, degenerative, oncologic, or those with deformity. Thus, perioperative stresses follow a more individual distribution and vary significantly from patient to patient.

Aside from the usual insults inherent to major surgery, such as massive blood loss and subsequent resuscitation, pulmonary compromise is of special concern. In a nationally representative study of patients undergoing spine fusions, the lungs were the second most commonly affected organ system by procedure-related complications [50]. This is likely due to the cumulative result of a number of perioperative factors, including transfusion and ventilator-associated related lung injury, direct mechanical contusion associated with a potential intrathoracic surgical approach, and the effect of pulmonary embolization of bone debris.

It is of no surprise that surgical extent and invasiveness are thus closely correlated with the risk for adverse events. It has been shown that more extensive procedures, especially those necessitating invasion of the thoracic cavity, are burdened with higher rates and risk of complications [50]. Indeed, approximately 3% of patients will develop ARDS after anterior/posterior spine surgery compared to approximately 1% after a posterior or 1.6% after an anterior approach only [50].

It is well established that significant lung injury does occur, especially during anterior/posterior spine surgery [51–55]. While the exact mechanism of lung injury associated with spine surgery remains unclear and is likely multi-

factorial, Urban and colleagues [52] were able to demonstrate an adverse pulmonary effect of perioperative events in the form of an increase in pulmonary vascular resistance in 15% (8/55) of patients, usually during or after posterior instrumentation. In a follow-up study, the same author analyzed bronchoalveolar specimens and linked the presence of lipid-laden macrophages to possible embolization of fat and debris entering the bloodstream during the surgical procedure. This mechanism of lung injury is supported by echocardiographic studies, in which 80% of spine surgery patients experienced moderate to severe embolic events during instrumentation of the spine [53]. Markers of lung catabolism showed a significant increase in the postoperative period compared to baseline [55]. Roentgenographic abnormalities of the lung can be found in 64% of patients undergoing anterior and posterior spine surgery [53].

Additional culprits contributing to pulmonary damage include ventilator-associated injury [56], the effect of blood product transfusions [57], and massive resuscitation [58]. It should be mentioned that coagulopathies and pulmonary circulatory disease were identified as the two disease states with the highest predictive risk for mortality after spine fusion (odds ratios of 5.46 (CI 4.34–6.86) and 8.37 (CI 5.95–11.78), respectively) [50]. The former may be viewed as a marker of invasiveness of the procedure and extent of blood loss, while the latter is likely an indicator of reduced end-organ reserve.

Timing of Complications

Although embolization of debris particles occurs primarily intraoperatively surrounding the implantation process, most clinical complications manifest in the days following surgery [59]. Indeed, in a report published by Parvizi, only 3 out of 47 mortalities undergoing total knee arthroplasty occurred intraoperatively [32]. In a study of over 30,000 hip arthroplasty patients, 88% of mortalities occurred during the patients' hospitalization. When looking at the timing of life-threatening complications, the same author concluded that 90% occurred within the first 4 postoperative days [59].

These observations suggest that the injury following systemic embolization of debris surrounding hip and knee arthroplasty may have a stepwise effect.

The intraoperative acute phase may be marked by mechanical obstruction of blood vessels, acutely leading to vasoconstriction in the lungs and other organs. Following this initial insult, protracted cardiopulmonary strain and the evolution of an inflammatory process may explain the delayed occurrence of complications including pulmonary embolism, lung injury, and delirium [32]. Supporting this hypothesis are findings which suggest that the maximum levels of lung catabolism were found on day 3 postoperatively [25, 55] and systemic markers of inflammation peak postoperatively [60].

Interventions

Opportunities for interventions to affect the relationship between embolic load and outcomes exist at the various perioperative stages. Careful patient selection is the cornerstone of optimizing outcomes. Therefore, it seems prudent to attempt to especially reduce embolic exposure in patients with decreased end-organ reserve [3, 21]. One example of such an approach would be to avoid bilateral procedures in the very old or those with significant comorbidity burden, thus increasing their chance to absorb perioperative insults [30, 31]. The use of non-cemented implantation techniques, although attractive in an attempt to reduce embolic exposure, may depend on bone quality and thus be of limited value in elderly patients [34]. However, if cement is utilized, vacuum drainage during prosthesis insertion seems to be a viable option to reduce the intramedullary pressure gradient [34]. Intensive monitoring with pulmonary artery catheters or transesophageal echocardiography may increase detection of fat emboli [34, 44], but no evidence exists that these interventions improve outcome. However, in selected cases invasive monitoring may aid to guide hemodynamic management.

Although some studies suggest that prophylactic use of steroids in patients with fractures may be beneficial in reducing markers of systemic inflammation [61] and the risk for the development of FES [62], more research is needed in this arena before clinical recommendations on routine administration of these drugs can be made. The use of intravenous alcohol, heparin, dextrans, and hypertonic dextrose is not recommended at this time. Therapy for FES remains supportive. Mortality is primarily from pulmonary sources, while long-term morbidity is secondary to cerebrovascular sequelae [40].

Further, the intraoperative use of epidural anesthesia may be advantageous as animal models have shown superior hemodynamics in the presence of pulmonary embolization, a situation not dissimilar to that encountered during intraoperative debris exposure [63, 64].

Interventions to reduce secondary organ injury due to stress and inflammation may be warranted. In this context, additional insults which can aggravate stress to the cardiovascular system, including pain and fluid overload, should be avoided. The use of peripheral nerve blocks has proven to positively affect levels of inflammatory markers [65].

Major blood loss remains a concern especially during major spinal surgery. While interventions such as use of anti-

fibrinolytics, controlled hypotension, use of cell savers, and hemodilution techniques remain therapeutic options [62], the use of recombinant factor VII is being evaluated in the spinal surgery arena [66, 67].

Summary

A large number of insults including tissue trauma, blood loss, and activation of various neurohumoral cascades may present the underlying causes for perioperative complications. While patients undergoing orthopedic procedures are not exempt from exposure to these stresses, a number of specific events, especially the embolization of cement and marrow material during instrumentation and manipulation of osseous structures, make this patient population unique and thus warrant special attention and discussion.

In this chapter we discuss issues surrounding the role of intravasations of bone, cement, and fat into the systemic circulation and its effects on various organ systems. The relationship of overall embolic load and end-organ reserve in the context of clinical outcomes is presented. Further, additional pathophysiological components relevant to spine surgical patients are reviewed. And finally, interventions to reduce the impact of intraoperative insults on clinical outcome are being presented.

We conclude that the rate and risk of perioperative complications in orthopedic patients are affected by the magnitude of intraoperative and postoperative insults and ability of various organ systems to absorb the derangements caused. The systemic embolization of debris material, extent of surgical invasiveness, and blood loss play major roles in the pathophysiology of these procedures.

Attempts should be made to find a balance between these two components and adopt management strategies including adequate patient selection, selection of surgical technique, and postoperative management.

Summary Bullet Points

- The intravasation of bone, cement, and marrow during the surgical process occurs frequently and may contribute to the pathophysiology of complications seen in the perioperative period.
- The risk of perioperative complications may be dependent on the level of the operative insult on one hand and end-organ reserve on the other.
- Identifying interventions that can reduce perioperative insults and instituting programs to identify patients at risk may result in a decrease in the odds for perioperative complications.

Case Study

A 58-year-old male with a history of obstructive sleep apnea, hypertension, and obesity presented for right total knee arthroplasty. His preoperative evaluation was unremarkable, except a right bundle branch block on the electrocardiogram. A recent nuclear stress test was negative for inducible ischemia.

After admission to the hospital, he proceeded to the operating room where a combined spinal and epidural was placed to provide surgical anesthesia. A femoral nerve block was added for postoperative pain control, and a radial arterial line was inserted for close hemodynamic monitoring. Intravenous sedation was provided with midazolam 5 mg, while supplemental oxygen at 3 L/minute was delivered via nasal cannula. Because of the tendency for airway obstruction with deeper levels of sedation, the patient was kept mostly awake during the procedure. The total knee arthroplasty procedure was conducted uneventfully under tourniquet inflation. Hemodynamics, respiration, and oxygenation remained normal throughout surgery. After implantation of the hardware, the tourniquet was released and closure of the wound commenced. Shortly after, the patient's blood pressure dropped from previously 112/65 to 76/43 mmHg, and his heart rate increased from 65 to 101 beats per minute. A concomitant drop in the pulse oximetry reading to 82% was noted. Ephedrine 10 mg was given intravenously, and a mask was placed over the patient's nose and mouth in order to deliver 100% oxygen. The patient's blood pressure improved to 94/52 and his oxygenation to 92%. After conclusion of surgery, the patient was brought to the recovery room where his O_2 saturation was noted to be 90% on a non-rebreather mask. On exam, diffuse rales were noted on chest auscultation, and a chest radiograph revealed bilateral, diffuse edema. Diuresis with intravenous furosemide was initiated. The patient became agitated and confused, and given his persistent hypoxia, the decision was made to intubate his trachea.

Laboratory tests revealed a hematocrit of 29%, a white cell count of 18,000, and a platelet count of 76,000/dL. A cardiac echo revealed a normal left ventricular function, moderate pulmonary hypertension, and right heart dilatation. A pulmonary embolism was ruled out by computed tomography with contrast. Based on these clinical findings, the diagnosis of fat embolism syndrome was made. Imaging of the brain was negative for an intracranial process. The patient remained intubated utilizing a lung protective ventilation approach with low tidal volumes, and he was successfully extubated on postoperative day 2. Supportive care consisted of diuresis and empiric use of bronchodilators. His central nervous system symptoms subsided. He was transferred to the ward and discharged from the hospital on postoperative day 7.

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Part II

Anesthesiologic Management

Anesthesia in the Orthopedic Patient

6

David Shapiro and Richard L. Kahn

Objectives

- Discuss perioperative anesthetic concerns of common orthopedic populations.
- Examine how orthopedic surgery is amenable to regional anesthesia.
- Review the advantages and risks of regional anesthesia.
- Understand the use of anticoagulation in the setting of regional anesthesia.
- Review proper positioning for orthopedic surgery.
- Discuss blood conservation strategies for orthopedic surgery.
- Examine the current state of Enhanced Recovery After Surgery for the orthopedic surgery patient.

Key Points

- A thorough preoperative evaluation should be performed in order to evaluate for preexisting comorbidities and identify risk factors for potential anesthetic implications.
- Orthopedic surgery is well suited for neuraxial and peripheral regional anesthetic techniques. These techniques offer many advantages including early mobilization, decreased time to discharge, and improved postoperative analgesia.
- Ultrasound guidance offers advantages over traditional regional techniques and may allow more patients to benefit from regional anesthesia.
- Orthopedic patients are at an increased risk for thromboembolism. The anesthesiologist must be aware of the choice of pharmacologic prophylaxis in order to coordinate regional anesthetic techniques.
- Several blood conservation strategies are available to minimize blood loss and blood transfusion and may be combined depending on the proposed surgery and specific patient.

Introduction

Managing the orthopedic patient can present a wide variety of challenges to the anesthesiologist. Orthopedic patients are a heterogeneous group with individuals varying greatly in regard to age, comorbidity profile, and surgical need. Patient outcome is affected by multiple factors including preexisting conditions, type of surgery, and anesthetic and perioperative management. While it remains unclear as to whether or not neuraxial and regional anesthesia reduce perioperative mortality [1–4], studies have shown that regional nerve blocks can improve postoperative functional recovery [5, 6], reduce the need for intensive care services [7] and hospital stay [5, 6], and decrease postoperative systemic infections [8], pulmonary complications, ileus, opioid consumption, inflammation, and the incidence of venous thrombosis [9–14]. Regional anesthesia also facilitates the usage of controlled hypotension which can reduce intraoperative blood loss, perioperative transfusion requirements, and postoperative deep venous thrombosis (DVT), improves surgical field visualization, and may improve patient outcomes [7, 8, 13–16].

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Despite the known advantages of regional anesthesia, the anesthesiologist must perform a comprehensive evaluation of each patient to determine the optimal anesthetic plan. When tailoring an anesthetic to the patient, one must consider the patient's age, comorbidities, expectations, surgical procedure, postoperative disposition, rehabilitation, and anticoagulation plans. In this chapter, we will discuss various aspects of anesthesia for the orthopedic patient, including special considerations of common presenting comorbidities in the orthopedic patient population; the advantages and risks of regional anesthesia; strategies to minimize intraoperative blood loss including hypotensive anesthesia, pneumatic tourniquets, and anti-fibrinolytic therapies; special intraoperative considerations including proper patient positioning; and finally, the future care pathways currently in development through the Enhanced Recovery After Surgery (ERAS) initiative.

The Orthopedic Population

The orthopedic patient population encompasses a wide range of individuals. Presenting patients can range from a healthy child who fell off a swing set presenting with a Colles' fracture to the elderly patient with multiple medical comorbidities presenting with a hip fracture. Regardless, it cannot be overemphasized that a complete and comprehensive preoperative evaluation of every patient is mandatory while taking care to not focus solely on the area of injury or surgery. This section will focus on several comorbidities commonly associated with orthopedic patients.

Advanced Age

The elderly population in the United States continues to grow. According to the Population Reference Bureau report "Aging in the United States," the number of Americans 65 years and older is projected to almost double from over 45 million today to over 90 million in 2060 [17]. Since the vast majority of joint arthroplasties performed in the United States occur in patients older than 50 years, it is an almost certainty that the demand for joint arthroplasty and other orthopedic care will continue to increase [18]. It is therefore important to note the physiologic changes that occur as a result of aging and the anesthetic implications of those changes to better manage the challenges and perioperative complications that may arise.

Aging is associated with a progressive decline of functional reserve in all major organ systems. Age-related changes in the brain result in increased sensitivity to anesthetic agents. In general, elderly patients are more sensitive to medications that act on the central nervous system and therefore require reduced dosages to achieve a desired clinical response. In addition, the agent may require a longer time to metabolize, thereby leading to a prolonged effect [19]. The increased CNS sensitivity to anesthetics helps to explain the impaired response to hypercapnia and hypoxemia. This has implications throughout the perioperative period.

Changes in the cardiovascular system are significant and progressive. In addition to an increased incidence of cardiovascular disease, the heart becomes less responsive to beta-adrenergic agonists (referred to as "dysautonomia of aging") and demonstrates an increased incidence of cardiac conduction abnormalities [19, 20]. Furthermore, these patients are prone to develop chronic hypertension. Hypertension places increased afterload on the heart, resulting in left ventricular hypertrophy and diastolic dysfunction which can lead to greater myocardial oxygen demand. Elderly patients also experience a greater incidence of blood pressure lability under anesthesia that can result in significant hypotension requiring treatment [21].

Since it is well founded that patients presenting with cardiac comorbidities are at increased risk of perioperative adverse cardiac events, patients should receive appropriate preoperative cardiac testing based on clinical risk profile, functional status, and type of surgery [22]. While the details of a proper perioperative cardiac evaluation are beyond the scope of this chapter, it should be noted that orthopedic surgery is defined as an intermediate risk surgical category due to the potential inflammatory response, blood loss, fluid shifts, and postoperative pain [23]. The functional status of these patients is often difficult to assess due to the physical limitations that require them to have surgery. Extensive universal preoperative cardiac testing has not been shown to improve outcome. Therefore, each patient must be evaluated on an individualized basis prior to surgery. In general, cardiac tests should only be ordered if the results would alter management. Judicious use of invasive monitors and close postoperative monitoring may also affect perioperative morbidity and mortality. Depending on the patient's medical comorbidities and operative course, certain patients should be admitted to a step-down or intensive care unit setting for closer postoperative monitoring and management

The pulmonary system undergoes profound changes with aging as well. These include stiffening of the chest wall; reduced lung parenchymal surface area, elasticity, and respiratory muscle strength as well as increased lung residual volume and ventilation to perfusion mismatching; and work of breathing. Additionally, elderly patients are more likely to have sleep apnea and chronic obstructive pulmonary disease (COPD) [19]. Such changes must be recognized and managed appropriately in order to avoid potential perioperative respiratory complications associated with anesthesia and surgery [24].

Both renal function and hepatic system function decline with age. Hepatic blood flow declines over time, as does

renal glomerular filtration rate. These changes lead to slower metabolism and clearance of a wide variety of medications commonly administered by anesthesiologists, including, but not limited to, anesthetic induction agents, opioids, local anesthetics, benzodiazepines, neuromuscular blockers, and nonsteroidal anti-inflammatories. One must be cautious and thoughtful when administering these agents to elderly patients [25, 26].

Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a relapsing and remitting, chronic inflammatory disease which affects 1% of adults with a greater preponderance in women [27]. The etiology of the disease is unknown but is believed to be due to a combination of genetic, immunologic, and environmental factors [28]. It primarily affects joints, resulting in persistent synovial tissue inflammation resulting in pain and stiffness which often worsens with rest. Other inflammatory arthropathies, such as systemic lupus erythematosus and scleroderma, share many of the same clinical features, and much of the following discussion applies.

The disease may also affect multiple other organ systems of the body as well. In the cardiovascular system, it can manifest as pericarditis, myocarditis, accelerated coronary atherosclerosis, coronary artery disease, and heart failure [29]. It addition, rheumatoid nodules can form on the cardiac conduction system, resulting in cardiac arrhythmias and heart block [30]. In the pulmonary system, RA may present as a pleural effusions, dyspnea, or pulmonary fibrosis resulting in restrictive lung disease. Costochondral involvement can limit chest wall movement, resulting in diminished vital capacity and lung volumes as well as significant ventilation to perfusion mismatching. RA patients may also have anemia of chronic disease [28].

The rheumatoid patient presents for orthopedic surgery throughout various stages of this progressive and disabling disease. Depending on the severity of the disease, these patients can present a challenge to the anesthesiologist. Airway management can be extremely difficult in this patient population. Patients may have atlantoaxial subluxation due to ligament destruction in which neck flexion can result in the odontoid process impinging on the spinal cord [15, 31]. It remains controversial whether flexion and extension cervical spine x-rays should be performed in all rheumatoid patients. Regardless, it is prudent to thoroughly assess the patient for the presence of any symptoms and obtain radiographs if appropriate. Due to their abnormal anatomy, mask ventilation and intubation can be extremely difficult. The combination of micrognathia with protruding top teeth can make direct laryngoscopy impossible. Fifty percent of rheumatoid patients have jaw symptoms usually presenting as inability to fully open the mouth, thus further complicating airway management [15]. Additionally, patients with this disease often have laryngeal deviation and cricoarytenoid synovitis. The upper airways of individuals affected by the disease can become completely obstructed even with conscious sedation.

If an airway exam is consistent with potentially difficult intubation, insertion of an endotracheal tube is best done utilizing indirect laryngoscopy via a video laryngoscope or an awake fiberoptic technique and employing a small gauge endotracheal tube. Besides airway considerations, the anesthesiologist must ensure that the patient has an adequate cardiac and pulmonary evaluation and risk stratification prior to surgery. Depending on the severity of disease and the surgical procedure, the patient may require invasive monitoring such as an arterial line or central line. In addition, preanesthetic evaluation must include discussion of any preexisting neuropathy which may preclude the usage of peripheral nerve blockade or neuraxial anesthesia. In this era of effective disease modifying drugs, particularly biologics, the incidence of severe manifestations of the disease process had been markedly decreased. There is now extensive experience confirming the safety of regional anesthesia combined with careful sedation in many of these patients [31]. The benefits of regional anesthesia, including decreased hemodynamic perturbations and avoidance of airway instrumentation, can outweigh the rare risk of an airway emergency [27].

Osteoarthritis

Osteoarthritis (OA) is the single most common disease process seen among the orthopedic population. More than 50 million adults in the United States have physician-diagnosed arthritis [32]. OA is a degenerative disease involving the loss of articular cartilage, leading to the loss of joint function. It differs from RA in that osteoarthritis is a degenerative condition characterized by a breakdown of articular cartilage and underlying bone, whereas RA is secondary to an autoimmune inflammatory reaction. Pain is usually present with movement and improved with rest unlike that of RA which is associated with morning stiffness that typically improves throughout the day. Women are slightly more frequently affected than men, and the prevalence increases with age. OA typically affects the large joints of the body, namely, the hip and knee, as well as the spine and joints of the hands and feet [33]. While osteoarthritis is not a systemic disease, the anesthesiologist should be aware of which joints are painful and/or have limited mobility [23]. Positioning patients may be extremely difficult and if at all possible, the patient should be allowed to position himself. Airway management may also be more challenging due to the decreased range of motion of the patient's neck and decreased glottic opening. A

thorough airway exam should be performed prior to surgery. Additionally, the placement of neuraxial anesthesia may be challenging due to the decreased disk height and an increased number of osteophytes surrounding the vertebrae. Often, using a paramedian approach is more successful. Finally, these patients may require chronic NSAIDs or opioids for their arthritic pain. This should be taken into account when tailoring an intraoperative anesthetic plan and postoperative analgesic regimen.

Although other diseases are common in the orthopedic arena, including ankylosing spondylosis, scoliosis, and obstructive sleep apnea among others, detailing these disease processes is beyond the scope of this chapter. In sum, it falls upon the anesthesiologist to recognize the anesthetic implications and challenges that each disease presents and employ the skills necessary to provide a safe and effective anesthetic.

Positioning

Patients are placed in a variety of positions for orthopedic procedures in order to help provide better surgical exposure. However, improper positioning can lead to intraoperative and postoperative complications including bony or ligamentous injury, tissue necrosis or ischemia, neuropraxia, or hemodynamic changes. Therefore, proper positioning should seek to absorb compressive forces, prevent excessive stretching or compression by maintaining normal body alignment and preserve hemodynamic and respiratory mechanics as much as possible [34].

There are several common operative positions utilized in orthopedic surgery; each position has its own set of unique considerations that the anesthesiologist should be aware of. A few simple rules apply to all positions: maintain position as neutral and natural as possible, pad areas where nerves are superficial and may be compressed, protect the eyes from corneal abrasion, position arms with less than ninety degrees of elbow and shoulder flexion, and check the positioning frequently.

The beach chair position is often used during shoulder surgery. In this position, the head, neck, and hips should be secured and maintained anatomically neutral. The operating room team must ensure neutral head and neck positioning to allow venous drainage from the head and prevent neuropathy from excessive brachial plexus stretching [35]. As the operative field is above the heart, air embolism is possible due to subatmospheric venous pressure and the presence of noncollapsible venous sinuses in bone. Thus, the anesthesiologist must maintain a high index of suspicion of an air embolism with any hemodynamic changes. In addition, in this position, there is a high degree of venous pooling in the lower extremities which can result in refractory hypotension. The decreased venous return to the heart can trigger the Bezold-Jarisch reflex, resulting in sudden hypotension and severe bradycardia [36]. Depending on the procedure as well as the patient's cardiac and neurologic comorbidities, invasive hemodynamic monitoring may be prudent in this position.

The lateral position is commonly employed for total hip arthroplasties performed from a posterior surgical approach. This positioning requires careful attention to maintaining neutral neck alignment. An axillary roll should be placed to relieve pressure on the down shoulder, brachial plexus, and vascular structures. Padding should also be placed below the dependent leg to prevent damage to the common peroneal and saphenous nerves. This position is associated with the greatest number of ocular complications, primarily corneal abrasions; the eyes should be protected and checked frequently [35].

Prone positioning is mainly utilized for spine surgery, and infrequently for foot and ankle surgery. The head and shoulders should remain neutral. Careful attention should be paid to ensure the eyes and ears are free from excessive pressure. The chest, abdomen, breast, and genitalia should remain free to prevent traumatic injury and hemodynamic changes due to compression of large vessels. Joints should be anatomically neutral, and proper padding should be placed to avoid postoperative neuropathy. Proper positioning and access to intravenous lines and monitors should be obtained prior to the surgeon preparing and draping the patient as it is difficult to adjust the position once the drapes have been applied.

The supine position is used for a large variety of orthopedic procedures. Main concerns in this position include eye protection and arm positioning as described above. It should be noted that roughly one quarter of all perioperative nerve injuries involve the ulnar nerve [35], although the etiology is generally not felt to be related to improper positioning.

Regional Anesthesia

Regional anesthesia has a wide application in orthopedic surgery. Its components, consisting of neuraxial and peripheral nerve blocks, can be used as adjuncts to postoperative pain relief or as the primary anesthetic during surgery. Utilizing regional anesthesia may allow the anesthesiologist to avoid instrumentation of the airway and delivery of positive pressure ventilation, as well as to avoid opioid-based pain medications, thereby leading to fewer systemic side effects. Although the influence of the mode of anesthesia on mortality remains unclear, a large body of literature has found regional anesthesia to have significant advantages over general anesthesia, including a decreased incidence of deep venous thrombosis and fatal pulmonary embolism, systemic infection, myocardial infarctions, postoperative confusion, and improved postoperative analgesia [3, 8, 12]. Rodgers

suggests that these benefits are gained due to the presence of regional anesthesia, and not the absence of general anesthesia [14]. Peripheral nerve blocks are associated with improved rehabilitation and reduced length of hospital stay [3, 6, 37]. That said, general anesthesia can be delivered safely and effectively to the orthopedic patient and is a reasonable alternative, particularly when regional anesthesia carries increased risk. Specific outcomes and the potential impact of regional anesthesia are discussed next.

Mortality

Mortality following orthopedic surgery varies based on the preoperative condition of the patient, his or her comorbidities, and the procedure performed. The 1-year mortality rate after hip fracture ranges from 17% to 27% based on several population-based studies in elderly patients [38–40]. Currently, based on the literature, there is no proven difference in mortality for hip fracture patients receiving regional or general anesthesia. While some studies have concluded that regional anesthesia is safer [3, 14, 41], other studies have found no clinically significant difference in mortality [1, 4, 42]. As a result of this ongoing debate and limited high-quality evidence on the subject, several researchers are conducting an international, prospective, multicenter, randomized control trial to further elucidate the benefits, if any, of regional anesthesia on mortality [43]. In addition to the possible benefit of reduced mortality, regional techniques may confer other benefits to patients.

Postoperative Analgesia and Rehabilitation

Pain management following orthopedic surgery can be extremely challenging. Failure to provide adequate analgesia can prevent early mobilization and rehabilitation, which are important factors for maintaining joint range of motion and ensuring the general success of surgery. Severe pain occurs in up to 60% of patients undergoing total knee arthroplasty [5]. Patient-controlled epidural analgesia, generally a low concentration of a local anesthetic combined with an opioid, can provide excellent pain relief for lower extremity surgery. This requires careful titration of the local anesthetic dose in order to minimize weakness and orthostatic hypotension during physical therapy. Although there is an increased level of concern for postoperative falls, there is no evidence to suggest that the placement of peripheral nerve blocks or neuraxial anesthesia increases the risk of such events, assuming standard fall precautions are utilized within the institution [44].

Peripheral nerve blocks using catheters or long-acting local anesthetics with or without additive may provide excellent postoperative analgesia with significantly reduced need for opioid administration. By taking fewer opioids, patients experience less nausea, vomiting, sedation, and urinary retention [5, 10]. Patients who have received peripheral nerve blocks have shorter hospital stays and decreased time to hospital discharge [45–49], reduced incidence of readmissions to the hospital [48], earlier ambulation [50], and improved early postoperative range of motion [51]. However, it must be noted that no study to date has demonstrated a difference in long-term joint function as a result of regional anesthetic techniques [52].

There is great interest in regional nerve blocks that provide anesthesia and analgesia while minimizing motor weakness in order to encourage early postoperative ambulation. One such regional technique, the adductor canal block, is increasingly utilized in patients undergoing total knee replacement. This nerve block anesthetizes the saphenous nerve and its branches to the vastus medialis while avoiding more proximal motor branches of the femoral nerve that supply the quadriceps [53] and is now more commonly used than a femoral nerve block in patients undergoing total knee replacement. A second motor-sparing regional technique that has been increasingly utilized for total knee arthroplasty as well as anterior cruciate ligament repairs at our hospital in an effort to encourage early postoperative ambulation is the infiltration between the popliteal artery and capsule of the knee (iPACK) block. Early data suggest that the iPACK coupled with an adductor canal block provided similar analgesia to a femoral nerve block. In addition, patients performed better during physical therapy which allowed for earlier hospital discharge [48]. According to a recent study, when combined with a periarticular injection by the orthopedic surgeon, patients who received both adductor and iPACK peripheral nerve blocks had decreased pain scores on postoperative days 0 and 3 and lower pain scores after physical therapy on postoperative days 1 and 3, compared with patients who received periarticular infiltration alone [54].

In addition to improving early postoperative analgesia, increased joint range of motion, and earlier hospital discharge, regional nerve blocks may theoretically decrease the incidence of chronic postoperative pain by inhibiting the local inflammatory response to injury that occurs after surgery. Blocking postoperative inflammation is believed to inhibit the development of hyperalgesia and chronic pain [55].

Respiratory Complications

Preexisting respiratory disease and general anesthesia are significant predictors of morbidity in hip fracture patients [56]. The risk of respiratory complications including pneumonia, acute exacerbation of COPD, and respiratory failure

has been found to be significantly higher when general versus regional anesthesia was used [57]. This respiratory benefit may be related in part to superior analgesia, which results in improved pulmonary function and decreased atelectasis, particularly in patients with limited respiratory reserve. Further explanation for this difference between the modes of anesthesia is likely attributable to the impact of mechanical ventilation on pulmonary injury.

Postoperative Confusion

Postoperative cognitive confusion and delirium exist on a continuum that is not yet fully understood. However, the incidence can be as high as 30% and has been associated with longer hospital stays, higher costs, and worse outcomes. The majority of studies report no difference in long-term postoperative confusion between regional and general anesthesia [58, 59]. However, a few studies have found a lower incidence of short-term confusion after regional anesthesia [4, 60–62]. This is likely due to patients receiving fewer opioids, benzodiazepines, and other anesthetics, leaving them more alert and cognitively aware.

Deep Vein Thrombosis

Postoperative DVT is common after orthopedic surgery. It has been well established that regional anesthesia significantly reduces the incidence of DVTs compared to general anesthesia [9, 10, 12, 14, 60, 63]. Hypotheses as to how regional anesthesia reduces the incidence of DVTs include the following: (1) increased blood flow to the extremities in combination with a reduced venous tone, (2) alterations in blood viscosity and coagulability secondary to neuroendocrine response to surgery [64], and (3) attenuation of the stress response to surgery showing decreased serum catecholamine and cortisol levels versus general anesthesia [65]. Despite the reduced incidence of DVTs in patients receiving regional anesthesia compared to those receiving general, regional anesthesia should not be viewed as an anticoagulation modality, and standard thromboprophylaxis should still be used.

Pulmonary Embolism

Many studies throughout the literature show a weak tendency toward a decrease in the incidence of PE for regional anesthesia. Furthermore, subgroup analysis demonstrates a large reduction in fatal PE following regional anesthesia [9, 10, 12, 14]. Reasons for this finding may be attributable to the effects on coagulation discussed previously.

Drawbacks to Regional Anesthetics

While regional anesthesia offers many benefits, one should also be aware of the potential adverse effects associated with their use. Besides offering anesthesia and analgesia, most peripheral nerve blocks are likely to impair motor function as well. This may limit the usefulness of some peripheral blocks in specific situations, especially when motor function needs to be assessed rapidly during and in the immediate postoperative period. In certain surgical procedures including those that involve nerve grafting or transposition, orthopedic trauma, or a patient with preexisting neuropathy at the surgical site, a regional nerve block may be contraindicated as it may prevent early diagnosis of postoperative nerve ischemia, compartment syndrome, or additional postoperative surgical complications that may warrant emergency intervention.

Although rare, both neuraxial and peripheral regional techniques may result in neurological injury. The mechanism of this complication is often unclear and multifactorial. Direct trauma to neural tissue during placement of a neuraxial block is rare. Contributing factors may include preexisting neuropraxias and neuropathies, diabetes mellitus, extremes of body habitus, male gender, and advanced age. Similarly, surgical factors such as direct surgical trauma, a compressive cast or sling, tourniquet inflation, and improper positioning can also contribute to neurological injury [66]. The rates of neurological complications after neuraxial blockade and peripheral nerve block are estimated to be 0.04 and 3%, respectively [67]. While the injury caused by the compressive lesions of an epidural hematoma or abscess can be elucidated, other causes of injury after neuraxial anesthesia often remain elusive. Transient neurological symptoms (TNS) are one of the most common complications after spinal anesthesia and present as pain in the buttocks and legs. The incidence of TNS is increased in ambulatory surgery, most commonly after knee arthroscopy, as well after spinals utilizing lidocaine as compared with bupivacaine, procaine, or prilocaine [68]. The pain can vary from mild to severe, is usually self-limited, and is best treated with nonsteroidal anti-inflammatory agents, suggesting an inflammatory component as its etiology. When actual neurological injury is suspected after neuraxial anesthesia, rapid diagnosis and treatment is essential. Particularly in the setting of an epidural hematoma or abscess, the likelihood of a recovery decreases significantly after 8 hours [63, 66]. Magnetic resonance imaging is the preferred diagnostic modality, but treatment should not be delayed if it is not available.

Causes of peripheral nerve injuries are assumed to be due to local anesthetic toxicity, complications of needle placement, or injury to surrounding structures by the local anesthetic or additives. However, no localization method

or monitoring technique has proven to be superior, and the pathophysiology of nerve injury remains unclear. It is extremely difficult to predict which patients will develop a neuropraxia. Some evidence suggests that patients with preexisting neurological deficits are more likely to develop a neuropraxia, with a suggested mechanism often referred to as the double crush theory [66, 69, 70]. Therefore, performing regional anesthesia on patients with preexisting neurological deficits is controversial and should be decided on an individual basis after fully discussing the risks with both the patient and the surgeon. Additionally, reducing the dose or concentration of local anesthetic as well as eliminating vasoconstrictive additives may be prudent [71].

Recovery from a nerve injury depends on a number of factors, including whether or not the axon of the affected nerve is preserved. It seems that if the axon is transected, recovery is slow and often incomplete. Similarly, if the neuronal fascicle is penetrated, neurons are exposed to injury from the local anesthetic that can be exacerbated by vasoconstrictors such as epinephrine [66]. Complete or worsening neural deficits should be immediately assessed by a neurologist, while mild symptoms often require only patient reassurance as the prognosis for improvement is excellent. If the injury does not resolve after 2–3 weeks, neurophysiologic testing can help to better define the nerve damage. Although neurophysiologic changes may not appear for a few weeks after the injury, nerve conduction studies and electromyography testing can help establish a baseline and rule out preexisting disease [66, 70]. While an exhaustive list of adverse effects of peripheral anesthetic techniques is beyond the scope of this chapter, it is essential to be knowledgeable on the limitations and risks of each block in order to properly and safely anesthetize the patient.

Anticoagulation

As stated previously, thromboembolic prophylaxis is essential because the risk of DVT and PE is high after major orthopedic surgery compared to other types of procedures. Total hip and knee arthroplasty as well as hip and pelvic fracture surgery have the highest incidence of thromboembolism [23]. Further, a number of patients are chronically on anticoagulation and antiplatelet therapy for various conditions including atrial fibrillation, previous history of venous thromboembolism, valvular heart disease, or history of percutaneous coronary intervention. Pharmacologic anticoagulation therapy has a significant impact on the use of regional anesthesia (particularly neuraxial anesthesia) and, in some cases, can preclude its use. While the incidence of an epidural hematoma in the general population remains exceedingly small, this incidence is significantly higher for patients on anticoagulation. The actual incidence of neurologic dysfunction resulting from hemorrhagic complications associated with neuraxial blockade is unknown.

The fourth edition guidelines from the American Society of Regional Anesthesia and Pain Medicine (ASRA) for regional anesthesia in patients receiving antithrombotic or thrombolytic therapy were published in 2018. They reflect the ever-changing treatment standards for thromboembolic prevention and provide guidance to providers caring for these patients. It must be mentioned, however, that due to the rarity of spinal and epidural hematomas and the likelihood of underreporting of such events, many of the guidelines are based on pharmacokinetic, pharmacodynamic, and hematologic studies, as well as case reports, small case series, and expert opinion. Given this, the guidelines should be used as a framework to help make clinical decisions based on the specific patient and clinical context, not as a blueprint in which certain decisions will lead to a certain outcome [63].

Factor Xa inhibitors, including rivaroxaban, apixaban, edoxaban, and betrixaban, are increasingly used over warfarin for the primary prevention of venous thromboembolism after total hip replacement. As compared to warfarin, they have safer bleeding profiles, more rapid onset, and shorter half-lives and do not require frequent laboratory monitoring [63]. They all have FDA black box warnings regarding the risk of spinal hematoma formation. However, due to the paucity of reports of spinal hematomas in patients who have received neuraxial anesthesia while on these agents, the new ASRA recommendations are pharmacologically based. To date, only two case reports of spinal hematomas have been reported in patients who received neuraxial anesthesia while on these new oral anticoagulants [72, 73]. The newly released guidelines are deliberately conservative in their recommendations on these new agents due to the lack of clinical data. These will likely change in the future as we learn more about the use of these drugs in the clinical arena.

While spinal hematoma formation is the most catastrophic complication of regional anesthesia due to the nature of bleeding into a fixed and noncompressible space, the risks associated with peripheral nerve blockade remain undefined. The fear of significant bleeding into a noncompressible space and/or nerve ischemia as a result of a nerve block (particularly in deeper plexus and peripheral nerve blocks) gives many clinicians pause. Based on the 18 case reports of patients with complications following peripheral or plexus blocks in patients on anticoagulation, morbidity from significant blood loss is more of a risk than long-term neurologic deficits. The ASRA guidelines recommend that when performing deep plexus or deep peripheral nerve blocks, the same guidelines for neuraxial techniques should be followed [63]. However, with the advent of ultrasound and the ability

to visualize the anatomy surrounding a nerve block target site, many anesthesiologists will apply a more liberal standard, depending on his or her individual skill, the clinical situation, and the complexity of the proposed regional anesthesia block.

As the options for postoperative anticoagulation continue to evolve, it is important to remain informed on the medications available, their mechanisms of action, pharmacologic properties, and case reports and series available in order to make educated risk-benefit analyses and decisions regarding regional anesthesia. Additionally, many patients may be on several medications affecting various parts of the coagulation cascade. The additive effect of these medications should be considered, although no recommendations have been made to address this issue. The need for prompt diagnosis and intervention is imperative to preserve neurological function and reverse spinal cord ischemia in the event of a spinal hematoma. This requires having a high index of suspicion and diligent assessments of the neurologic status after regional anesthesia.

Ultrasound-Guided Regional Anesthesia

The use of ultrasound-guided peripheral nerve blocks has increased dramatically over the past two decades and has become the gold standard technique in performance of regional anesthesia [74]. Ultrasound offers the ability to guide the needle placement; identify important anatomical structures such as the muscles, nerves, and major blood vessels within the field of interest; and monitor the injection of local anesthetic. Usage of ultrasound has led to fewer intravascular punctures and decreased time to onset of blocks when compared to traditional nerve stimulation techniques [75–77]. It has reduced the number of needle passes during block placement and the incidence of local anesthetic systemic toxicity (LAST) due to inadvertent intravascular administration of local anesthetic [78]. Furthermore, block quality has improved [79–82].

The faster onset time is likely due to a closer approximation of the needle and nerves with use of ultrasound. Several studies have also shown a dramatic reduction in the dose of local anesthetic necessary to achieve a successful block for surgical anesthesia or analgesia. Gautier found only 5 mL was necessary to achieve surgical anesthesia with an ultrasound-guided interscalene block for shoulder arthroscopy [83]. Similarly, Renes used an up-down method to show the minimum effective volume of local anesthetic for shoulder analgesia to be 3.6 mL [84]. These volumes are significantly lower than the traditional 40–60 mL used with paresthesia and nerve stimulator techniques. The ability to use lower doses may also explain the reduced incidence of LAST with the advent of ultrasound-guided nerve blocks. However, the incidence of local anesthetic toxicity is already extremely low (0.03%) [85]. Another benefit of low-dose blocks may be a reduced motor blockade, leading to increased patient satisfaction and fewer adverse effects of the block. However, these advantages have yet to be elucidated.

Historically, anesthesiologists have used anatomical landmarks to elicit paresthesias or electrical nerve stimulation in order to place the needle as close to a nerve as possible. However, this approach provides no information regarding the actual position of the needle tip, raising concern that the needle may be in an intraneural or intrafascicular location. Although the consequences of injecting local anesthetic intraneurally are controversial, it is acknowledged that injecting intrafascicularly is associated with an increased risk of nerve injury and neuropraxia. With the utilization of ultrasound, it has also become evident that even with a visually confirmed needle to nerve contact, a paresthesia is felt by only 38% of patients and an electrical stimulation of <0.5 mA elicits a visible muscle twitch in only 75% of patients [76]. Despite the absence of a muscle twitch, this does not affect the success rate with ultrasound. While some clinicians combine both nerve stimulation and ultrasound when performing blocks, nerve stimulation is insensitive, and the addition of nerve stimulation likely offers no advantage.

Although the data do not show conclusive superiority of ultrasound, it has become the preferred technique. Ultrasound allows those who are not regional anesthesia experts to feel comfortable performing a variety of blocks. This will likely increase the amount of regional anesthesia being performed and allow more patients to benefit from the technique.

Blood Conservation Strategies

Blood loss during orthopedic surgeries can be significant, particularly with revision procedures. According to a large study of over 320,000 patients in the United States, about one out of every five patients who undergo a total joint replacement surgery require a blood transfusion during surgery [86]. Allogeneic blood transfusions, while sometimes necessary, are associated with a number of risks, including but not limited to acute hemolytic transfusion reactions, transfusion associated circulatory overload, transfusion-related acute lung injury, infections, development of autoantibodies, and febrile reactions. In addition, according to one study, allogeneic blood transfusions were independently associated with longer hospital stays and higher hospital costs, which may be attributed to a higher incidence of infection in transfused patients [87]. Given this information, it is in the best interest of all parties to mitigate the need for transfusion. In the section to follow, several different blood conservation strategies that can be utilized will be discussed.

Controlled Hypotension

Hypotensive anesthesia is a technique that lowers the mean arterial blood pressure to 50–60 mmHg and results in a significant reduction in blood loss that can decrease transfusion requirements [88]. By reducing intraoperative blood loss, surgical exposure is improved and surgical time is reduced. Studies have also shown that a dry surgical field facilitates the penetration of cement into cancellous bone, improving the fixation during a total hip arthroplasty [16].

Prior to discussing the technique to achieve controlled hypotension, it is important to review the concept of oxygen delivery. Maintaining adequate oxygen delivery has been shown to improve prognosis [89]. Arterial oxygen delivery is dependent on cardiac output, hemoglobin concentration, and arterial oxygen saturation. If a decrease in cardiac output accompanies a decrease in blood pressure, oxygen delivery will also be decreased. Both general anesthesia and many antihypertensive medications are cardiac depressants and lead to a decrease in end-organ perfusion. Neuraxial anesthesia dilates the arterioles and veins and, when the level of sympathetic blockade includes the mid-thoracic level and above, also suppresses both the inotropic and chronotropic activity of the heart. However, it has been well described that by obtaining hypotension with a high sympathetic blockade approximating T4 and then titrating in an epinephrine infusion, cardiac output, and thus blood flow, is maintained despite hypotension [16]. Additionally, by utilizing neuraxial anesthesia, the negative effects of positive pressure ventilation on cardiac output and oxygen extraction are avoided.

When utilizing this technique, invasive monitoring is required. A reliable arterial line is essential to carefully titrating the epinephrine infusion and intravenous fluids to an acceptable mean arterial blood pressure. Maintenance of intravascular euvolemia is essential. With neuraxial anesthesia, the patient can be kept awake to assess neurological status in high-risk situations. The technique should be used with caution in people with a history of cardiac, cerebrovascular, renal, hepatic, or severe peripheral vascular disease.

The optimal mean arterial pressure for hypotensive anesthesia is controversial. The estimated intraoperative blood loss has been found to be 179 mL when the MAP was maintained at 50 mmHg and 263 mL when the MAP was kept at 60 mmHg [16]. This reduction may not be considered clinically significant. Cerebral blood flow is thought to be maintained constant over a range from 70 to 150 mmHg, but this assumption has recently been challenged. Some researchers suggest that during induced hypotension, the systolic blood pressure should not be reduced more than 20% from baseline [90].

Hypotensive neuraxial anesthesia has also been found to reduce the incidence of deep vein thrombosis. Virchow's triad describes thromboembolism occurring in the setting of venous stasis, vessel injury, and a hypercoagulable state. All three of these components exist during total hip arthroplasty but can be offset by obtaining controlled hypotension using neuraxial anesthesia and an epinephrine infusion. The neuraxial technique reduces the incidence of thrombosis as previously described, and the epinephrine infusion increases the skeletal muscle blood flow, reducing stasis and lessening thrombogenesis [16]. Additionally, the reduction in blood loss limits the dilution and consumption of coagulation factors, thus limiting rebound hypercoagulability.

The major cardiovascular risks with the hypotensive neuraxial technique are obtaining a high level of sympathetic blockade and severe bradycardia. The high spinal or epidural should be managed by assisting ventilation and supporting the circulation with epinephrine until resolution of the block. Early treatment of bradycardia with a beta-agonist is essential.

Intraoperatively, hypotension is also used during shoulder surgeries in the sitting position. The sitting position gives the surgeons better access to the shoulder, and hypotension helps decrease the blood loss and create an optimized surgical field. Several case studies have attributed ischemic brain or spinal cord injury to hypotensive anesthesia in the sitting position [91]. However, a recent study showed no strokes in over 4000 patients having outpatient shoulder surgery in the sitting position with hypotensive anesthesia [90]. Most of these cases were done under brachial plexus block and sedation with spontaneous ventilation, as positive pressure ventilation can theoretically adversely affect cerebral blood flow. Although this technique appears to be safe, it should be individualized to the patient taking into account comorbidities and risks.

Pneumatic Tourniquet

Applying a pneumatic tourniquet prior to incision is another strategy to minimize blood loss during orthopedic surgery. The tourniquet creates a relatively bloodless surgical field when inflated to 100 mmHg above the patient's systolic blood pressure. The tourniquet, however, is not without complications. It can cause significant pain that is often resistant to regional anesthesia and narcotics but is relieved with deflation. Although the etiology of this pain is unclear, a significant sympathetic response occurs 60 min after the inflation of the tourniquet. Other complications associated with usage of a pneumatic tourniquet include postoperative swelling, compression neuropraxia (which is often transient but, in rare cases, permanent), wound hematoma, vascular injury, tissue necrosis, rhabdomyolysis, muscle weakness, and compartment syndrome. Contributing factors are related to the height of the inflation pressure and duration of inflation [92]. In patients who have had prolonged application of a tourni-

quet, "post-tourniquet syndrome" may occur, resulting in swollen, pale, and weak limbs in the absence of paralysis. This syndrome typically resolves within a month of surgery. Postoperative edema distal to the applied tourniquet is the suspected etiology [93]. Wider cuffs require lower inflation pressures to stop flow and may help to minimize these complications [92, 94]. After 2 hours of tourniquet inflation, ischemic neuropraxia, edema, stiffness, pallor, and weakness, otherwise known as post-tourniquet syndrome, may occur [92]. When the tourniquet is deflated, both the mean arterial pressure and central venous pressure are decreased, and there is an increase in $PaCO_2$, $EtCO_2$, lactate, and potassium, leading to a transient metabolic acidosis. This is due to the circulation of the metabolic waste released from the ischemic extremity. Deflation is also associated with thrombolytic activity, activation of antithrombin III and protein C which may lead to post-tourniquet bleeding [94]. Whether these effects become clinically significant is highly variable. Therefore, the anesthesiologist should anticipate these changes when evaluating each patient preoperatively, and careful perioperative monitoring is required, particularly in patients with poor cardiopulmonary reserve. Despite the risks associated with use of pneumatic tourniquets, when used properly, they can improve surgical field visualization and reduce blood loss, thereby hastening surgical procedure and minimizing the need for transfusion.

Cell Salvaging

Cell salvaging is the process by which autologous blood lost during surgery is collected, processed, concentrated, and then administered back to the patient. Consideration for using this equipment should be based on availability, the patient's medical history regarding cardiac and hematologic comorbidities, starting hematocrit, religious beliefs (which may preclude transfusion of allogeneic blood), and anticipated intraoperative blood loss. In addition, patients with infected joints or malignancy may not be candidates for cell salvage as this can seed infection or malignancy to other parts of the body. Based on this assessment, a conversation with the surgical team should be held regarding the use of intraoperative cell salvaging. While the available studies investigating the utility of intraoperative cell salvage only contain small numbers of patients, they do suggest that it reduces the need for allogeneic blood transfusion in total joint arthroplasty [95, 96].

Tranexamic Acid

Tranexamic acid (TXA) is an antifibrinolytic agents that acts by competitive antagonism of plasminogen and plasmin binding sites on fibrin. By preventing this binding, TXA reduces bleeding by preventing the activation of plasmin, which normally acts to break down fibrin-bound clots. It has become more widely used in orthopedic surgery over the past several years, particularly in total joint arthroplasties and spine surgery. Several large studies found that usage of the agent reduced intraoperative blood loss and allogeneic blood transfusion [97, 98], and reduced thromboembolic complications, need for mechanical ventilation, and admission to the intensive care unit after surgery [99].

Overall, there is a substantial amount of evidence in the literature to suggest that TXA is effective at reducing perioperative blood loss and thus the need for blood transfusion in patients undergoing total joint arthroplasty. However, further research will be required to answer several questions regarding its administration including optimal dosing and frequency, route of administration (intravenous versus topical versus oral), and risk factors which may preclude its use in certain patient populations, particularly those with a history of coronary artery and/or cerebrovascular disease or patients who are hypercoagulable.

Enhanced Recovery After Surgery

ERAS is a multimodal, multidisciplinary perioperative care pathway designed to achieve early recovery for patients undergoing major surgery and lends itself to earlier, yet safe, hospital discharge. Its implementation requires effort from the entire healthcare team that includes hospitalists, surgeons, anesthesiologists, nurses, physician assistants, physical therapists, nutritionists, and other unit staff to help patients achieve superior recovery, decrease morbidity, reduce hospital length of stay, and provide cost savings. ERAS pathways have had success in various surgical subspecialties but are in the early stages of development for orthopedic surgery, particularly hip and knee arthroplasty [100].

While still in the early stages of development of an official ERAS pathway for elective primary hip and knee arthroplasty, the Hospital for Special Surgery already has many facets of such a pathway in place. Some of these include preoperative education classes and counseling and preoperative carbohydrate loading (permitting patients to consume energy dense clear liquids up until 2 hours before surgery). In the operative period, standardized anesthetic protocols consisting of neuraxial anesthetic and peripheral nerve blocks (as deemed appropriate) are utilized, assuming there are no contraindications and the patient is amenable. In the perioperative period, there is a strong focus on aggressive PONV prophylaxis and providing adequate postoperative analgesia using a multimodal approach including opioids, acetaminophen, nonsteroidal anti-inflammatory drugs, peripheral nerve

blocks, and patient-controlled epidural analgesia in order to promote early ambulation and rehabilitation. In addition, venous thromboembolism prophylaxis is administered as early as safely possible, and sequential compression devices are applied to patients who are not ambulating [100].

There remains a significant amount of work to be done to develop and optimize an ERAS pathway for the high volume of patients undergoing an elective total joint arthroplasty. The groundwork has been laid by countless studies that have elucidated what interventions improve outcomes and promote better patient care. The future of orthopedic care will rely on these standardized care plans as our aging population grows and demands high-quality yet efficient healthcare.

Summary

As the population continues to age, the volume of orthopedic surgery will continue to increase. Each orthopedic patient presents different challenges but should be managed by the anesthesiologist with knowledge of the surgical technique, position, predicted blood loss, and associated complications. The elderly are at an increased risk for perioperative complications making a thorough preoperative evaluation and use of appropriate intraoperative invasive monitors essential. Additionally, the anesthesiologist should appreciate the anesthetic challenges each disease process presents, including the airway challenges in the rheumatoid arthritis patient or the difficult neuraxial placement in individuals with osteoarthritis.

In orthopedic surgery, both general and regional anesthesia techniques are widely used in clinical practice. While the regional versus general anesthesia debate continues, regional anesthesia has some clear advantages. These include decreased early mortality, fewer cases of deep vein thrombosis and fatal PE, fewer respiratory complications, and improved rehabilitation. Sharrock showed a statistically significant decrease in the death rate at the Hospital for Special Surgery after making several changes, including performing 96% of all surgeries under regional anesthesia and utilizing perioperative invasive hemodynamic monitors more liberally [15]. Particularly in orthopedic surgery, regional anesthesia seems to have a strong indication. However, regional anesthesia is not a panacea and the anesthetic plan should carefully consider the operation, the patient's comorbidities, and patient and surgeon preference.

Although the incidence of neurologic dysfunction following epidural hematoma after neuraxial blockade is rare, the catastrophic consequences associated with compression of the spinal cord demand attention be paid to anticoagulation in the setting of regional anesthesia. A complete review of every patient's medication list to assess for medications that affect components of the clotting cascade is essential. Currently, the recommendations regarding neuraxial anesthesia and anticoagulants are based on expert opinion and are not evidence-based. As new medications continue to emerge, the anesthesiologist must be vigilant when making decisions regarding the use of regional anesthesia based on the pharmacological profile of each drug and must weigh the risks and benefits on an individualized basis.

Use of ultrasound for the placement of peripheral nerve and plexus blocks has been shown to reduce local anesthesia doses, complication rates, speed of block onset, and needle passes. In addition, its use is associated with a higher block success rate. Ultrasound will allow the occasional regional anesthesiologist to feel confident in the success of the blocks making regional techniques more accessible.

As orthopedic surgery is often associated with the potential for large blood loss, fluid shifts, and complications such as fat and air embolism, an anesthesiologist should have a low threshold for using invasive monitors, particularly if controlled hypotension or a pneumatic tourniquet is being used. Controlled hypotension leads to less blood loss and transfusion requirements, decreased rates of thrombotic phenomena, and improved fixation during total hip arthroplasty. Hypotension accomplished by neuraxial anesthesia with an epinephrine infusion results in a normal cardiac output and oxygen delivery despite low blood pressure. A pneumatic tourniquet provides a bloodless field but may lead to tissue, nerve, and blood vessel damage. Attempts to limit tourniquet time and pressure as well as to ensure proper fitting and placement of the tourniquet may help decrease these complications.

As the field of orthopedic surgery continues to evolve, there is an increased demand for joint replacements in an aging population, more procedures are being performed in an ambulatory setting, and the public seems to have a decreasing tolerance for postoperative pain. The anesthesiologist should be an active participant in the entire perioperative care of these patients to help improve the patient's operative experience and outcome.

Case Study

A 63-year-old gentleman with a history of osteoarthritis, hypertension, obesity, and a deep venous thrombosis 1 year ago presents for a left total knee replacement. The patient has suffered from osteoarthritis for the past 7 years, and his pain has been well managed with ibuprofen. His other daily medications include amlodipine, valsartan, and rivaroxaban. The patient's vital signs and laboratory tests are normal. His airway exam is normal; he has full range of motion of his neck and has a Mallampati 2 airway. The patient's exercise tolerance is limited by his left knee pain. His preoperative pharmacologic stress test is negative for ischemia, and

electrocardiogram is within normal limits. He discontinued his rivaroxaban 3 days prior to the surgery.

After transporting the patient to the operating room, standard monitors are applied. A nasal cannula with end-tidal carbon dioxide monitoring is placed. He is positioned supine on the operating room table and sedated with 4 mg of midazolam. The anesthesiologist then performs adductor canal and infiltration between the popliteal artery and capsule of the knee (iPACK) blocks, utilizing 20 mg of 0.25% bupivacaine and 2 mg of preservative free dexamethasone for each injection. Subsequently, a spinal is performed utilizing 4 mL of 1.5% isobaric mepivacaine. While positioning the patient, special care is taken to ensure that the head and neck remain neutral and that the ulnar nerves are properly padded. A forced air warming blanket is placed on the patient prior to surgical draping. Intravenous sedation for the operation is maintained using a propofol infusion. Intravenous antibiotics and 1 gram of tranexamic acid are administered to the patient prior to surgical incision. The surgery proceeds uneventfully, lasting for 80 min. The tourniquet time is 30 minutes. Estimated blood loss is 100 mL. Eight hundred mL of lactated Ringer's is given intraoperatively. Upon completion of surgical closure, intravenous ketorolac, acetaminophen, and ondansetron are administered and sedation is weaned. The patient awakens and is transported to the recovery room.

Two hours after arrival in the recovery room, the spinal anesthetic begins to wear off. Shortly thereafter, the patient begins to experience discomfort at the surgical site for which he receives intravenous acetaminophen, ketorolac (6 hours after his last dose), and 7.5 mg of oxycodone (which is available to him as needed every 3 hours in three dose strengths, depending on his pain score and nursing assessment). Deep venous thrombosis prophylaxis consists of aspirin on postoperative day 1 and lower extremity intermittent compression devices. Postoperative laboratory results are unremarkable. The patient is visited by the physical therapist 5 hours after arriving in the recovery room, and range of motion exercises are performed. The next morning, the physical therapist and nursing assistant help the patient out of bed for the first postoperative ambulation. He is able to complete physical therapy and remains comfortable with a visual analog pain score of 2–3/10. The patient is again seen by the physical therapist later that afternoon for a second ambulation trial, during which he is successful. The patient is discharged the afternoon of postoperative day 1 without issue with a plan for home physical therapy.

Summary Bullet Points

- Orthopedic surgical patients pose specific anesthesia-related concerns that the perioperative team should be aware of.
- Many orthopedic patients are candidates for regional anesthetic techniques, and the literature suggests potential benefits associated with their use.
- To avoid potential bleeding complications, perioperative physicians need to be aware of the effects of a growing number of anticoagulants and antiplatelet agents.
- There are several blood conservation techniques that can be employed in orthopedic surgery to optimize the surgical field as well as minimize blood loss and the need for transfusion.

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Pediatric Anesthesia for Orthopedic Surgery

7

Kathryn R. DelPizzo, Naomi Dong, and Carrie Rowe Guheen

Objectives

- To highlight the unique aspects of performing regional anesthesia in children, including local anesthetic properties in the young patient
- To review neuraxial anesthesia and the risks and benefits in children
- To illustrate potential complications of regional and neuraxial anesthesia in the pediatric population
- To introduce the anesthetic implications of special populations in the pediatric orthopedic setting, including cerebral palsy, osteogenesis imperfecta, arthrogryposis, myopathies, and patients with ventriculoperitoneal shunts
- To present the perioperative considerations related to pediatric spine patients

Key Points

- The anesthetic care of the pediatric orthopedic patient is challenging and differs in important ways from adults.
- Preemptive analgesia in the form of neuraxial anesthesia and peripheral nerve blockade can be utilized in the young patient on a routine basis. Practitioners of pediatric anesthesiologists must have in-depth knowledge of pediatric anatomy and the pharmacology of local anesthetics to prevent complications.
- Performing regional anesthesia on children who are sedated or under general anesthesia has become common practice in pediatric operating rooms. Several studies in the literature support the safety of this technique.
- Patients with syndromes such as cerebral palsy frequently present for orthopedic surgery. Understanding the spectrum of these syndromes and their anesthetic implications will help the clinician tailor safe and effective perioperative care of this patient population.
- Surgery for patients undergoing scoliosis correction is a common procedure performed on both healthy and medically complex teenagers. Although the surgical procedure has become routine, rare and potentially fatal complications can occur.

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Introduction

Unlike most adult patients, children frequently require an orthopedic operation because of a congenital abnormality or syndrome. Common syndromes with orthopedic involvement include osteogensis imperfecta (OI), cerebral palsy (CP), achondroplasia, muscular dystrophies, and Charcot–Marie–Tooth disease. Some of these patients will present with other neurological sequelae such as seizure disorders, ventriculoperitoneal (VP) shunts, developmental delay, and intrathecal baclofen pumps. Each of these entities has specific anesthetic implications.

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In the last few decades, concern has been raised about the effects of anesthesia on the developing brain. Early research centered on animal studies which showed impaired synaptogenesis and apoptotic neurodegeneration during neonatal neuronal development secondary to inhaled anesthetics, ketamine, benzodiazepines, and propofol [1–5]. The need for further scientific study led to the formation of SmartTots, a collaboration between the US Food and Drug Administration (FDA) and International Anesthesia Research Society (IARS) to fund and coordinate ongoing research. Clinical studies have shown reassuring results for children undergoing short, single anesthetics [6, 7]. Nevertheless, experts remain divided over the clinical implications of animal studies and the interpretation of human studies [8–11]. Due to concerns about these anesthetics, the FDA issued safety warnings for young children undergoing prolonged or repeated anesthetics in late 2016 [12]. It is in this context that the use of regional anesthesia is proposed as an alternative to a general anesthetic approach and as a modality to minimize overall anesthetic requirements [13].

Children presenting for surgery at our institution have received regional anesthesia in the same fashion as adult patients for over 30 years. The French-Language Society of Pediatric Anesthesiologists (ADARPEF), first published articles about safety in pediatric regional anesthesia in the 1990s, after Bernard Dalens wrote the first and only edition of the textbook Pediatric Regional Anesthesia [14–17]. More recently, the Second Edition of the New York School of Regional Anesthesia (NYSORA) Textbook of Regional Anesthesia and Pain Management dedicated four chapters to topics related to this patient population [18]. In addition, the multi-institutional Pediatric Regional Anesthesia Network (PRAN) was founded in 2006 and is now contributing large-scale data to the field [19–21].

Not all orthopedic procedures are amenable to regional anesthesia. Idiopathic scoliosis correction is a commonly performed surgery on healthy teenagers in the orthopedic setting. The incidence of idiopathic scoliosis has been estimated to be 1.9–3%; females who require surgery outnumber males by at least 2:1 [22]. Neuromuscular scoliosis is less commonly seen and can be neuropathic (cerebral palsy) or myopathic (muscular dystrophy) [23]. These patients usually have associated comorbidities and warrant a comprehensive preoperative evaluation using a multidisciplinary team approach.

This chapter is not intended to be a comprehensive review or a complete reference for pediatric practitioners in an orthopedic setting; our goal is to summarize and provide a starting point for the reader interested in the field of pediatric anesthesia for orthopedic surgery. The pertinent texts and literature will be emphasized for the reader who would like to access more in-depth information. Here, we will highlight common anesthetic techniques and unique circumstances that are more likely to be seen in an orthopedic operating room. Although beyond the scope of this chapter, the basic premises of pediatric anesthesia—airway management, preoperative parent–child preparation, pain assessment, and physiological differences between children and adults—are of paramount significance.

This chapter will focus on the discussion of the following: (1) the impact of regional anesthesia on the perioperative care of children undergoing orthopedic surgery, (2) neuraxial anesthesia and its risks and benefits in children, (3) common anesthetic and postoperative pain management techniques used at our institution for children, (4) possible complications of these techniques, and (5) aspects surrounding specific patient populations, including the risk of life-threatening events such as anaphylaxis.

Regional Anesthesia

The Impact of Regional Anesthesia in the Pediatric Patient

It is important to understand the concept of preemptive analgesia and that effective pain management begins before the child emerges from anesthesia. Preemptive analgesia can decrease morbidity and the development of chronic pain in the surgical patient of any age [24]. In the form of regional anesthesia, it may attenuate the stress response to surgery, resulting in improved postoperative outcomes [25].

Children have been identified to be excellent candidates for the use of regional anesthesia in order to modulate the stress response to surgery for over two decades. Early publications in the literature focused on neonates and young infants undergoing cardiac surgery [26–28]. Wolf and colleagues found lower levels of stress markers and less morbidity and mortality in infants who received neuraxial anesthesia [29]. Evidence exists that shows regional anesthesia combined with general anesthesia is more effective at suppressing neuroendocrine stress responses compared to conventional general anesthetic techniques using opioids alone [25]. Although perioperative events surrounding orthopedic surgery may differ from those that activate the intense physiologic response seen with cardiac surgery, we recommend the use of neuraxial and peripheral nerve blocks as valuable components in a comprehensive approach to the perioperative management of pediatric orthopedic patients.

Safety in Pediatric Regional Anesthesia

Pediatric regional anesthesia should not be performed without understanding key differences between adults and children. The most obvious one is the timing of block placement.

Although at one time considered controversial, it is now widely accepted among anesthesiologists to perform regional anesthetics in children who are anesthetized [21, 30].

In 1996 Giaufré and colleagues presented their findings from a multicenter study in France. Of 24,409 regional anesthetics (60% caudal blocks), none were associated with major complications, and minor complications were rare (0.9%). Eighty-nine percent of the blocks were placed under general anesthesia or heavy sedation, the majority of events occurred secondary to human error (overdose of local anesthesia or improper equipment usage), and none of the adverse events occurred secondary to peripheral nerve blocks [15]. In a follow-up study, Ecoffey and colleagues reported a similarly low incidence of serious complications (0.12%) with no patients having sequelae 1 year later [14]. Additionally, anesthesiologists in the UK published the National Epidural Audit in 2007. Between 2001 and 2005, they studied over 10,000 children who had an epidural catheter with a postoperative infusion in the caudal, lumbar, or thoracic areas. Of 56 incidents, they found only five to be serious (0.05%) and only one patient suffering sequelae 1 year later [31].

In the USA, the Pediatric Regional Anesthesia Network (PRAN) was organized in 2006. This is the first system of its kind to collect prospective data from multiple institutions on regional anesthetics performed in children. In its first 2 years, PRAN reported on data from 7500 nerve blocks in children with no permanent injuries [20]. A decade later, the PRAN investigators published data from over 100,000 blocks. There were no permanent neurologic deficits reported. Further, the incidence of transient neurologic deficits were very low and (2.4:10,000) did not differ between peripheral and neuraxial blocks. The risk of severe local anesthesia systemic toxicity was also low (0.76:10,000) and occurred mostly in infants [19].

Ultrasound

One cannot discuss safety of regional anesthesia in children without giving credit to the advent of portable ultrasound technologies. In the early 2000s, this topic dominated the pediatric regional anesthesia literature as an increasing number of providers used it per routine. In 2012, data in the USA demonstrated a 2.5-fold increase in the use of this tool for lower extremity single-shot blocks over the previous 4 years [32].

The advance of ultrasound-assisted regional anesthesia technique has made the performance of blocks in children easier, safer, and more effective. By visualizing the needle and its target anatomy, local anesthetic spread can be assessed in real time while avoiding vital structures (blood vessels, the lungs, etc). In addition, the needle may be repositioned more effectively as needed. The literature shows clear benefits of the use of ultrasound for the performance of peripheral nerve blocks; its use for neuraxial procedures, however, is less persuasive [33, 34].

It has been advocated that ultrasound guidance be mandatory for peripheral nerve blocks in children, arguing that the following benefits outweigh the cost of purchasing the machines and training clinicians: (1) clinically relevant reduction in onset time, (2) improvement in success rate, (3) reduction in volume of local anesthesia required, and (4) potential decrease in complication rates [35].

Compared to previous conventional techniques in children, ultrasound-guided blocks provide prolonged sensory blockade with lower volume of local anesthesia [36, 37]. Because the complication rates are very low even with conventional techniques, no study in pediatric patients has proven that ultrasound is superior; however, it is used for the majority of nerve blocks in many practices, including ours.

As with any tool, its benefit is only as good as its operator. Major complications with ultrasound-guided blocks are rare, but when operator error occurs, it is usually in the hands of the novice practitioner. It is imperative that providers using ultrasound in children have an understanding of the anatomy and block technique, as well as competence using the machine and the ability to mentally construct a three-dimensional image from the two-dimensional one obtained on the screen. Conventional techniques should not be forgotten, as the simultaneous use of nerve stimulation can be extremely helpful in the confirmation of the needle-nerve relationship [38].

Neuraxial Anesthesia

Neuraxial Anesthesia in Children

Neuraxial anesthesia is routinely used at the Hospital for Special Surgery. It reduces the requirements for anesthetics agents, muscle relaxants (and hence reversal agents,) and intraoperative opioids. Benefits include a faster return to a lucid mental status, appetite, bowel function, and less postoperative nausea and vomiting (PONV).

Most providers comfortable with pediatric anesthesia find the placement of a neuraxial block in a child to be easier than in an adult. Usually the patients are deeply sedated or under general anesthesia, have less adipose tissue, have no osteophytes or ligament calcifications, and have fewer spinal deformities. However, clinicians need to use care and understand that the depth of needle insertion is but one of many considerations. For most children, loss of resistance will be obtained more superficially than in adults. Although we do not recommend using a strict formula, some experts have developed one to assist the novice [39]. The ligamentum flavum is less tensile in children, but it can feel "tighter" and offer more resistance than expected. It can be difficult for beginners to differentiate between ligament and bone with the epidural needle. There may not be a distinctive "pop"

relied upon in the loss-of-resistance technique, so clinicians need to pay attention to *any* change in resistance rather than a specific qualitative sensation they have become accustomed to with adult patients. When an epidural catheter is passed and secured, an insertion depth of no more than 3–4 cm past the epidural needle tip is recommended to increase the likelihood of a midline location. This shallow placement can cause leaking at the epidural site if a postoperative infusion is used, thus requiring the education of nursing staff and parents. Securing the catheter at the insertion site is important, and if desired, there are commercial adhesive devices on the market that can be used for this purpose.

The frequencies of serious or major complications after lumbar epidural analgesia in children are 1:10,000 and 1:100,000, respectively [40]. Epidural blockade in children and adolescents produces less hemodynamic disturbance than in adults. In children less than 8 years of age, hypotension due to sympathectomy is less frequently encountered for the following two reasons: (1) a lower circulatory volume in the legs and splanchnic system and (2) an already relatively vasodilated systemic vasculature. If a significant change in the blood pressure or heart rate is observed in a child receiving neuraxial anesthesia in the operating room, other causes, including life-threatening events such as anaphylaxis or acute blood loss, must be considered.

The dosing of neuraxial anesthesia medication is different in children compared to adults. Although children require more frequent dosing in the operating room to achieve adequate anesthesia, they are at greater risk for toxicity of local anesthesia with repeated doses [41]. Infants and young children have a larger volume of cerebrospinal fluid than adults per kilogram weight (4 ml/kg vs. 2 ml/kg) with presumed higher daily turnover rates. They have a lower epidural fat content, which facilitates the spread of local anesthetic within and out of the epidural space. Further, with the absence of restrictions to distribution, such as spinal stenosis seen with older individuals, local anesthesia diffuses out of the epidural space faster, leaving the site of action more quickly. Spinal cord myelinization is not complete until 12 years of age. Therefore, local anesthetics do not last as long as they do in adults due to increased endoneurium permeability. For these reasons, spinal anesthesia alone is only helpful for cases that last less than 90 min [42].

The use of postoperative epidural catheters is a good solution for these challenges, as long as one follows the established dosing guidelines for children. (See the section "Pediatrics and Local Anesthesia" in this chapter.) Infusions avoid the problem of decreased latency and duration of local anesthetics in these patients, as well as the toxicity associated with repeated boluses. Because children require higher volumes of local anesthetic for neuraxial anesthesia and analgesia, it is important that the tip of the catheter is as close to the site of surgery as possible. At our institution, these catheters are used for lower extremity surgeries, so lumbar placement is our primary site of insertion, and combined spinal epidurals are used routinely. More information about thoracic or caudal epidural placement in children can be found elsewhere [39].

Caudal Epidurals

Although considered to be the "bread and butter" of most pediatric anesthesia practices, caudal anesthesia is not widely used at our institution mainly due to the age distribution of our patient population and clinician comfort with lumbar epidural placement. The majority of our infants and toddlers having lower extremity surgery undergo clubfoot reconstruction and will receive ultrasound-guided popliteal and sometimes saphenous nerve blocks after induction of general anesthesia (Table 7.1). Infants undergoing surgery for congenital hip dysplasia will sometimes receive a caudal anesthetic if deemed beneficial.

Perioperative Care

Perioperative Blocks and Postoperative Pain Management

To ensure that the benefit of the regional anesthetic is not overshadowed by intense untreated pain during block resolution, the transition period needs to be managed proactively. Parents and nurses caring for the child need to anticipate the recession of the block. If the patient has a catheter, perineural or epidural, the weaning process can be controlled gradually. If the patient received a single-injection block, the provider needs to give the caretakers a timeline for when to expect the block to recede. This can be difficult, as the recession of peripheral blockade is very unpredictable in the younger pediatric population. In general, recognizing pain in children can be challenging, and while a block recedes, this population may describe their limb as "itchy," or "cold" as opposed to "tingling" like many adults will.

The transition from epidural or perineural analgesia is best bridged with an oral narcotic offered on a regular basis, usually every 3–4 hours. Barring any contraindications, acetaminophen and nonsteroidal anti-inflammatory agents should be given around-the-clock for the first few days postoperatively. We recommend beginning the nonnarcotic analgesics as soon as possible in the operating or recovery room, and then begin the narcotics as soon as the patient reports any of the following: pain, tingling in the blocked extremity, or resumption of motor function (e.g., moving toes after popliteal block, bending nonoperative knee after neuraxial anesthesia, moving fingers after upper extremity block).

Table 7.1 Common anesthetic techniques in children at HSS

Procedure	Age	Common indications	Anesthesia	Postoperative pain	Notes
Clubfoot repair	Infant	Club foot	General anesthesia, U/S[a]-guided, popliteal	Acetaminophen, oxycodone motrin	
Hip closed reduction, arthrogram, spica cast	Infant	Congenital hip dysplasia	General anesthesia, +/− Caudal	Acetaminophen, motrin	
Foot reconstruction	Predominantly school-aged (10–15 years)	Flat foot deformity	Neuraxial anesthesia, popliteal +/− catheter, saphenous[b] at end of case	IV PCA[c], oral oxycodone, acetaminophen	
Knee ACL MPFL[d]	Predominantly teenagers	ACL injury, patella instability	Spinal, saphenous ACL +/− IPACK[e]	Ambulatory surgery, goes home with oral narcotic, acetaminophen	
Hip varus rotational osteotomy, femoral osteotomy	Usually 5–10 years	Spastic hip subluxation	General anesthesia, neuraxial, fascia iliaca	Epidural PCA, 0.1% bupivacaine, diazepam, oxycodone, acetaminophen, ketorolac	Cerebral palsy patients
Hip arthroscopy	Usually teens—early 40s	Labral tear, impingement	Neuraxial anesthesia	Ambulatory surgery	Majority are healthy and active
Hip preservation PAO[f] Surgical dislocation	Teens—early 40s	PAO—dysplasia, dislocation—impingement	Neuraxial anesthesia	Both receive [c]PCEA, diazepam, narcotics and ketorolac, acetaminophen	Mostly women
Limb-lengthening, external fixator placement	Usually age 10–13	Unequal limb length or short limbs	Combined spinal–epidural, IV sedation or general anesthesia	IV PCA, oxycodone, acetaminophen, ketorolac	Some patients have achondroplasia
Elbow, hand surgery	Varies	Fractures, cerebral palsy, elbow contractures	Infraclavicular or supraclavicular block depending on patient age and anatomy +/− GA	IV PCA, oral narcotics, acetaminophen, ketorolac. May avoid block if risk of compartment syndrome	Surgeons may ask for infraclavicular catheter for continuous passive motion therapy (contractures)

Unless indicated, all cases are done with IV sedation unless general anesthesia required for airway control
Regional anesthesia not performed if contraindicated
[a]*U/S* ultrasound
[b]*Saphenous* subsartorial approach, ultrasound-guided. For foot surgery, it is often performed at the end of the case, because it benefits the patient longer in the postoperative period and the local anesthetic load at induction is already maximized
[c]Patient-controlled analgesia, patient-controlled epidural analgesia
[d]Medial patellofemoral ligament
[e]*IPACK* infiltration between the popliteal artery and the capsule of the posterior knee
[f]Periacetabular osteotomy

Complications

Neurological Injury

There are few contraindications to regional anesthesia that are specific to pediatrics. The incidence of neurological injury as a result of these techniques is difficult to quantify; in closed claims databases, perioperative nerve damage is more frequently associated with surgical factors and general anesthesia [43]. In an international review, the incidence reported in adults ranged from 0.04 to 0.5% [44]. Current efforts to quantify the risks of regional anesthesia in pediatrics rely on multicenter databases such as the Pediatric Regional Anesthesia Network [19].

Peripheral nerve blocks are performed on children with chemotherapy-induced and other peripheral neuropathies including Charcot–Marie–Tooth [45]. Preexisting central nervous system disorders were once considered a contraindication to regional anesthesia, but in adults with these disorders, neuraxial anesthesia and analgesia do not appear to cause a worsening of preoperative neurological symptoms [46].

Some authors postulate that children may be at a lower risk for neurological injury compared to adults because of higher nerve plasticity [47]. Nevertheless, the patient with preoperative neurological disease should be approached with care and considered on a case-by-case basis. Lirk and colleagues suggest the following strategies to minimize the risk in patients with preexisting neuropathies: (1) avoid epinephrine in the local anesthetic solution, (2) use the lowest effective dose and concentration of local anesthetic, (3)

use ultrasound guidance to place peripheral blocks, and (4) use lipophilic opioids to decrease the dose of local anesthetic [44].

Neuraxial Complications

When discussing complications of neuraxial techniques, postdural puncture headaches (PDPH) and transient neurologic symptoms (TNS) are common concerns. For adults, the frequency with which PDPH occur is often quoted as less than 2% for neuraxial anesthesia. TNS has an incidence as high as 7% when using mepivicaine 1.5% [48], and this risk is typically much lower with bupivacaine. For pediatric patients, these frequencies are less clear.

In general there are several risk factors that can increase the likelihood for a PDPH: pregnancy and young age, with a peak incidence in the teenage years [49, 50]. Patients over 50 years of age have a markedly lower incidence. The use of a small gauge (25–27), non-cutting, pencil-point spinal needles, such as a Whitacre, appears to decrease the incidence of PDPH in adults and likely pediatric patients [39]. Ascertaining the presence of a PDPH or TNS can be challenging in the pediatric population due to their age, maturity level, and presence of developmental delays. PDPHs have a very characteristic positional quality to them that is not always easy to determine in the pediatric population. Other causes of postoperative headache should be considered, including sinusitis, pneumocephalus, and, of higher acuity, meningitis and subdural or subarachnoid hematoma [39]. Diagnosing and treating these complications in children often represent challenging tasks.

Much of the literature associated with PDPH in children reflects those who have had lumbar puncture for either diagnostic testing or intrathecal chemotherapy, performed with large-bore needles. Studies from this population have found an incidence as high as 8% [39]. Several studies in the past 15 years have attempted to determine the incidence and treatment of postdural puncture headaches in children undergoing spinal anesthesia with needles no larger than 25 gauge. See Table 7.2.

It should be noted that some authors maintain that children under 10 years of age do not develop PDPH [54].

Table 7.2 Incidence of PDPH and TNS in children and adolescents[a]

Lead author	Year	Country	PDPH[b] (%)	TNS[a] (%)
Puncuh [51]	2004	Italy, Finland	0.4	0.8
Kokki [52]	2005	Finland	4[a]	2
Imbelloni [53]	2006	Brazil	0.9	n/a
Llewellyn [31]	2007	UK	0.06	n/a
DelPizzo [49]	2017	USA	4.9[a]	n/a

[a]Adolescents included
[b]Incidence

In children, performing an epidural blood patch must be carefully considered. Unlike adults, pediatric patients often require heavy sedation for the performance of a blood patch and at least two practitioners. Furthermore, the appropriate amount of blood to use in the pediatric population is unclear. Most authors recommend 0.2–0.3 ml/kg of blood [39, 55]. Fortunately PDPH is uncommon in children, but if it occurs, conservative management including bed rest, hydration, and analgesics, such as acetaminophen, is the first course of action before the use of epidural blood patches is considered.

Contraindications to neuraxial anesthesia are the same as for adults. At the Hospital for Special Surgery, a high risk of compartment syndrome is the most common reason not to use an epidural in children postoperatively. This is due to the fear that the symptoms of compartment syndrome—increasing pain in the affected limb—will be masked and therefore delay the diagnosis. Spina bifida and myelomeningocele are absolute contraindications, but the presence of a ventriculoperitoneal (VP) shunt is not, although the risks and benefits of spinal and epidural anesthesia should be carefully considered on an individual basis. The concerns with VP shunts include changes in intracranial pressure and infection. Despite these concerns, there is literature to support the use of spinal and epidural anesthesia in these patients [56–58].

Pediatrics and Local Anesthesia

Safe doses of local anesthetics are computed based on weight in kilograms. Most children receive blocks after they are sedated or anesthetized, making the early signs of toxicity difficult or impossible to recognize. General anesthesia may modify the hemodynamic responses to epinephrine-containing test doses, leaving the methods used for adults (changes in heart rate and blood pressure) less reliable for children [59]. In children, ECG changes, specifically T-wave changes, may be the first sign of intravascular injection during a test dose [60]. Even if a child is awake, the prodromal warning signs for toxicity can be confused with irritability that can be attributed to other factors.

Unlike opioids, which may be titrated around a weight-based starting point, local anesthetics have a "maximum allowable dose" (single-injection bupivacaine/ropivacaine with epinephrine 2.5–3 mg/kg, lidocaine/mepivacaine with epinephrine 7 mg/kg). Neurologic and cardiac toxicity from local anesthetics are rare in pediatrics when providers are cautious. In a pivotal article by Berde in 1993, guidelines for local anesthetic infusions were introduced based on analysis of a series of convulsions associated with pediatric regional anesthesia and further study of pharmacokinetic data [41, 61]. The risk of toxicity with repeated doses or with continuous infusion is greater in children than in adults, even though the clearance for amide local anesthetics reaches adult matu-

ration around 8 months of age. For infusions, the maximum amount of epidural bupivacaine should be no greater than 0.4 mg/kg/h, and in neonates, 0.2 mg/kg/h. Many pediatric hospitals use chloroprocaine, an ester instead of an amide local anesthetic, for babies younger than 3 months of age because chloroprocaine is rapidly metabolized in this age group. Additives such as opioids and clonidine are frequently used in these infusions to enhance the analgesic effect.

Prepubertal children present a unique challenge when contemplating peripheral nerve blockade, because the total volume of local anesthesia allowable is less than for adults, and the blocks recede faster. The block duration is proportional to the absolute dose given, not the dose based on body weight [62]. To the authors' knowledge, there are no human studies on duration of the analgesic effect of peripheral nerve blockade stratified by age. Berde reports evidence in animals that show when dosed proportional to body weight, infant rats have a shorter duration of blockade of the sciatic nerve compared to older rats [62, 63].

In our experience, peripheral nerve blocks for prepubertal children provide shorter duration of postoperative pain relief, compared to those performed on adults. Anecdotally, children under the age of 12 years of age tend to experience surgical pain within 6–10 hours after block placement, compared to approximately 18 hours in our adult population when using bupivacaine. If the patient is expected to experience considerable pain postoperatively, a perineural catheter can be placed, or clonidine (maximum 1 μg/kg) may be added to the local anesthetic solution to extend analgesic effects.

In the past decade, cases of local anesthetic systemic toxicity (LAST) successfully treated with a 20% lipid emulsion (Intralipid®, Fresenius Kabi AB, Uppsala, Sweden) have been reported with increasing frequency. These include a 13-year-old girl who received a posterior lumbar plexus block under general anesthesia and developed a ventricular arrhythmia 15 min later and a 40-day-old baby who received a caudal epidural block under general anesthesia and immediately developed tachycardia, T-wave inversions, ST segment elevations, and hypotension [64, 65]. Lipid emulsion and all necessary resuscitative equipment and medication should be readily available when performing these procedures.

In summary, when administering these medications to children in the operating room, it is important to (1) adhere to dosing guidelines, (2) use slow, fractionated doses with regular aspiration, (3) monitor patients for ECG changes and signs of neurological toxicity, (4) have Intralipid® readily available, and (5) consider that the risk for toxicity is increased with concomitant hypoxemia and hypercarbia [66].

The surgeon often relies on her anesthetist to recommend the quantity of local anesthetic she can use for infiltration. If a regional block has been performed, this step may be unnecessary. If it is deemed beneficial, the total doses of local anesthetic given are additive.

For further information about pediatric-specific local anesthesia dosing, the European Society of Regional Anesthesia and Pain Therapy and the American Society of Regional Anesthesia and Pain Medicine published recommendations intended to provide guidance to reduce variability observed in clinical practice [67].

Special Patient Groups and Considerations

See Table 7.3 for a summary of common pediatric disease entities with orthopedic involvement.

Cerebral Palsy

Cerebral palsy (CP) is a nonprogressive disorder of motion and posture that results from an injury to the developing brain, first described in the 1860s by the English surgeon William Little. The condition was called Little's disease for many years and is now known as spastic diplegia. In developing countries, the incidence is two for every 1000 live births, and almost half of the cases present in babies who are premature [74]. Early theories postulated that the disorder was caused by an event during birth that led to lack of oxygen delivery to the motor cortex, but in 1897 Sigmund Freud disagreed. Noting that children with cerebral palsy often had other problems such as mental retardation, visual disturbances, and seizures, Freud postulated that the disorder begins during the brain's development in the womb. "Difficult birth, in certain cases," he wrote, "is merely a symptom of deeper effects that influence the development of the fetus." [75]

However, the belief that birth complications cause cerebral palsy was widespread among physicians, families, and medical researchers until recently. It was not until the 1980s when scientists analyzed extensive data of more than 35,000 births and discovered that birth complications account for only a fraction of cases—probably less than 10% [74]. In most cases of cerebral palsy, no etiology could be found. These findings from the National Institute of Neurological Disorders and Stroke (NINDS) perinatal study have profoundly altered medical theories about cerebral palsy and have motivated researchers to explore alternative causes.

There are four different types of CP: spastic, ataxic, dyskinetic, and mixed. Spastic CP is the most common type (over 70% of cases) and usually involves contractures in the elbows, wrists, hips, knees, and ankles. Spasticity is caused by an imbalance between inhibitory neurotransmitters like gamma-aminobutyric acid (GABA) and excitatory neurotransmitters like glutamate. This imbalance leads to excessive stimulation of alpha motor neurons causing contraction of agonist and antagonist muscle groups simultaneously.

Table 7.3 Common pediatric disease entities with orthopedic involvement

Disease or syndrome	Characteristics	Genetics	Orthopedic implications	Anesthetic concerns	Regional anesthesia contraindicated?
Osteogenesis imperfecta	Abnormal collagen/connective tissue disorder, fragile brittle bones that fracture easily Incidence 1:15,000 to 1:20,000 children	More than 90% of cases are *type I* or *type IV* *Type I*: autosomal dominant, mild *Type II*: autosomal dominant (can be recessive), lethal, most severe form; can affect heart valves/aorta leading to CHF/death *Type III*: autosomal dominant (can be recessive), severe kyphoscoliosis/limb deformities *Type IV*: autosomal dominant, moderate, onset in newborn period with fractures in utero *Type V–VII*: do not have type I collagen mutation but demonstrate similar phenotypes	Surgical treatment of fractures with osteotomies, realignment of fragments, and medullary nail fixation Spinal fusion to prevent progression of spinal deformity	Risk of fracture with positioning, transfer, tourniquet, NIBP (use arterial line), and succinylcholine (fasciculations causing fractures) Difficult airway (large head, short neck, large tongue) Limited neck extension (risk of cervical spine or mandibular fracture) Spine deformity (poor respiratory function, restrictive lung disease, evaluate cardiac and respiratory function especially with type II) Increased bleeding due to platelet dysfunction Hyperpyrexia (not MH associated, thought due to elevated thyroid hormones)	No, but can be technically difficult; positioning and needle trauma can be fracture risk
Arthrogryposis multiplex congenita (multiple congenital contractures)	Nonprogressive syndrome with persistent multiple limb contractures, atrophied or absent muscles, deformed/dislocated joints Incidence 1:3000 live births	Most cases sporadic	Rigid foot deformity (clubfoot most common) Knee deformity (fixed flexion contracture most common) Hip deformity (flexion contracture, developmental hip dysplasia, hip dislocation) Upper extremities corrected after patient ambulating Spinal fusion to prevent progression of spinal deformity	Difficult airway (micrognathia, limited TMJ mobility, atlanto-occipital instability) Difficult vascular access secondary to contractures Hyperpyrexia (not MH associated) Evaluate cardiac and respiratory function	No
Achondroplasia	Short-limbed dwarfism, macrocephaly, frontal bossing, depressed nasal bridge, midface hypoplasia, thoracolumbar kyphosis	Autosomal dominant, but >80% cases are sporadic	Surgical treatment of progressive thoracolumbar kyphoscoliosis. Surgery required anteriorly and posteriorly Limb-lengthening procedures Treatment of fractures	Difficult airway (macroglossia, midface hypoplasia, short neck, limited cervical mobility, airway obstruction from choanal atresia/stenosis) Difficult vascular access in obese patients Possible hydrocephalus/elevated ICP and foramen magnum stenosis	Neuraxial contraindicated in presence of hydrocephalus/elevated ICP; use with caution in presence of severe spinal stenosis

Neurofibromatosis	Spectrum of disorders with neurofibromas of skin/nerves, café au lait spots, Lisch nodules, and axillary freckling/ incidence NF-I 1:4000, NF-II 1:50,000	Usually autosomal dominant, classified as *NF type I–VII (type I and II most common)* *NF-I* (von Recklinghausen disease): peripheral type (orthopedic manifestations common) *NF-II*: central type, (bilateral acoustic neuromas in >90% patients, usually no bony involvement)	Scoliosis most common osseous defect Must rule out presence of intraspinal lesions (pseudomeningocele, dural ectasia, or intraspinal neurofibroma) with MRI or CT myelogram due to risk of lesion compression with spine instrumentation	Evaluate cervical spine and spinal cord for compressive neuromas Suspect pheochromocytoma (MEN IIb) with hypertension Evaluate airway for laryngeal or pharyngeal neurofibromas (possible difficult ventilation and/or intubation) Neck extension during laryngoscopy may cause cervical spine compression if intramedullary lesions present CXR to rule out mediastinal masses (especially in newborns)	Neuraxial contraindicated in presence of compressing spinal lesions
Marfan syndrome	Connective tissue disorder associated with FNB-1 (fibrillin) gene mutation, skeletal abnormalities (joint laxity/subluxation, tall stature, arachnodactyly, scoliosis), eye lens dislocation, cardiac disease (mitral valve prolapse, aortic root dilation, aortic dissection), spontaneous pneumothorax	Autosomal dominant with variable expression but can occur sporadically	Severe kyphoscoliosis and thoracic deformity, scoliosis occurs in 40–60% of Marfan's patients	Cardiovascular assessment (echocardiogram) for presence of mitral valve prolapse (present in 80% of cases) and aortic root dilation CXR and pulmonary function test if severe kyphoscoliosis Intubation may be difficult, risk of TMJ subluxation/dislocation	No; however, presence of dural ectasia may be cause of inadequate spinal anesthesia
Duchenne muscular dystrophy	Absence of dystrophin protein and destruction of muscle fibers that are replaced with scar tissue and fat, leading to pseudohypertrophy Incidence 1:3500 live male births	Sex-linked recessive but 30% occur from spontaneous mutation	Proximal muscle weakness, difficulty standing up Development of contractures, joint deformities, muscle retractions, and degenerations Collapse of spine leading to severe scoliosis and restrictive lung disease	Cardiovascular assessment (ECG, echocardiogram), dilated cardiomyopathy and conduction abnormalities common in adolescents Pulmonary function test (chronic respiratory muscles weakness and decreased ability to cough/clear secretions) Assess for sleep apnea, pulmonary hypertension Expect difficult airway (macroglossia) Avoid succinylcholine (absolute contraindication) and halogenated agents due to hyperkalemic response (cardiac arrest) and rhabdomyolysis with severe hyperthermia and myoglobunuria (have dantrolene available) Joint deformities and contractures can make positioning and vascular access difficult	No

(continued)

Table 7.3 (continued)

Disease or syndrome	Characteristics	Genetics	Orthopedic implications	Anesthetic concerns	Regional anesthesia contraindicated?
Myotonic dystrophy	Inability of muscles to relax after contraction, progressive involvement of skeletal, cardiac, and smooth muscle	Autosomal dominant but may be autosomal recessive	Possible clubfoot deformities, hip dysplasia, and scoliosis	Cardiovascular assessment (ECG and echocardiogram) for conduction abnormalities, mitral valve prolapse, cardiomyopathy Respiratory function (restrictive lung disease) Assess for sleep apnea CXR (silent aspiration) Risk of perioperative aspiration (dysphagia and gastric distension) Avoid hypothermia to avoid shivering and myotonic crises Respiratory drive sensitive to all intravenous agents, consider reduced doses Avoid succinylcholine (risk of prolonged generalized myotonia)	No, but will not relieve Myotonic contractions
Charcot–Marie–Tooth disease (peroneal muscular atrophy)	Hereditary polyneuropathy, presenting with distal weakness, muscular atrophy, loss of proprioception (foot weakness and unsteady gait)	Inherited in different patterns (autosomal dominant, autosomal recessive, and X-linked), dominant form is most common	CMT is most common neuromuscular cause of cavovarus foot deformity in children	Neurologic, cardiovascular, and respiratory evaluation (pulmonary function tests, CXR, EKG, and ABG if respiratory involvement suspected) Echocardiogram indicated based on clinical evaluation Anesthesia may exacerbate any preexisting respiratory disease; postoperative mechanical ventilation may be required	No
Arnold–Chiari malformation	Herniation of posterior lobe of cerebellum through foramen magnum, elongation of fourth ventricle, and noncommunicating hydrocephalus	Few reported cases of autosomal recessive inheritance associated with myelomeningocele and prenatal onset Classified as type I, II, III, IV	Type II most often in children with myelomeningocele, dysfunction of lower cranial nerves (vocal cord weakness/paralysis, difficulty feeding, crying, breathing). Ventriculoperitoneal shunt to control hydrocephalus resolves brain stem symptoms. If brain stem symptoms persist after shunting surgical decompression indicated	Preoperative evaluation for signs of elevated ICP and brain stem and/or cervical cord compression Prone positioning with careful head positioning (risk of brain stem compression) Risk of venous air embolism depending on level of surgical field (avoid nitrous oxide)	Please refer to *Neuraxial Complications* section of text
Hydrocephalus/VP shunt	Caused by either overproduction or obstructed drainage of CSF from brain	80–90% of patients with myelomeningocele have hydrocephalus requiring shunting	Treatment to relieve obstructive hydrocephalus requires shunting, either to external ventricular drain (temporary relief) or internal shunt within brain (third ventriculostomy) to peritoneum or right atrium	Signs of shunt failure can include nausea, vomiting, severe headaches, increased irritability, increased level of paralysis (emergent neurosurgical intervention required)	Please refer to *Neuraxial Complications* section of text

Data from Refs. [68–73]

The spectrum of severity in these patients is broad. It is important to note that the causative brain injury itself is nonprogressive, but the clinical picture can change over time and is different for each individual. Some children are intellectually on par with their peers, others may understand their surroundings but are nonverbal, and some of these children will be developmentally stunted in infancy. Caring for these patients in the perioperative setting requires that all providers be sensitive to these variations and look to the caregiver for guidance on how the patient reacts to pain, separation from the caregiver, new surroundings, etc.

It is particularly important for perioperative orthopedic clinicians to understand issues associated with CP, because this patient population often presents for orthopedic surgery: lower extremity tenotomies and osteotomies are the two common procedures, and there is an overall incidence of 20% for scoliosis in these children [76]. Patients require heightened attention due to their associated comorbidities. Besides developmental delays, some patients have other neurological issues such as seizure disorders, deafness, visual loss, and hydrocephalus treated with VP shunts. Many have feeding difficulties with poor nutritional status requiring gastrostomy tubes or gastroesophageal reflux and difficulty handling oral secretions with resulting pulmonary complications such as aspiration pneumonia. Respiratory disorders are a common cause of death. Patients with CP are sensitive to narcotics and anesthetics and have a higher risk for oversedation and respiratory depression. They often have intact sensation, with postoperative spasms being common. They often present with surgical pain that is difficult to manage. Interestingly, most patients with CP tolerate benzodiazepines well and need doses in the high-normal range to have relief from postoperative spasms, especially if they were taking them preoperatively.

The medications used to treat these comorbidities also complicate these patients' care. Antiseizure medications and antispasticity drugs such as baclofen and diazepam are frequently used. Anticonvulsants need to be continued throughout the perioperative period especially for children with generalized seizures. Fortunately most of these drugs have long elimination half-lives (24–36 hours), and if not given for 24 hours, the risk of significant seizure may not be significantly increased, provided the preoperative drug levels were within the recommended range.

Balcofen acts on the GABA receptors in the dorsal horn of the spinal cord to decrease spasms and pain. It can be given orally or via the intrathecal route with a pump usually inserted subcutaneously in the anterior adominal wall [56]. Baclofen and benzodiazepines can potentiate central nervous system depression, contributing to a slower emergence from general anesthesia. Regardless of their medications, patients with CP have been shown to have a lower minimum alveolar concentration (MAC) compared to normal controls [77].

Baclofen pumps present a contraindication to neuraxial anesthesia. These pumps are rarely discontinued for surgery, and if the patient is undergoing spine surgery, a neurosurgeon should be involved. Disruption of intrathecal baclofen administration can have life-threatening consequences. There are case reports of severe morbidity from disruption of the pump resulting in acute overdose or withdrawal [78, 79]. The diagnosis of pump malfunction might be difficult unless the symptoms are placed into context and the providers have complete knowledge of the patient's medical history. Acute overdose can manifest as hypotension, bradycardia or tachycardia, hypotonia, respiratory depression, somnolence, flaccid paralysis, and coma. Acute withdrawal can manifest as generalized seizures, malaise, dysphagia, hypertonia or rigidity, hyperthermia, hypertension, tachycardia, headaches, and hallucinations.

Treating hypothermia in the perioperative period can be a challenge in these patients due to hypothalamic dysfunction and lack of adipose tissue. Patients with CP should be treated in a latex-free environment; latex allergies are more common in this patient population, likely due to having had multiple exposures during procedures in hospital settings.

Regional anesthesia is extremely beneficial for these patients. General anesthesia is usually required for airway control, but epidurals and peripheral nerve blocks should be considered in addition, barring any contraindication. It must be noted that with these children, postoperative narcotics should be administered with caution. Postoperative epidurals using a mix of bupivacaine (0.06–0.1%) and clonidine (1 μg/ml) or plain bupivacaine along with oral diazepam are the mainstay of treatment at our institution, along with peripheral nerve blocks when deemed beneficial. Neuraxial opioids are rarely used. Once again it is important to note that it can be difficult to interpret pain in these patients especially if they are nonverbal, and in these cases, the caregiver's input is essential.

Surgery for Scoliosis Correction

Surgery for scoliosis correction is one of the most common operations performed on healthy teenagers. Anesthetic implications unique to this procedure include spinal cord monitoring and positioning. In general, teenagers have higher anesthetic and narcotic requirements in the operating room than adults undergoing this procedure. Some children presenting for scoliosis correction have underlying medical syndromes that add complexity to the patient's care.

It is important to elicit a complete history, including the patient's exercise tolerance. Healthy teenagers are usually still able to exercise with mild restrictive pulmonary disease and may only have respiratory symptoms at full exertion.

Identifying the location of the spinal deformity, the age of onset, and the direction and severity of the curve will provide

valuable information about the patient's pulmonary function and potential associated congenital anomalies. Most curves in adolescent idiopathic scoliosis are convex to the right. A left thoracic convexity should raise ones index of suspicion to look for other underlying conditions and congenital anomalies [23].

Knowing the type or etiology of the scoliosis is essential. In many teenagers, the etiology of scoliosis is unknown, or idiopathic. However, neuromuscular scoliosis may occur as a result of diseases such as cerebral palsy and muscular dystrophy [23]. This type of scoliosis is associated with significantly increased intraoperative blood loss compared with idiopathic scoliosis. These patients are also at higher risk for perioperative neurological and respiratory complications [80].

The two monitoring techniques most commonly used to monitor spinal cord function are somatosensory evoked potentials (SSEPs) and motor evoked potentials (MEPs). The functional integrity of the somatosensory pathways in the posterior column of the spinal cord can be continually assessed by SSEPs. Normal intraoperative SSEPs are good predictors of normal postoperative sensory function [23]. MEPs assess the integrity of the spinal motor pathways in the anterior columns. It is important to monitor these signals for thoracic spine surgery. The routine use of MEPs intraoperatively has virtually replaced the "wake-up test" previously relied upon to assess spinal cord insult during surgery.

All anesthetic agents affect spinal monitoring to varying degrees, and usually an anesthetic compatible with these modalities involves low-dose volatile agents with intravenous medications. TIVA may be used especially if there is suspicion of malignant hyperthermia (MH.) Of all anesthetic agents, narcotics may be least likely to adversely affect the somatosensory evoked potentials (SSEPs). Cortical SSEPs and motor evoked potentials (MEPs) are very sensitive to nitrous oxide and potent inhalational agents. Ketamine enhances MEPs and is used almost routinely at our institution for spine cases. Four out of four twitches using a monitor to assess the intensity of neuromuscular blockade are still maintained for MEPs. Hypothermia, anemia, hypoxia, and significant decreases in arterial pressure below levels of cerebral autoregulation may affect both SSEPs and MEPs and should be considered when evaluating changes in these signals.

As opposed to following a prescribed technique, it is more important to provide a safe, effective anesthetic that is unchanged throughout the operation. The stability of the anesthetic makes evaluating any changes in the signals less complex. A baseline set of SSEPs and MEPs should be performed by the neuromonitoring technician as early as possible so that changes to the anesthetic and/or monitoring technique can be made before the most critical part of the operation, spine distraction, and instrumentation.

Patients with coexisting diseases such as CP and muscular or myotonic dystrophy introduce special challenges. Patients with CP can have significant comorbidities and those with VP shunts or intrathecal baclofen pumps may need neurosurgical involvement. Although rare, there have been case reports of life-threatening hydrocephalus following posterior spinal fusion in children [81]. The shunt can malfunction during correction of the spinal deformity via disconnection, fracture, kinking, or inadequate length. The disruption of an intrathecal baclofen pump can also have catastrophic effects if not recognized and treated immediately.

Patients with muscular and myotonic dystrophies should be carefully evaluated preoperatively for cardiomyopathy and pulmonary insufficiencies. Patients affected by the most severe forms of the disease may succumb to cardiopulmonary problems in late adolescence or early adulthood [82]. Of note, the severity of muscle weakness does not correlate with the severity of cardiac dysfunction. These patients are at risk for nonmalignant hyperthermia and may be predisposed to malignant hyperthermia; triggering agents should be avoided. Aspiration precautions must be taken, and due to preexisting muscle weakness, muscle relaxants are usually not needed. Postoperative mechanical ventilation is almost always necessary. This group of patients is sensitive to virtually all anesthetic agents including narcotics and benzodiazepines. In summary, caring for this particular patient population during spine surgery is usually more challenging than for those with idiopathic scoliosis.

Because scoliosis surgery is an operation associated with significant pain and prolonged hospitalization, high-volume pediatric centers have developed enhanced recovery after surgery (ERAS) pathways to facilitate early mobilization and multimodal analgesia which some argue should become standard of care [83, 84]. Antifibrinolytic use is also becoming more prevalent as more studies are showing that the risk-benefit ratio is favorable [85].

Allergic Reactions

Anaphylaxis is a severe, life-threatening, systemic hypersensitivity reaction. This is characterized by rapidly developing life-threatening airway and circulation failure usually associated with skin and mucosal changes. The incidence of perioperative anaphylaxis is similar in children and adults, but in children, latex is more often the causative agent [86]. Sensitization mainly occurs by wound or mucosal contact with latex devices during surgery or by inhalation of airborne allergens released from powdered latex gloves.

Higher-risk patients frequent the orthopedic operating room, including those with spina bifida and cerebral palsy. Other risk factors include individuals who had neonatal sur-

gery or multiple operations in childhood, particularly urological, spinal, or rectal. Atopic individuals and those with allergies to avocado, banana, chestnut, kiwi, papaya, peach, or nectarines are also in this group.

The initial cutaneous symptoms of anaphylaxis are not always seen under surgical drapes, and the first signs in the operating room may be severe hypotension and bronchospasm. Adverse latex reactions during anesthesia usually occur between 30 and 60 min after exposure. Treatment in the acute phase consists of the removal of latex from the environment and administration of intravenous epinephrine. In the late phase, histamine blockers and corticosteroids can be helpful. Allergy testing should be performed at least 6 weeks after the event and should include all agents used in the operating room, as neuromuscular relaxants are also frequently responsible [87]. The best method of prevention is complete avoidance of latex. In centers where a latex-free environment has been adopted, a significant decrease in the incidence has been proven [88].

Summary

In an orthopedic setting, children often present for surgery that is amenable to regional anesthesia. Performing these techniques in children is safe, and the majority of practitioners place the blocks after the patient is asleep. The ultrasound machine has made the performance of peripheral nerve blocks easier, more effective, and safer in this age group. However, utilizing these blocks in children still requires the physician to possess a thorough understanding of the basic principles of pediatric anatomy and physiology, as they relate to regional anesthesia and local anesthetics.

Neuraxial anesthesia remains a widely used technique in the pediatric population, with low complication rates. Postdural puncture headache is the most common complication and can be difficult to diagnose and treat in a child. A postoperative epidural catheter is an important component of the postoperative analgesic regimen in an orthopedic setting.

When regional anesthesia is used for postoperative analgesia in children, the transition period from limb blockade to full sensation should be managed with early initiation of oral/intravenous acetaminophen, NSAIDs, and narcotics. If a perineural or epidural catheter is in place, this process may be easier to manage. Educating the caretakers about the recession of the block is essential.

Neurological injury from regional anesthesia is rare in adults, and the risk is difficult to quantify in children. Multiinstitutional databases, such as the Pediatric Regional Anesthesia Network (PRAN), are contributing important information regarding the safety of regional anesthesia practice to the field of pediatric anesthesia.

Patients with cerebral palsy and other syndromes are often cared for in the orthopedic setting. Understanding the sequelae of these diseases is essential. Surgery for scoliosis correction is common in these patients and in healthy teenagers. The anesthetic technique for spine surgery is unique in that it must be tailored to the spinal cord monitoring.

Summary Bullet Points

- Pediatric patients undergoing orthopedic procedures have their own unique considerations compared to adults. Providers should understand these differences before caring for children in the operating room.
- The use of regional anesthesia in children, particularly ultrasound-guided, is beneficial and recommended. Evidence-based data regarding the use of regional anesthesia and its safety are being compiled on a more routine basis due to the creation of the Pediatric Regional Anesthesia Network (PRAN).
- Congenital syndromes are common in pediatric orthopedic patients, and providers should be familiar with their anesthetic implications.

Case Study

An 11-year-old female presents for a left pelvic osteotomy, left hip varus derotational osteotomy, and left hamstring and iliopsoas tendon releases. She suffers from spastic cerebral palsy and was born prematurely at 27 weeks postconception. After birth, she remained intubated and mechanically ventilated in the NICU for 2 weeks. She is developmentally at the kindergarten level. She ambulates, but walking has become difficult in the last few weeks due to increasing weakness. She has a seizure disorder that is well controlled with medication. She uses bronchodilators for asthmatic events that occur with upper respiratory infections. Her last use was 1 month ago, and the patient has no history of pneumonia or obstructive sleep apnea. She weighs 30 kg and her height is 128 cm. She routinely takes oxcarbazepine, and she took albuterol and budesonide for 3 days before surgery prophylactically. Her only past surgical history is for strabismus. An allergy to penicillin was reported, but her mother reports that she has taken cephalosporins and amoxicillin without problems.

In preparation for surgery, the patient received 2 mg of intravenous midazolam in the holding area. In the operating room she was induced with propofol without muscle relaxant and the trachea was intubated. The epidural space was easily accessed via the loss-of-resistance technique, and 25 mg of

bupivacaine was given through the epidural needle. An epidural catheter was threaded smoothly. A 22-gauge radial arterial line and an additional peripheral venous catheter, 18 g, were easily placed. Cefazolin was given for antibiotic prophylaxis. Surgical incision was made, and the patient showed no hemodynamic response. She was maintained on oxygen and nitrous in a 50% mixture, with isoflurane 0.3% end-tidal. Glycopyrrolate was given to reduce secretions and diazepam for the treatment of postoperative spasms. Forty-five minutes after the start of surgery, the patient became hypotensive with an increase in peak airway pressures. One hundred percent oxygen was administered and isoflurane was discontinued. There was no wheezing, but hand ventilation was difficult. A latex reaction was suspected and surgery was halted. The wound was flushed with saline, and all surgeons changed their gloves. Epinephrine was administered in small doses (0.5 μg/kg) with a slight increase in the blood pressure. When larger doses were given (1–2 μg/kg), the patient's blood pressure stabilized and her airway pressures decreased. An infusion of epinephrine and intravenous fluids was maintained, serum tryptase levels were checked, and other routine blood laboratory tests were performed. The patient was taken to the pediatric intensive care unit and remained on the epinephrine infusion for 24 hours. Her serum tryptase and IgE levels were elevated. She was extubated on postoperative day 2 and went home on postoperative day 5. Six weeks later, she underwent allergy testing which revealed a level 5 reaction to latex. She was not allergic to neuromuscular blockers or any antibiotics.

Five months later, she returned for surgery in a latex-free environment with the same anesthetic technique without sequelae.

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8 Anesthetic Techniques and Their Clinical Application for Specific Orthopedic Procedures

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Objectives

- To introduce the rationale for the choice of specific anesthetics and techniques.
- To discuss frequently encountered contraindications and complications of regional anesthesia.
- To describe techniques used to perform various regional anesthetics.
- To provide an overview of the use of anesthetics for specific orthopedic procedures.

Key Points

- Many different local anesthetics with various effect profiles are available for the practice of regional anesthesia, as well as a number of additives. Main considerations in choosing the appropriate agent are dosage/volume, speed of onset, duration, and side effects.
- Absolute or relative contraindications include infection, coagulation disorders, and preexisting neurologic deficits. Among the potential hazards of regional anesthesia are local anesthetic systemic toxicity and neuropathy.
- Four methods to determine the right injection sites have been developed over time: anatomic landmarks, the paresthesia technique, electric nerve stimulation, and ultrasound guidance. The insertion of catheters allows for a prolonged period of regional anesthesia or analgesia.
- Numerous block techniques can be carried out to provide anesthesia to different body parts. For the upper extremity, several approaches to anesthetize the brachial plexus have been described, including interscalene, supraclavicular, infraclavicular, and axillary blocks. Apart from neuraxial anesthesia, lumbar plexus block, femoral nerve block, saphenous nerve block, popliteal nerve block, and ankle block are among the techniques available for the lower extremity.

Introduction

The practice of anesthesia at the Hospital for Special Surgery is primarily one of regional anesthesia (RA) techniques. Regional anesthesia—whether neuraxial (spinal, epidural) or peripheral nerve blocks—can decrease the stress response to surgery and, as such, is considered beneficial in the perioperative period. Neuraxial anesthesia is associated with decreases in (early) mortality, deep vein thrombosis/pulmonary embolism, myocardial infarctions, respiratory morbidity, and postoperative confusion. Peripheral nerve blocks (PNB) are associated with improved rehabilitation and reduced length of hospital stay. The safe and successful practice of regional anesthesia relies on anesthetizing nerves without damaging their structure. Disruption of the nerve structure or the surrounding tissue architecture with the needle can cause undesirable neurological consequences. Anesthesiologists trained in regional anesthesia achieve this goal by relying on anatomical landmarks, the patient's feedback, and the use of nerve stimulators or ultrasonography to locate the targeted nerves. This chapter introduces the reader to the practice of regional anesthesia at a single institution—it is neither meant to be all inclusive or to provide a detailed

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"cookbook" approach to regional anesthesia—rather it is meant to provide an overview of its use at the Hospital for Special Surgery. Specific attention will be paid to the presentation of various techniques used for a variety of orthopedic procedures while discussing (1) the choice of local anesthetic, (2) the contraindications for the use of regional anesthesia, (3) the complications and side effects associated with regional anesthetics, (4) the performance and indications for various peripheral nerve blocks and neuraxial techniques, and (5) the utilization of techniques in the setting of specific orthopedic surgeries as practiced at the Hospital for Special Surgery.

Local Anesthetics

Choice of Local Anesthetic

Medium- and long-acting amide local anesthetics (LAs) are most frequently used to achieve peripheral nerve blockade, whether for surgical anesthesia or for postoperative analgesia. The choice of LA is dependent upon a number of factors, including speed of onset, duration of surgery, toxicity profile, and patient comorbidities. In general, at our institution, medium-acting LAs, such as mepivacaine, are used for cases of relatively short duration (<2 h) and long-acting LAs, such as bupivacaine, are used for cases of longer duration (>2 h). In the case of peripheral nerve blockade, the choice to use longer-acting LAs depends on the desired prolonged length of postoperative analgesia. Please refer to Table 8.1 for a summary on characteristics of different local anesthetics in peripheral nerve blocks and epidural and spinal anesthesia.

Drug Dosage

Depending on age and comorbidities, in general, a volume of 30–50 ml of a number of commercially available LAs can be used to anesthetize peripheral nerves close to the trunk in an average-sized adult. The doses of different types of anesthetics are shown in Table 8.1 [1].

Latency

The latency to block onset can be decreased by (1) carbonization of the local anesthetic, (2) alkalinization of the LA, and (3) warming of the LA. A fourth option to hasten block onset of shorter-acting LA includes the use of higher volumes and has become common practice at the Hospital for Special Surgery, where anesthetic blocks are performed in the operating room with surgery following in short order, allowing limited time for block onset.

Adjuvants

Different medications have been used as adjuvants to LA in peripheral nerve blocks with the goal to either enhance or prolong the effect of a block. Possible adjuvants include epinephrine, dexamethasone, ketamine, neostigmine, opioids, and clonidine. In general, the practice at HSS includes the use of epinephrine, clonidine, or dexamethasone to increase the duration of peripheral nerve blocks.

Contraindications for the Use of Regional Anesthesia

Infection

Infection at the needle puncture site is an absolute contraindication to the use of any type of regional anesthetic [2]. Bacteremia or infection in the region to be blocked is not absolute, but rather relative contraindications to the use of regional anesthesia or peripheral nerve blocks—after weighing the overall risks and benefits of the use of either neuraxial or peripheral nerve block. Conservative practice dictates that indwelling catheters should be avoided in the setting of infection, unless the patient has begun a course of antibiotics. It should be noted that, in the case of neuraxial anesthesia without indwelling catheter, where infection without signs of systemic involvement is present, the risk of bacterial spread to the neuraxial space is probably low [3]. Indeed, in a series of almost 500 patients presenting for surgical treat-

Table 8.1 Local anesthetics

Agent	Nerve block				Epidural anesthesia				Spinal anesthesia			
Lidocaine	1–2%	30–50	10–20	120–240	1–2%	15–30	5–15	60–180	1.5–5%	1–2	1–4	30–90
Mepivacaine	1–1.5%	30–50	10–20	180–300	1–2%	15–30	5–15	60–180	4%	1–2	1–4	30–90
Prilocaine	1–2%	30–50	10–20	180–300	1–3%	15–30	5–15	60–180	1–2%	2–4	2–7	60–130
Bupivacaine	0.25–0.5%	30–50	20–30	360–720	0.25–0.5%	15–30	15–20	180–350	0.5–0.75%	2–4	3–9	90–200
Levobupivacaine	0.25–0.5%	30–50	20–30	360–720	0.25–0.75%	15–30	15–20	180–350	0.5–0.75%	2–4	3–9	90–200
Ropivacaine	0.2–0.5%	30–50	20–30	360–720	0.2–0.75%	15–30	15–20	180–350	0.5–0.75%	2–4	3–9	90–200

Data from Refs. [39–41]

*Subject to hypobaricity, isobaricity, or hyperbaricity

ment of an infected joint and in whom a neuraxial anesthetic was performed, no cases of meningitis or epidural abscess were encountered at our institution [4].

Coagulation Disorders

Problems with coagulation, whether iatrogenic or pathologic, remain a relative contraindication to the use of regional anesthesia or peripheral nerve blockade. The American Society of Regional Anesthesia and Pain Medicine (ASRA) provides recommendations and practice guidelines on this topic [5]. This is especially important in the setting of newer anticoagulants which carry broad indications for use (atrial fibrillation, DVT, etc.). Details on regional anesthesia in the setting of anticoagulant are frequently updated and should be followed closely [6].

Preexisting Neurological Deficits

Previous neurological disease or peripheral nerve injuries of either acute or chronic nature are not absolute contraindications to the use of regional anesthesia or peripheral nerve blockade. Some evidence suggests, however, that preexisting neurologic abnormalities may increase the risk of anesthesia-related neuropathies after neuraxial anesthesia [7]. Therefore, given the obvious advantages of regional anesthesia, the risks and benefits should be carefully weighed, and thorough documentation should be performed before an anesthetic is performed. In general, due to the conservative nature of the practice of regional anesthesia at HSS, we do not perform peripheral nerve blocks in the setting of preexisting neurological deficits.

Complications and Side Effects Associated with Regional Anesthesia

Local Anesthetic Systemic Toxicity

Local anesthetic systemic toxicity (LAST) is a relatively rare but a potentially life-threatening complication of regional anesthesia. It can range from neurological symptoms to cardiovascular collapse. While the pathophysiology of LAST is not fully clear, there is evidence that some of its mechanisms relate to the drugs' sodium channel blocking activity. Local anesthetic agents readily bind to voltage-gated sodium channels and decrease transmembrane sodium flux, thus impairing depolarization and producing the desired anesthetic action when applied to peripheral nerves. Depending on concentration they also interact with a multitude of other ion channels, drug receptors, and enzymes. In the central nervous and cardiac tissues, where the local anesthetic is redistributed to in a dose-dependent manner after adsorption, a number of unfavorable side effects can occur. In the brain, disruptions of inhibitory and excitatory circuits evoke either seizure activity or cerebral depression and coma. Cardiac toxicity comprises mainly impairment of contractility and generation of arrhythmias, for which different mechanisms are thought to play a role [8]. In general, LA agents have variable side effect profiles. Longer-acting LAs like bupivacaine and ropivacaine are reportedly more prone to produce cardiac toxicity even at low doses; further, they rather affect conductance than myocyte contractility, resulting in sustained arrhythmias. On the contrary, shorter-acting LAs like lidocaine and prilocaine have a higher central nervous system to cardiac toxicity ratio and in the latter organ predominantly affect cardiac contractility. The optimal treatment for LAST might therefore not only depend on the predominant site of toxicity but also on the type of LA involved [9]. According to the ASRA practice advisory, airway management and prevention of hypoxia and acidosis are among the most crucial first steps to treatment [10]. Both cardiac and central nervous system toxicities have been successfully treated with the use of Intralipid® (Fresenius Kabi AB, Uppsala, Sweden) [11]. It is the currently recommended treatment for all cases of LAST except minor central nervous system toxicity [12]. It is thought that Intralipid will extract lipophilic LA from the plasma, thus reducing concentrations and its effect on neurons and cardiac cells. Other treatment options include benzodiazepines to terminate seizures; positive inotropic support with epinephrine, which is believed to be particularly beneficial where LAs are causing myocardial depression; or, as a last resort, intermittent maintenance on cardiac bypass. At the Hospital for Special Surgery, Intralipid® (and an algorithm for its use) is easily accessible at all anesthetizing locations where regional anesthesia is performed.

Neuropathy/Neurological Injury

Prevention and education are the keys to management of neurologic injury. Nerve injury from anesthetic sources is very rare and often multifactorial [13]. A careful and considered discussion of the risks and benefits relating to neurological injury and their incidence should involve every patient to be anesthetized [14]. There are often situations (i.e., professional athletes and dancers) in which even the potential for risk of injury makes regional anesthesia an unacceptable choice.

Regional Anesthesia Techniques

Anatomical Landmarks

Anatomic landmarks were the original means of guiding the location of injections for regional anesthesia. They are still

used with marked success in certain situations (placement of spinals and epidurals, axillary nerve blocks, etc.). Increasingly, they are an adjunct to newer technologies for identification of neural structures (i.e., femoral artery palpation to guide placement of ultrasound probe), especially in situations involving the teaching of residents and fellows.

Paresthesia Techniques

Eliciting a paresthesia from probing of the needle is a time-tested technique—hence the dictum "no paresthesia, no anesthesia." It is thought that the paresthesia develops when the tip of the needle comes in contact with the nerve. Theoretically, there is an increased risk of nerve damage (decreased margin of safety) when attempting to elicit paresthesias, and, as a result, its use has somewhat fallen out of favor. Further, utilizing a paresthesia technique requires the patient's cooperation, which limits the level of sedation provided during block performance.

Nerve Stimulator

The nerve stimulator works on the principles of electrostimulation. A nerve stimulator discharges an electrical current that is transmitted through tissue structures via a needle. When the needle tip approaches the nerve, the electrical current causes a twitch of the muscle that is innervated by a particular nerve, providing localizing information to the anesthesiologist. Using this technique, the anesthesiologist can target specific nerves and deliver a dose of local anesthetic to anesthetize the surgical site. Nerve stimulation has been used to locate nerves for many years and is currently the most commonly utilized technique [15]. However, there are drawbacks to this technique, one of which is the inability to directly visualize the path of the needle as it passes through tissue.

Ultrasound Guidance

Ultrasound-guided techniques were historically used to either diagnose side effects or avoid vascular puncture. They have more recently become the technique of choice for identifying nerves and their surrounding anatomy [16]. Ultrasonography helps visualize the targeted nerves and the needle as it moves through tissues and associated vital structures. It can also help determine the adequacy of spread of the local anesthetics around the nerves. Ultrasound imaging relies on the ability of tissue to reflect sound waves. Sound waves are emitted from the ultrasound probe into the tissue over which it is applied. These sound waves then reflect back toward the probe as they cross different areas of the body. The probe receives the reflected waves and an image is created on the screen of the ultrasound machine. The angle and intensity of the reflected sound waves transmitted through tissues determine the clarity of the picture. When using this technique, the anesthesiologist can visualize, in real time, the structures that he/she is looking for, pass the needle toward the targeted nerves, and avoid vital structures that may be in the way and avoid, for example, vascular puncture [17]. This ensures success of the block by confirming an adequate spread of the local anesthetic solution around the nerve. However, it must be noted that no data are available to suggest that using ultrasound decreases the risk of neuropraxias [18].

Catheter Techniques

Continuous nerve catheter techniques can be used for either intraoperative management (depending on surgical duration and postoperative pain plan) or postoperative pain management (severe postoperative pain, posttraumatic pain states, sympathetic blockade, amputation/stump pain, etc.). Different types of administration are available—intermittent bolus administration, continuous administration, or patient-controlled administration [19]. The method of choice for a given institution most often depends on organizational factors. Continuous peripheral catheters are frequently used at our institution for patients who cannot receive epidural analgesia when undergoing lower extremity arthroplasty. Further, patients with extensive foot reconstructions benefit from this approach, as the location of pain is difficult to control with neuraxial techniques.

Upper Extremity Nerve Blocks

The Brachial Plexus

There are four commonly used primary approaches to regional anesthesia of the brachial plexus: interscalene, supraclavicular, infraclavicular/coracoid, and axillary. Nerve stimulator and/or ultrasound approaches can be used for each of these blocks; however, at the Hospital for Special Surgery, ultrasound techniques are used primarily for interscalene, supraclavicular, and infraclavicular approaches, while nerve stimulator techniques are most commonly reserved as adjuncts and for teaching purposes.

Review of Anatomy

The brachial plexus is formed by the anterior rami of the C5–C8 and T1 spinal nerves. It contains a contribution from

C4 in 60% and from T2 in nearly 30% of individuals. The roots of the spinal nerves exit from the spinal canal behind the vertebral artery and cross the transverse process of the corresponding vertebrae. They join to form three trunks and run together toward the first rib. The upper trunk arises from the union of the roots of C5/6, while the middle is comprised of the root of C7 and the lower of the roots of C8/T1. The trunks (which lie on top of each other) pass between the scalenus anterior and scalenus medius muscles in the interscalene groove. Just above the clavicle, the trunks divide into an anterior and posterior division. The three posterior divisions join to form the posterior cord, the anterior divisions of the upper and middle trunks form the lateral cord, and the medial cord is the continuation of the anterior division of the lower trunk. The cords lie close together in the infraclavicular region, surrounding the subclavian artery [20].

Interscalene Nerve Block

The interscalene nerve block (ISB) was first introduced by Winnie as a puncture site in the interscalene groove at the level of the cricoid cartilage and the sixth cervical vertebra, with the needle directed perpendicular to the skin [21]. It has been modified and revised multiple times since then. The block provides anesthesia and analgesia for both arthroscopic and open procedures of the shoulder and proximal upper arm. Its use can also be indicated for closed reduction of shoulder dislocations, physical therapy, or as a diagnostic tool in the evaluation or therapy of certain chronic pain syndromes (e.g., complex regional pain syndrome (CRPS)). Interscalene nerve blocks are contraindicated in certain situations, including contralateral phrenic nerve paresis, contralateral recurrent laryngeal nerve paresis, and severe chronic pulmonary obstructive disease. The reason for this is a high rate of temporary paralysis of the phrenic and/or recurrent nerve on the side of the block, thus exposing the patient to respiratory failure and upper airway obstruction [22–24]. Interscalene nerve blocks can also be associated with a number of complications, including vertebral artery injection (resulting in immediate seizure), local anesthetic toxicity, direct intrathecal or epidural injection (with subsequent high or total epidural or spinal), and even permanent quadriplegia [25]. Interscalene nerve blockade is achieved by injecting 15–40 ml of LA solution into the interscalene groove at the level of a line drawn laterally from the transverse process of C6 (the external jugular vein often overlies the intersection site). The site of injection can be localized via paresthesia, nerve stimulator, and/or ultrasound technique. If a paresthesia approach is used, sensory signs should be elicited before injection of LA solutions. The site can be superficial in many people. One should aim for a paresthesia of the hand or forearm, although a paresthesia of the shoulder—which does not necessarily reflect direct stimulation of the brachial plexus—may be sufficient for anesthesia needed for shoulder surgery. If a nerve stimulator technique is used, the brachial plexus in the interscalene groove should ideally contract the biceps (flexion at the elbow) before local anesthesia is deposited. If the brachial plexus is localized by using an ultrasound technique, one is classically looking for the "stop light" configuration of the C4, C5, and C6 nerve roots. Deposition of local anesthesia around these roots will achieve the desired surgical anesthesia. Smaller amounts (5 ml) of local anesthesia deposited around each nerve root have been found equally efficacious in achieving surgical anesthesia [26]. Regardless of the technique used, when the interscalene block is achieved, a catheter may be placed for those situations in which a prolonged block of the brachial plexus is desired (i.e., re-anastomosis of digits). The interscalene block of the brachial plexus can be performed with the arm at the patient's side, and the risk of pneumothorax is remote. However, a pneumothorax should be considered if cough or chest pain is produced while exploring for the location of the brachial plexus. Phrenic nerve and/or recurrent laryngeal nerve block with associated ipsilateral hemiparesis of the diaphragm and laryngeal musculature are common side effects of the interscalene approach to the brachial plexus, but remain clinically irrelevant in the majority of cases [27]. Accidental epidural anesthesia and spinal anesthesia are also possible using this approach, and if local anesthesia is accidentally injected into the vertebral artery, convulsions are likely to follow. At HSS, the interscalene nerve block is used in conjunction with sedation for most arthroscopic and open procedures of the shoulder.

Supraclavicular Nerve Block

The supraclavicular nerve block (SNB) is used to provide anesthesia for surgery on the shoulder, arm, and even forearm. It is approached by paresthesia, nerve stimulator, or ultrasound techniques. This block's popularity has increased with the recent introduction of ultrasound. Classically, a SNB is achieved by injecting 15–40 ml of LA at a point just behind the midpoint of the clavicle where the nerves cross the first rib. The midpoint of the clavicle can be confirmed by palpating the subclavian artery in thin individuals or by extending an imaginary straight line from the end of the external jugular vein. Paresthesias of the forearm or hand should be elicited before the injection of LA. Pneumothorax is the most common complication of SNB (about 1% incidence) [28], initially manifesting as cough, dyspnea, and pleuritic chest pain. Block of the phrenic nerve occurs frequently but generally does not cause clinically significant symptoms. Advantages of SNB are rapid onset and ability to perform the block with the arm in any position. Historically, the high risk of pneumothorax limited the use

of SNB. The use of ultrasound has theoretically reduced the incidence of pneumothorax by allowing visualization of the supraclavicular artery and nerve and, just as importantly, visualization of the first rib, clavicle, and apex of the lung [29]. This permits localization of the nerves while avoiding needle puncture of the lung. Ultrasound approaches either use hydrodissection (advancement of the needle while injecting) of the classic "cluster of grapes" lying next to the artery or deposition of all local anesthesia at a "12 o'clock" position above and adjacent to the neural structures [30]. Nerve stimulation can be used as an adjunct to ultrasonography to confirm needle position by eliciting an appropriate contraction of the muscles supplied by the brachial plexus. SNB is used for most closed procedures of the shoulder in conjunction with sedation.

Infraclavicular Nerve (Coracoid) Block

Coracoid blocks are often used to provide anesthesia for surgery involving the arm, elbow, wrist, and hand. The introduction of ultrasonography has made blocking of the brachial plexus in this location relatively risk-free in comparison to earlier approaches [31]. Using the ultrasound probe, the subclavian artery is visualized medially to the coracoid process, and 5–7 ml of LA is deposited next to the medial, lateral, and posterior cords of the brachial plexus, which lie circumferential to the artery. Alternatively, a single injection of 20–30 ml LA posterior to the artery may be equally effective [32]. Appropriate visualization of surrounding tissues and control to where the needle is directed are keys to the success of this block.

Axillary Nerve Block

Use of the axillary nerve block for upper extremity surgery has decreased at the Hospital for Special Surgery concomitant with the increased use of ultrasound-guided infraclavicular nerve blocks. Both nerve blocks remain useful for operations involving the hand, wrist, forearm, and/or elbow; however, the newer ultrasonographic technology allows direct visualization of the nerve structures while avoiding the theoretical complications associated with the axillary nerve block. There remain two primary techniques—the perivascular "single-injection" technique and the transarterial technique [33]. The axillary block of the brachial plexus is achieved by injecting 25–40 ml of LA in the axillary sheath of the axilla. The nerves are anesthetized around the axillary artery. The primary "problem" with the axillary block is that significant anatomic variation exists. Individual septa may surround different nerves, necessitating multiple injections when compared to single injection approaches. In order to perform the block, the upper extremity is abducted to 90° and externally rotated, the axillary artery is palpated and traced back toward the axilla, and the needle is inserted just anterior to the vessel. Entrance of the needle into the axillary sheath transmits a "popping" sensation to the anesthesiologist's fingers, and the needle transmits the pulsation of the artery. Paresthesias are useful but not mandatory for confirming correct placement of the needle. Digital pressure applied distal to the needle during and after injection should promote proximal flow of LA solutions, within the sheath toward the side, where the musculocutaneous nerve exits. Alternatively, one can transfix the axillary artery (aspirating on both sides of the artery before placement of local anesthesia) with the needle and deposit 10–15 ml of local anesthesia on either side of the vessel, theoretically within the confines of the axillary sheath.

Typically, a small cuff of LA is deposited in the subcutaneous tissues over the proximal medial aspect of the axilla during withdrawal of the needle to block the intercostobrachial nerve. The musculocutaneous nerve is sometimes not blocked because it leaves the sheath proximal to the point of injection. This nerve is important because it provides sensory innervations from the radial side of the forearm to the thenar eminence. It should be blocked as it emerges from between the elbow crease with 5–10 ml of LA. The axillary approach carries the lowest risk of pneumothorax, making it useful for outpatients undergoing surgery on the forearm and hand.

Extremity Nerve Blocks

The Lumbosacral Plexus

The lumbosacral plexus (lumbar, sacral, and pudendal plexus) is formed by a set of conjoining nerve roots that arise from the lower lumbar and sacral spinal nerves (T12–S5), passing communicating branches between each other. Together, they account for the sensory and motor support of the lower extremity.

Unlike in the upper extremity, it is not easily possible to provide anesthesia to the entirety of the lower extremity via one single injection or block. Combinations of various peripheral nerve blocks with or with neuraxial anesthesia are therefore frequently utilized.

Review of Anatomy

After assembling lateral to the intervertebral foramina, the lumbar plexus proceeds downward in the psoas compartment between the psoas major and quadratus lumborum muscles. Aside from short, direct muscular branches, six major nerves branch off: the iliohypogastric, ilioinguinal, genitofemoral, lateral femoral cutaneous, obturator, and femoral nerves. While the former three pierce the abdominal wall or psoas muscle, the latter exit the pelvis through the obturator fora-

men (obturator nerve) and the muscular lacuna underneath the inguinal ligament (femoral nerve), respectively. The lumbar plexus provides innervations to the anterior portions of the hip joint, groin, most regions of the anterior and medial thigh, as well as parts of the knee joint and medial lower leg.

The adjacent sacral plexus innervates posterior and lower portions of the leg through nerves and direct branches. Two branches are most relevant for blockade, the posterior cutaneous femoral and sciatic (containing common fibular and tibial) nerves, which leave the pelvis together through the greater sciatic foramen.

Lumbar Plexus Block

Different ways to anesthetize parts of the lumbar plexus have been described, including the psoas compartment and perivascular (3-in-1) blocks. For the psoas compartment block, a nerve stimulator needle is inserted 3 cm inferior and 5 cm lateral to the fourth lumbar spine, which is commonly located at the height of an imaginary line between the iliac crests. After contact with the fifth lumbar transverse process, the needle should be advanced in cephalad direction, sliding off the transverse process, until a quadriceps motor response can be seen. Complications of this technique include risk of intravascular, epidural, or subarachnoid injection and nerve damage [34]. The 3-in-1 block, in contrast, is based on the assumption that a large volume of local anesthetic injected into the femoral perineural sheath will migrate in lateral and cephalad directions, toward the lumbar plexus, or at least toward its terminal branches femoral, obturator, and lateral femoral cutaneous nerve, providing anesthesia to three peripheral nerves with only one injection (hence, 3-in-1 block). The reliability of this block is subject to controversy [35].

However, the nerves of the lumbar plexus do not fully cover the posterior hip, so neither of these blocks will provide full anesthesia for hip surgery; rather, they are often used in conjunction with either a spinal or epidural approach. A lumbar plexus block is sometimes performed at the Hospital for Special Surgery to help alleviate hip pain. It can be used alone or in combination with epidural anesthesia for postoperative pain control in patients after hip replacement surgery, open reduction and fixation of the femur, and closed reduction of the hip joint.

Saphenous Nerve Block

At the Hospital for Special Surgery, the saphenous nerve block is the nerve block most commonly used for surgeries of the knee and medial foot. It is most often anesthetized at the level of the adductor canal. The saphenous nerve is a sensory branch of the femoral nerve, responsible for sensation from the inner aspect of the knee to the inner aspect of the lower leg and foot. As a purely sensory nerve, its blockade is not associated with motor blockade. As such, it is often used in the outpatient setting when early rehabilitation/motor control of the knee (i.e., knee ligamentoplasty) is requested. The saphenous nerve can be localized in the subsartorial region with the ultrasound probe 7–10 cm above the medial epicondyle of the femur. It is located between the vastus medialis and the gracilis muscles, on the inner aspect of the thigh [36]. Ten to fifteen milliliters of LA is deposited in this space to achieve blockade.

IPACK Block

At the Hospital for Special Surgery, local infiltration between the popliteal artery and capsule of the knee (IPACK) block is often used to provide analgesia for knee operations with a component of posterior knee surgical pain. Using ultrasound, the IPACK block targets the articular branches of the tibial, common peroneal, and obturator nerves in the popliteal region, allowing for analgesia by controlling posterior knee pain following knee surgery. Because the block is done under ultrasound visualization, it is associated with a very low incidence of nerve injury, arterial injury, and foot drop.

Femoral Nerve Block

At the Hospital for Special Surgery, the femoral nerve block is also used for surgeries of the knee and medial foot. However, concerns relating to its potential for prolonged motor blockade and subsequent delayed rehabilitation have seen the femoral nerve block fall out of favor. The femoral nerve is blocked by the injection of 20–30 ml of LA immediately laterally to the femoral artery, just below the midpoint of the inguinal ligament. A line drawn from the anterior superior iliac spine to the symphysis pubis will approximate the ligament. The block itself can be performed by using anatomic landmarks with either nerve stimulator or ultrasonography. With a nerve stimulator, electrical stimulation resulting in contraction of the quadriceps in the prepatellar groove at 0.5 mA is considered sufficient to block the femoral nerve. As with other nerve blocks, the concentration of LA determines the clinical effect. A lower concentration is associated with analgesia of the surgical site, while a higher concentration is associated with both surgical anesthesia and motor blockade in the femoral distribution [37].

Popliteal Nerve Block

Sciatic nerve blocks in the popliteal fossa are used at the Hospital for Special Surgery to help alleviate pain after foot

and ankle surgery, whether reconstructive or arthroscopic. Occasionally, they are used as the primary surgical anesthetic. Patients who have a popliteal block will usually have analgesia to approximately 85% of surface area of the foot. Because the sciatic nerve does not supply sensation to the entire foot, this block is often used in combination with a saphenous nerve block for postoperative pain control. The popliteal nerve is blocked in the popliteal fossa, an anatomical site that is bordered laterally by the biceps femoris muscle and medially by the semimembranosus muscle. This is also where the sciatic nerve splits into its two major components, the tibial and common peroneal nerves. Needle entry for the popliteal nerve block should be proximal to the splitting of these two nerves to avoid a partial block. With a nerve stimulator, electrical stimulation resulting in dorsiflexion of the foot at 0.5 mA is considered sufficient to block the popliteal nerve. When this is achieved, 30–40 ml of LA is injected—a large volume is required to ensure adequate anesthesia of both branches of the sciatic nerve. As with other nerve blocks, the concentration of LA determines the clinical effect. A lower concentration is associated primarily with analgesia of the surgical site, while a higher concentration is associated with both surgical anesthesia and motor blockade in the popliteal distribution.

Ankle Block

The ankle block is often used at the Hospital for Special Surgery to either provide surgical anesthesia and/or postoperative analgesia for surgeries of the forefoot. It is a combination of multiple injections around the foot and ankle area. All five nerves of the foot can be blocked at the level of a line connecting the medial and lateral malleoli. The posterior tibial nerve is the major contributor of sensation to the sole of the foot. To block this nerve, the needle is introduced just behind the posterior tibial artery and advanced until a paresthesia to the sole of the foot is elicited or bone is encountered, at which point the needle is slightly withdrawn and 5 ml of LA is injected. The sural nerve is blocked by injecting 5 ml of LA between the lateral malleolus and calcaneus. Infiltration of 5 ml of LA anterior to the medial malleolus blocks the saphenous nerve. The deep peroneal nerve is the major nerve to the dorsum of the foot and is blocked by injecting 5 ml of local anesthesia just lateral to the anterior tibial artery. Superficial branches of the peroneal nerve are blocked by a subcutaneous ridge of local anesthesia injected between the anterior tibial artery and lateral malleolus.

Neuraxial Anesthesia

Spinals, epidurals, and continuous spinal epidurals (CSE) are the mainstay of anesthesia for surgery of the lower limb at the Hospital for Special Surgery. Their techniques are well described elsewhere. As with peripheral nerve blocks, the choice of LA depends upon many factors, including availability, practitioner comfort, duration of surgery, positioning, and patient comorbidities. At our institution, epidurals facilitate the practice of controlled hypotension and are sometimes used to ensure patient comfort in settings where the use of a tourniquet is required. As a generalization, combined spinal/epidural techniques allow for continuous infusions of opioids and LAs for postoperative pain in the postoperative period.

Regional Anesthesia for Specific Procedures

As mentioned previously, regional anesthesia is used for most procedures performed at the Hospital for Special Surgery except spine surgical interventions, which require general anesthetics and are not discussed here.

Following is a brief description of the anesthetic techniques routinely used for various procedures commonly performed. Variations of the techniques described will depend on details of the surgery and patient comorbidities. A summary of anesthetic techniques used by procedure type is presented in Table 8.2.

Anesthetic Techniques: Upper Extremity

Total Shoulder Arthroplasty

As regional techniques, interscalene or supraclavicular nerve blocks are possible approaches for total shoulder arthroplasty, both for surgical anesthesia and postoperative pain control. Additionally, deep sedation or general anesthesia and airway management by laryngeal mask should be con-

Table 8.2 Anesthetic techniques for common procedures carried out at HSS

Total knee arthroplasty	Total hip arthroplasty
Femoral nerve block Combined spinal and epidural Arterial blood pressure monitoring (if ASA ≥3)	Combined spinal and epidural Controlled hypotension ± lumbar plexus block Arterial blood pressure monitoring ± central line
Total shoulder arthroplasty	*Foot and ankle surgery*
Interscalene/supraclavicular block ± general with laryngeal mask Arterial blood pressure monitoring	Spinal Popliteal block ± catheter
Knee arthroscopies	*Shoulder arthroscopies*
Spinal or general with laryngeal mask Sedation	Interscalene block Sedation
Hand and forearm surgery	
Infraclavicular block Sedation	

sidered, given that the patient position and proximity of the surgical intervention to the airway can be very discomforting. An arterial line attached to a continuous blood pressure monitoring device is commonly utilized to duly detect and counteract blood pressure variations, which commonly appear in the sitting (beach chair) position.

Shoulder Arthroscopy

Similar to total shoulder arthroplasty, an interscalene or supraclavicular block in conjunction with sedation is used for diagnostic or interventional shoulder arthroscopy, providing adequate surgical anesthesia and postoperative analgesia to the shoulder region. Longer procedures or those requiring relaxation of the shoulder musculature, including shoulder stabilizations, may require the addition of a general anesthetic.

Elbow, Forearm, and Hand Surgery

Depending on the exact location of surgical intervention, a supraclavicular, infraclavicular, or axillary block can be taken into consideration. At HSS, the supraclavicular block is predominantly used for proximal, and an infraclavicular block for distal procedures, while the axillary block decreases in importance.

Anesthetic Techniques: Lower Extremity

Total Hip Arthroplasty

For total hip arthroplasty, combined spinal and epidural anesthesia has proven beneficial. On the one hand, given the complex nerve supply to the hip joint, surrounding tissue, and muscles, neuraxial anesthesia provides advantages compared to peripheral nerve blocks in practicality and ease of use. On the other hand, controlled hypotensive epidural anesthesia can reduce bleeding. Further, a lumbar plexus block can contribute to excellent postoperative analgesia, especially in cases where anticoagulation requires removal of the epidural catheter shortly after the procedure. Arterial blood pressure monitoring is obligatory with the use of controlled hypotension and with regard to invasiveness of the surgery and potential blood loss.

Total Knee Arthroplasty

The knee joint is supplied by both the femoral and sciatic nerves. Pain often extends to the thigh, for instance, when a tourniquet is used to reduce bleeding. Complete surgical anesthesia and postoperative pain control are most easily achieved by combination of neuraxial anesthesia (spinal and epidural) and peripheral (femoral or saphenous) nerve block. Catheters make prolonged postoperative application of local anesthetic possible. Arterial blood pressure monitoring is applied in patients classified as American Society of Anesthesiologists Class 3 or above.

Knee Arthroscopy

Outpatient knee arthroscopy can, as a minor painful procedure, most frequently be managed by spinal anesthesia alone at the Hospital for Special Surgery. Advantages are fast recovery and low incidence of complications. However, depending on patient preference or comorbidity profile, general anesthetics with a laryngeal mask airway may be used.

Foot and Ankle Surgery

Nerve supply to the lower leg, ankle, and foot is provided by the saphenous nerve (medial side), the sciatic nerve, and its branches, respectively. Blockade of one or more of these nerves is sufficient for complete surgical anesthesia, as long as no thigh tourniquet is applied. Depending on the location of the surgery, a popliteal block, an ankle block, or a saphenous block is chosen. For more extensive procedures, a spinal or combined spinal and epidural is added.

Spine Surgery

The transversus abdominis plane (TAP) block is a peripheral nerve block designed to anesthetize the nerves supplying the anterior abdominal wall (T6 to L1). It is often used in spinal surgical procedures that incorporate an anterior surgical approach to the spine. The anterior rami of spinal nerves T6–L1 innervate the anterolateral abdominal wall. The anterior divisions of the intercostal nerves (T7-11) enter the abdominal wall between the internal oblique and transversus abdominis muscles. The goal of the TAP block is to inject local anesthetic in the plane between the internal oblique and transversus abdominis muscles, targeting the spinal nerves in this plane. The injection interrupts innervation to the abdominal skin, muscles, and parietal peritoneum; however, it will not block visceral pain. The TAP block can be performed using a blind approach or with ultrasound guidance. Using an anatomic approach, a single point of entry is at the lumbar triangle of Petit. The triangle is bounded inferiorly by the iliac crest (IC), anteriorly by the external oblique muscle, and posteriorly by the latissimus dorsi. The costal margin (CM) is just superior to the triangle of Petit. The classic description is the feel of a "double pop" as the needle traverses the fascia extensions of the external oblique and the internal oblique muscles. However, the ultrasound approach, in which the probe is placed in a transverse plane to the lateral abdominal wall in the midaxillary line, between the lower costal margin and iliac crest, allows for a more accurate deposition of local anesthesia.

Summary

Orthopedic surgery is undoubtedly one of the specialties where regional anesthesia is used most frequently and most successfully. Not only does the practice of selectively anesthetizing specific regions of the body mitigate the systemic stress associated with surgery, but it also allows for more focused and sustained postoperative analgesia. Especially the elderly and people suffering from comorbidities like cardiovascular or respiratory disease benefit most. Furthermore, many studies demonstrated reductions in demand for analgesics and other systemically administered drugs, exerting a positive influence on perioperative well-being and diminishing associated side effects like nausea, vomiting, or constipation [38]. However, in order to achieve optimal acuity, duration, and minimal side effects, it is essential for the anesthesiologist to gain knowledge about a number of influencing factors: selection of appropriate block technique; choice of the right local anesthetic agent, concentration, and dosage; locating injection sites by use of anatomical landmarks, paresthesia technique, ultrasound, or a combination of these methods; determining block success and, if in doubt, resorting to another method of regional or even general anesthesia; ensuring sustained analgesia; and, last but not least, awareness of side effects associated with injection and/or drugs. The most cumbersome immediate complication of regional anesthesia is LAST. LAST can rapidly lead to catastrophic situations, only manageable by means of the full-scale application of intensive care services. The mainstay of treatment is Intralipid, and its availability is mandatory in areas where regional anesthesia is administered. Moreover, although infrequently occurring, permanent nerve damage is a matter of concern and potentially disqualifies some patients from receiving regional anesthesia.

Comprehensive unilateral anesthesia to the whole limb can more easily be achieved in the upper extremity. Possible approaches include the interscalene, supraclavicular, infraclavicular, and axillary plexus block and should be chosen according to type of surgery and desired distribution of anesthesia. In the lower limb, several techniques are available for the lumbosacral plexus as well as for peripheral nerves. However, a multimodal approach combining one or more of these peripheral blocks with neuraxial anesthesia is applied frequently.

In conclusion, regional techniques are cornerstones of orthopedic anesthesia; their development and advancement establish new possibilities and make orthopedic surgery available to more patients. While widely used at the Hospital for Special Surgery, variations of these approaches have to be tailored to individual patient comorbidities, preferences, anatomic variations, as well as surgical cofactors like patient positioning.

Summary Bullet Points

- Regional anesthesia provides focused and sustained pain relief for patients undergoing orthopedic surgery.
- Choice of specific anesthetics and techniques is the key to successful regional anesthesia.
- Complications and contraindications must be kept in mind in order to minimize potential harm.

Case Study

A 27-year-old woman (68 kg, 165 cm) with a history of shoulder pain over several months presented for ambulatory diagnostic shoulder arthroscopy. Her preoperative vital signs, clinical examination, and routine laboratory workup were unremarkable.

The patient was monitored as per routine and a 20-gauge intravenous cannula was placed. The injection site for an interscalene block was determined using a 30 mm insulated needle attached to a nerve stimulator. After biceps response was evoked at 1.8 mA and intravascular needle position was ruled out by negative aspiration, 30 mL of 0.375% bupivacaine was injected, with aspiration occurring at 5 mL intervals.

The patient immediately began to complain about acoustic sensations as well as feelings of dry and itchy mouth and eyes. The injection was interrupted and the needle withdrawn; within 20 s, generalized convulsions resembling a grand mal seizure developed, and the patient was found to be apneic. Mask ventilation with 100% oxygen was initiated, midazolam 5 mg was administered, and the anesthesia technician was instructed to get a lipid rescue kit from the cardiac arrest cart located outside the room. The convulsions stopped and the anesthesiologist noticed broad complex tachycardia with a heart rate of 140 bpm on the ECG; a pulse was difficult to palpate at the carotid artery. Intralipid® 20% 500 mL intravenously was started. Attempts to place a radial arterial catheter failed at that point. An attempt of cardioversion was unsuccessful. After 50 mL of Intralipid® was infused, a brief period of ventricular fibrillation was immediately followed by asystole. After commencement of cardiac compressions, administration of epinephrine 1 mg, and successful tracheal intubation, another 150 mL of Intralipid® was infused rapidly. Return of spontaneous circulation occurred approximately 45 s after initial appearance of ventricular fibrillation. A narrow complex tachycardia was present on the ECG; a radial arterial catheter was successfully placed. The initial blood pressure obtained was 140/90 mmHg, but rapidly declined to 80/40 mmHg. Circulation was supported with repetitive boluses of phenylephrine and epinephrine, until a central line and continuous epinephrine infusion was estab-

lished. Analysis of arterial blood samples revealed the following values: pH 6.8, $PaCO_2$ 116 mmHg, PaO_2 144 mmHg, and lactate exceeding 15 mmol/L. Intermittent positive pressure ventilation was maintained to counteract hypercapnia and acidosis. To facilitate ventilation and prevent reoccurrence of convulsions, another 7.5 mg bolus of midazolam was administered. The remaining 300 mL of Intralipid was infused over 20 min (0.22 mL/kg/min). The patient was transferred to the intensive care unit. A repeated arterial blood sample after 2 h revealed a pH of 7.33, $PaCO_2$ of 48 mmHg, PaO_2 of 222 mmHg, lactate of 9.2 mmol/L, potassium of 2.7 mmol/L, and glucose of 90 mg/dL. The ECG showed a sinus tachycardia at a rate of 110 bpm with occasional ventricular ectopy. An amiodarone loading dose (300 mg) and potassium were subsequently administered, and the patient was maintained on continuous inotropic support (epinephrine 0.02 μg/kg/min) and sedation (propofol 50 μg/kg/min). Epinephrine and propofol were gradually decreased and eventually discontinued 4 h after admission to the intensive care unit. The patient was extubated shortly thereafter. The patient was transferred to a cardiac ward on day 3 and discharged 7 days after the initial event. The surgical procedure was carried out 4 weeks later using general anesthesia without any incident.

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The Role of the Postanesthesia Care Unit in the Perioperative Care of the Orthopedic Patient

9

Michael K. Urban

Objectives

- To provide an overview of the goals of postoperative care and discuss commonly encountered challenges in the care of postoperative orthopedic patients
- To discuss common perioperative complications and the care of specific patient populations as approached at the Hospital for Special Surgery
- To introduce the concept of the model of postoperative care unique to the Hospital for Special Surgery

Key Points

- The traditional role of the postanesthesia care unit (PACU) is to provide a safe transition from the highly monitored operating environment to the routine management on the patient ward.
- The goals of such transition include observation and monitoring of the resolution of anesthesia, resuscitation of blood loss and its consequences, and adequate pain management.
- Common complications after orthopedic surgery affect the cardiopulmonary and other organ systems, requiring that perioperative physicians are familiar with diagnosis and treatment of these entities.
- At the Hospital for Special Surgery, the PACU also functions as an extended monitored care facility, providing care and observation for specific surgical patient populations such as extensive spinal procedures and bilateral knee arthroplasties and patients with increased postoperative medical risks such as ischemic heart disease and pulmonary.
- In the role as an intensive care unit, the recovery room at the Hospital for Special Surgery may also care for unstable patients, including those with respiratory failure.

Introduction

The orthopedic patient can be particularly challenging with regard to postoperative care. This patient group is diverse and may present with a variety of challenges. The spectrum includes the geriatric patient with multiple comorbidities scheduled for total joint replacement to the young deceptively healthy trauma patients who may have multiple associated injuries. Thus, it becomes clear that a host of different factors may significantly impact on an individual's postoperative course.

Despite general concerns associated with any postoperative patient, the perioperative clinician's greatest challenges continue to be related to the care of the elderly with significant medical problems who seek surgical resolution for their chronic musculoskeletal problems, most commonly osteoarthritis. As of 2016, 15.2% of the US population are over 65 years old, and 49% of these individuals have "physician" diagnosed arthritis. According to the Department of Health and Human Services, the number of US citizens over 65 years of age is expected to increase to 71.5 million by the year 2030. Hence, it is virtually certain that an increasing number of elderly patients with multiple comorbidities will seek orthopedic surgeries.

Traditionally, the role of the postanesthesia care unit (PACU) is to provide monitored care for the patient recovering from an anesthetic after surgery. It further represents the bridge between single practitioner monitoring in the opera-

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tive theater environment and periodic observational monitoring in a hospital room.

The PACU at the Hospital for Special Surgery, however, serves multiple purposes with an expanded scope compared to more traditional recovery rooms. Although its primary functions focus on the recovery of patients after surgery and anesthesia, patients are admitted postoperatively for overnight observation for potential surgical or comorbidity-related complications. Further functions include those traditionally provided by a step-down unit (SDU) for patients who require additional physiological monitoring. Further it is used as an overflow unit for high-acuity and unstable patients with complications when the intensive care unit (ICU) is at capacity. The latter functions apply to complicated patients both directly admitted from the operating room and those transferred from patient wards within the hospital. During a 1-year period, approximately 2% of the patients discharged from the PACU after nonambulatory orthopedic surgery required readmission to a higher level of care, which includes ICU, SDU, and PACU [1]. Cardiac complications were the most common reason for transfer, followed by pulmonary and neurological adverse events.

The goal of this chapter is not to provide an in-depth discussion of components of routine postoperative care, such as monitoring the recovery from anesthesia, maintaining cardiopulmonary and hemodynamic stability, and controlling pain, but instead to entertain a brief overview of the most common problems and complications encountered in the care of specific orthopedic patient populations. Further, a specific objective of this chapter is to discuss the above points in the context of current practice at the Hospital for Special Surgery (HSS).

Recovery from Anesthesia and Fluid/Blood Management

The role of the PACU is to provide patients with a safe transition of care from the operating room to the patient ward. During this transition, many acute effects of surgery and anesthesia, including traumatic and drug-related factors affecting patient physiology, need to be addressed. Since many PACUs care for patients after a variety of surgical procedures which often require general anesthesia, airway problems constitute a large number of complications, and hence respiratory management is often the focus of attention. In an Australian database of 419 recovery room incidents, 43% were related to airway and respiratory complications [2]. At this orthopedic institution, where the majority of the patients receive a regional anesthetic, although oxygenation and ventilation remain the most important concerns of the PACU staff, the incidence of PACU incidents related to the airway is much lower. Of the nonambulatory surgical procedures performed at HSS in 2010, the majority were performed under regional anesthesia (Fig. 9.1).

Since patients undergoing lower extremity surgery will usually have been anesthetized with neuraxial anesthesia, these individuals require PACU observation until both the hemodynamic and neural blockade effects of the local anesthetic have resolved. For patients undergoing a posterior approach total hip arthroplasty, the anesthetic often includes controlled hypotensive anesthesia via a neuraxial block which is dosed through the epidural catheter with the goal to achieve sympathectomy. In this particular patient population, the mean arterial blood pressure may decrease 25% with either no change or a slight decrease in heart rate [3]. With this technique, blood pressure and heart rate are controlled

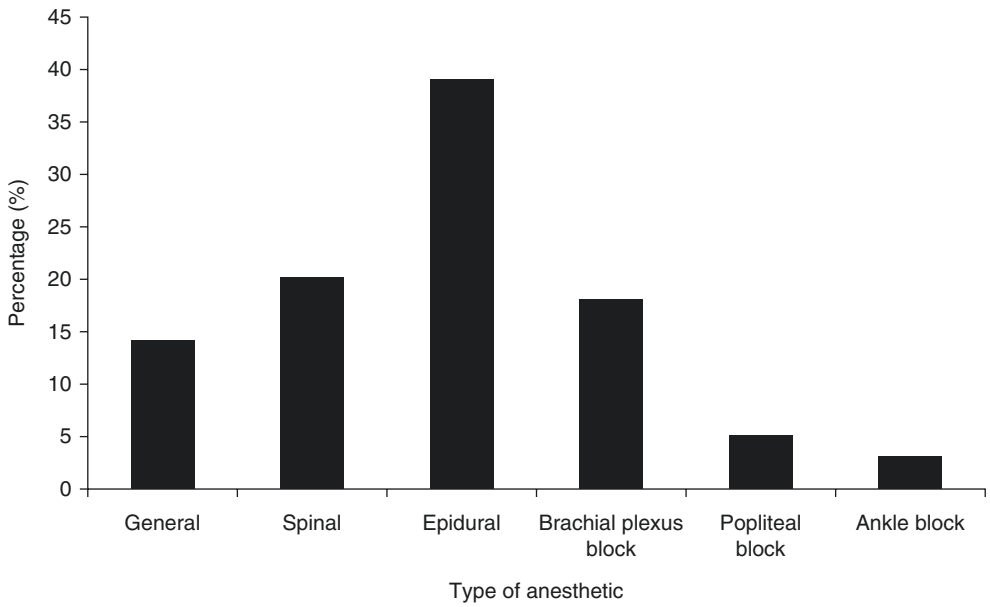

Fig. 9.1 Distribution of types of anesthetics performed at the Hospital for Special Surgery

and stabilized using epinephrine infusions in the operating room, while in the PACU these patients are at risk for continued episodes of hypotension until the neuraxial block resolves. In the PACU, blood pressure is supported with ephedrine, intravenous fluids, and when applicable blood transfusions, respectively. Crystalloid infusions are limited because of the notion that once systemic vascular resistance is normalized and volume returns to the central circulation, elderly patients, especially those with preexisting cardiac dysfunction, may be at risk for postoperative congestive heart failure.

In the past, the majority of arthroplasty patients predonated autologous blood, and this blood was transfused in the PACU. However, an autologous blood donation system is expensive, and if the surgery is rescheduled, the donated blood is wasted. Further, there remains the risk of clerical transfusion errors and contamination of the blood units. Finally, preoperative anemia is a consequence of predonation and is associated with increased morbidity and mortality after orthopedic surgery [4]. Nevertheless, blood loss has been reduced through the combination of regional anesthesia with controlled hypotensive anesthesia and the perioperative administration of tranexamic acid [5]. Since the majority of the blood transfusions still take place in the PACU, our customary practice is to withhold homologous blood transfusion in asymptomatic adult patients with hemoglobin levels above 8gm/dl as per the results of the TRICC and FOCUS trials [6, 7]. A recent review supports a restrictive approach to blood transfusions after major orthopedic surgery [8]. The same conservative approach is applied to postoperative fluid management in the PACU, where the goal is to provide goal-directed therapy resulting in adequate tissue perfusion without inducing the complications of fluid overload, including pulmonary congestion, CHF, bowel edema and ileus, hyponatremia, and tissue edema [9]. In addition to the traditional methods of assessing intravascular volume status (physical examination, urine output, acid-base status), point-of-care, bedside transthoracic echocardiography (TTE) is frequently utilized [10]. Although the colloid-crystalloid debate continues, albumin is often considered as a resuscitation fluid to provide acute volume expansion with reduced interstitial edema.

Pain Management

Pain management should be addressed and planned in the operating room, but the PACU is where most of that plan is implemented. The goal is to establish an analgesic plan which will treat pain effectively, ameliorate the postoperative stress response, facilitate postoperative rehabilitation, minimize the side effects, improve outcome, and decrease hospital stay. This includes a multimodal approach, which will vary depending on the surgical procedure, but often includes acetaminophen, a NSAID, a gabapentinoid, and an opioid [11]. The initial dose of acetaminophen is frequently administered intravenously in the OR or PACU. At the Hospital for Special Surgery, many of the patients are followed by the Anesthesia Department managed with acute pain service, and the pain after lower extremity surgery may be managed with patient-controlled epidural analgesia (PCEA). An important element of this postoperative pain protocol is the institution of PCEA before the level of pain experienced by the patient becomes difficult to control and is usually initiated before complete resolution of the operative neuraxial blockade. Attention is paid, however, to frequent evaluation of the resolution of the motor blockade in order to detect rare neuraxial complications. Recently, a trend towards application of periarticular local anesthetic injections and/or more extensive combinations of peripheral nerve blocks has led to a decrease in the need for PCEA [12], which has also reduced the number of bladder catheters placed in the perioperative period.

Postoperative pain management is challenging in patients with preoperative narcotic dependency after spinal fusion surgery. The persistent nociceptive and neuropathic pain which these patients experience as well as perioperative opioid-induced hyperalgesia may in part be mediated through N-methyl-D-aspartate (NMDA) receptors. Ketamine is a noncompetitive NMDA receptor antagonist, which has been used in the treatment of chronic pain syndromes and at subanesthetic doses in the management of acute pain [13, 14]. At the Hospital for Special Surgery, we have shown that a perioperative infusion of subanesthetic ketamine is effective at reducing pain in narcotic-tolerant patients after posterior spinal fusions. It aids in counteracting unacceptable levels of pain in patients resistant to conventional narcotic treatment. These patients typically spend the night following surgery in the PACU on a ketamine infusion with concomitant use of a PCA with intravenous hydromorphone. On the first postoperative day, the chronic pain patients who were treated with ketamine continue to have improved analgesia during physical therapy compared to the non-ketamine-treated patients [15].

Common Complications

Cardiac Complications

As previously discussed, our PACU serves not only as a recovery room but also as the location of care when SDU and ICU are at capacity. Analyzing institutional data, monitoring for cardiac complications – including myocardial ischemia – was the major reason patients remained in the PACU after having recovered from anesthesia. During a 1-year period,

7.6% of the patients undergoing major nonambulatory orthopedic procedures were entered into a rule-out myocardial infarction (ROMI) protocol [16]. Of these patients, 20% had elevated serum troponin levels and about one third had postoperative cardiac complications, the majority of which were arrhythmias. However, the incidence of a myocardial infarction was low (1.2%). Although speculative, it is feasible that aggressive postoperative management of these patients in the PACU (β-blockade; ASA, statin, treatment of anemia, and hemodynamic instability) assisted in achieving these results. The diagnosis of a postoperative myocardial ischemia is important in the orthopedic population since these events are often associated with further cardiac morbidity if not treated appropriately (Fig. 9.2). Two prospective studies of patients undergoing noncardiac surgery reported that postoperative cardiac troponin elevations were strongly associated with mortality within 30 days and 12 months after surgery [17, 18]. Furthermore, the decision to initiate postoperative physical therapy which is important for a favorable outcome in orthopedic patients may depend on the correct diagnosis of postoperative myocardial ischemia (PMI).

Arrhythmias, specifically atrial fibrillation (A-fib), is a common postoperative cardiac complication in the PACU. These patients are initially treated with either metoprolol or diltiazem to slow the ventricular response. A treatable etiology is then sought, including electrolyte abnormalities, anemia, hypovolemia, and myocardial ischemia. A pulmonary embolism is considered in those who present after the first postoperative day and have associated pulmonary signs and symptoms suggestive of a thrombotic event. Patients not converting to sinus rhythm are considered for amiodarone infusion. Since postoperative new-onset A-fib can be indicative of subclinical paroxysmal A-fib and an increased risk of an ischemic stroke within 1 year of surgery [19, 20], a cardiologist is consulted who can discuss the risks and benefits of long-term anti-coagulation.

Respiratory Complications

As most patients in a PACU will have received a variety of intraoperative medications and interventions which potentially compromise the respiratory system, related problems constitute some of the most commonly encountered postoperative complications. At an orthopedic institution where the majority of the patients receive a regional anesthetic with minimal to moderate sedation, the incidence of PACU complications related to the airway and respiratory system is relatively low. However, given the high prevalence of obesity and obstructive sleep apnea among patients undergoing arthroplasty and spine surgery, respiratory concerns and complications remain a primary concern. Furthermore, in patients with rheumatological diseases (i.e., rheumatoid arthritis, ankylosing spondylitis), both airway management and issues regarding oxygenation and ventilation secondary to restrictive lung disease can be particularly challenging. Elderly patients undergoing hip procedures are affected more commonly by hypoxic events compared to patients undergoing non-orthopedic procedures [21]. This hypoxia may reflect embolization of bone marrow debris into the pulmonary system. In some of these patients, preexisting pulmonary arterial hypertension will be exacerbated by the

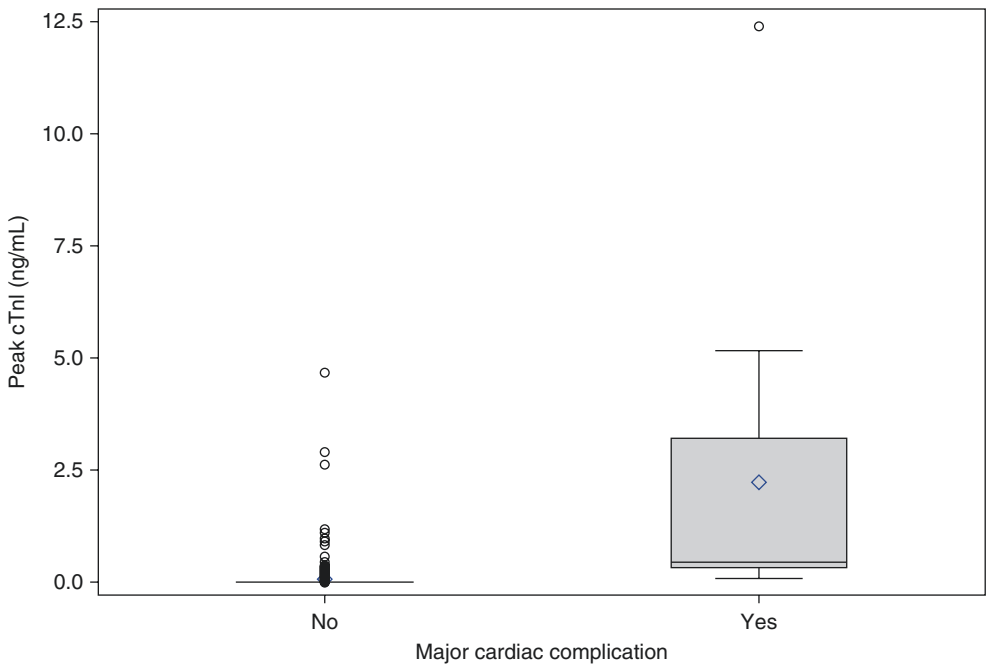

Fig. 9.2 Troponin (cTnI) levels in postoperative patients with (yes) and without (no) cardiac complications

embolization of cement and bone marrow particles during hip and knee arthroplasty. Thus, our practice dictates that this patient population requires at least 12–24 hours of monitoring in the PACU.

Fat embolization is a well-known complication of skeletal trauma and surgery involving instrumentation of the femoral canal [22]. Patients undergoing bilateral hip and knee arthroplasty, revision hip arthroplasty, and pelvic reconstructions are at increased risk for fat (bone marrow) embolism syndrome [23]. The clinical manifestations of FES include respiratory symptoms, ranging from mild hypoxemia to adult respiratory distress syndrome; cardiac derangements, including tachycardia, arrhythmias to heart failure; neurologic abnormalities, ranging from somnolence and confusion to obtundation and coma; and hematologic symptoms, including thrombocytopenia and disseminated intravascular coagulation [24]. The signs and symptoms of FES in relation to the incidence of presentation are described in the Schonfeld Index [25] (Table 9.1). Since the management of the FES is supportive with early intervention resuscitation and stabilization to minimize the deleterious effects of the systemic inflammatory response to the initial insult, patients at increased risk are monitored in the PACU for 24 hours.

Renal Complications

In an analysis of 1636 patients undergoing lower extremity joint arthroplasty, acute renal failure (ARF) constituted one of the major postoperative life-threatening complications [26]. Using the RIFLE criteria to classify patients into ARF severity categories, many orthopedic patients fall into the group at risk for ARF [27]. Risk factors include advanced age, elevated body mass index, preoperatively elevated creatinine, and significant perioperative blood loss. The operative procedures which are most likely to result in ARF include bilateral knee arthroplasty, revision knee and hip arthroplasty, and posterior spine fusions. These procedures not only involve significant blood loss but may also induce FES and/or an inflammatory response which produces capillary leakage and decreased intravascular circulating volume. Hence, in the majority of cases, oliguria and anuria are the result of hypoperfusion of the kidney secondary to relative hypovolemia. Perioperatively, it is important to restore appropriate intravascular volume through the infusion of crystalloid, colloid, and when required blood products to prevent the development of acute renal dysfunction. Bedside TTE and laboratory tests are often utilized to assess intravascular volume status and determine subsequent care and interventions.

Table 9.1 Schonfeld FES Index

Sign	Score
Petechial rash	5
Diffuse alveolar infiltrates	4
Hypoxemia paO_2 < 70 mmHg, FIO_2 100%	3
Confusion	1
Fever >100.4 F	1
Heart rate > 120 bpm	1
Respiratory rate > 30	1

Data from Ref. [25]
Score >5 required for diagnosis of FES

Obstructive Sleep Apnea

After the patient group with cardiac disease, the next largest category of patients who are monitored in the PACU for an extended period at the Hospital for Special Surgery are those with obstructive sleep apnea (OSA). OSA is a chronic condition resulting in partial or complete obstruction of the airway during sleep with potential adverse cardiovascular complications. The prevalence of OSA in our population may approach 10%. These patients may be at risk for adverse postoperative cardiorespiratory complications, including death. However, there are insufficient evidence-based data in the literature to provide guidelines with regard to the postoperative management of patients with diagnosed OSA. In a retrospective analysis of patients undergoing total hip or total knee arthroplasties, OSA was associated with increased incidence of postoperative transfer to an ICU [28]. The accepted diagnosis of OSA requires an overnight polysomnography analysis which generates an Apnea-Hypopnea Index, AHI, the number of pharyngeal collapses lasting more than 10 seconds per hour during sleep. However, the STOP-BANG questionnaire for OSA has been advocated by some as a simple bedside means of identifying those patients at risk for having OSA [29]. All patients for nonambulatory surgery at the Hospital for Special Surgery have a STOP-BANG score in their medical record; a score of ≥5 places a patient at high risk for OSA. Most clinicians agree that patients with severe OSA, AHI >30, or obesity hypoventilation syndrome (OHS) should be monitored with oximetry and adequate respirations for at least the night after surgery [30]. The postoperative management of those with mild-to-moderate OSA remains controversial; however, a conservative approach suggests a monitoring period of one sleep cycle. At the Hospital for Special Surgery, we have established an OSA unit which provides continuous pulse oximetry and respiratory rate monitoring with nurse-activated alarms. Patients who have known or suspected mild-to-moderate OSA, ASA 2, or BMI ≤45 and do otherwise not require SDU or ICU monitoring for additional diagnosis (ROMI, large EBL) are monitored in this unit (Box 9.1). Patients who use continuous positive airway pressure at home are asked to bring their masks to the hospital, thus facilitating continuation of care during their stay.

Box 9.1 Criteria for Admission to the OSA Unit

1. Diagnosed OSA with stable, chronic use of CPAP at home
2. Diagnosed OSA but noncompliant with CPAP
3. Suspected OSA (STOP-BANG ≥5; clinician decision)
4. BMI ≤45
5. ASA ≤2 (unless ASA of 3 based on BMI only)
6. Exclusion:
   (a) Requiring SDU monitoring other medical reasons
   (b) EBL >20%
   (c) Chronic pain patient

Patients After Bilateral Joint Arthroplasty and Revision Arthroplasty

Patients undergoing bilateral lower extremity or revision arthroplasty are observed overnight in our PACU, based on the fact that these operations are associated with increased blood loss, longer surgical duration, and an increase in the perioperative inflammatory response. Single-stage bilateral lower extremity arthroplasty, particularly that involving the knee joints (SBTKA), has been reported to be associated with increased morbidity and mortality [31]. The major postoperative complications after SBTKA include myocardial infarction, fat embolization, respiratory insufficiency, and thromboembolic events. As these complications may be the result of multiple comorbidities, increased blood loss and fluid shifts, pain, and cardiopulmonary stress compared to unilateral joint arthroplasty, careful patient selection and increased postoperative vigilance seem prudent in an attempt to improve outcomes. At our institution all SBTKA recipients are screened by an anesthesiologist preoperatively with the goal to restrict these higher-risk procedures to patients without significant comorbidities [32] (Box 9.2). Although younger patients are being selected for SBTKA, some of the complications are still increasing. The increased complication rate may be the result of the rising levels of obesity and associated, often undiagnosed, conditions like pulmonary hypertension [33].

Box 9.2 Exclusion Criteria for SBTKR

1. Patients ≥80 y.o.
2. ASA 3
3. Active ischemic heart disease (h/o angina or positive stress test)
4. Reduced LV function (LVEF<45%; DOE; h/o CHF)
5. Poor functional capacity
6. Pulmonary disease
   (a) Moderate to severe pulmonary hypertension
   (b) O_2 dependent
   (c) Steroid-dependent asthma
   (d) Exercise-limiting COPD
7. Morbid obesity
8. Renal insufficiency: Cr >1.8
9. Liver disease: child's class B or greater
10. Poorly-controlled DM; HbA1c >7%
11. Cerebral vascular disease (h/o stroke)
12. Major peripheral vascular disease

Data from Ref. [32]

Postoperative Delirium

Another significant patient population requiring extended postoperative monitoring and interventions is the population suffering from postoperative delirium. Delirium is a common complication in the geriatric population following orthopedic surgery, with a reported incidence of up to 50% particularly after the repair of femoral neck fractures [34]. Postoperative delirium usually presents after 24 hours post surgery and resolves within 48 hours. However, in some of the patients, evidence of confusion and cognitive dysfunction may persist for up to 6 months. Postoperative delirium is associated with longer hospital stay, increased risk for complications, poor recovery, increased mortality, and increased healthcare costs [35, 36]. The diagnosis can be challenging as postoperative delirium can present in various forms. A fluctuating hyperactive state is often associated with agitation, sweating, and tachycardia, but a hypoactive type may present with passive confusion and is often overlooked. Since in most cases patients present with a change in mental status without a clear etiology, they are often subjected to an extensive neurological evaluation including brain imaging. At the Hospital for Special Surgery, patients with delirium are identified by nurses using the CAM algorithm [37]. Next a neurological examination is conducted by a physician to rule out focal deficits. Further, blood laboratory analysis may be performed to exclude electrolyte abnormalities, hypercarbia, and hypoxemia. A review of all medications to eliminate unnecessary centrally acting medications is mandatory. And finally, care should be taken to assure adequate pain management [38].

At our institution over a 6-year period in a cohort of 78,492 adult patients undergoing nonambulatory orthopedic surgery, the incidence of POD was 1.2%. Many of the risk factors identified have been cited in previous reports and are not amendable to modification. They include advanced age,

medical comorbidities, and a history of preexisting psychiatric disease. However, some risk factors such as preexisting narcotic dependence, alcoholism, and hyponatremia are potentially modifiable. In addition, the surgical procedure, type of anesthesia, and type of postoperative analgesia may affect the incidence of delirium, and as such these factors can be targeted in an attempt to reduce its incidence [39].

Once the diagnosis of postoperative delirium has been established, the managing physician is faced with the problem of treatment options. If removal of the delirium-inciting agents (i.e., narcotics, benzodiazepines) does not improve the confusion and/or the patient's hyperactive state, pharmacological treatment has traditionally constituted in the use of neuroleptic medications such as haloperidol. At our institution, however, we have had significant success with low-dose (<0.5 μg/kg/h) infusions of dexmedetomidine for 6–8 hours. This approach is used primarily in hyperactive patients and produces mild-to-moderate sedation, control of agitation, and associated hypertension and tachycardia while allowing the patient to rest without significant depression of the respiratory system.

Readmission to the PACU

As mentioned previously, the PACU functions as the place for monitoring and treatment when the ICU and SDU are at capacity. As such its staff provides care for patients whose medical condition deteriorates during the remainder of their hospitalization. When studying all patients undergoing major orthopedic surgery over a 1-year period (n = 12,229) at our institution, 1.7% (n = 206) were readmitted to the PACU within 6 days of discharge. This represented 1.6% of all total hip arthroplasties, 1.8% of all total knee arthroplasties, and 3.4% of all spinal fusion surgeries (3.4%) [40]. Patients readmitted to the PACU after surgery had multiple comorbidities, including cardiac disease (40.3%), diabetes mellitus (18.4%), chronic renal insufficiency (14.1%), and pulmonary disease (12.6%) (Fig. 9.3). Approximately 9% of the returning patients had ≥3 comorbidities. Of the patients with a final diagnosis of myocardial ischemia, 80% had at least one cardiac risk factor. Patients requiring PACU readmission were also significantly older and had a longer length of hospital stay. Since there is increased pressure to reduce the length of the hospital stay after major orthopedic procedure, it is important to identify which patients are at risk for acute postoperative complications. This study represents the first step in identifying the incidence of postoperative complications after major orthopedic surgery, the patients at risk for these complications, and possible interventions which may reduce poor outcome.

Summary

The PACU at the Hospital for Special Surgery functions as a recovery room, SDU, and overflow ICU. Much of our emphasis is devoted to the recovery of patients from regional anesthesia and the institution of adequate postoperative analgesia. Common problems encountered in the orthopedic patient population often stem from blood loss and fluid resuscitation. Complications are infrequent but are often related to respiratory or cardiac events. In contrast to a traditional PACU, our recovery room devotes resources to the observation and management of patients after more invasive procedures, such as bilateral lower extremity arthroplasty, or

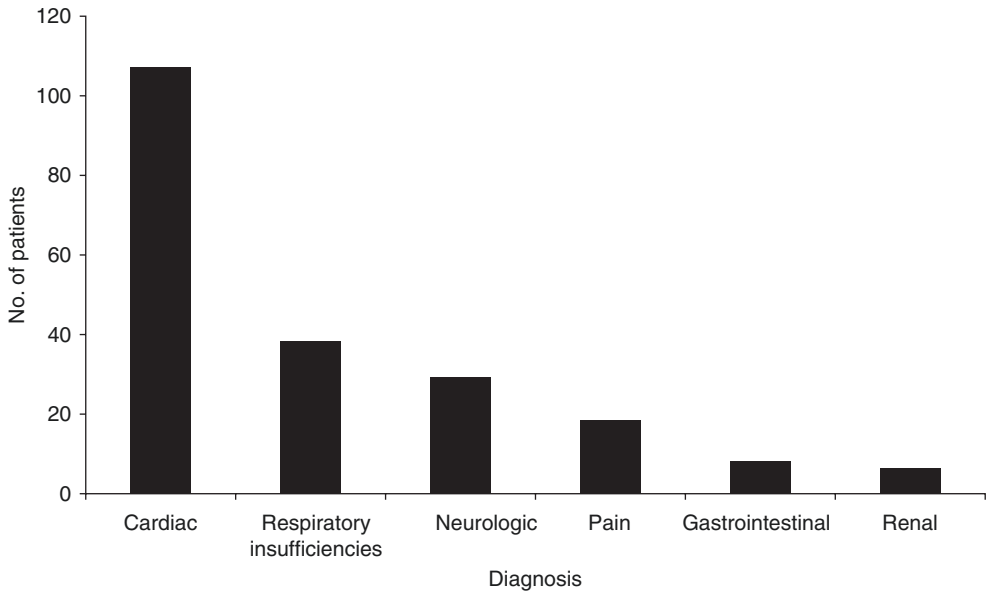

Fig. 9.3 Return to a monitored setting

patients with specific medical problems such as OSA and postoperative delirium as well as those at high risk for postoperative myocardial infarction. Our critical care is focused on complications prevalent among patients undergoing orthopedic surgery. Patients frequently found in this category are those requiring mechanical ventilation due to pulmonary insufficiency and those suffering large blood loss. Further, patient categories are those with severe complications related to fat embolism syndrome and those presenting with cardiopulmonary resuscitative emergencies. However, since many of our arthroplasty patients are geriatric, we also provide monitored care for the common medical complications associated with this age group. This careful attention to the postoperative issues of our specific patient population is paramount in attempting to reduce perioperative complications.

Summary Bullet Points

- In order to optimize patient outcomes, the postoperative care of orthopedic patients should focus on observation of organ function, monitoring of the resolution of anesthesia, resuscitation of blood loss and its consequences, and adequate pain management.
- Physicians caring for orthopedic patients need to be familiar with common perioperative complications in order to address them expediently.
- The model of postoperative care at HSS which allows for the adjustment of recovery room resources to care for problems encountered at various stages of the hospitalization has proven to be efficient and successful.

Case Study

An 80-year-old female with a past medical history significant for hypertension, coronary artery disease, depression, and elevated cholesterol was scheduled for right total knee arthroplasty. The surgical course was uneventful, and the anesthesia was performed using a combined spinal epidural technique with 12 mg of bupivacaine and a femoral nerve block with 30 mL of 0.25% bupivacaine. The patient's surgery ended at 10:30 am, and she was admitted to the PACU for an overnight stay for a rule-out myocardial infarction protocol and observation.

At 10 pm on the night of surgery, the patient was complaining of extensive pain despite an epidural infusion of 0.06% bupivacaine and 10 μg/mL of hydromorphone. The PACU team decided that the epidural was not adequately functioning, and she was switched to an intravenous patient-controlled pump containing hydromorphone.

By 1 am the PACU team was called to the patient's bedside for assessment of aggressive and combative behavior. Her vital signs included a blood pressure of 190/100 mmHg, a heart rate 100 bpm, a temperature of 37.8 °C, and oxygen saturation of 90%. The patient complained that she was being held captive in a hotel in Chicago and demanded to have the police called so that she could be released immediately. An arterial blood gas was obtained and revealed a pH of 7.36, a CO_2 of 44 mmHg, and an O_2 of 66 mmHg. A chest radiograph demonstrated bilateral lower lobe atelectasis.

The differential diagnosis included pulmonary embolism, a cerebrovascular event, fat embolism syndrome, and postoperative delirium. Since the patient had been ambulatory prior to surgery and when taking the timing of events into account, a thromboembolic event was considered to be unlikely. The symptoms of hypertension and confusion could be the result of cerebrovascular occlusion and/or cerebral hemorrhage; however, the patient's neurological exam was non-focal. In addition, the elevated blood pressure was more likely the result of her pain. With regard to infection, her chest radiograph was clear except for atelectasis, the knee incision was clean, and the wound was not hot or tense. Fat embolism syndrome was also considered, but as other signs like alveolar infiltrates on chest radiograph and hematologic signs such as thrombocytopenia were missing, this was also considered less likely.

The team decided that her primary problem was postoperative delirium, secondary the stress of surgery, inconsistent and inadequate analgesia, and sleep deprivation in the PACU. The patient was given intravenous enalapril and metoprolol for her elevated blood pressure and heart rate. An infusion of dexmedetomidine at 0.5 μg/kg/h was initiated, and once the patient was sedated, she was placed on noninvasive positive pressure ventilation. At 7 am the following morning, the infusion was stopped, and by 8 am the patient was awake, oriented, and alert. Her pain was well controlled with intravenous hydromorphone. Her vital signs had normalized and she was discharged to the ward.

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Postoperative Pain Management in the Orthopedic Setting

10

David H. Kim, Sang J. Kim, and Douglas S. Wetmore

Objectives

- Provide a comprehensive overview of pain management in the orthopedic patient population.
- Describe multimodal analgesic techniques that help minimize the reliance on opioids in the immediate postoperative period.
- Provide support for the use of regional anesthesia and analgesia and describe newer motor-sparing nerve blocks.
- Discuss the novel formation of the recuperative and transitional pain service.

Key Points

- An optimal pain management regimen is critical in order to facilitate rehabilitation, recovery, and discharge in both in- and outpatients.
- Addressing pain through various techniques provides opioid-sparing analgesia.
- Literature supports the use of regional anesthesia over general anesthesia.
- Chronic postsurgical pain (CPSP) is a well-known phenomenon after major orthopedic surgery and can partially be addressed by instituting pain management services throughout the perioperative period.

Introduction

Available postoperative pain management modalities vary depending on the surgery type and anesthesia technique utilized. In this chapter, we present the general principles of postoperative pain management and review currently available forms of analgesic approaches including the use of preemptive and multimodal analgesia, local anesthesia infiltration, regional and neuraxial anesthetic and analgesic techniques, and peripheral nerve catheters. We based our review on evidence-based review of the literature whenever possible.

Additionally, we discuss postoperative pain management techniques and regimens used at the Hospital for Special Surgery and highlight some of the successes and limitations we have had with our own patient population.

General Principles of Pain Management

Pathophysiology of Pain

Pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in such damage" [1]. Pain is also subjective, and it may not be a result of potential injury or tissue damage. In the absence of potential injury and involvement of noxious stimuli, pain maybe due to psychological reasons [1]. Given

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that pain is subjective and influenced by emotions and psychologic factors, clinicians are often bound to accept descriptions of pain as reported by the patient.

During surgery, direct tissue damage leads to the release of inflammatory mediators including peptides, lipids, and neurotransmitters [2]. These molecules initiate a cascade of neural processes that encode the noxious stimuli known as nociception [1]. The nociceptive stimulus is transmitted by peripheral somatosensory receptors. Ultimately, these signals are transmitted to the central nervous system via pain neurons. Inflammatory mediators act peripherally and induce local neurogenic inflammation which leads to vasodilatation and plasma extravasation [2]. Pain signals evoked by tissue damage can lead to central and peripheral sensitization, which is defined as increased responsiveness of nociceptive neurons compared to the normal or subthreshold afferent input [1, 3]. According to some literature, such sensitization may be reduced with the use of preemptive analgesia [3].

Pain is further classified as acute or chronic pain. Acute pain is defined as "pain that is present in a surgical patient after surgery" [4]. Chronic pain, per American Society of Anesthesiologists, is defined as pain "extending in duration beyond the expected temporal boundary of tissue injury and normal healing, and adversely affecting the function or well-being of the individual" [5].

Chronic Postoperative Pain

The incidence of chronic postsurgical pain (CPSP) varies depending on the surgery performed and is believed to occur in between 394,000 and 1.5 million cases per year in the USA [6]. After hip replacement procedures, the estimated incidence of CPSP was 12% [6]. The working definition of CPSP proposed by Macrae and colleagues included the following criteria: (i) pain development after a surgical procedure, (ii) at least 2 months of duration, and (iii) exclusion of other causes including malignancy after surgery or chronic infection. The authors suggested further that the possibility of the pain being a continuation from a pre-existing problem should be evaluated and potentially excluded [6]. According to a French cross-sectional cohort study using a survey of 2100 patients who underwent orthopedic procedures, 1292 patients reported suffering from chronic pain after 3 months [7]. Authors noted statistically significant odds ratios for developing CPSP to be associated with arthrodesis, knee arthroplasty, and leg fracture (OR = 2.7, OR = 1.8, OR 1.9, respectively; $P < 0.05$) while noting increased neuropathic pain with elbow surgery, meniscectomy, amputation, and neurolysis [7]. Recent evidence has shown that young age, obesity, female sex, the presence of anxiety, depression, stress, and catastrophizing characteristics have been strongly correlated with CPSP with about one in five patients developing CPSP [8]. A strong risk factor for developing CPSP was found to be severe acute pain, leading the authors to recommend that acute pain should be effectively controlled using regional anesthesia, local anesthetic infiltration, and gabapentin [8].

Variation of Perioperative Pain for Orthopedic Procedures

A patient's experience with perioperative pain can vary dramatically for different orthopedic procedures with different anesthetic and analgesic techniques as well as use of various protocols. A recent meta-analysis that compared adductor canal nerve blocks versus femoral nerve blocks for total knee arthroplasty showed a visual analog scale (VAS) score in various studies ranging from 20 to 48 mm at 48 hours [9]. A recent meta-analysis of patients receiving gabapentinoids for postoperative pain in total knee arthroplasty showed a numerical rating scale (NRS) score in various studies ranging from 3.6 to 5.7 at 72 hours [10]. Other orthopedic procedures can involve a lower level of perioperative pain. A randomized controlled trial of patients receiving periarticular injections in total hip arthroplasty showed mean VAS scores of 2–3 within the first 24 hours, approaching a VAS score of 0–1 by day 5 [11]. The varying pain scores highlight the challenge of knowing when to institute different modalities for the same procedure (i.e., knee replacements). Variable pain scores also underscore that some procedures do not elicit severe pain (i.e., hip replacements) and may not require the same modalities for different procedures. Hence, one protocol may not fit the needs for all procedures and patients. Instead of generalizing orthopedic pain management into one pathway, it is important to understand what differentiates various procedures (pain severity) and tailor the procedure-specific pathways accordingly (e.g., total knee pathways versus total hip pathways).

Preemptive and Preventive Analgesia

Preemptive analgesia describes the concept that the timing of a specific pain intervention can prevent peripheral and central sensitization from noxious nociceptive surgical stimuli [12]. The effectiveness of preemptive analgesia has been studied with mixed results [13, 14]. The concept of preventive analgesia includes a preoperative intervention that may reduce the impact of noxious nociceptive stimuli throughout the perioperative period [12]. Preventive anal-

gesia can include systemic medications and regional anesthesia and analgesia techniques. There is some evidence that hyperalgesia is prevented by regional analgesic techniques [15].

Multimodal Analgesia

Systemic Analgesic Techniques

Opioids

Opioids remain the main systemic analgesic used in the treatment of postoperative pain. Opioids act on multiple receptors in the central nervous system, including the mu, kappa, and delta subtypes. There are multiple receptors within each subtype with some producing analgesia and others producing undesirable side effects such as respiratory depression and reduced gastrointestinal motility. Mu receptors are associated with analgesia, smooth muscle tone, sedation, mood alteration, and nausea and vomiting. Delta receptors are associated with decreased colonic transit time. Kappa receptors have a central analgesic effect, decrease colonic transit time, and have visceral nociception antagonism. Opioids produce effective analgesia and can be administered through multiple different routes with the most common in the postoperative period being the oral and parenteral routes. The parenteral route is ideal for acute postoperative pain due to its rapid onset of action. Morphine and synthetic analogues such as hydromorphone and fentanyl are the most commonly used opioids. Onset of action, half-life, and bioavailability vary by drug and route of administration. Most anesthesiologists have considerable experience with the administration of these drugs. Less commonly used drugs such as methadone which have a long half-life and N-methyl-D-aspartate (NMDA) antagonism have a role in patients on chronic opioids and patients undergoing larger, more painful procedures such as multilevel spine surgeries [16]. While very effective, opioids have significant potential for abuse and misuse contributing to the current opioid epidemic in the USA [17]. Concerns about abuse and misuse of opioids have led to increasing interest in opioid-sparing modalities and enhanced recovery after surgery (ERAS) pathways. These endeavors have shed light on common misbeliefs that NSAID use will increase postoperative bleeding [18, 19].

Intravenous Patient-Controlled Analgesia (PCA)

Intravenous (IV) patient-controlled analgesia (PCA) has become the standard of care for delivery of parenteral opioids on an individualized basis. Typical IV PCA regimens provide patients with autonomy while preventing side effects with "lockout" settings. Successful patient-controlled analgesia requires the availability of special pumps as well as patient and staff education. When compared to staff-administered prn opioids, IV PCA results improved analgesia and patient satisfaction [20, 21]. Dangerous effects such as respiratory depression are not eliminated with IV PCA [21]. Common PCA settings are presented in Table 10.1.

Table 10.1 Common IV PCA settings

Opioid concentration	Demand	Lockout (min)	Basal infusion
Morphine (1 mg/mL)			
Adult	0.5–2.5 mg	5–10	
Pediatrics	0.01–0.03 mg/kg (max = 0.15 mg/kg/h)	5–10	0.01–0.03 mg/kg/h
Hydromorphone (0.2 mg/mL)			
Adult	0.05–0.25 mg	5–10	
Pediatrics	0.003–0.005 mg/kg (max = 0.02 mg/kg/h)	5–10	0.003–0.005 mg/kg/h
Fentanyl (0.01 mg/mL)			
Adult	10–20 μg	4–10	
Pediatrics	0.5–1 μg/kg (max = 4 μg/kg/h)	5–10	0.5–1 μg/kg/h

Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used agents which inhibit cyclooxygenase (COX) reducing prostaglandin synthesis. Prostaglandins are mediators of inflammation and peripheral nociceptive sensitization. Many NSAIDs irreversibly and nonselectively bind COX, while newer drugs such as celecoxib are selective for COX-2 which is primarily involved in pain and inflammation pathways. NSAIDs are important components of multimodal analgesia and show well-documented opioid-sparing effects [22, 23]. While most NSAIDs are administered orally, ketorolac is an injectable NSAID with excellent analgesic properties [23]. Many of the side effects of NSAIDs including bleeding and disruption of gastric mucosa come from inhibition of COX-1 [24, 25]. Renal dysfunction and disruption of osteogenesis occur with all NSAIDs [26–28]. Bleeding and disruption of osteogenesis may not be of clinical relevance [29, 30].

Acetaminophen

Acetaminophen's analgesic and antipyretic effects are likely mediated through many central mechanisms although its exact mechanism of action remains undetermined. Acetaminophen can be administered orally, rectally, and parenterally. Acetaminophen has been shown to have significant opioid-sparing effects and reduction of side effects when combined with opioids [31, 32]. The main serious side effect of acetaminophen is hepatotoxicity, limiting the maximum dose to

4000 mg/day in adults. The IV formulation has increased bioavailability resulting in a faster onset and avoids first-pass metabolism through the liver which decreases its hepatotoxicity [33]. A recent systematic review showed no clinically significant difference between the IV and oral formulations in postoperative pain management [33].

Tramadol and Tapentadol

Tramadol and tapentadol are synthetic opioids with a unique mechanism of action as a mu agonist and a serotonin-norepinephrine reuptake inhibitor. Tramadol has been shown to be an effective analgesic in the perioperative period [34, 35]. Advantages of tramadol over traditional opioids include decreased respiratory depression and decreased GI side effects. Tramadol can lower the seizure threshold, and there is a risk of serotonin syndrome when it is administered with other pro-serotonergic medications [36]. While previously thought to have a low potential for abuse, tramadol is abused at rates similar to other opioid medications [36]. Tapentadol has similarly been shown to be an effective analgesic in the perioperative period with a reduced side effect profile compared to classical opioids [37, 38]. Tapentadol may have a lower potential for abuse compared to classical opioids [38].

Gabapentinoids

Gabapentin and pregabalin are anticonvulsants that are thought to mediate analgesia through interaction with specific subunits of calcium channels, inhibiting the release of excitatory neurotransmitters. There is evidence that gabapentin decreases postoperative opioid use, but there is conflicting evidence on the degree to which it does [39–41]. Postoperative dosing for 72 hours was shown to promote opioid cessation in a mixed surgical cohort [42]. Pregabalin has a similar method of action to gabapentin but with greater oral bioavailability [43]. Pregabalin has been shown to reduce pain scores and opioid consumption at multiple dosing regimens [43–45]. The main side effect of gabapentinoids is sedation.

Steroids

Systemic corticosteroids such as dexamethasone are primarily used in the perioperative period as antiemetics, but they also have analgesic and anti-inflammatory properties [46]. Dexamethasone acts on the glucocorticoid receptor to suppress the immune response and reduce inflammation. Glucocorticoids can have several side effects including hyperglycemia, immunodeficiency, and adrenal insufficiency if used for an extended period of time. Systemic dexamethasone has also been shown to prolong the duration of action of perineural local anesthetics [47, 48].

Muscle Relaxants

Muscle relaxants are centrally acting drugs used to decrease skeletal muscle tone. These drugs work centrally through different and sometimes poorly understood mechanisms to suppress muscle spasms and relax skeletal muscle. Tizanidine, an alpha-2 agonist, is the only muscle relaxant that has been shown to also be an effective analgesic [49, 50].

Dexmedetomidine

Dexmedetomidine is a centrally acting alpha-2 agonist. Dexmedetomidine is widely used for sedation in critical care and procedural sedation in medically complex patients due to its relative lack of respiratory depression. In a recent meta-analysis, dexmedetomidine was shown to reduce opioid consumption in the postoperative period [51]. Dexmedetomidine has been shown to have an opioid-sparing effect in spine surgery and total knee arthroplasty [52, 53]. This drug is typically administered as a bolus dose followed by an infusion intraoperatively. Dexmedetomidine's most significant side effects is related to its hemodynamic effects leading to bradycardia, hypotension, and hypertension mediated by peripheral alpha-2 receptor stimulation.

Ketamine

Ketamine, originally developed as an anesthetic, is now used in the treatment of postoperative pain, chronic pain, and depression. Ketamine blocks nociceptive stimuli through NMDA receptor antagonism [54]. Ketamine may also act on opioid receptors [55]. A recent systematic review of 39 randomized controlled trials showed that ketamine infusions result in powerful opioid sparing for a variety of surgical procedures [54].

Local Anesthesia Infiltration/ Periarticular Injection

Periarticular Injection

Periarticular injections have become an important part of multimodal analgesia in hip and knee arthroplasty. Typical injection agents include local anesthetics, opioids, NSAIDs, and corticosteroids. A systematic review of 21 randomized controlled trials in hip and knee arthroplasty concluded that PAI improves pain relief, reduces opioid consumption, and results in a larger range of motion and lower rates of nausea and vomiting than placebo [56]. Combining periarticular injection with motor-sparing blocks such as the IPACK and adductor canal blocks may confer further benefits such as earlier ambulation in total knee arthroplasty [57, 58].

Liposomal Bupivacaine

Liposomal bupivacaine is a drug delivery system for the amide local anesthetic bupivacaine that uses lipid bilayers to encapsulate drug resulting in slow release, increased duration of action, and lower plasma concentration than plain bupivacaine [59]. Many of the initial studies in liposomal bupivacaine showed decreased pain scores and opioid consumption when compared to placebo [59]. While there is some evidence of an advantage over traditional pain protocols in the plastic surgery literature, multiple reviews in the orthopedic surgery literature have not shown a difference when compared to plain bupivacaine [60–62]. Moreover, one study looked at over 80,000 total knee arthroplasties done with a peripheral nerve block and showed no clinically meaningful reduction in inpatient opioid prescription, opioid-related complications, and length of stay with liposomal bupivacaine [63].

Regional Anesthesia Techniques

Peripheral Nerve Blockade

Peripheral nerves can be blocked at various sites for upper and lower extremity surgery. The brachial plexus can be blocked via the interscalene, supraclavicular, infraclavicular, and axillary approach. Lower extremity peripheral nerve blocks include the lumbar plexus, femoral, fascia iliaca, adductor canal, sciatic, popliteal, IPACK (interspace between the popliteal artery and the capsule of the posterior knee), saphenous, and ankle blocks. Peripheral nerve blockade provides improved analgesia, side effects, and patient satisfaction when compared to systemic opioids [64–68]. Complications are rare and depend on the site of blockade (e.g., phrenic nerve paresis in interscalene block) [69]. Motor-sparing blocks such as the adductor canal block and IPACK result in similar analgesia to previous peripheral nerve blocks (e.g., femoral and sciatic nerve blocks) with the added advantage of early ambulation and physical therapy due to their motor-sparing effects [58, 70]. Upper extremity motor-sparing blocks such as the superior trunk block and suprascapular block offer similar pain relief yet may spare the phrenic nerve [71, 72] and preserve hand strength. Truncal blocks such as the transversus abdominis plane block and quadratus lumborum block may have a role in postoperative analgesia in orthopedic surgery, including anterior spine surgery [73, 74]. Perineural additives to prolong peripheral nerve blocks include alpha agonists, buprenorphine, and dexamethasone. While each of these additives has been shown to be effective in prolonging the action of local anesthetics when administered perineurally, dexamethasone is by far the most well-studied additive and has been shown to prolong nerve blocks up to 22 hours [75, 76].

Neuraxial Anesthesia and Analgesia

Ambulatory Lower Extremity Procedures

With the increase in the number of ambulatory surgical centers and ambulatory procedures, there is a need for shorter-acting spinal anesthesia to prevent any delays in discharge. Since it has been accepted for spinal use in Europe in 2012, there has been a resurgence in the use of chloroprocaine [77, 78]. Several retrospective and prospective studies demonstrate its safety and efficacy [79–81]. Some studies demonstrated lower risk for transient neurologic symptoms (0–1.9%) and less incidence of urinary retention (0%) [79, 82]. With chloroprocaine dosages of 30–60 mg and length of action ranging from 45 to 90 min, duration is shorter than mepivacaine, lidocaine, and bupivacaine [81]. One randomized controlled trial demonstrated its ability to facilitate earlier discharge and reduce cost in comparison with general anesthesia [83]. To prolong analgesia and spare motor blockade, anesthesiologists are adding opioids (fentanyl, morphine) to their spinal anesthetics [84]. Adding preservative-free morphine has been shown to decrease opioid consumption and pain up to 1 day after surgery [84], but the possibility of delayed respiratory depression precludes its use in the ambulatory setting since all patients require prolonged observation in a monitored setting. Another common side effect of spinal opioids is pruritus which can be debilitating in the immediate postoperative period [84].

Total Hip and Knee Arthroplasty

Recent studies in hip and knee patients comparing general anesthesia to neuraxial anesthesia showed a favorable perioperative outcome in those who underwent neuraxial anesthesia [85]. A database analysis of over 380,000 patients who underwent neuraxial anesthesia had a lower 30-day mortality, shorter length of stay, less cost, and less in-hospital complications compared to general anesthesia recipients [86]. The use of neuraxial anesthesia in hip surgeries has been associated with lower mortality, thromboembolic events, blood loss, cardiopulmonary complications, and infections [87]. A retrospective review of more than 3000 hip and knee replacements showed surgical site infections were less than half as likely if an epidural or spinal was used instead of general anesthesia [88]. It is for these reasons that the primary anesthetic utilized at the Hospital for Special Surgery for lower extremity joint surgeries involves neuraxial techniques.

Peripheral Nerve Catheters

Although multimodal analgesia and motor-sparing blocks have allowed for earlier discharge to home or to rehabilitation centers, there are concerns about possible severe rebound

pain and possible readmission for unrelenting pain control or opioid-related adverse effects when the blocks wear off on the day after surgery. Hanson and colleagues [89] compared patients with an ambulatory adductor canal catheter to a control group (sham catheter group) after total knee arthroplasty. Patient satisfaction –which is as high as 94% when the blocks are functioning with the catheter – was notably lower after the resolution of the block while in the hospital.

Rebound pain is a phenomenon first described by Williams and colleagues in 2007 [90]. The study described it as the moderate to severe acute pain a patient encounters after nerve block analgesia resolved. The study was comparing the use of a single-shot femoral nerve block versus a femoral nerve ambulatory catheter after anterior cruciate ligament (ACL) reconstruction. Patients were educated in the use of multimodal analgesia, including NSAID, acetaminophen, and opioids. The study subjects were instructed to keep a pain diary and note the moment when they believed the block did not provide analgesia. A linear regression model identified predictors of rebound pain syndrome (RPS) and only nerve block duration was a predictor. The authors concluded that increased duration of block leads to reduction in rebound pain.

Therefore, the goal of implementing an adductor canal catheter program (as planned at our institution) is not only to prolong analgesia but also prevent rebound pain, further reducing the use of opioids. By sending patients home with an adductor canal catheter, the cost savings to the hospital would be significant. A study done at Virginia Mason in Seattle described how ambulatory adductor canal catheters placed in total knee arthroplasty patients resulted in the ability to discharge of 11.9% of the patients (69 patients) to home on the day after surgery [91]. These patients were educated on home catheter care and were followed closely up to 4 days. Patients removed the catheter after the 50-hour infusion completion on day 3. Remarkably, there were no dislodgments, no major complications such as local systemic toxicity, no infections, and no block attributable falls. No patients had to be seen prior to the 14-day routine follow-up visit with the surgeon. And there was no readmission for pain control. Pain scores were less than 2 at rest and less than 4 out of 10 with activity throughout the infusion period, as well as on postoperative day 4. Most notably, 18.8% of the patients did not take any opioids while at home. This study demonstrated the efficacious use of a catheter with the goal to prevent rebound pain and possibly provide a non-opioid pain regimen at home.

Despite literature suggesting successful use of catheters for managing postoperative pain, there are also studies that show that catheters require more patient education, time for placement, and availability of a healthcare providers for consultation, have higher risk of bacterial colonization, and are prone to dislodgment [92]. With the increased use of additives such as dexamethasone to prolong single-shot nerve blockade, there need to be future studies comparing additive single-shot nerve blocks to those using catheters. If a single-shot block with a dexamethasone additive prolongs the block long enough to minimize rebound pain, the use of a catheters might prove to be unnecessary.

Currently, at the Hospital for Special Surgery, peripheral catheters for certain procedures to prolong the benefits of the block for 2–3 days are used selectively. Placed for elbow surgery, it is used to allow patients to comfortably perform passive range of motion for several days. If it is placed for tissue flap surgeries, the associated sympathectomy promotes vasodilation and improves circulation in the operative site. In the setting of ankle, knee, or hip surgeries, catheters achieve minimization of opioids.

HSS Pain Management for Specific Procedures

Postoperative pain management at the Hospital for Special Surgery is dependent on surgery type, surgeon and patient preference, expected level of pain, the patient's medical history (prior spine fusion surgery, cardiac disease requiring anticoagulation, difficult airway, etc.), planned surgical thromboprophylaxis, and lastly the rehabilitation goals and discharge plans. The postoperative pain management planning for patients without chronic pain or those who do not require a visit (ASA 1 or 2 without history of chronic pain) to our presurgical screening center occurs at the preoperative holding area. Upon discussing the anesthetic plan with the patient, one or more of the following modalities of pain management are provided: epidural PCA, IV PCA, peripheral nerve block, or peripheral nerve catheter. A service to follow the patients is selected to be either the acute pain service (APS), the chronic pain service (CPS), or in straightforward cases the surgical service. Furthermore, when appropriate, incorporation of multimodal analgesia utilization (acetaminophen, NSAIDs, ketamine, dexmedetomidine, etc.) is maximized to reduce systemic use of opioid medication. All patients who receive a regional anesthetic are educated that, once the analgesic effect begins to wear off, the patient will experience pain that will require transitional pain interventions (oral pain medication, IV PCA, redosing of local anesthetic via catheter, etc.). Lastly, close communication with the surgical team is crucial to ensure that there is an adequate postoperative analgesic regimen in place.

Total Joint Replacement

At HSS, more than 90% of hip and knee replacements are performed using regional anesthesia. With the overarching goal of promoting early ambulation postoperatively, there have been attempts to decrease the use of IV PCAs while

increasing the use of long-acting, motor-sparing peripheral nerve blocks. For similar reasons, some surgeons have moved away from the use of epidural catheters for postoperative pain management and have relied on the use of peripheral nerve blocks, multimodal analgesia, and periarticular injections to achieve the goal of early ambulation and physical therapy.

Total Hip Arthroplasty

If the total hip arthroplasty is performed using a combined spinal epidural technique (CSE), and the epidural catheter is left in place to be used as a postoperative pain regimen, then the PCEA will be initiated in the recovery room postoperatively. An ifusate of 0.0625% bupivacaine with 0.01 mg hydromorphone at a continuous rate of 4 ml/h with a demand dose of 4 ml every 10 minutes with an hourly maximum of 20 ml is used [93]. On the morning of postoperative day (POD) 1, all the patients with PCEA are followed by the acute pain service, the continuous infusion is stopped, and the demand dose is kept available until noon. Upon encouraging patients to request and use oral pain medication with the use of epidural demand dose as the backup, the patient is transitioned to an oral pain medication regimen (oral acetaminophen, oxycodone, hydrocodone, hydromorphone, NSAIDs, etc.) with discontinuation of the epidural catheter. If the patient cannot tolerate the transition, the epidural may be left in place until the afternoon on POD 1 or the next morning at the discretion of the acute pain service attending physician.

Quadratus Lumborum Block (QLB)

While periarticular injections (PAI) are becoming the standard analgesic regimen for THA, use of novel blocks to supplement the analgesic has been recently reported and since has been adopted for intermittent use at the Hospital for Special Surgery. The successful ultrasound-guided transmuscular quadratus lumborum block (QLB) for postoperative pain management has been previously reported and since has gained popularity for THA procedures [94, 95]. Although there is currently a lack of prospective trials that demonstrates the efficacy of QLB in THA, some anesthesiologists have incorporated the block to optimize the analgesic regimen without compromising the patient's ability to ambulate.

Suprainguinal Fascia Iliaca Block (SIFI)

Another novel block technique that is being used for hip surgery is the SIFI block. The proposed benefit of this block is the ability to provide the same analgesic coverage as a fascia iliaca block but spare quadriceps strength [96], allowing patients to ambulate earlier while consuming less opioids. The literature is scarce on this technique, except for cadaveric dye studies [97] describing the nerves this compartment block may be targeting. There are several retrospective and volunteer studies that validate its potential analgesic benefits, but its motor-sparing capabilities are questioned [98]. Indeed, 2 out of 19 volunteers in one study demonstrated significant quadriceps weakness. Further prospective randomized controlled trials need to be pursued to help elucidate this novel block for hip surgeries.

Total Knee Arthroplasty

Depending on the surgeon's preferences and use of PAI, the postoperative pain regimen may or may not encompass the use of PCEA. Patients whose postoperative anticoagulation regimen allows for use of a PCEA will receive it in the recovery room with similar epidural infusion mixture and settings as aforementioned for THA procedures. However, on POD 1, the basal infusion is started at a higher rate but is still discontinued in the afternoon. Demand dosing is maintained until the POD 1 afternoon, while an oral pain regimen is encouraged to achieve a similar transition. If the surgeon prefers not to use the PCEA, the patients will receive a single-shot spinal anesthetic (usually using an intermediate local anesthetic such as mepivacaine) along with an adductor canal block (ACB) with or without the infiltration between popliteal artery and capsule of the posterior knee (IPACK) block. These non-epidural patients usually have periarticular injections along with their motor-sparing blocks. Most practitioners have changed their practice from performing femoral nerve blocks to using ACB. While femoral nerve blocks were routinely performed in the past [99], recent studies demonstrated similar postoperative analgesia with less quadriceps muscle weakness and perhaps lower risk of neuropraxia with ACB [100–102]. However, the use of large volumes of 0.5% bupivacaine in the ACB has resulted in occasional motor blockade. This is thought to be attributable to proximal spread of local anesthetic to the femoral nerve. The newly developed IPACK block performed under ultrasound guidance has been shown to improve postoperative analgesia by providing improved pain relief to the posterior aspect to the knee without loss of motor function [58, 103]. Prior to its use, however, a close communication with the patient and the surgeon should take place to ensure the discussion of risks and benefits. A foot drop can occur after IPACK or PAI due to anesthetic spread to the peroneal nerve found in the area of injection. Most anesthesiologists do not perform the IPACK block on severely valgus deformed knees, as injury of the peroneal nerve during correction can occur, making early diagnosis difficult.

Shoulder Surgery

Total Shoulder Arthroplasty

Total shoulder surgeries are either done under supraclavicular, interscalene, or superior trunk block. The latter is a novel

approach to the brachial plexus that targets the C5–C6 components at the trunk level. This technique not only spares the distal hand but decreases the risk for phrenic nerve blockade or injury [71]. At times, general anesthesia is induced upon block placement at the surgeon's request for additional muscle relaxation. Many practitioners have moved away from using interscalene nerve blocks in favor of supraclavicular or superior trunk approaches as the latter techniques have shown to provide adequate anesthesia and analgesia for surgery with reduced risk of intrathecal injections or phrenic nerve injury due to direct needle trauma. Most patients will require IV PCA as a backup with oral pain medication regimen, as they will experience pain with receding effects of the peripheral nerve block.

Shoulder Arthroscopies

Most shoulder arthroscopies are performed with a supraclavicular or superior trunk block with sedation. Patients are usually ambulatory and are discharged shortly after the procedure; hence, surgeons provide prescriptions for oral multimodal pain medications.

Elbow Surgery

Most procedures are performed with either a supraclavicular or infraclavicular nerve block. Given the high success rate of these techniques under ultrasound guidance, axillary approaches to the brachial plexus have gone out of favor. Supplemental cutaneous nerve blocks are also performed to supplement the brachial plexus block such as the intercostobrachial nerves to aid in tourniquet pain. Patients are usually provided with a prescription for oral pain medications. As with all cases, patients with extensive surgery with expected high postoperative pain levels will be admitted and an IV PCA ordered overnight.

Foot and Ankle Surgery

Depending on the specific case, surgeons may have differing preferences for anesthesia. Close communication with the surgeons ensures that a successful postoperative analgesic plan is implemented. For any procedure involving the forefoot, an ankle block can be performed with or without ultrasound guidance. For any major ankle surgeries such as total ankle replacement, most of the anesthetic plans encompass the use of a single-shot sciatic nerve block in the popliteal fossa, ACB or distal saphenous nerve block (analgesia to medial ankle), as well as a spinal anesthetic. Adjuvants such as clonidine or dexamethasone can be added to popliteal sciatic nerve blocks to lengthen the analgesic duration [104, 105]. Especially with the addition of preservative-free dexamethasone, popliteal nerve blocks have been shown to last as long as 48 hours. Patients will either have an IV PCA and/or oral analgesics for pain once nerve blocks begin to wear off.

Spine Surgery

Patients undergo various types of spine surgery from simple single-level discectomies to multilevel spinal fusion revisions. For nonambulatory spine patients, adequate postoperative analgesia may be difficult to achieve, especially given the limited feasibility for regional anesthesia modalities. Most perioperative pain regimens for spine surgeries encompass the use of opioids. Patients undergoing spine surgery have frequently had chronic low back pain and have been on long-term opioids at home, thus requiring higher than normal doses of perioperative opioid doses. However, every attempt is made to maximize the incorporation of multimodal analgesic approaches including local and regional anesthesia whenever possible. The uses of acetaminophen, NSAIDs, ketamine, gabapentin, and long-lasting local anesthetics injected at the surgical site have been added to protocols in the perioperative setting [106, 107]. The use of NSAIDs, especially ketorolac for spine fusion surgery, varies depending on the surgeons' preference given the concern for increased risk for nonunion at high doses (>120 mg per day) within 14 days of surgery [107]. Although epidural anesthesia above the level of surgery is a feasible option, it impedes neuromonitoring of spinal cord integrity and is rarely performed. Recently, transversus abdominis plane (TAP) blocks have been used for extreme lateral interbody fusion (XLIF) and anterior lumbar interbody fusion (ALIF), with some patients receiving opioid-free anesthesia with adequate analgesia postoperatively.

Recuperative Pain Model

Patients transitioning from IV PCA to oral pain medications may often have difficulty with inadequate pain control. The transition from IV PCA to oral pain medication may also occur on the day of discharge, and patients may find themselves needing additional doses of pain medications at home. Given that the acute pain service does not continue to follow patients after discontinuation of IV PCAs, patients may not be attended to at the time they need it the most to ensure proper and satisfactory analgesic regimen for discharge. For this reason, HSS created a recuperative pain medicine (RPM) service in 2007 with the goal to bridge the gap with specific goals targeted to improve patient and staff satisfaction [108]. After one and a half years of implementing RPM, Press Ganey scores increased from the 87th percentile to 99th percentile among peer institutions. This increase was attributed to the administrative and educational endeavors that focus on providing an adequate oral pain medication regimen in the hospital or at home utilizing in-house staff and telephone helpline services. Furthermore, if a patient continues to have postsurgical pain, the recupera-

tive pain team provides consultations and support for this patient population up to 8 days after surgery. Should longer care be needed, the team initiates a seamless transfer to a chronic pain specialist.

Orthopedic Patients with Chronic Pain

Given the challenges in managing pain in opioid-tolerant patients in the postoperative period, HSS has instituted selection criteria for preoperative chronic pain consultations. Any patient who has been taking opioids daily for more than 6 months or with a current or recent history of substance use disorder, illicit drug use, or use of opioid agonist-antagonists or methadone is required to see one of our chronic pain specialist prior to undergoing surgery. This serves to educate the patient regarding pain expectations for the surgical procedure and the development of a well-outlined plan prior to surgery. This plan usually entails the use of regional, multimodal analgesics and patient-controlled analgesia (intravenous or epidural). Intraoperative and postoperative ketamine and dexmedetomidine infusions have been used to assist in managing patients who were on high doses of opioids prior to surgery. Management usually entails a monitored setting in which increased doses of respiratory depressant medications can be safely titrated.

Transitional Pain Service

The opioid crisis has led clinicians to spearhead several opioid-sparing protocols and pathways for the most painful procedures [109]. HSS is currently piloting a novel home catheter program to assist in transitioning total knee arthroplasty patients from hospital to home through the use of telemedicine. This program will be the first to utilize telemedicine for ambulatory pumps, to continue providing the services of the acute pain service at home via an electronic application that is downloaded on the patient's smartphone or tablet and allows HIPAA-compliant text messaging and voice and video calls. This step is targeted to ease the transition from hospital to home and provide the patient with further guidance and direction in managing and weaning opioids and catheter care as an outpatient [110, 111]. This transitional pain service (TPS) will not only ensure that ambulatory pumps are functioning, and help patients transition off of opioids, but also will help identify patients at risk for chronic postsurgical pain (CPSP). It is postulated that a TPS may even assist in preventing readmissions and CPSP [111, 112].

Summary

HSS postoperative pain management has evolved from primarily focusing on optimizing pain control via peripheral nerve blocks to expanding its attention to not only analgesia but also ambulation (motor-sparing blocks), ambulatory surgery (short acting spinals), and opioid-sparing pathways (long-acting blocks, peripheral nerve catheters). By reviewing the literature, conducting our own studies (retrospective and prospective), and implementing perioperative protocols, HSS has developed a comprehensive understanding for managing all types of patients (both opioid naïve and tolerant) and for several different orthopedic procedures. Focusing not just on the intraoperative anesthetic but also the preoperative education and postoperative analgesic care and long-term outcomes, the goal is to improve patient satisfaction, minimize opioid reliance, and facilitate return to function.

Summary Bullet Points

- Controlling acute postoperative pain will minimize acute and chronic effects of postoperative pain and facilitate physical therapy.
- A multimodal approach to the pain management regimen may include systemic opioids and non-opioids and/or regional analgesics.
- The analgesic agents and techniques chosen will depend on a variety of factors including the type of surgery, patient's comorbidities, and preferences.
- There will be a subset of patients who will require a recuperative pain medicine or chronic pain medicine consult to manage the postoperative pain regimen and to transition to an appropriate outpatient regimen.

Case Study

An 80-year-old woman with a history of Parkinson's disease, dementia, and osteoarthritis sustained a left femoral-neck fracture after a fall. She was scheduled to undergo open reduction and internal fixation (ORIF) of her femur. She weighed 55.8 kg (123 lb.), with a body mass index of 18.7. Her medications taken at home included amantadine and carbidopa–levodopa for Parkinson's disease. The patient had received morphine and hydromorphone prior to hospital transfer, and during her initial assessment at our institution, she was confused, but oriented to person and place. Her son noted that she had underlying dementia and became easily confused during prior hospitalizations. Given concerns for

prolonged postoperative delirium related to her age and cognitive dysfunction, the goal of the anesthesia plan was to minimize postoperative opioids. The patient's intraoperative anesthetic plan consisted of spinal anesthesia (1.5% mepivacaine 4 mL). She received mild intravenous sedation with a propofol infusion. At the end of the procedure, an ultrasound-guided suprainguinal fascia iliaca (SIFI) block using 0.25% bupivacaine 30 mL was performed, and a catheter was placed for postoperative analgesia. Postoperatively, a solution of 0.2% ropivacaine at 6–8 mL/hour. was infused through the peripheral nerve catheter, which provided excellent analgesia. The catheter remained in place with a continuous infusion for 2 days, during which time she did not require opioids. The catheter was subsequently removed, and she was transitioned to oral acetaminophen 650 mg (every 6 hours scheduled) and tramadol 50 mg (every 4 hours as needed).

With resumption of her medication and frequent reorientation, her cognitive status improved during the hospitalization, with a return to baseline by POD 2. The patient was discharged on POD 3.

It is well established that postoperative delirium is associated with increased hospital length of stay, morbidity, and long-term neurologic sequelae [113]. In particular, hip fractures are common among the elderly, and the use of psychotropic medications including opioids can predispose patients to postoperative delirium [114]. Therefore, strategies that provide effective analgesia while minimizing exposure to such medications are critical. Our case illustrates how the use of a SIFI catheter can provide prolonged analgesia and reduce opioid consumption after surgery for hip fracture.

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Enhanced Recovery After Surgery (ERAS) Protocols in Orthopedic Patients

11

Ellen M. Soffin

Abbreviations

ASA	American Society of Anesthesiologists
ERAS	Enhanced recovery after surgery
LIA	Local infiltration analgesia
NOF	Neck of femur
NSAID	Nonsteroidal anti-inflammatory drug
THA	Total hip arthroplasty
TJA	Total joint arthroplasty
TKA	Total knee arthroplasty
TSA	Total shoulder arthroplasty
UTI	Urinary tract infection

Objectives

- To review the fundamental principles of enhanced recovery after surgery (ERAS) protocols
- To describe how ERAS pathways are structured
- To present the evidence linking ERAS and positive outcomes after orthopedic surgery
- To reveal knowledge gaps in ERAS-related care of the patient undergoing orthopedic surgery

Key Points

- ERAS represents a leading example of evidence-based, multidisciplinary, multimodal perioperative care.
- ERAS pathways include standardized elements with demonstrated benefits in respect to recovery, tailored to the individual surgical subtype.
- Within orthopedic surgery, ERAS has been most widely applied to elective total hip and knee arthroplasty, with consequent reductions in length of hospital stay and complications.
- ERAS protocols are also emerging within other orthopedic surgery subspecialties, including femoral neck fracture surgery, total shoulder arthroplasty, revision joint arthroplasty, and spine surgery.
- ERAS has the potential to improve the quality of care for patients undergoing orthopedic surgery.

Introduction

Over the last 20 years, enhanced recovery after surgery (ERAS) pathways have gained considerable influence over the perioperative care of the surgical patient. Pioneered by Danish surgeon Henrik Kehlet in 1997, ERAS was originally intended as a core set of interventions for optimizing recovery after colorectal surgery [1]. Kehlet hypothesized that the benefits of ERAS are realized by multimodal interventions, each of which alone may not affect outcomes after surgery but when provided together exert a synergistic effect on recovery [2]. A major goal of ERAS is to reduce unwanted variation in care, thereby guaranteeing similar outcomes to patients undergoing similar procedures. Variation in perioperative care has been interpreted as evidence of uncertainty about optimal care. Variation is minimized by delivering standardized, multidisciplinary, evidence-based interventions to every patient as a formal pathway of care. The ERAS pathway covers every aspect of a patient's surgical journey, from the preoperative phase through to discharge from the

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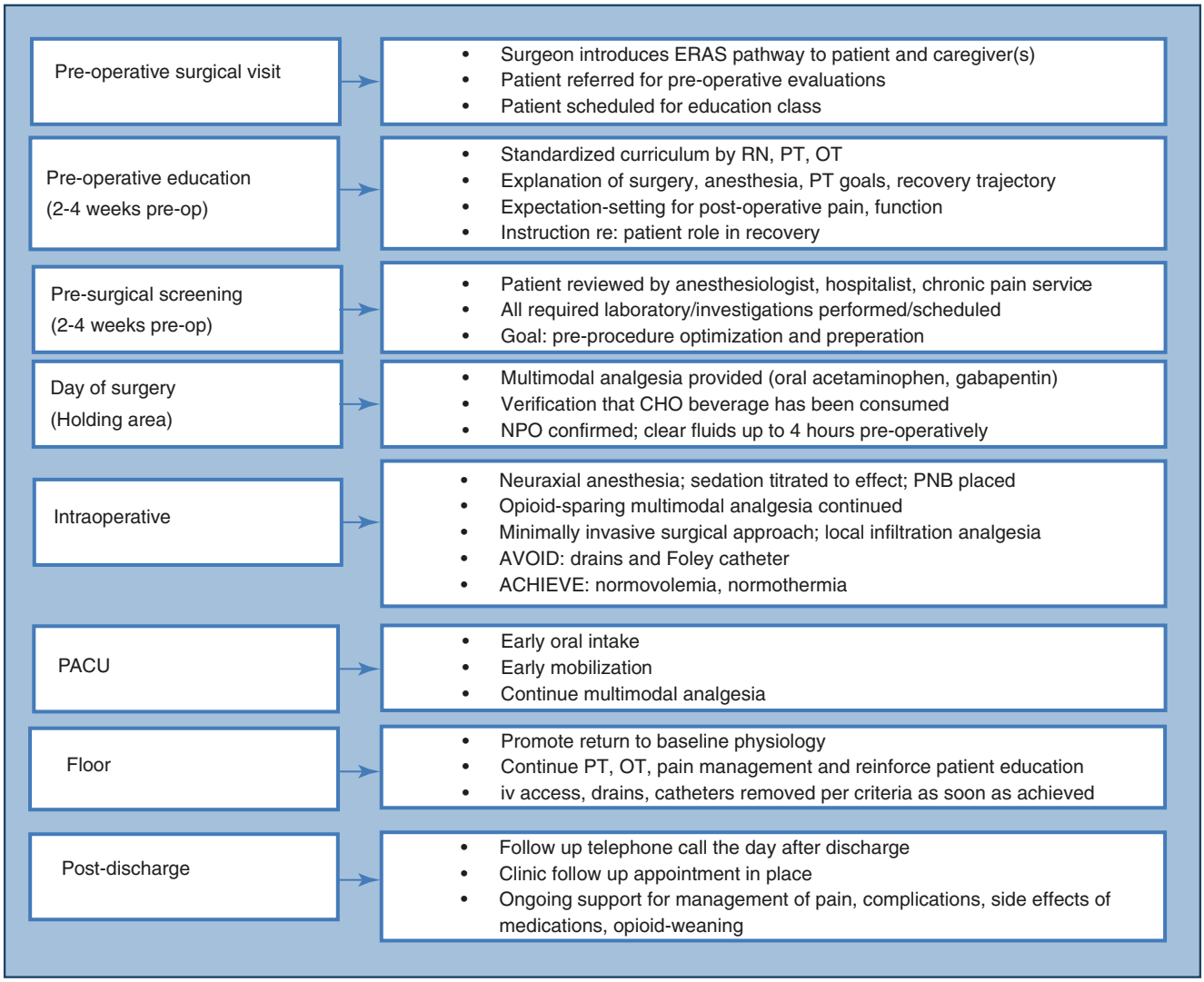

Fig. 11.1 Example of a general ERAS for orthopedic surgery template. The pathway includes standard pre-, intra-, and postoperative elements of care. PNB, peripheral nerve block. CHO, carbohydrate

hospital (Fig. 11.1). ERAS has been consistently associated with accelerated postoperative recovery, shortened length of hospital stay, higher patient satisfaction, and enhanced clinical outcomes, all without increasing hospital readmission rates [3].

The successes of ERAS in colorectal surgery have spread rapidly to other subspecialties. The core components and strategies are shared across surgical disciplines, with adaptation and tailoring of individual components to specific surgeries, as needed. Within orthopedic surgery, elective hip and knee arthroplasty have been the most prominent surgical subtypes to benefit from ERAS pathways. However, reports of ERAS as applied to other domains within orthopedic surgery are now apparent.

This chapter will review the history, design, and efficacy of ERAS pathways. The past, present, and future applications of ERAS to orthopedic surgery are discussed.

What Is Enhanced Recovery After Surgery?

According to ERAS principles, surgery disrupts the baseline physiologic processes of the patient, producing the surgical stress response [1–3]. An imbalance between pro- and anti-inflammatory cytokines and a metabolic shift toward a catabolic state lead directly to the systemic dysfunction that limits recovery. It follows that more invasive surgeries will produce a larger stress response.

The physiology proposed to underlie ERAS efficacy is modulation of the surgical stress response. Kehlet hypothesized that "organ dysfunction" slows postoperative recovery [1, 2]. Dysfunction is expressed across organ systems as pain, fatigue, confusion/delirium, immobilization, hemodynamic disturbances, and constipation/ileus. The use of surgical drains and catheters and logistical issues surrounding hospital care further combine and contribute to the dysfunction, which ultimately inhibits recovery and timely discharge from the hospital after surgery.

To minimize the stress response, multiple interventions are made with each component contributing to a reduction in the overall surgical stress burden. For this purpose, the major complications and factors limiting recovery are identified for each surgery. Subsequently, the evidence for interventions that benefit outcomes is reviewed, selected, and incorporated into the ERAS pathway.

There are several examples of effective pathway-based care in evidence today and no consensus definition of ERAS within the literature. Several terms exist, including "accelerated rehabilitation," "fast track," and "rapid recovery." These models of care share several key elements, which form the basis of ERAS programs [3, 4]:

1. *Preoperative optimization of the patient:*
   (a) A comprehensive preoperative assessment includes consultation with an anesthesiologist and allied specialists as needed, to optimize general health and comorbidities.
   (b) Patient education, counseling, and expectation-setting regarding the course of recovery, with an emphasis on how the patient can be an active participant in their care and recovery.
   (c) Formulation of a discharge plan with resources in place for anticipated obstacles to recovery.
2. *Minimizing the stress response to surgery:*
   (a) Use of minimally invasive surgery, where possible
   (b) Use of surgical and anesthetic techniques to minimize surgical duration
   (c) Selection of anesthetic modalities targeted toward blunting the sympathetic response to surgery (e.g., neuraxial anesthesia with sedation and peripheral nerve blocks)
   (d) Maintenance of homeostasis: normovolemia, normoglycemia, and normothermia.
3. *Promotion of early postoperative mobilization and nutrition:*
   (a) Multimodal, opioid-sparing analgesics to achieve pain control and reduce opioid-induced side effects (e.g., local infiltration analgesia, peripheral nerve blocks, epidural analgesia, acetaminophen, nonsteroidal anti-inflammatory drugs [NSAIDs], and gabapentinoids)
   (b) Advance oral nutrition as soon as oral intake is tolerated by the patient
   (c) Multimodal prophylaxis against nausea and vomiting
4. *Ongoing optimized postoperative care:*
   (a) Encourage baseline nutritional and hydration status.
   (b) Early and ongoing mobilization.
   (c) Promotion of physiologic sleep-wake cycle.
   (d) If used, early removal of catheters, surgical drains, intravenous infusions/medications.
   (e) Foster independent activities of daily living (e.g., self-care, washing, dressing).
   (f) Clarify discharge and post-discharge expectations and logistics.

The improvements in patient outcomes achieved by ERAS programs cannot be made without supportive organizational structures. The most highly standardized, evidence-based pathway will only be successful with input and acceptance from all members of the multidisciplinary team [5]. This is traditionally accomplished by creating "champions" representing the frontline clinical providers: surgeons, anesthesiologists, nurses, physical therapists, pharmacists, nutritionists, and pain management practitioners. The partnerships that develop from the integration of the care team help drive the success of ERAS and distinguish ERAS from traditional perioperative (often siloed) care.

Enhanced Recovery After Surgery for Orthopedic Surgery

ERAS may be best associated with colorectal surgery, but multidisciplinary clinical pathways of care in orthopedic surgery are not new. Integrated pathways of care and positive effects on outcomes have been supported by evidence for decades [6]. Much of the ERAS focus in orthopedic surgery has been applied to elective total hip arthroplasty (THA) and total knee arthroplasty (TKA). More recently, ERAS has emerged as an effective tool to optimize care for other orthopedic procedures, including fractured neck of femur (NOF), revision joint arthroplasty, total shoulder arthroplasty, and spine surgery. Next is a consideration of the benefits of ERAS in each of these surgical populations.

Elective Total Hip and Knee Arthroplasty

As our knowledge regarding the benefits of ERAS has evolved, interest in applying the concepts to joint arthroplasty has also grown. This growth has been driven in part by an increase in the volume of evidence-based and narrative

reviews which present the literature supporting individual ERAS components, linked with positive outcomes after elective total joint arthroplasty (TJA) [7–10].

ERAS protocols for elective hip and knee arthroplasty typically include neuraxial anesthesia, opioid-sparing analgesia, local infiltration analgesia (LIA), peripheral nerve blocks, and a strong emphasis on early postoperative mobilization [7]. Effective pain control with multimodal, non-opioid analgesics is a prominent theme within ERAS pathways for TJA. This can be accomplished via including several classes of analgesics within the pathway: acetaminophen, ketamine, lidocaine, magnesium, and gabapentinoids (pregabalin or gabapentin) [9, 10]. The case for the safety and efficacy of these individual components of ERAS pathways for THA and TKA seems clear on an individual basis. However, their effectiveness within a pathway requires further consideration.

Several studies compare ERAS pathways with usual care for TJA. An early combined cohort study compared 1500 patients presenting for THA or TKA to 3000 patients on a traditional protocol [11]. The ERAS pathway emphasized neuraxial over general anesthesia, minimizing opioid use with multimodal analgesics given throughout the perioperative period, selective use of urinary catheters and surgical drains according to need, and implementation of prespecified discharge criteria. Patients cared for under the ERAS pathway experienced fewer postoperative complications and lower 90-day mortality. The median duration of hospital stay decreased from 6 days to 3 days, without any change in subsequent readmission rates.

Length of stay has been a frequent endpoint in studies of ERAS efficacy. On average, ERAS for TJA results in a decline in median length of stay of 1–2 days (from a median length of stay of 4–6 days to 2–4 days), with no significant increase in the incidence of complications or readmissions [12–16]. At the same time, studies show that ERAS preferentially benefits the majority of TJA patients, including older patients, patients with baseline cardiopulmonary disease or diabetes mellitus, as well as those with tobacco, alcohol, or other substance misuse disorders [17].

Several studies confirm and extend these findings in THA and TKA. Most studies have shown that ERAS is safe and effective, accelerates the recovery process, minimizes reliance on opioid pain medication, and improves patient satisfaction. Khan and colleagues retrospectively analyzed 1744 patients who underwent TKA under an ERAS pathway [18]. Not only did ERAS significantly reduce length of stay and rates of revision surgery, but readmission and important complications (including transfusion and cardiac events) were also significantly lower, compared to 1631 patients managed with traditional perioperative care. The first meta-analysis of ERAS for total joint arthroplasty was published in 2017 and confirmed that ERAS is associated with reduced length of stay and complications without any effect on 30-day readmission [19].

Fractured Neck of Femur

ERAS principles may be particularly beneficial for patients presenting with a fractured neck of the femur (NOF). These patients are typically older, with a higher median American Society of Anesthesiologists (ASA) grade (ASA 3), and are often confined to bed by their injury [20]. Their risk of complications is higher than for patients presenting for elective THA, who are typically younger, fitter, more mobile and have benefited from the phase of preoperative preparation and optimization [21]. ERAS, with its emphases on opioid-sparing modalities for pain control, early mobilization, and normalization of physiology, may be particularly beneficial for elderly patients – especially those with significant comorbidities. Components of care which positively impact on outcomes after surgery include prompt review by an orthogeriatrician, early surgical intervention, opioid-sparing anesthesia and analgesia, maximization of regional analgesia, and mobilization on the day of surgery [22, 23].

Despite these benefits, there is a paucity of published descriptions of full ERAS interventions for patients undergoing fractured NOF repair. This represents a missed opportunity, given the significant burden of complications, morbidity, and length of stay associated with fractured NOF [22, 23]. In an early pre-post study design, Pedersen and colleagues evaluated a “fast-track” protocol in 535 consecutive patients presenting for emergency hip fracture surgery compared to historic, conventional institutional care (which emphasized systemic opioids) [24]. The pathway included early assessment by the anesthesiologist, femoral nerve catheter placement for pain control, and a standardized approach to nutrition, urinary retention, and fluid and oxygen therapy. The pathway was associated with a reduction in any in-hospital complication (from 33% to 20%), including lower incidence of confusion, pneumonia, and urinary tract infection (UTI). Length of stay was likewise significantly shorter for patients cared for under the pathway (9.7 vs. 15.8 days). Similar results were concluded in a case-control study of 232 patients which assessed the impact of an ERAS-for-fractured NOF pathway [25]. The pathway included early anesthetic and analgesic assessment, a fascia iliaca compartment block, carbohydrate loading, and early mobilization after surgery. Although the ERAS program reduced postoperative complications, there were no significant differences in mortality or length of stay. Interestingly, this protocol did not include a global opioid-minimizing strategy or local infiltration analgesia. Significant reductions in complications with a modest reduction in length of stay were recently described in 5002 patients undergoing

emergency hip fracture repair under an ERAS pathway in a large integrated healthcare delivery system [26].

Revision Joint Arthroplasty

Revision joint arthroplasty is logically associated with more extensive surgical trauma and a corresponding increase in the magnitude of the surgical stress response. There are minimal data exploring the effects of ERAS on this patient population; however, reports are starting to emerge. A recent feasibility study of 29 patients undergoing revision TKA concluded that the use of a fast-track protocol could produce outcomes that were similar to primary TKA [27]. It is important to emphasize that all included patients were undergoing revision for non-septic indications and the study was not designed or powered to detect meaningful differences between outcomes after primary or revision TKA. Nonetheless, the median length of stay was 2 days, there were no deaths within 3 months of surgery, readmission rates were low, and there were high levels of patient satisfaction. More recently, a retrospective study of 132 patients associated an ERAS pathway with reduced length of stay after both hip (1 vs. 6 days) and knee (6 vs. 8 days) revision arthroplasty [28]. Finally, investigators in Norway evaluated a fast-track care pathway for 82 patients undergoing revision hip and knee arthroplasty, as part of a larger 1-year follow-up study [29]. Compared to a median length of stay of 3.1 days for patients undergoing primary joint arthroplasty, the ERAS pathway was associated with median stays of 4.2 days for revision hip and 3.9 days for revision knee surgeries. The authors additionally reported low revision rates of 3.7% and 7.1% for the revision hip and knee cohort, respectively. Patient-reported outcomes, satisfaction, and functionality scores were better for all patients cared for under the ERAS pathway, irrespective of the type of surgery. Although impressive, it is important to note that the indication for surgery and underlying pathology are likely to be highly variable for revision joint arthroplasty (compared to primary elective TJA). The gains described here may be (at least in part) attributable to these variations. Indeed, the reduction in length of stay from 6 days to 1 day after revision hip arthroplasty reported above [28] is more likely to reflect patient selection, patient factors, and surgeon factors than the ERAS pathway itself.

Total Shoulder Arthroplasty

Currently, minimal data are available to describe the potential benefits of ERAS for total shoulder arthroplasty (TSA). Much of the available evidence focuses on anesthetic and analgesic regimens and their effects on pain, opioid consumption and related side effects, and length of stay. TSA is primarily performed as an inpatient procedure with an average length of stay exceeding 2 days [30]. This extended length of hospital stay has been attributed to the difficulty in achieving and maintaining adequate pain control [31]. Published data associate several factors including age, comorbid burden, pain-related behaviors, and baseline opioid use with higher pain scores and longer length of stay after TSA [30–33]. Length of stay was also shown to be an independent predictor of 30-day complications after TSA, including UTI and blood transfusion [31].

A pilot study in ten patients described and evaluated a clinical pathway for TSA [34]. The pathway featured a long-acting interscalene block and standardized, multimodal analgesia, including regularly scheduled non-opioid analgesics (meloxicam, acetaminophen, pregabalin) and opioids as needed. Patient recovery was remarkable for low pain scores and minimal opioid use in the first 24 hours after surgery in half of included patients. Nonetheless, the mean length of stay was 63 ± 18 hours in this cohort, suggesting that factors other than analgesic control contribute to length of stay after TSA. This raises the possibility that fully comprehensive ERAS pathways may produce further gains in recovery after TSA.

Spine

The synergy of ERAS and improving care and outcomes after spine surgery seems intuitively obvious. There is increasing demand for spine surgery, and there are regional variations in length of stay, complications, pain, and functional recovery [35]. Spinal fusion is a painful procedure, which relies on opioids (and, frequently, opioid monotherapy) for postoperative analgesia. Concerns regarding fusion and bleeding risk in the setting of NSAID use and limited opportunities for peripheral nerve blocks restrict the available choices for multimodal analgesia [36]. Finally, in contrast to elective total joint arthroplasty, "spine surgery" encompasses a heterogeneous group of procedures with a range of anticipated postoperative recovery trajectories. In contrast to TJA, it may be necessary to tailor pathways of care to particular spine surgery subtypes and/or to selected groups of patients.

A paucity of data examines the use of ERAS applied to spine surgery. One of the earliest comparative studies evaluated a comprehensive multimodal analgesic and antiemetic pathway in 41 consecutive patients undergoing major spine surgery vs. historic institutional care [37]. The multimodal regimen included acetaminophen, NSAID, gabapentin, dexamethasone, ketamine, and postoperative epidural patient-controlled analgesia. Results supported a postoperative reduction in opioid consumption in the intervention group, along with

lower incidence of nausea, sedation, and dizziness. The length of stay was reduced to 2 days in the ERAS group, from 7 days in the non-ERAS group (a clinically but not statistically significant reduction). A second study evaluating an ERAS pathway in lumbar fusion included patient education classes 1 week prior to admission, mobilization on the day of surgery, and an early discharge plan based on predetermined criteria [38]. Here, length of stay was reduced by 4.7 days.

ERAS has also been applied to less invasive spinal procedures and may represent a care model which can facilitate safe same-day discharge. A recent case series of 42 patients highlights these concepts [39]. The authors described a partial ERAS pathway comprising a minimally invasive approach for lumbar fusion, sedation anesthesia, and liposomal bupivacaine for local infiltration analgesia. Compared to historic data, the ERAS pathway was associated with improved functional scores and low rates of complications. Recently, a fully comprehensive ERAS pathway for lumbar decompression has been evaluated in 61 patients undergoing lumbar microdiscectomy, laminectomy, or laminotomy at the *Hospital for Special Surgery* [40]. Unlike earlier reports in spine surgery, the pathway included full standard ERAS elements from across the pre-, intra-, and postoperative phases of care. The pathway was associated with short median length of stay (4.65 hours; interquartile range 3.3–6.6 hours) for the cohort, minimal complications, and no readmissions within 90 days of surgery.

Limitations of ERAS Research Methodology

Although the results that have been ascribed to ERAS are impressive as a body of work, there are major design limitations inherent in much of the research. Chief among these is that the vast majority of studies rely on a retrospective cohort design. The typical study evaluates outcomes of interest before and after implementation of an ERAS pathway. Studies frequently compare the same outcomes measured years apart, without controlling for naturally evolving perioperative care processes and/or patient factors. Each and any of these may profoundly affect results. As is highlighted in this chapter, two major endpoints in ERAS research are the incidence of complications and hospital readmission. An underlying assumption in ERAS research is that all complications and readmission are captured in the datasets. Allied to this, readmission is considered as a surrogate marker of complications in many studies. Thus, any patient presenting to hospitals outside the primary facility would be missed and the impact of an individual ERAS program overstated. Finally, since ERAS is delivered as a package of care, the research does not permit a critical evaluation of which components positively affect outcomes and which are adjuncts. Given the complexity and cost associated with ERAS implementation and maintenance, this is an important area for future focus.

Conclusions and Summary

Although pioneered in colorectal surgery, ERAS was quickly embraced by the orthopedic surgery community as an effective model to improve the care and outcomes after total joint arthroplasty patients. ERAS has been successfully applied to THA and TKA with reductions in length of stay. These gains have been achieved without increasing complications or rates of readmission. There is currently limited procedure-specific evidence for ERAS benefits in other elective procedures, such as (1) total shoulder arthroplasty, (2) more complex and heterogeneous procedures including spine surgery, and (3) nonelective procedures including fractured NOF repair and revision joint arthroplasty. Entirely absent from the literature is an understanding of ERAS benefits for total ankle replacement, sports, and ambulatory surgeries. Given the demonstrated gains achieved by ERAS in other orthopedic procedures, these patient populations are likely to benefit as well.

ERAS goals of reducing the surgical stress response, improving the quality of care, and minimizing unwanted variation in care are achieved by putting evidence into practice. This requires input and cooperation between specialists from multiple disciplines using multiple interventions. Numerous sources of evidence support the premise that when orthopedic care teams adopt ERAS, patients may recover more quickly with a lower incidence of postoperative complications. Optimism regarding these benefits must be tempered with a knowledge of the drawbacks associated with ERAS research methods. Reports of ERAS pathways are burgeoning in the literature. In the future, unimodal studies in which single elements are compared within multimodal pathways are required to guide our understanding of how ERAS can maximally benefit the care of the patient undergoing orthopedic surgery.

Summary Bullet Points

- ERAS is multimodal, multidisciplinary care directed toward accelerating postsurgical recovery and reducing morbidity and length of stay.
- ERAS has been successfully applied to orthopedic surgery; the best characterized evidence for ERAS benefits is on patients undergoing elective TKA and THA.
- Emerging evidence suggests ERAS may positively affect outcomes after other orthopedic procedures, including hip fracture, TSA, and spine surgery.
- Gaps in ERAS knowledge include how or if pathways may benefit orthopedic patients undergoing less invasive or ambulatory surgery.

Case Study

An 83-year-old woman presented with an intertrochanteric hip fracture after a fall at home. She was independently mobile at baseline, without ambulation aids or assistive devices. She lived with her husband in a private home. Her past medical history was significant for diabetes mellitus, well controlled on metformin; angina; low body mass index (17); 40 pack year smoking history and chronic obstructive pulmonary disease, on inhaled cortico-steroid and mucolytic therapies.

The patient was admitted to directly to the Orthopedic Surgery Special Care Unit (OSCU). Surgery was planned for the following morning. Intravenous access was established, and full laboratory investigations were performed, including complete blood count, complete metabolic panel, coagulation factors, EKG, and chest X-ray. Consultations from a hospitalist, nutritionist, physical therapist, and anesthesiologist were obtained. Recommendations included optimization of preoperative hemoglobin (Hb), pulmonary function, cardiac status, and nutritional support. A pain assessment prompted initiation of regularly scheduled acetaminophen plus tramadol, as needed. A fascia iliaca block was performed under ultrasound guidance (20 mL 0.25% bupivacaine).

The morning after her admission, the patient underwent dynamic hip screw fixation under spinal anesthesia. Intraoperatively, she received propofol (10 μg.kg.min^{-1}) and dexmedetomidine (0.3 μg.kg.hr^{-1}) sedation. No benzodiazepines or opioids were administered. Antiemetic prophylaxis (ondansetron 4 mg) tranexamic acid (1 g), the scheduled dose of acetaminophen (1000 mg) and toradol (15 mg) were given, intraoperatively. Local infiltration analgesia was administered by the attending surgeon at the end of the procedure.

One hour after arrival in the postanesthesia care unit (PACU), the patient was alert and comfortable and the spinal anesthetic has fully resolved. She was able to sense bladder fullness and voided without requiring catheterization. She was assessed by a physical therapist in PACU within 3 hours of arrival, at which time she was able to actively sit up in bed and dangle her feet over the edge of the bed. Six hours later, with physical therapy assistance, she was able to transfer to her chair and mobilized with an assistive device. Oral nutrition was permitted when the patient was deemed able to tolerate intake (after bedside nursing assessment). Multimodal analgesia was continued. The hospitalist continued to follow and guide medical management.

On post-operative day 1, she mobilized 30 ft with a walking frame, under supervision. Her Hb was 8.1 (from 9.9, preoperatively) with mildly increased heart rate (99 beats per minute at rest) and she endorsed dizziness. She was given 1 unit packed red blood cell transfusion, due to her symptoms and underlying angina. This was tolerated well with an appropriate increase in Hb to 9.1. All medications were successfully transitioned to oral formulations.

She was discharged to a skilled nursing facility, on post-operative 4.

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Part III

Medical Management in Specific Clinical Settings

Perioperative Care of the Orthopedic Patient with Connective Tissue Disease

12

Susan M. Goodman

Objectives

- To discuss the characteristics of patients with systemic lupus erythematosis (SLE) and inflammatory arthritis (IA) such as rheumatoid arthritis (RA), spondyloarthropathy (SpA) including ankylosing spondylitis (AS), and psoriatic arthritis (PsA) to predict the need for orthopedic surgery
- To characterize the multisystem involvement common to these patients, enumerate the appropriate preoperative evaluations, and discuss the relevance of disease control to perioperative optimization

Key Points

- Patients with connective tissue disease frequently require orthopedic surgery due to the presence of poorly controlled inflammatory arthritis.
- Occult multisystem involvement, including cardiac and pulmonary disease [1], increases the risk of surgical complications.
- Patients with rheumatic diseases are likely to be on medications that may affect wound healing or raise the infection risk, an important consideration in the perioperative setting.
- The results of orthopedic surgery in such patients are gratifying with respect to pain relief, but functional improvements may not be as complete as seen in patients with osteoarthritis.
- Patients with inflammatory muscle diseases, scleroderma, and vasculitis are not disproportionately likely to undergo orthopedic surgery and will not be discussed in this chapter.

Introduction

Patients with SLE and inflammatory arthritis (IA) comprise 3% of the general population, but 15% of the patients undergo orthopedic surgery. Although advances in medical therapy have decreased the severity of IA [2], up to 30% of patients fail to respond fully and are at ongoing risk for joint damage. Historically, up to 50% of RA patients could expect to undergo orthopedic surgery, most commonly arthroplasty, over the course of their illness, but current surveys reveal a decrease in small joint reconstructive surgery and soft tissue procedures for RA patients [3–6], concurrent with more widespread use of potent medical therapies [7]. While rates of large joint procedures have remained stable in RA, rates of arthroplasty utilization have increased for patients with SLE and spondyloarthritis [8]. The risk for multisystem disease and joint destruction is greatest in those patients with persistent inflammation who have failed to respond to medical therapy, placing the patient who requires orthopedic reconstruction at highest risk for occult multisystem disease.

Arthroplasty is a major surgical procedure with recognized risks. Serious and potentially life-threatening cardiopulmonary complications include myocardial infarction, arrhythmia, and pulmonary embolization. Arthroplasty is recognized by the American College of Cardiology/American Heart Association as an intermediate-risk procedure, which indicates a 1–5% incidence of cardiac death or nonfatal myocardial infarction [9] (MI). The risk of an ischemic cardiac event has been reported as 0.6% overall in patients undergoing arthroplasty [1]. The prevalence of occult atherosclerotic

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disease in the population of patients with inflammatory arthritis and SLE is high, estimated to be equivalent to the risk seen in patients with diabetes. The national inpatient sample reveals that the in-hospital mortality for SLE patients undergoing total hip arthroplasty (THA) is significantly increased, a risk associated with renal dysfunction [10]. Atherosclerotic disease is increased in patients with persistent inflammation typical of SLE, RA, AS, and PsA patients; their excess mortality is largely due to the increase in cardiovascular disease. In patients with SLE and RA, cardiac risk is independent of traditional risk factor but is magnified by them [11, 12]. AS and PsA are not as strong an independent cardiac risk factor as RA and SLE, but these patients are more likely to have multiple traditional risk factors such as metabolic syndrome and dyslipidemia. Additional risk factors such as obesity, smoking, hypertension, and diabetes are also increased in PsA patients [13–16]. PsA patients with severe skin involvement are at an increased risk for ASCVD, but mildly affected PsA patients are not. Prolonged therapy with disease-modifying drugs (DMARDS) and biologics, however, decreases the cardiac risk in patients with RA [17, 18], improves the lipid profile in patients with AS [19], and may prevent the progression of atherosclerosis [20]. Cardiac risk assessment and risk modification in the perioperative period will be addressed.

Patients with connective tissue diseases are at risk for pulmonary disease. Respiratory disease is estimated to be present in up to 80% of SLE patients and can affect the airways, parenchyma, as well as the bellows function with diaphragm compromise [21]. Patients with RA have an estimated 30–46% incidence of interstitial lung disease [22–24] and may have upper airway compromise due to involvement of the cricoarytenoid joints [25, 26]. AS patients may have significant chest wall restriction when the costovertebral joints fuse or the thoracic spine becomes ankylosed. Pulmonary function impairment increases the risk of postoperative atelectasis and pneumonia, which is more frequent when patients mobilize slowly. The majority of patients studied undergoing hip arthroplasty reveal transient hypoxemia during THA, related to fat embolization occurring during pressurization of the femoral canal, which is magnified in the presence of underlying pulmonary impairment [27]. However, regional anesthesia is the technique of choice for extremity surgery and is less likely to be associated with pulmonary complications. Extremity surgery is generally well tolerated in the presence of pulmonary disease, as perioperative pulmonary risk is greatest in procedures performed near the diaphragm, but spine surgery may increase the risk of postoperative pulmonary complications. Upper airway management can pose complex challenges when general endotracheal anesthesia (GETA) is necessary in patients with cervical spine fusion, as seen in SpA patients, or instability which is present in 40% of RA patients undergoing arthroplasty [28]. Pulmonary and airway evaluation and risk assessment and considerations to mitigate risk by preoperative optimization and planning will be discussed.

Thromboembolic risk is increased in patients with the anticardiolipin antibody syndrome (ACLA) and mandates aggressive anticoagulation. For patients with APS, preoperative planning with anesthesia and surgery to minimize the risk of postoperative hemarthrosis by restricting activities including physical therapy may be necessary. However, patients with SLE who do not have ACLA are also at increased VTE [29]. Pulmonary artery hypertension (PAH) may complicate SLE and is characterized by marked elevations in right heart pressure and decreased venous return to the heart, which can result in catastrophic hypotension and shock when magnified by the effects of anesthesia [30]. These complex manifestations of systemic connective tissue disease are addressed in detail elsewhere.

Renal impairment may increase perioperative risk in the connective tissue disease patient undergoing orthopedic surgery [10]. Underlying renal dysfunction is a significant risk factor for perioperative renal damage [31]. Renal compromise may be intrinsic to the disease state, such as glomerulonephritis in a patient with SLE. SLE patients rarely undergo TJA due to erosive joint disease but are more likely to sustain joint damage due to organ-preserving therapy including high-dose corticosteroid therapy, which is the major risk factor for osteonecrosis (ON). SLE patients undergoing THA are therefore largely drawn from this pool of severely affected patients with intrinsic renal disease who have received high-dose corticosteroid therapy [32–34]. Renal functional impairment may also be attributed to medications such as nonsteroidal anti-inflammatory drugs (NSAIDS) or renin-angiotensin blocking agents (ACEI/ARA), which can increase the likelihood of perioperative renal damage [35]. Finally, medications used to treat IA and SLE can impair wound healing and increase the risk of infection [36]. Strategies to minimize perioperative risk while avoiding disease flare will be discussed.

Rheumatoid Arthritis

Cartilage erosion by untreated or unresponsive rheumatoid synovial pannus typically leads to joint destruction, resulting in pain and loss of function. Reports drawn from large cohorts reveal that 34–58% of RA patients will undergo an orthopedic intervention, usually arthroplasty. Those patients most likely to undergo surgery were those who had persistent elevations in ESR and CRP, positive rheumatoid factor, nodules, worse function scores on the Health Assessment Questionnaire (HAQ) scores, and erosions on serial radiographs [3, 4, 37]. Gratifyingly, as aggressive therapy has become the standard of care, the natural course of RA has changed. Comparing a

cohort of patients treated in 1985, only 10% of whom were taking MTX, to a cohort studied in 2000, 76% of whom were taking MTX, revealed that the 2000 cohort had better function on HAQ scores, lower ESR, fewer swollen joints, and fewer radiographic erosions [2]. The introduction of widespread TNF inhibitor therapy as well as more aggressive approaches to therapy has further improved RA status, with improved function on HAQ scores and more frequent remissions. For example, in those treated with TNFis, concurrent treatment with methotrexate significantly reduces the incidence of arthroplasty [38]. Nonetheless, only small joint and soft tissue procedures, but not large joint surgery rates, have decreased [7, 39]. However, up to 30% of patients fail to respond to therapy, comprising the group with persistent inflammation who are most at risk for joint damage [5].

The reported all-cause mortality after TJA is 0.7%, largely related to VTE and major acute cardiac events (MACE) [40]. RA, underlying cardiovascular disease, and age >80, as well as bilateral surgery, have been identified as factors associated with an increased surgical mortality [41, 42]. Patients with RA have an increased risk of VTE overall, but the risk is not increased after surgery [43–45]. RA patients have a significant increase in atherosclerotic cardiovascular disease (ASCVD) and coronary artery disease (CAD) compared to normal controls. Carotid atherosclerosis has been demonstrated in 44% of RA patients compared to 15% of matched controls and may be subclinical [11, 46]. The patients at greatest risk of ASCVD are those patients with persistent active inflammation and active RA, while patients in remission are less likely to bear ASCVD risk markers such as elevated CRP or elevations of brachial blood pressure. Treatment with MTX or TNFis decreased ASCVD risk [17, 18]. RA therapy and low disease activity decrease cardiac risk, reinforcing cardiac concerns in the RA patients who require orthopedic surgery, who are characterized by persistent inflammation and treatment failure [47].

Patients with RA may not be able to exercise sufficiently to predict cardiac risk under the ACC/AHA guidelines. Demonstration of the ability to perform 4 METs of energy, achieved by walking upstairs, is sufficient for an intermediate-risk surgery such as arthroplasty [9]. RA patients are frequently unable to demonstrate this and may require formal cardiac imaging. Echocardiography can provide information on valve anatomy and cardiac function measured as ejection fraction, but stress testing is required to provide information regarding ischemic risk. Beta-blockade, which is protective in regard to cardiac events, can be considered in cases where ischemic cardiac risk outweighs the risk of significant hypotension, bradycardia, and stroke associated with beta-blocker use [48].

Patients with RA are at an increased risk of infection after arthroplasty [45]. Risk factors for infection include age and poor functional status, but the relationship to medication use is not clear [49]. While exposure to TNF therapy increased the risk of infection in a meta-analysis that pooled data from over 3681 patients with recent exposure to such therapy and 4310 with no such exposure [50, 51], recent pharmacoepidemiologic studies have not confirmed this association. By linking the date of surgery to infliximab billing records for 4288 patients, of whom 270 (6.3%) had infection requiring hospitalization or prosthetic joint infection (PJI), infection rates were no different for patients who had received their infliximab within 1 month, 6 months, or a year of therapy [50]. Medication management is discussed below.

Pulmonary involvement is common in RA patients, with a reported prevalence of 50%. When patients are screened by high-resolution computed tomography (HRCT), 67% of scans are abnormal, most commonly revealing a reticulonodular pattern and ground glass opacities typical of interstitial lung disease (ILD) or bronchiectasis [22, 52]. When respiratory symptoms are used to screen for the presence of pulmonary disease, 42% of the population of RA patients, 29% of whom had abnormalities on pulmonary function testing (PFT), reported cough, phlegm, dyspnea, or wheezing on a validated questionnaire (PFT) [24]. Patients with high titer RF positivity and high Larson or Sharp score indicating cartilage erosion, ESR, or CRP elevations are more likely to have pulmonary abnormalities. These characteristics therefore identify patients at high risk for pulmonary involvement and thus pulmonary complications after surgery. The risk of perioperative pulmonary complications is not only increased in patients with underlying pulmonary disease but also those who smoke, are in a poor functional state, and are of advanced age. Surgical site is the greatest predictor of pulmonary complications, and extremity surgery is therefore low risk for pulmonary complications, which increase with proximity to the diaphragm. Spine surgery places the patient at greater risk for pulmonary complications [53]. Patient with RA undergoing extremity surgery can be screened by history, but those in whom spine surgery is planned may benefit from more comprehensive evaluation. Pulmonary function testing may be useful in estimating pulmonary reserve.

Airway obstruction is a rare but potentially fatal complication of upper airway involvement in RA. Patients may have a history of hoarseness as the only indication of cricoarytenoid arthritis. The cricoarytenoid joints, small diarthrodial joints, may be affected in patients who have longstanding polyarticular disease. Edema produced at the time of intubation may result in airway closure after extubation. Preoperative evaluation with pulmonary function testing or fiberoptic laryngoscopy may provide information needed for airway management [25, 26]. Regional anesthesia is preferred for extremity surgery, but when general anesthesia is necessary, nasotracheal intubation may be employed with direct fiberoptic visualization of the airway to lessen airway trauma. Preoperative consultation with anesthesia is helpful in preparation for safe airway management.

Cervical spine involvement in RA patients accompanies severe erosive disease and can be prevented by aggressive use of DMARDS [54]. Asymptomatic cervical spine involvement has been reported in 44% of RA patients screened at the time of referral for arthroplasty [55, 56]. Screening should be performed on RA patients using lateral flexion and extension X-rays; those at highest risk are the patients with erosive hand and foot deformities [41]. Lateral films in neutral missed 48% of 65 known cases of atlantoaxial subluxation and failed to fully characterize the severity of the subluxation in 66% [28]. MRI is a better modality to fully characterize cervical spine pathology such as instability as well as basilar invagination. Cervical spine instability may be a rare cause of sudden death or paraplegia. Although there are no randomized controlled trails comparing conservative therapy to surgical therapy or addressing optimal timing for intervention, neurologic deterioration occurs consistently in symptomatic patients [57]. In severely affected patients, loss of mobility, attributed to involvement of weight-bearing joints, may be the result of cervical spine involvement with myelopathy. This requires evaluation by neurology and treatment, usually by surgical stabilization, prior to extremity surgery. Extremity surgery should be performed when possible under regional anesthesia, but if general anesthesia is required, fiberoptic guided nasotracheal intubation avoids hyperextension of the neck.

The rheumatoid shoulder may remain clinically silent, in spite of progressive soft tissue destruction which will eventually impact function and cause pain. Shoulder involvement may be tolerated as patients may compensate with scapulothoracic motion until significant damage to the soft tissue shoulder envelop has occurred. Damage to the structures of the rotator cuff cannot be visualized without ultrasound or MRI, which reveal three times the incidence of supraspinatus tendon rupture and five times the incidence of infraspinatus tendon rupture when compared to OA patients [58]. The relatively silent nature of shoulder involvement in RA has implications at the time of total shoulder arthroplasty (TSA) surgery. Improvement in pain, decrease in sleep disturbance, as well as improvements in activities of daily living (ADL) such as personal hygiene were reported for patients with RA undergoing shoulder replacement over a 20-year period of observation [59]. Functional improvement after TSA depends on the status of the rotator cuff. Hemiarthroplasty remains a good option when the glenoid is severely eroded and the rotator cuff is irreparable [60]. Complications are rare, and no significant difference has been seen when OA patients are compared to RA patients undergoing TSA [61].

RA patients undergoing arthroplasty have an excellent response in terms of pain relief as measured by VAS pain scales, but THA patients may lag in functional measures, although outcomes after TKA are as good as OA patients [62, 63]. When measurements of global well-being such as the SF-36 are studied by RA patients after arthroplasty, the scores predictably improve. Functional measurements such as the HAQ lag behind the scores of osteoarthritis patients [64]. Long-term outcome for THA and TKA in RA patients, measured as implant durability, is equivalent or better than implant survival for OA patients [4, 64]. Expectations of TKA are lower for patients with RA [65], but satisfaction is high, even when objective measures lag behind the less satisfied OA arthroplasty patients [66].

Systemic Lupus Erythematosus

Although 90% of SLE patients have joint inflammation, it is typically benign and does not erode cartilage. Some SLE patients, however, may have RA features, leading to joint destruction. Joint destruction severe enough to warrant arthroplasty, however, occurred in only 3.8% of 500 SLE patients in a well-studied cohort, significantly fewer than the 58% of RA patients who undergo orthopedic surgery. Of the 19/500 SLE patients undergoing arthroplasty, osteonecrosis (ON) was more likely to lead to surgery, in 10/19 patients, than SLE-RA overlap [34, 66]. ON occurs early in SLE patients beginning therapy with corticosteroids. MRI, a very sensitive technique for diagnosing ON, reveals asymptomatic ON in 40% of studied patients, as early as 1–3 months after starting corticosteroid therapy [66]. Symptomatic ON is less common, present in 12.8% of patients [67]. The risk of symptomatic ON is primarily conferred by corticosteroid dose alone [32, 68]. Although other factors such as renal involvement, cushingoid appearance, and Raynaud's phenomenon have been linked to an increase in ON, careful analysis of 570 SLE patients, 11.5% of whom had ON, failed to demonstrate any other factor associated with ON when matched for corticosteroid dose [69]. Unlike the RA population, the need for arthroplasty may reflect successful aggressive organ-preserving therapy in SLE, rather than demonstrating a failure to respond to treatment. There are few successful interventions to lessen ON, although small series suggest bisphosphonates may play a mitigating role [70].

Patients with large ON lesions occupying more than two-thirds of the weight-bearing surface of the femoral head are likely to develop subchondral collapse and will usually require TJA to preserve function. Non-arthroplasty surgical interventions for ON such as core decompression remain a possible option when pain is intractable but should be reserved for cases where subchondral fracture and collapse have not occurred. Free vascularized fibular grafts have been described to treat ON, but the results have not been widely reproducible [67, 71, 72]. In our experience, all joint-sparing procedures are less likely to succeed in SLE patients who require ongoing steroid therapy.

SLE patients undergoing TJA have higher in-hospital mortality as revealed in a recent analysis of a national inpatient database, and the risk is greatest among those with kidney disease [10]. Excess mortality in SLE is due to atherosclerotic cardiovascular disease, independent of the presence of traditional risk factors such as diabetes or hypertension [73]. Arthroplasty is an intermediate-risk procedure in the risk stratification strategy proposed by the American College of Cardiology/American Heart Association, which correlates with a 1–5% risk of cardiac death or nonfatal MI. SLE patients should be screened, as should all patients, by history. When exercise tolerance permits 4–10 METs of exertion, achieved by walking upstairs or performing vigorous sports, no further cardiac evaluation may be necessary. As many of these patients are not capable of exercise due to their arthritis, inclusion of pharmacologic stress testing to identify subclinical ischemic disease should be considered in these patients whose risk is estimated to be analogous to that of diabetic patients [9].

Chronic kidney disease is a comorbidity known to increase postoperative renal damage and perioperative mortality in settings such as non-SLE hip fracture. SLE patients frequently have impaired renal function, as well as hypertension, increasing the risk of postoperative renal dysfunction [31, 74]. Careful preoperative identification of impaired renal function in SLE patients permits discontinuing other modifiable nephrotoxic agents such as NSAIDS and ACEI/ARA [75].

Secondary antiphospholipid antibody syndrome (APS) may be seen in SLE and increases the risk of vascular thrombosis. APS is a prothrombotic state defined by both the presence of antibodies directed against phospholipid and plasma proteins, in a patient with either vascular thrombosis or pregnancy loss. These antibodies include the antiphospholipid antibodies and b-2 glycoprotein [76]. However, patients with SLE are at increased risk for VTE even if they do not have antiphospholipid antibodies. And smoking and obesity are additional risk factors [29, 34]. The lupus anticoagulant interferes with phospholipid-dependent clotting factors, resulting in a prolongation of the APTT, and, less frequently, the PT. Not all patients who have evidence of a lupus anticoagulant are at increased risk of thrombosis, but the presence of these antibodies in a patient considering arthroplasty or any surgery raises concerns [77, 78]. Those patients with "triple positivity" – positive lupus anticoagulant, high titer anticardiolipin antibody, and B2 glycoprotein antibodies – are at the highest risk of VTE [79]. When patients with known APS are indicated for surgery, careful coordination with anesthesia and orthopedics is mandatory. Exacerbations of APS can occur in the setting of perioperative hypercoagulability and may include recurrent thrombosis due to withdrawal of anticoagulation, as well as breakthrough thrombosis, in spite of anticoagulation due to the prothrombotic state induced by surgery. Catastrophic APS consisting of widespread thrombosis has also been described after surgery in susceptible patients. Risk of thromboembolic events can be diminished by bridging the patient from coumadin to heparin or low-molecular-weight heparin prior to surgery, thus minimizing the time off anticoagulants. Postoperative and intraoperative use of ancillary measures such as venous compression devices and limiting tourniquet time when possible may be helpful in decreasing the thromboembolic risk [77]. Statins and hydroxychloroquine may confer an additional antithrombotic effect, although this has not been proven. Aggressive anticoagulation is necessary in these patients, with the attendant risk of post-op hemarthrosis. Experience gained at our institution suggests that this can be minimized by slowing the postoperative physical therapy regimen and should be discussed prior to surgery. Additional compromises in terms of anesthesia and post-op analgesia may be necessary, as spinal or epidural regional anesthesia and epidural analgesia should not be employed when the patient is receiving heparin for prophylaxis or therapy in light of the risk of spinal or epidural hematomas. Bridging heparin or low-molecular-weight heparin may be discontinued 24 h prior to anesthesia and surgery so that regional anesthesia can be utilized and restarted 3 h after the epidural catheter is removed. In some cases, placement of an inferior vena cava filter may be indicated.

Surgical outcome patients with SLE achieve relief of pain and improved function after arthroplasty [80]. When revision is used as the endpoint, SLE patients have the same arthroplasty survival as other patients and have a 94% 5-year arthroplasty survival [81–83]. Outcome for bipolar prosthesis is poor, however, with a 27% failure rate, and bipolar prosthesis is no longer recommended for ON patients [72]. Early complications have been reported to be increased in some series, however. In 47 THA performed in 36 patients, there were two intraoperative fractures which did not require further surgery; delayed wound healing was reported in three patients, one of whom required debridement 3 weeks after surgery; and two patients had early, nonrecurrent dislocations and one late deep infection [84]. Another series of 19 THA reported a complication rate of 21%, with two surgical site infections, one hematoma, and one DVT [34]. Complications are higher in patients with SLE undergoing THA than those undergoing TKA [85, 86] Risks of all complications are highest in those with recent SLE-related hospitalizations, suggesting that complications are increased in the setting of active SLE [87].

Spondyloarthropathy

The SpA group includes patients with AS, PsA, reactive arthritis, and arthritis associated with Crohn's disease (CD) and ulcerative colitis (UC). The clinical unifying features

include prominent enthesitis, peripheral arthritis that is frequently asymmetric, and sacroiliitis with or without ankylosis, as well as extra-articular features. This includes psoriasiform skin lesions and nail pitting, mucosal ulceration extending throughout the GI tract as well as the genitalia, inflammation of the genitourinary (GU) tract, absence of RF and nodules, and ocular inflammation such as uveitis and conjunctivitis. The recognition of the high frequency of HLA-B27 positivity and familial clustering has strengthened the association. Specific clinical features, such as the presence of psoriasis, permit division into clinically relevant subgroups.

Ankylosing Spondylitis

AS is characterized by vertical spinal syndesmophytes, which may lead to spinal ankylosis as well as inflammatory and erosive axial and peripheral arthritis. The goal of medical therapy is to prevent spinal ankylosis and prevent destruction of peripheral joints, for which a combination of modalities has been employed including NSAIDS, traditional and biologic DMARDS, and physical therapy modalities. There has been little success in treating the progression of spinal ankylosis, however [88]. Younger age of onset of AS and severity of spine involvement predict hip involvement [89].

Hip arthritis is present in 30–50% of AS patients and may progress in spite of therapy [88]. The characteristic exaggerated lordosis seen in advanced AS may result in the development of a flexed knee and flexed hip gait which magnifies symptomatic arthritis in the hips or knees. Hip involvement may include significant flexion contractures and ankylosis of the hips. Bilateral hip involvement is common, and in our experience, correction of both hips under the same anesthesia should be considered when there are significant contractures, to decrease the likelihood of recurrent contracture in the operated leg. THA is usually performed for pain, poor posture, and poor function, with multiple series reporting benefit in these areas. Pain relief is reported in 83–90% of patients. Durability of the implant is also very good, with 90% survival of the implant at 10 years, 79% survival of the implant at 15 years, and 61% survival of the implant at 20 years. Function is not necessarily improved as significantly as pain, however. Although ambulatory status improved in all patients, one study observed that only 42% of AS patients who had undergone THA were employed, compared to 64% of AS patients who had not undergone THA [90, 91].

Knee involvement may also be severe in patients with AS. TKA performed on 30 knees in 20 patients with AS were reported to provide excellent pain relief, demonstrated by an improvement in Knee Society Scores (KSS). This scale assesses pain and function and ranges from 0 to 100, with 100 indicating excellent function and no pain. Patients improved from an average score of 14 prior to surgery to 87.5 points on postoperative study. Function improved from a score of 16 pre-op to 80 points at 2 years. There was minimal change in range of motion, however. The average arc of motion was 84° prior to surgery, and although the average range of motion was 94° at 2 years, this deteriorated to an average of 86° when last seen by the authors in follow-up [92]. When patients have advanced arthritis in both the hips and the knees, hip replacement should generally be performed first to restore hip motion and correct contractures, which will facilitate rehabilitation after knee replacement surgery.

Surgery may be undertaken for spine deformities in AS and may be indicated to restore balance or restore horizontal gaze. Opening wedge osteotomy, closing wedge osteotomy, or polysegmental wedge osteotomy may be performed to correct exaggerated spinal kyphosis. This is a high-risk surgery, however, with 4% mortality and 33% incidence of instrumentation failure [93]. Spine surgery may be indicated for osteoporotic spine fractures, which typically occur after low impact trauma. Spine fractures are significantly increased in AS patients, but fractures of the wrist and hip are not [94]. Fracture diagnosis is frequently delayed, due in part to difficulty visualizing fracture on standard X-rays in an ankylosed spine. There is a 50% complication rate for patients who require surgery due to neurologic deficits and a 17.7% 3-month mortality [95, 96].

Heterotopic ossification (HO) is reported in AS patients and may contribute to a compromised range of motion. Revision surgeries and surgery performed in young men increase the risk of developing HO. Prophylaxis with low-dose radiation or indomethacin can be used to decrease the rate of HO formation [97].

Although patients with AS frequently have pulmonary involvement, the greatest contribution to perioperative pulmonary risk is the site of surgery, with the greatest risk conferred by surgical procedures near the diaphragm [53, 98]. Extremity surgery is therefore generally well tolerated. Pulmonary manifestations of AS include chest wall restriction, and patients may develop severe restrictive ventilatory impairment due to fusion of the costovertebral joints, ankylosis of the thoracic spine, or involvement of the anterior chest wall and become obligate diaphragmatic breathers when the costovertebral joints fuse [99]. AS patients should be mobilized quickly with attention to bowel function in light of concern for postoperative abdominal distention or ileus which might compromise the respiratory status of these patients by upward pressure on the diaphragm. There are no available studies determining the perioperative risk

conferred by restrictive pulmonary or chest wall pathology, however. In addition, a common cause of restrictive pulmonary physiology, obesity, has not been shown to increase perioperative pulmonary risk [53, 100].

Upper extremity surgery, frequently performed with scalene nerve block anesthesia, typically paralyzes the ipsilateral diaphragm and may not be well tolerated in patients with the chest wall restriction frequently seen in AS. AS patients should be evaluated by anesthesia prior to surgery, and regional anesthesia should be used whenever possible for lower extremity surgery. Fiberoptic visualization may be necessary for intubation when general anesthesia is necessary when the cervical spine is fused to prevent injury and fracture.

Patients with AS have an increase in cardiac disease compared to those without chronic inflammatory diseases, which may be responsible for the doubled mortality reported in AS patients. The incidence of cardiovascular disease is three times higher than the risk predicted by traditional risk factors contained in the Framingham Risk Score, reflecting the risk associated with chronic inflammation [101]. Aortic valve disease with regurgitation and aortic root dilatation has been described historically. More recent studies have not confirmed these findings, although there is a high prevalence of diastolic dysfunction [102, 103]. Conduction abnormalities such as 1′ A-V block and prolongation of the QRS interval are described and are associated with prolonged disease duration [104]. The prevalence of coronary artery disease in AS may be related to an increase in traditional risk factors such as hypertension and the presence of chronic inflammation with persistent elevations of CRP, as well as dyslipidemia with lower levels of protective high-density lipoproteins (hdl) [105]. Preoperative cardiac evaluation should include careful assessment of AS patients for traditional cardiac risk factors, and imaging studies such as echocardiography or stress testing should be performed when history or physical exam suggests cardiac symptoms or limitation or when the patient is unable to achieve 4 METs of exertion necessary to undertake orthopedic surgery.

Osteoporosis and osteopenia is highly prevalent in AS, described in the spine in 57% and the femoral neck in 47% of patients [106]. Osteoporosis is associated with male gender, high levels of inflammatory markers such as CRP, high disease activity score, and low functional capacity [107]. Diagnosis may be difficult due to concurrent spinal syndesmophytes, which can lead to overestimation of bone mineral density (BMD), but bone turnover markers such as collagen cross-links and low vitamin D levels may be helpful [108–110]. The role of osteoporosis in arthroplasty outcome or the rate of periprosthetic osteolysis is not clear, but evaluation of BMD and vitamin D levels with treatment where indicated may have benefits in arthroplasty outcome.

Psoriatic Arthritis

PsA has variable presentations. Skin lesions may be the dominant clinical feature or may be absent at the time of diagnosis. Arthritis typically develops 10 years after the skin lesions have been present. Observational cohort studies are ongoing to define the course and prognostic features of this disease. Careful longitudinal study has demonstrated the development of severe erosive disease in 20% of patients. Additionally, over half of the patients followed for greater than 10 years will progress to joint damage. Those patients with more than five involved joints at the time of onset, persistent joint inflammation, and persistent elevations of CRP are the patients likely to progress [109, 110]. Although only 17% of patients in this large observational cohort were able to sustain a remission, another 34% had minimal disease activity, indicating a substantial benefit from therapy [111]. In a cohort of 504 PsA patients, only 32 patients, or 6.3%, developed hip arthritis, of whom only 9 patients, or 1.8%, of the total cohort underwent THA. Patients likely to progress to THA were those with an earlier age at onset of PsA and spondylosis [112]. Outcomes of pain and function are similar to those for patients undergoing THA for OA [113].

Patients with psoriatic arthritis appear to have an increase in subclinical cardiovascular disease, similar to patients with other systemic inflammatory diseases. Cardiovascular disease in PsA correlates with the severity and extent of the skin disease. Cohorts including patients with mild disease are less likely to show an increase in cardiovascular disease or an excess mortality [16, 114]. Although cardiovascular disease in severely affected PsA patients is independent of traditional risk factors, PsA patients also have an increase in known cardiac risk factors such as diabetes, hypertension, smoking, and hyperlipidemia [115]. Patients undergoing arthroplasty should therefore be evaluated for cardiac disease following the American College of Cardiology/American Heart Association guidelines when a history demonstrating adequate exercise tolerance is not available.

The orthopedic literature is of little help in guiding an approach to optimizing arthroplasty outcome in infection rate in patients undergoing TKA. Early reports revealed a high rate of both superficial (9.1%) and deep (5.5%) infection in PsA patients undergoing THA. PsA patients undergoing TKA were reported to have an infection rate of 17% [116–118]. When perioperative antibiotics were employed, this extreme rate of infection was not duplicated [117]. Current routine precautions include treatment of the psoriatic skin prior to surgery, with particular attention to the operative site, as well as routine use of perioperative antibiotics, which have resulted in a decrease in infection. Antibiotic-laden cement may be appropriate for selected cases.

Medications

Medications that suppress the immune system and may affect wound healing are frequently prescribed for the treatment of systemic rheumatic diseases and may contribute to the increase in perioperative complications seen in these patients. The three major drug categories used in these patients are corticosteroids; DMARDs including synthetic molecules such as methotrexate, hydroxychloroquine, azathioprine, leflunomide, and tofacitinib; and the biologic agents including the TNF blocking agents. Careful medication management may be an opportunity to mitigate infection risk common to all rheumatic disease patients, but medication management has not been consistent [119]. However, there is little direct evidence to guide medication management decisions. The American College of Rheumatology (ACR) and the American Association of Hip and Knee Surgeons (AAHKS) collaborated on a guideline for the perioperative management of antirheumatic therapy for patients with rheumatic diseases undergoing THA or TKA and used a consensus-based process after a systematic literature review to make the recommendations that follow (Table 12.1) [120]. The aim was to balance the risk of infection, which is uncommon but can be severe, with the risk of disease flare, which occurs frequently after surgery [121].

Table 12.1 Antirheumatic medications, dosing interval, and surgical recommendation

DMARDs: *Continue* these medications through surgery	**Dosing interval**	**Continue/withhold**
Methotrexate	Weekly	Continue
Sulfasalazine	Once or twice daily	Continue
Hydroxychloroquine	Once or twice daily	Continue
Leflunomide (Arava®)	Daily	Continue
Doxycycline	Daily	Continue
Biologics: *Stop* these medications prior to surgery and schedule surgery at the end of the dosing cycle. *Resume* medications at minimum 14 days after surgery in the absence of wound-healing problems, surgical site infection, or systemic infection	**Dosing interval**	**Schedule surgery (relative to last biologic dose administered)**
Adalimumab (Humira®, AbbVie Inc., North Chicago, IL, USA) 40 mg	Every 2 weeks	Week 3
Etanercept (Enbrel®, Amgen, thousand oaks, CA, USA) 50 mg or 25 mg	Weekly or twice weekly	Week 2
Golimumab (Simponi®, Janssen Biotech, Inc., Horsham, PA, USA) 50 mg	Every 4 weeks (SQ) or Every 8 weeks (IV)	Week 5 Week 9
Infliximab (Remicade®, Janssen Biotech, Inc., Horsham, PA, USA) 3 mg/kg	Every 4, 6, or 8 weeks	Week 5, 7, or 9
Abatacept (Orencia®, Bristol-Myers Squibb, NY, NY, USA) weight-based 500 mg; IV 1000 mg; SQ 125 mg	Monthly (IV) or Weekly (SQ)	Week 5 Week 2
Rituximab (Rituxan®, Genentech, San Francisco, CA, USA) 1000 mg	Two doses 2 weeks apart every 4–6 months	Month 7
Tocilizumab (Actemra®, Genentech, San Francisco, CA, USA) IV 4 mg/kg; SQ 162 mg	Every week (SQ) or every 4 weeks (IV)	Week 3 Week 5
Anakinra (Kineret®, Sobi, Inc., Stockholm, Sweden) SQ 100 mg	Daily	Day 2
Secukinumab (Cosentyx®, Novartis, Basel, Switzerland) 150 mg	Every 4 weeks	Week 5
Ustekinumab (Stelara®, Janssen Biotech, Inc., Horsham, PA, USA) 45 mg	Every 12 weeks	Week 13
Belimumab (Benlysta®, GlaxoSmithKline, Brentford, UK) 10 mg/kg	Every 4 weeks	Week 5
Tofacitinib (Xeljanz®, Pfizer, NY, NY, USA) 5 mg: *Stop* this medication 7 days prior to surgery	Daily or twice daily	7 days after last dose
Severe SLE- specific medications: *Continue* these medications in the perioperative period	**Dosing interval**	**Continue/withhold**
Mycophenolate	Twice daily	Continue
Azathioprine	Daily or twice daily	Continue
Cyclosporine	Twice daily	Continue
Tacrolimus	Twice daily (IV and PO)	Continue
Not-severe SLE: *Discontinue* these medications in the perioperative period	**Dosing interval**	**Continue/withhold**
Mycophenolate	Twice daily	Withhold
Azathioprine	Daily or twice daily	Withhold
Cyclosporine	Twice daily	Withhold
Tacrolimus	Twice daily (IV and PO)	Continue

Dosing intervals obtained from prescribing information provided online by pharmaceutical companies

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[a]2016 American College of Rheumatology/American Association of Hip and Knee Surgeons Guideline for the Perioperative Management of Antirheumatic Medication in Patients with Rheumatic Diseases Undergoing Elective Total Hip or Total Knee Arthroplasty

Corticosteroid

Corticosteroids are used in rheumatic diseases for their striking anti-inflammatory effect but are known to increase infection risk and to have a negative effect on wound healing. Patients who have received daily corticosteroid therapy have suppression of their endogenous adrenal function as demonstrated by ACTH stimulation tests. Because of the risk of hypotension, "stress-dose" or supraphysiologic steroid is typically administered at the time of surgery. Although suppression of the adrenal axis is easily demonstrated after relatively short courses of corticosteroid, it is less clear when supraphysiologic replacement doses of cortisone are actually needed. When patients on chronic daily steroid, all of whom had been demonstrated to have adrenal insufficiency by ACTH stimulation testing, underwent surgery such as arthroplasty and were randomized to receive either parenteral corticosteroid or saline plus their usual daily dose, there was no hemodynamic difference between the groups. Similar results were obtained when patients treated with long-term corticosteroid were hospitalized with significant stress such as sepsis [122, 123], suggesting that the supraphysiologic doses may not be warranted. Endogenous cortisol production has been measured in healthy patients undergoing surgery to determine the normal response to stress. Patients undergoing arthroscopy have no increase in their cortisol production, whereas patients undergoing arthroplasty have a 17-fold increase from baseline cortisol production [124].

Although the risk of infection associated with steroid has been well documented, a clear dose cutoff for risk mitigation is difficult to determine as there is a significant interaction between dose and duration of therapy. Using a weighted cumulative dose modeling method, the risk of infection increased for continuous prednisone 5 mg/day from 30% to 46% to 100% if the prednisone was taken for 3 months, 6 months, or 3 years, making it difficult to extrapolate risk from cross-sectional surgical studies [125]. Dermal and epidermal atrophy are seen with long-term glucocorticoid use, also contributing to infection risk by the effect on wound healing. Cut points for increased infection risk have been reported at 10, 15, and 20 mg/day [50, 126, 127].

The ACR/AAHKS guideline recommends that patients who are taking glucocorticoids for their rheumatic condition, but not those taking replacement therapy or those who were treated with glucocorticoids as a child, take their usual daily dose of glucocorticoids on the day of their THA or TKA and not supraphysiologic doses of glucocorticoids [120]. However, recent studies have revealed that glucocorticoids given on the day of surgery decrease nausea and pain and benefit knee range of motion in patients undergoing TKA. These clinical findings are associated with decreased inflammatory markers including Il-6. These previously unrecognized benefits may lead to an overall reassessment of the role of perioperative glucocorticoids to balance the benefits with the previously known harms [128–130].

Synthetic DMARDS

Methotrexate has been extremely well studied in the perioperative period [131, 132]. Continuing methotrexate in the perioperative period does not increase surgical site infections and has no negative impact on wound healing. Moreover, patients who discontinue methotrexate predictably flare, compromising their ability to participate in rehabilitation. The ACR/AAHKS guideline recommends continuing synthetic DMARDs, methotrexate, leflunomide, sulfasalazine, and hydroxychloroquine through surgery [36, 120, 132–134].

Biologic Agents

The use of anti-TNF agents in inflammatory arthritis has significantly decreased the disease burden for patients with IA, but there is a clear risk of severe infection which is highest within the first 6 months of therapy [2, 135–137]. Although there are no randomized clinical trials to test the impact on surgical site infections, there are multiple retrospective studies as well as studies drawn from large population databases that show an association of TNF inhibitor therapy with surgical site infection. The ACR AAHKS guideline recommends withholding all biologics at the time of surgery and planning the surgery at the end of the dosing cycle, given the relationship of dose and adverse effects, timing the operation for the end of the dose cycle when the drug effect is at its nadir [136–140]. These agents can be restarted 2 weeks after surgery once the wound has healed and there is no sign of infection or wound drainage or erythema [120].

Tofacitinib

Tofacitinib is a small molecule but functions as a targeted therapy, similar to the biologics. This is a recently approved drug with no published data regarding perioperative risk but clear increases in infection risk in nonsurgical settings. The duration of immunosuppression appears to last a week after stopping therapy, so the ACR/AAHKS guideline recommends scheduling THA or TKA 7 days after the last tofacitinib dose [120, 141].

Summary

Patients with systemic connective tissue diseases and inflammatory arthritis frequently require orthopedic joint reconstruction to restore function and diminish pain, either in the setting of poorly responsive IA or as a consequence of therapy in patients with ON. Multisystem involvement in these patients may include occult cardiopulmonary disease, which should be evaluated preoperatively so that the patients' status can be optimized. Results of surgery are gratifying in terms of

pain relief, although functional improvements may lag behind patients undergoing the same procedures for osteoarthritis. Careful collaboration between surgeons, anesthesiologists, and rheumatologists is fundamental to optimize outcome.

Summary Bullet Points

- Patients with rheumatoid arthritis undergoing orthopedic reconstruction are those who have failed to respond to medical management and typically have multiple affected joints, occult multisystem disease, and significant functional disability, all contributing to the perioperative challenge.
- Patients with systemic lupus erythematosus undergoing orthopedic reconstruction for osteonecrosis are typically those who have required high-dose corticosteroid therapy for organ-threatening manifestations and may have functional impairment in renal or cardiac systems at the time of surgery.
- Patients with ankylosing spondylitis undergoing orthopedic reconstruction of their hips or knees may have concurrent deformities of the spine, which can complicate mechanical alignment and additionally compromise respiratory function.
- Spondyloarthropathy patients with psoriatic arthritis undergoing orthopedic reconstruction may have active skin disease, a potential source of infection, and have a significant increase in associated obesity, diabetes, and smoking, all of which can increase perioperative risk.

Case Study

A 49-year-old man with a 25-year history of seronegative systemic-onset juvenile rheumatoid arthritis (JRA), treated with anakinra and methotrexate, was referred for therapy of a left prosthetic hip infection. His original surgery was performed in 1990. The patient also had a right hip arthroplasty in 1988, which was revised in 2007 for aseptic loosening of the prosthesis. He developed groin pain and fevers and was admitted to an outside hospital with Methicillin-sensitive staphylococcus (MSSA) was identified from blood cultures and a hip aspirate. The hip prosthesis was explanted and an antibiotic spacer was placed. He received 8 weeks of cefazolin 2 g three times a day, and he normalized his C-reactive protein and white blood cell count. He subsequently underwent an uncomplicated reimplantation of the left hip. No source for the infection could be identified.

One month later he developed pain in the left hip and underwent a debridement procedure; MSSA was cultured, and he was again treated with cefazolin resulting in improvement of symptoms. However, he developed recurrent pain with a draining sinus and was referred to HSS for further therapy.

At the time of his presentation, he was afebrile. His exam was remarkable for a draining sinus track at the left hip incision. The right hip incision was well healed, and the hip motion was pain-free. There was no evidence of active synovitis, but bilateral wrist and elbow motion were restricted.

Aspiration of the right hip revealed $125 \times 10^3/\mu L$ white blood cells, and a culture that was obtained at that time was negative for bacterial growth. His erythrocyte sedimentation rate was 110 mm/h and his C-reactive protein was 12.5 mg/L. He underwent explantation and debridement of the left hip prosthesis. MSSA was grown from all operative cultures, and he completed 6 weeks of cefazolin. Bactericidal titers were obtained. Lovenox was used for thromboprophylaxis. His anakinra was discontinued, and he was treated with methotrexate 12.5 mg BID once weekly and remained without flare. He was readmitted 3 months later for reimplantation, which was successful.

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Perioperative Care of the Orthopedic Patient with Cardiac Disease

13

Lawrence F. Levin

Objectives

- To identify cardiac conditions affecting postoperative outcomes
- To minimize adverse outcomes from cardiac conditions via pharmacologic therapy and interventional therapy
- To review postoperative considerations and conditions in light of cardiac revascularization, devices, valvular heart disease, atrial fibrillation, and myocardial ischemia

Key Points

- Significant cardiac morbidity and mortality are experienced by patients in the setting of orthopedic surgery.
- Risk to an individual patient can be stratified, incorporating clinical information including the patient's functional capacity as well as their medical history, specifically preexisting ischemic heart disease, heart failure, cerebrovascular disease, renal insufficiency, and diabetes.
- Supplemental testing beyond a thorough history and physical examination is necessary only in patients deemed to be at high risk based on the aforementioned clinical criteria.
- Maintenance of ongoing cardiac pharmacotherapy is generally appropriate; initiation of beta-blocker should be considered in the higher-risk population, ideally at least a week in advance of the procedure.
- Preoperative coronary revascularization does not reduce the risk of orthopedic surgery and therefore should be performed only to reduce the patient's lifetime risk of adverse cardiac events.

Introduction

Cardiac complications of surgery are a major public health concern. Two hundred million people undergo noncardiac surgery yearly with a cardiac complication rate reported from 0.5% to 3.5% [1]. Between 1996 and 2008, the Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echo (DECREASE) trials reported a 3.5% incidence of major cardiac complications among intermediate- and high-risk patients [2]. A review of all major non cardiac surgeries among patients older than 40 in the United States between 2004 and 2013 found an overall 3% incidence of major adverse cardiac events [3]. For orthopedic procedures, there were 1595 events per 100,000 surgeries, an incidence comparable to the event rate of genitourinary or otolaryngological procedures.

Orthopedic surgery increases the risk for cardiac events by multiple mechanisms. Catecholamines are significantly heightened due to tissue injury inherent to orthopedic surgery as well as perioperative pain. The increased catecholamines induce tachycardia and thus increase myocardial contractility and oxygen demand. Demand ischemia—the mismatch of myocardial oxygen demand and myocardial perfusion—accounts for half of cardiac complications of orthopedic surgery [1]. Additionally surgical stress induces a systemic inflammatory response, which can lead to rupture of previously stable atherosclerotic plaque. A significant portion of the orthopedic population suffers from underlying rheumatologic illness further heightening inflammatory responses and potentially destabilizing plaque. Inherent to

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all surgeries including orthopedic procedures are fluid shifts with fluctuating intravascular volume due to capillary leakage also related to postoperative inflammatory responses. Such surgery evokes a hypercoagulable response as fibrinogen levels and coagulation factors are upregulated. Platelets are activated with heightened aggregation. These influences, coupled with a decrease in fibrinolytic factors, all contribute to a hypercoagulable state.

With this in mind, the orthopedic patient is at risk for cardiac complications. The goal of this chapter is to help minimize this risk and to assist in the treatment of cardiac complications. The first step is to stratify the patient for risk of cardiac complications after which the preoperative measures used to minimize cardiac risk will be elucidated. A discussion of the management of those cardiac conditions commonly seen in orthopedic populations concludes this chapter.

The Identification of Cardiac Conditions Affecting Postoperative Outcome

The goal of perioperative cardiac care is to minimize the cardiac complications after surgery. Risk stratification for perioperative cardiac events is not only used in the implementation of perioperative therapies but is also useful in discussions with the patient and family as they consider different therapies for their orthopedic condition. If a patient's risk for perioperative cardiac events is significantly elevated and not modifiable, and if surgery is deemed elective, the patient, the clinician, and the orthopedist may decide not to pursue that procedure treating the patient conservatively. Likewise, if the patient's risk for perioperative cardiac events is high but the risk modifiable a decision to postpone surgery to pursue therapies, either pharmacologic or invasive, to minimize perioperative risk would seem in order. Lastly, a surgical patient deemed low risk for cardiac complications might have a lower threshold for pursuing surgery if on balance the benefit of surgery outweighs the risk.

The functional capacity of the patient has been shown in multiple analyses to predict perioperative cardiac events: the greater the preoperative exercise capacity of the patient, the lower the postoperative cardiac event rate [4–6]. The Duke Activity Status Index is often used to determine this parameter [7, 8]. The basal metabolic rate of an average-sized male is one metabolic equivalent. This is the average energy expenditure while lying down performing no physical activity. Inability to perform four metabolic equivalents of activity is considered a poor functional capacity, while climbing two flights of stairs without stopping (four to seven metabolic equivalents of exercise) has been associated with reduced cardiovascular complications (Fig. 13.1). Seven to ten metabolic equivalents are considered good, while >10 metabolic equivalents are excellent and place the patient at low risk for perioperative cardiac events.

In the orthopedic population, functional capacity is often limited not by cardiovascular reserve but instead by joint pain and deformities. In a patient with an unknown or a limited functional capacity, risk indices should be used to assess the risk of cardiac complications. In 1977, Goldman and colleagues developed the earliest validated model [9]. Subsequently Lee and colleagues modified the index presenting the Revised Cardiac Risk Index using primarily the patient history to assess the cardiac risk [10]. Variables include history of ischemic heart disease, congestive heart failure, cerebrovascular disease, diabetes on insulin, renal insufficiency, and the inherent risk of the surgical procedure (Box 13.1).

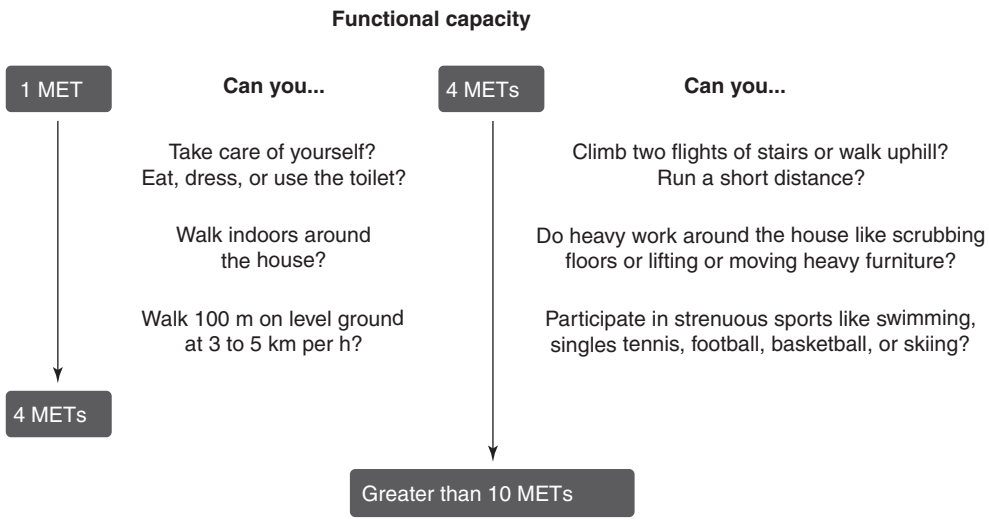

Fig. 13.1 Estimated energy requirements for various activities. *km per h* kilometers per hour, *MET* metabolic equivalent. (Based on, with permission of Elsevier and Wolters Kluwer, respectively, Hlatky et al. [7]; and Fletcher et al. [8]; Used, without objection, from Poldermans et al. [1]; Oxford University Press.)

Box 13.1 Variables in Patient History Used to Assess Cardiac Risk in Orthopedic Surgery

1. History of ischemic heart disease (history of MI or a positive exercise test, current complaint of chest pain considered to be secondary to myocardial ischemia, use of nitrate therapy, ECG with pathological Q waves; do not count prior coronary revascularization procedure unless one of the other criteria for ischemic heart disease is present)
2. History of HF
3. History of cerebrovascular disease
4. Diabetes mellitus requiring treatment with insulin
5. Preoperative serum creatinine >2.0 mg/dL (177 μmol/L)
6. High-risk type of surgery (examples include vascular surgery and any open intraperitoneal or intrathoracic procedures)

The presence of ischemic heart disease is defined as a history of myocardial infarction, ongoing chest pain or nitroglycerin use, abnormal preoperative stress test, or an ECG with evidence for an old myocardial infarction. Congestive heart failure is defined as a history of prior pulmonary edema or ongoing nocturnal dyspnea or a physical examination with edema, rales, or an S3 on cardiac auscultation. A chest X-ray with pulmonary vascular congestion can also be used as a marker for heart failure. While heart failure from reduced ejection fraction is an established risk factor, the role of heart failure with a preserved ejection fraction is less clear in the absence of ongoing symptoms. Significant diastolic dysfunction increases morbidity from high-risk vascular surgery [11]. A known history of cerebrovascular disease as demonstrated by a history of transient ischemic event or stroke has been strongly associated with peripheral vascular and cardiovascular atherogenesis, which increases the risk for perioperative events. Diabetics—particularly those on insulin—have an altered metabolism and hyperinsulinemia, factors that destabilize atherosclerotic plaque and increase the risk of cardiac events. Likewise, renal insufficiency—specifically with a creatinine level >2.0 mg/dL—is associated with atherosclerotic events.

In addition, the inherent risk of the specific surgery must also be considered. High-risk surgery clearly increases the risk of postoperative cardiac events. Orthopedic surgery overall is considered intermediate risk given the 1–5% cardiac event rate [12]. Not surprisingly, the greater the number of cardiac risk factors as defined by the risk index, the greater the incidence of major cardiovascular complications [13]. The patient with less than two risk factors has less than 1% incidence of major cardiovascular events. Greater than or equal to three risk factors carries a 5.4% incidence of cardiac complications.

The Revised Cardiac Risk Index has been reassessed and validated in multiple contemporary settings. In their prospective study of 9519 patients older than 50 undergoing elective noncardiac surgery at 2 major Canadian tertiary care centers, Davis and associates found that the RCRI accurately stratified risk; notably, however, the presence of insulin-dependent diabetes did not aid the accuracy of the model [14]. There are multiple minor risk factors whose role in cardiac risk assessment is unclear. These risk factors are clinically relevant but statistically do not contribute to risk assessment. Specifically, age greater than 70, suboptimally controlled hypertension, and the presence of atrial fibrillation with normal ventricular response do not increase the risk of cardiac complications. A chronically abnormal electrocardiogram——including a baseline bundle-branch block or ST changes in the setting of left ventricular hypertrophy—does not increase the risk of cardiac complications.

The routine physical examination of the patient also contributes to risk assessment by confirming the previously identified risk factors. Cardiac auscultation revealing an S3 suggests decompensated heart failure. Pulmonary auscultation with crackles suggests pulmonary edema particularly in the presence of an elevated jugular venous pressure. Given the association between peripheral arterial disease and adverse cardiac events, findings consistent with peripheral vascular disease increase the patient's risk for ischemic events. Therefore, auscultation and palpation of the carotid arteries as well as the distal extremities can be revealing.

Preoperative cardiac testing may be necessary in patients whose clinical evaluation places them at an unclear or increased risk for cardiac complications. The most basic cardiac test is a routine electrocardiogram. According to the 2014 ACC/AHA Guidelines on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery [15], routine preoperative electrocardiographic testing "may be considered" except in asymptomatic patients prior to low-risk surgery. An ECG is "reasonable" in patients with coronary artery disease, arrhythmias, peripheral artery disease including cerebrovascular disease, and any structural heart disease. The guidelines specifically note that ECG findings rarely affect risk stratification but can be useful as a baseline for comparison in the setting of postoperative complications. A retrospective review of 23,036 surgical patients identified a 1.8% incidence of cardiac complications among patients with an abnormal ECG and a 0.3% incidence of cardiac complications among patients with a normal ECG [16]. In patients undergoing low- or intermediate-risk surgery, there was only a 0.5% incidence of cardiac complications among the entire population. With this in mind, while electrocardiography is relatively inexpensive and available to most clinicians, its routine use in low-risk surgery for a low-risk population is not recommended.

The assessment of left ventricular function is also not required because in patients without evidence of active congestive heart failure, echocardiography will not affect clinical outcome. However, in patients with evidence of ongoing or recent heart failure, the preoperative optimization of cardiac status will improve not only the patient's long-term event rate but also the patient's risk for perioperative exacerbation of heart failure. For example in a study of patients undergoing high-risk vascular surgery, the echocardiographic determination of an ejection fraction less than 35% had only a 50% sensitivity and 91% specificity in predicting postoperative myocardial infarction or death [17]. Similarly, in a patient with a known cardiomyopathy and stable symptomatology, routine echocardiography is not necessary preoperatively though could be considered if deemed appropriate to optimize long-term care. Therefore, in patients with a history of congestive heart failure with a recent or ongoing exacerbation, preoperative echocardiography should be considered [18]. Additionally, in a patient with dyspnea from an unknown etiology, echocardiography could be used to exclude previously undiagnosed structural heart disease and is therefore indicated. In summary, preoperative assessment of left ventricular function is recommended only in patients with a recent change in their left ventricular function or a recent change in their clinical status suggesting congestive heart failure. Chronic, stable left ventricular dysfunction does not warrant routine assessment.

Preoperative stress testing is appropriate in a patient with elevated operative risk (with at least one or more unfavorable Revised Cardiac Risk Indices) with a limited or unknown exertional tolerance. In a patient able to complete at least 4 METS of activity, it is "reasonable to forgo" stress testing [15]. There is no role for stress testing in a low-risk patient awaiting low-risk surgery.

As there are multiple available modalities for preoperative stress testing, deciding which to perform requires both clinical judgment and a familiarity across a range of techniques. The gold standard is a routine treadmill test, the benefits of which include the determination of functional capacity, the measurement of blood pressure and the heart rate response to exercise, and assessment of ischemic burden. In a population awaiting vascular surgery, and thus patients enriched with coronary artery disease, routine treadmill testing has a 74% sensitivity and a 69% specificity for predicting cardiac complications [17]. While the negative predictive value is high (98%), the positive predictive value is only 10%. Therefore, routine treadmill testing is a reasonable way to reassure the patient and the surgeon that the operative risk is low. However, many patients proceeding with orthopedic surgery have a markedly reduced exertional tolerance based upon their underlying orthopedic condition. With this in mind, pharmacologic testing is often necessary. In such testing, vasodilators—including dipyridamole, adenosine, or regadenoson—are often combined with radiotracers (technetium or thallium in SPECT and fluorodeoxyglucose in PET) to localize regions of poor perfusion. Distal to an obstructive lesion in a coronary artery, the adenosine receptor is upregulated to maximize endogenous vasodilatation to optimize coronary flow. The amount of vasodilatation induced by exogenous adenosine or dipyridamole (which decreases the breakdown of adenosine) is inversely proportionate to the severity of the stenosis. Therefore, the greater the stenosis in an artery, the less the pharmacologic agent will induce vasodilation, and therefore the less the increase in perfusion seen with Adenosine or Dipyridamole.

In a study of 1179 patients undergoing vascular surgery, the extent of myocardial ischemia on vasodilator perfusion imaging strongly correlated with the risk of postoperative cardiac events [19]. If the extent of myocardial ischemia was less than 20% of the left ventricle, there was no significant increase in the risk of cardiac events. The likelihood ratio increased to 1.6 if 20–29% of the myocardium was ischemic, to 2.9 if the extent of myocardial ischemia was 30–50%, and to 11 when greater than 50% of the ventricle was at jeopardy. Perfusion imaging with vasodilators has been well validated to stratify risk for postoperative cardiac events in a high-risk population [20].

Dobutamine stress testing can also be used to risk stratify. Dobutamine increases myocardial oxygen demand by agonizing the beta-1 receptor. However, its beta-2 agonism has the disadvantage of potentially causing hypotension. Likewise, dobutamine stress testing is poorly tolerated by many patients with an incidence of refractory chest pain and arrhythmias approaching 2% [21]; dobutamine is therefore relatively contraindicated in patients with ventricular or atrial arrhythmias, refractory hypertension, or ongoing hypotension. In contrast, dobutamine stress echocardiography is well validated as a risk stratifier for perioperative cardiac events with a sensitivity of 85% and a specificity of 70% [17]. The negative predictive value is reported to be as high as 100% with a positive predictive value in the 25–48% range. Several studies have compared perfusion studies and dobutamine echocardiography for preoperative risk assessments [20]. Ultimately, the sensitivity and specificity are comparable, and choosing which study is appropriate should be determined by availability and local expertise.

A number of emerging modalities are also being more commonly used to assess ischemic burden and coronary anatomy. Coronary CT angiography has a reported 96% sensitivity and 74% specificity for predicting obstructive coronary artery disease in the individual patient [22]. CT angiography also has the advantage of characterizing and quantifying nonobstructive soft plaque which tends to be more unstable and at greater risk for rupture. In a 2015 prospective analysis of 955 patients older than 45 undergoing noncardiac surgery (56% orthopedic procedures), the addition of coronary CTA

to the RCRI significantly more accurately identified patients at risk for adverse cardiac events by 30 days post op [23]. However, the addition of CTA also significantly overestimated the risk in patients who did not experience adverse events. Interestingly, of the patients who had a post-op MI, 24% had nonobstructive CAD on CTA, and 4% had a normal CTA without CAD. In a meta-analysis, MRI has been reported to have a sensitivity of 83% and a specificity of 86% in predicting ischemia [24]. Further when weighted perfusion modalities are employed, test performance improves to 91% sensitivity and 81% specificity. While MRI has been analyzed preoperatively for major high-risk surgery [25], there are currently limited published data utilizing MRI in the intermediate-risk population. Data are currently too limited to recommend routine use of either coronary CTA or cardiac MR for preoperative risk assessment.

Stress testing and imaging modalities predict risk of myocardial ischemia which logically correlates with the risk of postoperative demand ischemia. However, stress testing does not necessarily predict the risk of plaque rupture, the pathological process accounting for up to 50% of postoperative myocardial infarctions. As such, biomarkers should therefore be considered to assess the risk of perioperative plaque rupture. High-sensitivity C-reactive protein (hsCRP), a marker for vascular inflammation, has received considerable attention. Expressed in smooth muscle cells and atherosclerotic arteries, the hsCRP has been associated with increased plaque vulnerability, increased expression of adhesion molecules, induction of nitric oxide, altered cardiac function, and inhibition of lipolysis [26]. All these histological variables increase the patient's risk for plaque rupture. Additionally, an elevated hsCRP is associated with an increased risk of postoperative MI following vascular surgery [27]. While statins have been shown to reduce hsCRP and reduce perioperative cardiac events in a high-risk population (to be discussed separately), there are no published trials supporting the routine assessment of perioperative hsCRP to guide surgical management—including the initiation of statin. Thus, while it is reasonable to consider checking hsCRP prior to high-risk surgery, no well-informed recommendations concerning its use in the preoperative setting have been formulated.

Brain natriuretic peptide (BNP) has been well validated as a marker for increased myocardial wall stress, which may at times be related to impaired compliance due to myocardial ischemia [28]. Specifically, N-terminal pro-BNP has been shown to be a predictor of heart failure and cardiac events in the general population [29]. Likewise, a severely elevated preoperative BNP suggests the presence of decompensated congestive heart failure and/or increased wall stress which increases the patient's risk for cardiac events. This has been validated in multiple trials of patients undergoing high-risk surgery [30–32]. In a meta-analysis of 2179 patients undergoing noncardiac surgery, a BNP >92 mg/L was associated with an increased incidence of death or MI at 30 days post-op [33]. The association is so strong that the Canadian Cardiovascular Society guidelines on preoperative cardiac risk assessment recommend checking pre-op BNP in patients older than 64, or patients age 45–64 with cardiovascular disease or at least 1 Revised Cardiac Risk Index [34]. While routine preoperative BNP determination is not recommended by the American College of Cardiology, assessing BNP in a patient with a limited exertional tolerance and a history suggestive but not diagnostic of CHF may confirm or exclude the diagnosis and alter treatment strategies.

Troponin is a sensitive marker of myocardial ischemia in patients with clinical evidence of obstructive coronary artery disease. Preoperative ischemia or unstable cardiac plaque increases the risk of postoperative myocardial events. Elevated preoperative troponin is associated with increased postoperative morbidity and mortality in a population with risk factors [35]. However, routine assessment of troponin preoperatively is not recommended. If a patient presents with evidence of acute onset or active ischemic heart disease, assessment of troponin is logical. A thorough history and physical examination as well as additional cardiac testing would routinely be implemented in such a patient. Routine assessment of troponin in a patient without additional evidence of myocardial ischemia awaiting orthopedic surgery is not appropriate.

The Optimization of Cardiac Conditions Affecting Postoperative Outcome

Pharmacologic Therapy

The goal of the perioperative management of the orthopedic patient is to optimize the patient's condition before proceeding to the operating room and thereby to minimize perioperative cardiac events. The potential benefits of a therapy include reducing the patient's risk of perioperative cardiac events as well as reducing the long-term consequences of the cardiac pathology. However, all interventions carry a risk. Whether pharmacologic or interventional in nature, the risk of these therapies must be weighed against the potential benefit.

One of the most hotly debated pharmacologic therapies for perioperative care is beta-blockade. There are multiple mechanisms via which such therapy could theoretically reduce the risk of cardiac events. Reduced heart rate and myocardial contractility decrease myocardial oxygen demand. The slower heart rate also allows increased diastolic flow through the epicardial coronaries, increasing myocardial perfusion. Additionally, the pharmacologically reduced adrenergic stimulation stabilizes plaque and reduces susceptibility to ventricular arrhythmias.

However, despite these advantages, there are conflicting data about the role of beta-blocker in the perioperative setting. The Perioperative Ischemic Evaluation (POISE) trial included 8351 surgical patients considered high risk based on their age (>45 years) and the presence of ischemic heart disease (≥3 risk factors) all undergoing major surgery [36]. High-dose beta-blocker was initiated immediately preoperatively. Specifically, metoprolol succinate 100 mg was given 2–4 h prior to surgery, as well as an additional dose 6 h postoperatively (and potentially 12 h later), achieving an average dose of 400 mg of metoprolol in the immediate perioperative setting. Not surprisingly there was a significantly increased incidence of bradycardia and hypotension in the treated group. While the 30-day cardiovascular event rate was reduced by 17% in patients receiving beta-blocker, this benefit was offset by an increased incidence of stroke as well as a 33% increase in all-cause mortality in the treated patients. Additional analysis suggests that the high and rapid dosing of the beta-blocker resulted in hypotension and thus caused cerebrovascular and cardiovascular hypoperfusion and the higher instances of stroke and mortality.

In the DECREASE trial [2], 112 patients with abnormal stress tests awaiting vascular surgery received bisoprolol at 2.5–5.0 mg daily for at least 1 week preoperatively titrated to a stable heart rate in the perioperative period. There was an 89% decrease in the incidence of cardiac events at 1 month which persisted at 3-year follow-up; notably there was no increased incidence of stroke seen with beta-blocker use [37]. Earlier Mangano and colleagues determined that atenolol given pre- and postoperatively to 200 high-risk patients—defined as having at least two cardiac risk factors or known ischemic heart disease—reduced cardiac events at both 6 months and 2 years postoperatively [38].

Beta-blocker therapy has also been evaluated in low surgical risk patients and found to be ineffective perioperatively. Examples include the POBBLE trial which enrolled 103 low-risk patients proceeding to vascular surgery who received metoprolol in the perioperative setting [39]. No change in the 30-day event rate was noted. Similarly the Metoprolol after Vascular Surgery (MaVS) trial confirmed that metoprolol did not reduce the risk of adverse events in a comparable low-risk population [40]. In this study, up to 90% of the patients had two or less risk indices and 60% had less than or equal to one.

In an attempt to reconcile these discrepant studies, Bangalore and colleagues [41] published a meta-analysis confirming that the greater the preoperative risk of the patient, the greater the risk reduction from preoperative beta-blocker therapy. Specifically, 16 fewer nonfatal myocardial infarctions per 1000 patients occurred in those treated with beta-blocker, a benefit occurring at the expense of three additional strokes and three additional fatalities. Multiple subgroup analyses suggest that heart rate control is appropriate but not at the expense of hypotension [42]. A 2014 review of 17 studies including 16 randomized controlled trials confirmed that initiating beta-blocker within 24 h of surgery decreases nonfatal MIs but increases stroke and all-cause mortality [43]. Based upon this review, the American College of Cardiology and American Heart Association recommend beta-blockade only in patients who are taking them prior to surgery in order to avoid rebound effects associated with early discontinuation [15]. According to the ACC/AHA, beta-blockers should be considered in patients with intermediate- or high-risk preoperative testing or at least three RCRI factors [15]. With this in mind, the early implementation of a long-acting beta-blocker without sympathomimetic activity can be considered. In such circumstances, bisoprolol, metoprolol succinate, or atenolol at low doses should be initiated more than 1 day (ideally >1 week) preoperatively to confirm tolerability. Beta-blockade should not be initiated on the day of surgery and should not be given at the expense of stable blood pressure or heart rate, as this increases the risk of hypoperfusion and cerebrovascular ischemia. While there is no data-based consensus on the duration of therapy, continuation of beta-blocker (assuming a stable blood pressure) for at least 28 days postoperatively seems reasonable as this is the timeframe during which catecholamines remain elevated.

Aspirin therapy in the perioperative setting should also be considered. Mechanistically, aspirin reduces vascular events by inhibiting platelet function and aggregation, thereby decreasing the risk of plaque destabilization and coronary thrombosis. Aspirin exhibits proven benefits in secondary prevention of cerebrovascular as well as cardiovascular therapy and is indicated in a high-risk population for primary prevention. However, aspirin also has inherent risks including increased risk of perioperative hemorrhage. Oscarsson and colleagues [44] randomized 220 high-risk patients to low-dose (75 mg) aspirin or placebo 1 week preoperatively and found a significantly reduced risk of cardiac complications (1.8% incidence) in the aspirin group vs. the placebo group (9% incidence). No greater incidence of bleeding was noted in the aspirin group. Burger [45] analyzed 41 studies including 45,590 patients who underwent surgery on aspirin and found a 1.5-fold increase in the incidence of bleeding complications without an increase in the severity of the hemorrhage. Most recently, Devereaux and associates in the POISE-2 trial evaluated approximately 10,000 patients at increased risk for vascular events undergoing noncardiac surgery, 39% of which were undergoing orthopedic procedures [46]. Patients who received perioperative aspirin not only experienced no reduction in perioperative death or nonfatal myocardial infarction but also suffered a greater incidence of major bleeding and acute kidney injury requiring dialysis. Notably, in patients who had been on aspirin preceding the test but who discontinued it during the trial period, there was no greater incidence of thrombotic events or

infarctions. Importantly, the trial did not include patients who had recently undergone implantation of a cardiac stent. With this in mind, perioperative aspirin cannot be recommended in patients who have not recently undergone stent implantation or recent acute coronary syndrome.

Inhibition of the renin-angiotensin system is an additional pharmacologic modality to be considered in the perioperative setting. The logic for angiotensin converting enzyme inhibition or angiotensin receptor blockade in the preoperative setting includes their role in improving endothelial function, their anti-inflammatory properties, and the potential inhibition of atherogenesis. Also in the setting of left ventricular dysfunction, ACE inhibitors improve myocardial function when employed long term. The QUO VADIS trial compared preoperative quinapril versus placebo in patients undergoing cardiac surgery. A reduced risk of cardiovascular events at 4 weeks as well as 1 year postoperatively was demonstrated [47]. However, this occurred at the expense of symptomatic hypotension and a decreased response to vasodepressors.

Perioperative ACE inhibition increases postoperative vasodilatation, particularly in the setting of epidural anesthesia. Paralleling the postoperative beta-blocker experience, the resulting postoperative hypotension may contribute to cerebral and coronary hypoperfusion. Additionally, the hypotension may interfere or delay mobilizing the patient. Physical therapy instituted early after surgery reduces the risk of venous thrombosis and hospital-acquired infections. Thus, hypotension, whether provoked by volume depletion, the effects of anesthesia/analgesia, or antihypertensive agents (beta-blockers, ACE inhibitors), delays mobilization due to symptomatic orthostasis. With this in mind, Hospital for Special Surgery guidelines recommend discontinuing ACE inhibitors at least 24 h prior to surgery and reinitiating them postoperatively only in the setting of stable hemodynamics. ACE inhibition should not be empirically initiated prior to surgery given this increased postoperative risk.

Calcium channel blockers reduce myocardial oxygen demand similar to beta-blockers. However, short-acting dihydropyridine calcium channel blockers increase chronotropy and may increase ischemia. There are very limited data supporting a cardiovascular benefit of calcium channel blockers in the perioperative setting. Wijeysundera published a meta-analysis of 11 trials (1007 patients) that suggests a reduction in perioperative ischemic events and supraventricular arrhythmias without a significant decline in myocardial infarctions or death [48]. Thus the continuation of calcium channel blockers in the perioperative setting is recommended. Conversely the preoperative initiation of calcium channel blockers is not appropriate given the risk of postoperative hypotension in the absence of proven clinical benefit.

Nitroglycerines create hemodynamic changes that theoretically benefit patients in the perioperative setting. Coronary vasodilatation increases coronary perfusion; selective venodilatation reduces preload and left ventricular wall stress. Both of these effects decrease myocardial oxygen demand and reduce ischemia. An early trial assessed intravenous nitroglycerin in the perioperative setting finding a decreased incidence of perioperative ischemia in high-risk patients with known angina or documented coronary disease but with no reduction in death or myocardial infarctions [49]. There was also an increased risk of hypotension. The American College of Cardiology guidelines state that nitroglycerine is not recommended but may be considered in the perioperative period.

Central acting alpha-2 agonists potentially afford perioperative benefits by decreasing noradrenergic stimulation by inhibition of the postganglionic receptor. This decreased catecholamine surge should empirically reduce the risk of cardiac events. In the European Mivazerol Trial [50], 1897 patients with known ischemic heart disease undergoing intermediate- or high-risk noncardiac surgery were randomized to the alpha-agonist or placebo with a decreased risk of death or MI noted only in patients undergoing vascular surgery; patients undergoing intermediate-risk surgery received no benefit from mivazerol. A meta-analysis of 23 randomized trials found no statistical benefit to alpha-agonism in nonvascular surgery [51]. Devereaux and associates [52] in POISE-2 found that administering clonidine immediately preoperatively not only did not reduce death or nonfatal myocardial infarction but also increased the incidence of nonfatal cardiac arrest as well as hypotension and bradycardia. The American College of Cardiology guidelines therefore state that alpha-2 agonists are not recommended at the time of noncardiac surgery.

3-Hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins) should logically reduce perioperative cardiac events due to their plaque stabilizing effects. They are currently indicated for secondary prevention as well as primary prevention in patients without previously established coronary artery disease but with known peripheral arterial disease. Histologically, their pleiotropic effects stabilize plaque and reduce the likelihood of plaque rupture. Statins decrease lipid oxidization making them less avidly absorbed by macrophages to form foam cells. Statins have an anti-inflammatory effect that reduces matrix metalloproteinase, and they reduce myocardial cell death. Each of these histological effects should logically be favorable in the perioperative setting.

Several trials have evaluated the role of statins in the perioperative setting. Fluvastatin has demonstrated a beneficial effect in vascular surgery [53]. Likewise, atorvastatin 20 mg daily reduced cardiac events immediately following vascular surgery as well as 6 months later [54]. A meta-anal-

ysis including over 223,000 patients demonstrated a 44% reduction in perioperative mortality among statin users (with a 59% reduction among statin users undergoing vascular surgery) [55]. An additional 2015 meta-analysis confirmed a reduced incidence of death, MI, and CVA among statin users following vascular surgery [56]. Data for intermediate- or lower-risk surgery are not as robust. In a retrospective analysis of patients undergoing intermediate-risk surgery, statin use was associated with a reduced risk of adverse cardiac events including 30-day mortality [57]. Statins do, however, have side effects. Rhabdomyolysis is a rare but very serious side effect with a reported incidence approximating 0.1%; however, there is no reported increased incidence of rhabdomyolysis in the perioperative setting. Myalgias are a frequent complication of statin therapy. In the orthopedic population specifically, the myalgias may be masked by perioperative or orthopedic pains. Likewise, myalgias from statins may complicate the routine treatment of perioperative pain.

With this in mind, the ACC/AHA recommends continuing statins perioperatively [15]. Initiating a statin is "reasonable" prior to vascular and high-risk surgery. Consistent with other cardiovascular guidelines, preoperative therapy should be consistent with routine cardiac therapy. If a patient should appropriately be prescribed statins for primary or secondary prevention, such therapy could be appropriate in the perioperative setting as well. Should a statin be initiated in the perioperative setting, a long-acting statin such as rosuvastatin or fluvastatin would be most appropriate as there is no intravenous statin formulation.

Interventional Therapy

Preoperative coronary revascularization improves myocardial perfusion and decreases the likelihood of demand ischemia. While plaque rupture accounts for at least 50% of postoperative ischemic events, revascularization does not prevent plaque rupture. In fact, disruption of stable plaque releases chemokines that precipitate plaque rupture in nonrevascularized and otherwise stable vessels. Therefore, following percutaneous revascularization, aggressive pharmacotherapy—typically including dual antiplatelet therapy (DAPT)—is critical and may necessitate postponing additional surgeries.

In the Coronary Artery Revascularization Prophylaxis (CARP) trial, 5859 patients from 18 Veterans Administration hospitals awaiting vascular surgery were screened [58]; the 510 patients found to have significant coronary artery disease were randomized to revascularization versus medical therapy. There was no difference in adverse cardiac events perioperatively. It is notable that patients with critical left main disease and severe LV dysfunction were excluded and that patients who underwent CABG had less adverse cardiac events on long-term follow-up.

From these observations, preoperative revascularization preceding intermediate- or low-risk surgery (such as most orthopedic procedures) is not recommended. However, revascularization could be considered if it would improve the patient's long-term risk for cardiac events as is recommended in left main or multivessel CAD with reduced LV function. This must be weighed against the likely need to postpone the orthopedic surgery with the implicit prolonged pain and immobility while awaiting surgery.

Postoperative Considerations and Conditions

Orthopedic Surgery After Coronary Revascularization

Orthopedic surgery after coronary revascularization increases the likelihood of coronary artery (target vessel) restenosis as surgical stress destabilizes atherosclerotic plaque and activates clotting factors. Plaque rupture from percutaneous transluminal coronary angioplasty (PTCA) requires at least 2 weeks to heal. Atherogenesis classically starts 8 weeks following angioplasty. Therefore, the optimal timing for orthopedic surgery after angioplasty is between 2 and 8 weeks after the percutaneous coronary intervention (PCI). Reports from the Cleveland Clinic [59] describe the early experience (1984–1999), when 13.4% of patients who underwent angioplasty a median 11 days prior to major vascular surgery suffered a major cardiovascular complication. In a description of their experience at Mayo (1988–2001), Brilakis and coauthors describe 350 patients who underwent noncardiac surgery within 2 months of angioplasty, including 188 who underwent angioplasty <2 weeks prior to surgery [60]. Only three patients suffered myocardial infarction or death; all three were among the patients who underwent coronary revascularization less than 2 weeks prior to the noncardiac surgery, for an event rate of 1.6% (3/188).

Coronary stenting markedly reduces the likelihood of such target vessel restenosis. However, it takes at least 6 weeks for a bare metal stent to endothelialize, a period during which there is a high risk of stent thrombosis and death in the absence of dual antiplatelet therapy (aspirin plus a P2Y12 receptor blocker). Stent stenosis due to smooth muscle cell proliferation and neointimal hyperplasia starts approximately 12 weeks after stent implantation. Therefore, the ideal time for elective orthopedic surgery is between 6 and 12 weeks following coronary revascularization with a bare metal stent. Note that the ACC/AHA Guidelines recommend delaying noncardiac surgery at least 30 days after BMS [15]. A review of the 207 patients who underwent non-

cardiac surgery within 2 months of PCI with a bare metal stent at the Mayo Clinic revealed eight patients who suffered death or myocardial infarction, all of which underwent surgery within 6 weeks of the stent implantation [61]. In a review from the Netherlands, van Kujik and coauthors report a >50% incidence of major adverse cardiac events after noncardiac surgery less than 30 days after implantation of a BMS [62]; the incidence dropped to 4% when surgery was delayed 3 months following BMS. While perioperative dual antiplatelet therapy did increase the risk of severe bleeding, it did not statistically reduce the high risk of cardiac events in patients with noncardiac surgery early after PCI with BMS.

Stents that elute drugs (drug-eluting stents, DES) to prevent neointimal hyperplasia have a markedly reduced rate of stent restenosis. However, the rate of stent thrombosis without periprocedural dual antiplatelet therapy is significant. First-generation drug-eluting stents (sirolimus-eluting stent [Cypher] and paclitaxel-eluting stent [Taxus]) were associated with significant thrombosis in the absence of 12 months of uninterrupted dual antiplatelet therapy. These stents have been phased out and have not been manufactured since approximately 2011. The currently used DES (everolimus-eluting stent and zotarolimus-eluting stent) require only 6 months of DAPT in patients with stable CAD [63]. Therefore, elective orthopedic surgery should not be performed within the first 6 months following DES implantation in a patient with stable coronary disease. Note that DES implanted in the setting of an MI or acute coronary syndrome requires 12 months of DAPT. The risk of stent thrombosis increases with the number and length of the stents and inversely with the width of the stents. Diabetic patients and smokers have a greater incidence of stent thrombosis. Also, thrombosis of a left main stent or a proximal left anterior descending artery stent is more clinically significant than distal artery or branch vessel restenosis. Therefore, timing of noncardiac surgery after DES should be based upon not only the type of stent but also the number and size of stents, the indication for the stent, and the medical history of the patient.

In summary, elective orthopedic surgery should be performed at least 2 weeks and ideally less than 8 weeks after balloon angioplasty. Surgery should be performed at least 6 weeks following implantation of a bare metal stent. Surgery should be performed at least 6 months following implantation of a drug-eluting stent, but consider a longer duration in a patient with diabetes or tobacco use, with multiple stents—particularly long and narrow stents, or with a prior acute coronary syndrome treated with primary stenting.

If the risk of hemorrhage is acceptable, aspirin should be continued perioperatively without interruption at a dose of at least 81 mg daily. If P2Y12 receptor blockers had been in place prior to surgery, they should be discontinued at the discretion of the surgical team. Typically, clopidogrel (Plavix®, Sanofi Aventis, Bridgewater, NJ, USA) is held for five doses prior to surgery, but consideration should be given to holding it for seven doses prior to spinal surgery or when epidural anesthesia is employed where the results of hemorrhage may be more catastrophic. Prasugrel (Effient®, Eli Lilly and Co, Indianapolis, IN, USA) is typically held for seven doses prior to surgery for full clearance. The decision as to whether to reinitiate DAPT after surgery depends upon many variables including the degree of hemostasis achieved and the concomitant use of additional anticoagulants (vitamin K antagonists, direct oral anticoagulants, heparin) for DVT prophylaxis.

If coronary revascularization is necessary prior to orthopedic surgery, the modality of revascularization should be influenced by the urgency of the orthopedic procedure. If surgery cannot be delayed for 6 months to allow a full course of uninterrupted dual antiplatelet therapy following DES implantation, a BMS is most appropriate but requires postponing surgery for at least 6 weeks (6 weeks of uninterrupted dual antiplatelet therapy plus an additional 5–7 days to allow clearance of the thienopyridine pre-op). If surgery cannot be delayed for 6 weeks, balloon angioplasty is most appropriate but requires delaying surgery 2 weeks to allow the ruptured plaque to heal. The clinician might consider coronary angiography after the patient has recovered from surgery to screen for restenosis and to consider definitive revascularization with a stent.

Patients who have undergone open revascularization with coronary artery bypass grafting (CABG) do not require special or additional consideration. In the Coronary Artery Surgery Study, of the nearly 25,000 patients in the registry, 3368 patients underwent noncardiac surgery over more than 4 years of follow-up [64]; 15% of the surgeries were orthopedic. The incidence of postoperative infarction or death was less than 1% following orthopedic surgery. Among patients who had undergone CABG and subsequent high-risk noncardiac surgery, 2.5% suffered adverse cardiac events. If agreeable with the orthopedic and anesthesia team, aspirin can be considered perioperatively in this population given their increased plaque burden. If open revascularization is necessary prior to orthopedic surgery, there is no empiric need to delay orthopedic surgery; bypass grafts and cardiovascular hemodynamics typically normalize by the time the patient is discharged from the hospital. However, sternotomy incisions and vein graft harvest sites may require weeks to stabilize, and the sternotomy in particular may interfere with the physical therapy necessary to recover optimally from orthopedic surgery [64, 65].

Devices

Monopolar electrical cautery during surgery may interfere with pacemaker or ICD function. Far-field electrical signals from the cautery may be spuriously interpreted by the device

as cardiac myocyte electrical activity [66]. If a patient is pacemaker dependent, the sensing of far-field activity may inhibit the pacing function of the device leaving the patient asystolic. An intracardiac defibrillator may interpret the far-field activity as ventricular arrhythmias and attempt electrical cardioversion. The American Society of Anesthesiologists therefore recommends that in a pacemaker-dependent patient, within 6 months prior to surgery, the device should be evaluated; during a surgery in which monopolar cautery is a possibility, the device should be reprogrammed to asynchronous mode, or a magnet should be placed over the device [67]. ICDs should have their anti-tachycardia algorithms turned off during surgery with ongoing continuous cardiac monitoring and an external defibrillator readily available. Preoperatively, it is therefore critical to determine if a patient with a device is pacemaker dependent. Likewise, details about defibrillator programming including model and manufacturer should be obtained because it is often necessary to interrogate the ICD and validate its function once its programming has been altered or a magnet applied.

Valvular Heart Disease

Valvular heart disease increases the risk of cardiac complications of orthopedic surgery. Catecholamine surges, fluid shifts, and afterload reduction due to peripheral vasodilatation can cause hemodynamic collapse, heart failure, and tachyarrhythmias more frequently seen in patients with significant valvular heart disease. Patients with regurgitant valve disease typically tolerate orthopedic surgery well because the associated afterload reduction from anesthesia reduces systemic vascular resistance allowing a compensatory increase in cardiac output. Stenotic valve disease on the other hand increases the risk of orthopedic surgery, because cardiac output is fixed and cannot compensate in the setting of peripheral vasodilatation.

Symptomatic aortic stenosis carries a very high short-term mortality and morbidity—independent of noncardiac surgery—and therefore requires valve surgery prior to proceeding with elective orthopedic surgery. Patients with asymptomatic severe aortic stenosis (defined as valve area <1.0 cm^2 with mean transvalvular gradient >40 mmHg) often safely wait years prior to elective valve surgery. However, noncardiac surgery carries an increased mortality and morbidity in the setting of severe aortic stenosis. Historically, rates of perioperative morbidity and mortality exceeded 11% and in some studies exceeded 30% [68, 69]. More recent studies, however, suggest a much lower risk. A propensity score-matched control study of all patients undergoing elective noncardiac surgery at Cleveland Clinic between 1998 and January 2009 found a 30-day mortality rate of 2.1% among patients with moderate or severe aortic stenosis (compared with a 1% 30-day mortality among matched controls) [70]. The composite endpoint of 30-day mortality plus nonfatal MI was 5.7% in cases with severe AS and 4.4% in cases with moderate AS. The clinical predictors of adverse events among AS patients include symptoms, severe mitral regurgitation, and significant CAD.

In a review of elective intermediate- and high-risk noncardiac surgeries at Mayo Clinic from 2000 to 2010, there was no statistically significant difference in the incidence of adverse cardiac events in patients with asymptomatic severe AS and matched controls [71]. Patients with symptomatic severe aortic stenosis not surprisingly had increased adverse events mostly driven by heart failure (12.9%) with a nonsignificant trend toward increased 30-day mortality (5.9% vs. 3.1%). Elective orthopedic surgery is therefore not recommended in a patient with symptomatic severe aortic stenosis. In a patient with asymptomatic severe stenosis, the risk of adverse cardiac events may be elevated but not prohibitive. The presence of concomitant obstructive CAD, significant mitral regurgitation, or LV dysfunction increases the risk [72].

Should the orthopedic surgery proceed in the setting of a stenotic aortic valve, strict attention to volume challenges and hemodynamic monitoring may mitigate some of the morbidity. Because cardiac output is preload dependent, the patient should be aggressively volume repleted with arterial blood pressure monitoring and consideration given to right-heart catheterization. Sinus rhythm should be maintained to avoid loss of atrial systole and diastolic function. Systemic vascular resistance should be maintained because the fixed cardiac output prevents a compensatory increase when SVR drops. Phenylephrine should therefore be used to increase SVR without increasing heart rate. Afterload reducing agents should be avoided.

Atrial Fibrillation

Postoperative arrhythmias increase the patient's morbidity, mortality, and length of stay in the hospital. Stress of anesthesia and surgery precipitates arrhythmias. Medical conditions including hypoxia, hypercarbia, electrolyte and acid–base disturbances, exogenous and endogenous catecholamines, and myocardial ischemia are all associated with arrhythmias. Ectopy—both atrial and ventricular—commonly extinguishes without intervention. Ventricular arrhythmias—including torsades de pointes—warrant immediate attention and treatment per Advanced Cardiac Life Saving guidelines.

Atrial fibrillation is the most commonly encountered postoperative arrhythmia and therefore will be discussed here. Its incidence following noncardiac and nonthoracic surgery is reported between 0.2% and 8% [73–78].

Specifically in an orthopedic population, Kahn and coauthors report an incidence of atrial fibrillation or supraventricular arrhythmias of 3.1% among 1210 consecutive total hip or knee arthroplasties; this analysis included patients with a preoperative history of arrhythmias [74]. Further Conwell reported a 0.36% incidence of new-onset atrial fibrillation among over 12,000 recovery room admissions; notably in this study, patients with a history of atrial fibrillation were excluded. A review of New York state discharge data from 1997 to 2013 revealed a 0.7% incidence of new-onset atrial fibrillation following total hip or knee arthroplasty [79].

Risk factors for postoperative atrial fibrillation (POAF) include a history of prior cardiac disease including preoperative paroxysmal atrial fibrillation and structural heart disease (left ventricular dysfunction, valvular heart disease, pericardial disease). Kahn's analysis suggests a possible clue on preoperative electrocardiography as he found a greater incidence of atrial ectopy as well as a left anterior hemiblock on preoperative testing among patients who developed postoperative arrhythmias [74]. Underlying pulmonary conditions including COPD are associated with POAF [76]. Conwell found a greater incidence of pulmonary emboli among her arrhythmia patients with an incidence of <5% among this cohort [78]. Advanced age increases the likelihood of postoperative atrial fibrillation [73, 74, 78].

Postoperative atrial fibrillation has potential significant consequences [75]. The tachycardia may cause myocardial ischemia by increasing myocardial oxygen demand. The loss of atrial systole may decrease cardiac output and increase left ventricular filling pressures causing congestive heart failure. Prolonged arrhythmia (particularly those persisting beyond 48 h) precipitates stunning of the atria with poor flow in the atrial appendage, thereby increasing the likelihood of thromboembolic episodes including strokes.

Rate control is the first step in therapy. Prior to starting pharmacotherapy, the preoperative ECG as well as an ECG in the arrhythmia should be reviewed to exclude an accessory pathway such as Wolff-Parkinson-White syndrome; administration of atrial-ventricular nodal blockers can precipitate conduction down the bypass tract converting the atrial fibrillation to life-threatening ventricular fibrillation. If a bypass tract is observed, most commonly amiodarone or procainamide are used with a low threshold for electrical cardioversion. In the absence of a bypass tract, beta-blockers are considered first-line therapy, though calcium channel blockers are a very good alternative given their availability in an inexpensive short-acting intravenous drip. Digitalis increases vagal tone and is therefore less effective in this population with heightened catecholamines; however, it is often used in patients with borderline hypotension because it will not lower blood pressure. Typically, intravenous dosing of medication is necessary to achieve rapid onset, but oral therapy should also be used concomitantly to allow the patient to be rapidly weaned off the IV medications.

Patient with POAF should be assessed for treatable etiologies. Electrolytes should be normalized with magnesium supplementation to keep the level >2.0 mg/dL. Significant anemia (typically Hgb <7.5 g/dL) or active hemorrhage may require transfusion of blood products. If there is clinical suspicion, pulmonary emboli or myocardial ischemia should be excluded. Hypoxemia should be corrected with supplemental oxygen and its cause clarified and corrected.

Anticoagulation should be considered because the likelihood of intracardiac thrombus increases after 48 h of atrial fibrillation. The risks of anticoagulation postoperatively must be weighed against the benefits. While there are no universally accepted standards, it is usually not necessary to initiate rapid-onset, full-dose anticoagulation in this setting because the arrhythmias are typically self-limited and the patients are often routinely already taking some form of pharmacologic DVT prophylaxis. If the arrhythmia persists beyond 48 h, with the agreement of the surgical team, a vitamin K antagonist (warfarin) or a full-dose direct oral anticoagulant should be started.

Postoperative atrial fibrillation may have long-term implications and requires outpatient follow-up. Mirroring the experience after cardiac surgery [80], postoperative atrial fibrillation after orthopedic procedures often resolves prior to discharge. However, patients with resolved POAF are still at greater long-term risk for thromboembolism [79], suggesting that although the surgery may have precipitated the arrhythmia, patients with POAF have an inherent predisposition. In patients who remain in atrial fibrillation, cardioversion is generally performed. The general approach is to wait approximately 4 weeks before attempting cardioversion. This period is sufficient to allow the postoperative catecholamine surge to abate, maximizing the opportunity for spontaneous conversion to sinus rhythm, thereby avoiding the procedure altogether; likewise the delay allows the volume status and hematocrit to normalize, increasing the likelihood that the rhythm will remain sinus following the cardioversion.

No therapies have proven to provide certain prophylaxis against atrial fibrillation. Beta-blockers logically afford some benefit by reducing the cardiac response to catecholamines. However, cardiac surgery patients who were first started on beta-blockers perioperatively were more dependent on mechanical ventilation and remained in the hospital longer postoperatively [81]. While beta-blockade is an appropriate therapy for atrial fibrillation, it is ineffective for prophylaxis against atrial fibrillation. Other agents have been studied in the cardiac and thoracic surgery patients including amiodarone, magnesium, and statins, but the role of these agents in orthopedic surgery is not defined, and they are not recommended solely for atrial fibrillation prevention.

Myocardial Ischemia

Postoperative myocardial ischemia (PMI) following orthopedic surgery is most commonly detected within 48–72 h of the procedure. The incidence of cardiac injury following orthopedic surgery is reported up to 53% in emergent cases and up to 9% in elective cases [82]. At the Hospital for Special Surgery, Urban and coauthors reported a 0.6% incidence among all surgical cases during a 12-month period with a 6.5% incidence among those patients considered high risk [83].

Myocardial infarction is classifically defined as the elevation of a biomarker (Troponin or CK-MB) beyond the 99th percentile of the upper reference limit in the setting of at least one of the following: typical symptoms, electrocardiographic changes, or cardiac imaging abnormalities [84]. A spontaneous MI (type I) is due to plaque rupture or instability and accounts for 5–30% of post-op MIs. A myocardial infarction secondary to an ischemic imbalance (type II) is due to a supply-demand mismatch, classically in the setting of fixed but stable obstructive coronary disease but also possibly due to coronary vasospasm; this accounts for the significant majority of PMI. Troponin is a very sensitive marker for myocyte injury as it detects increased cell membrane permeability with release of cytosolic components—the earliest stages of cell damage—as well as cell death. Following cell injury, troponin begins to rise after 4 h and peaks after 18–24 h and is detectable for 4–10 days. The height of the peak correlates with the severity and extent of myocardial damage. Troponin can be falsely elevated in the setting of pulmonary embolism, left ventricular hypertrophy, and chronic kidney disease. The immunoassay is also inhibited by circulating immunological factors including heterophile antibody and rheumatoid factor (an antibody disproportionately encountered in patients with rheumatic disease). The creatine kinase-MB fraction lacks specificity following orthopedic surgery given the significant skeletal injury inherent in these procedures.

Interestingly, elevated postoperative troponin is associated with an increased all-cause mortality. In the VISION Study of over 21,000 patients >45 years old who underwent noncardiac surgery from 2008 to 2013, severity of troponin elevation correlated with risk of 30-day all-cause mortality [85]. Notably, 93% of patients with elevated troponin were asymptomatic. In an intermediate- to high-risk population undergoing high-risk surgery, elevated troponins predicted 8-year all-cause mortality [86].

Electrocardiography has neither the specificity nor the sensitivity of troponin for postoperative myocardial injury. Although ECG changes do prognosticate for adverse cardiac outcomes in the setting of an abnormal troponin in patients who underwent vascular surgery, electrocardiography does not provide additional prognostic information [87].

Symptoms are also not a dependable indicator of postoperative myocardial ischemia. Typical ischemic symptoms may be masked by sedation or analgesics; atypical symptoms such as nausea or fatigue may be falsely blamed upon anesthesia. In the POISE trial, up to 65% of patients with documented postoperative myocardial infarction were asymptomatic at the time of the diagnosis.

Perhaps as a consequence of these ambiguities, there are no clear standards for postoperative MI screening. All patients with signs or symptoms suggesting ischemia should be screened with serial troponins and ECGs at 8-h increments for at least 16 h with additional measurements until the level plateaus. ACC/AHA Guidelines state that the usefulness of post-op ECG or troponin is "uncertain" in asymptomatic patients even in those at high risk for ischemia [15]. I favor screening high-risk patients because of the prognostic value of elevated postoperative troponin to predict adverse cardiac events as well as noncardiac mortality [83, 88]. Routine screening of low-risk patients or patients undergoing low-risk surgery is not recommended, however.

Treatment of postoperative myocardial infarction is similar to treatment of nonoperative acute coronary syndrome [89]. Pharmacologic therapy should include statins with beta-blockade for blood pressure and rate control. Antiplatelet therapy with at least low-dose aspirin should be strongly considered. Antithrombotic therapy with heparin as well as supplemental platelet inhibition with a thienopyridine should be considered if plaque rupture is suspected; these agents are likely not necessary in the setting of demand ischemia due to stable fixed coronary disease. They also carry a greater risk of hemorrhage and must be discussed with the surgical team. Revascularization should be considered in ST elevation myocardial infarction and a very high-risk non-ST elevation infarction; angiography with PCI is preferred over thrombolysis to clarify the cardiac anatomy and to minimize the high risk of surgical sight hemorrhage from thrombolytics. All patients with suspected or confirmed PMI should be watched in a monitored setting.

Summary

In closing, significant cardiac morbidity and mortality is experienced by patients in the setting of orthopedic surgery. The risk to an individual patient can be stratified incorporating clinical information. These clinical characteristics include the patient's functional capacity as well as their medical history, specifically preexisting ischemic heart disease, heart failure, cerebrovascular disease, renal insufficiency, and diabetes. Supplemental testing beyond a thorough history and physical examination are only necessary in patient deemed to be at high risk based on the aforementioned clinical criteria. The maintenance of ongoing cardiac pharmaco-

therapy is generally appropriate; initiation of beta-blocker should be considered in the higher-risk population, ideally at least a week in advance of the procedure. Finally preoperative coronary revascularization does not reduce the risk of orthopedic surgery and therefore should only be performed to reduce the patient's lifetime risk of adverse cardiac events.

Summary Bullet Points

- The risk of orthopedic surgery can be accurately determined based upon clinical assessment as well as diagnostic testing.
- Pharmacologic therapy may reduce the risk of cardiac complications when utilized in the appropriate setting.
- Interventional therapy does not reduce the risk of cardiac complications of orthopedic surgery and is appropriate only to reduce the patient's long-term risk of adverse cardiac events.
- Patients presenting for orthopedic surgery often have complex cardiac conditions that require preparation to manage optimally.
- The diagnosis and management of postoperative cardiac complications is similar to the management of these conditions in the nonoperative setting.
- Severe aortic stenosis increases perioperative morbidity and mortality, particularly if symptomatic and if accompanied by significant mitral insufficiency and coronary artery disease.

Case Study

An 80-year-old woman is seen for cardiac evaluation prior to hip replacement surgery. She has a history of hypertension managed with amlodipine and hyperlipidemia managed with rosuvastatin. She suffered an episode of confusion with near loss of consciousness 7 years prior and was told she had a TIA. She therefore takes a daily aspirin. Until 4 years ago, she had been very athletic, regularly walking 2 miles in 40 minutes with her husband. Her exertional tolerance has severely diminished mostly due to her orthopedic pains; she currently walks only around her house and last walked four blocks over 2 years ago. She reports mild, non-limiting dyspnea with walking without chest pain or dizziness. She has not seen a cardiologist since her TIA 7 years ago. Examination in your office is notable for stable vital signs with BP of 120/70 and HR of 65 and cardiac auscultation with a late-peaking crescendo-decrescendo murmur at the base with a diminished but audible S2 without a paradoxical split. A soft holosystolic murmur is appreciated at the apex. Her lungs are clear and extremities without edema.

Based upon her cardiac exam, she undergoes an echocardiogram that confirms aortic stenosis with valve area of 1.1 cm^2 and mean transvalvular gradient of 38 mmHg. LV is mildly hypertrophied with normal systolic function. There is mild mitral insufficiency. By strict criteria, her aortic stenosis is moderate (severe stenosis = valve area <1.0 cm^2 with mean gradient >40 mmHg); however, the stenosis is significant and borderline severe. She also reports mild exertional dyspnea. She therefore undergoes an adenosine technetium perfusion study which is normal and therefore excludes severe obstructive CAD.

So this 80-year-old woman has significant (but not severe), asymptomatic aortic stenosis in the setting of one RCRI risk factor (history of TIA = cerebrovascular disease) awaiting intermediate-risk surgery. Her risk of adverse cardiac events is elevated but not prohibitive. After discussions with the patient whose quality of life is compromised by her orthopedic condition and not responding to palliative medical therapy, the decision is made to proceed with surgery. She continues her medications including the calcium channel blocker and statin up until and including the day of surgery. Low-dose aspirin is continued as well, given her history of TIA; this decision is debatable based upon data from POISE-2. Beta-blocker is not initiated given her stable vital signs and the absence of ischemic heart disease.

The surgical course is notable for mild hypotension for which phenylephrine is initiated to maintain BP without compromising systemic vascular resistance. She is also volume loaded with saline. By post-op day 1, phenylephrine is weaned off. She is only tolerating clear liquids in the setting of a mild post-op ileus, so maintenance IVF is continued. On post-op day 2, she reports palpitations found due to atrial fibrillation with a rapid ventricular response. Her blood pressure remains normal, so amlodipine is stopped and diltiazem drip is initiated and titrated to maintain ventricular rate <80 bpm. Oral metoprolol tartrate is started in the meantime. Hypoxia, ischemia, and anemia are excluded. Electrolytes are corrected with intravenous magnesium to keep Mg >2.0. On post-op day 4, her rhythm converts to sinus, and metoprolol is changed to long-acting once daily succinate.

Notably, aspirin 325 mg bid had been started on post-op day 0 for DVT prophylaxis. On post-op day 2, when she converted to atrial fibrillation, this was changed to a direct oral anticoagulant (Xarelto®, Janssen Pharmaceuticals, Beerse, Belgium). For the first 24 h, prophylactic dose (Xarelto 10 mg) was given; once hemostasis was established, the dose was increased to full therapeutic dose (20 mg). Despite converting to sinus rhythm, she is at increased risk for atrial fibrillation after discharge. She is therefore discharged on full-dose oral anticoagulation with beta-blocker, and she will follow up with cardiology 2 weeks later.

This case demonstrates the perioperative management of a patient with aortic stenosis, a condition that increases oper-

ative risk but can typically be managed with strict attention to hemodynamics. The vignette also includes an episode of postoperative atrial fibrillation, which is commonly encountered and also effectively managed with medical therapies.

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Perioperative Care of the Orthopedic Patient with Chronic Pulmonary Disease

14

Kethy M. Jules-Elysée

Objectives

- To appreciate the contribution of chronic pulmonary disease to the genesis of postoperative complications
- To demonstrate the utility of such preoperative testing as serum albumin, arterial blood gases, and the spirometric assessment of pulmonary function
- To demonstrate the importance of chronic pulmonary disease such as asthma, chronic obstructive lung disease, and pulmonary hypertension in the perioperative context
- To present a logical approach to the preoperative evaluation of patients with chronic pulmonary disease

Key Points

- Chronic pulmonary disease is a potent contributor to problems of both a pulmonary and nonpulmonary nature in the postoperative setting.
- Pulmonary problems rival, if not exceed, the cardiac domain in their importance in the perioperative clinical setting.
- The preoperative evaluation should assess chronic pulmonary disease in its several variations, pulmonary hypertension, congestive heart failure, and impairment in cognitive and functional capacity as risk factors.

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Introduction

Although the prevention and management of postoperative cardiac complications have received more attention in the medical literature, postoperative pulmonary complications (PPCs) are associated with comparable mortality rates, similar prolongation in length of hospital stay, and may occur more frequently [1, 2]. One large study (1055 patients) reported a 2.7% incidence of pulmonary complications in patients whose surgery was rated to be low to moderate risk, for example, orthopedic surgery. Those who experience with such postoperative problems had a markedly longer length of stay (27.9 vs. 4.5 days) [3]. Further of all major postoperative medical complications, PPCs are the most costly. Box 14.1 shows that the most common pulmonary complications after noncardiac surgery are pneumonia (usually aspiration), respiratory failure, and atelectasis [4–6]. Respiratory failure is the most worrisome as it is associated with prolonged mechanical ventilation, increased length of stay in the intensive care unit, and higher mortality. A history of functional limitation, cardiac failure, COPD, current smoking practices, age ≥ 60 years, and an American Society of Anesthesiology (ASA) category ≥2 are associated with increased risks for such problems [7]. Duration of surgery is also important [8] as is the number of packed red blood cells given during surgery. The transfusion of more than four units also increases the risk of PPCs [9]. However, several additional problems are also relevant in the orthopedic setting where fat embolism syndrome [10] and venous thromboembolism [11] are more frequently seen, especially after total joint arthroplasty of the hip and knee. Further, obstructive sleep apnea (OSA), a problem associated with respiratory complications after surgery, is prevalent in the orthopedic patient population [12]. This is discussed in another chapter (Chap. 19). Finally, there is the underappreciated problem of pulmonary hypertension, a condition associated with OSA as well as several of the connective tissue diseases. Due to their relevance in the postoperative orthopedic setting, this chapter will focus on these major pulmonary conditions.

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Box 14.1 Postoperative Pulmonary Complications

- General complications
- Atelectasis
- Infection
- Bronchitis
- Pneumonia
- Bronchospasm
- Pulmonary embolism
- Exacerbation of underlying chronic lung disease
- Respiratory failure and prolonged invasive or non-invasive ventilation
- Fat embolism syndrome with acute respiratory distress syndrome (ARDS)

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The Preoperative Evaluation

Identification of Conditions That Affect Postoperative Pulmonary Outcome

The general approach to the preoperative evaluation is developed in Chap. 1. Nonetheless, with respect to the prediction of postoperative pulmonary complications, a number of pulmonary-specific considerations are noteworthy. For instance, the history should focus on such symptoms as wheezing, coughing, sputum production, exercise tolerance, orthopnea, and paroxysmal nocturnal dyspnea. The physical examination is focused on the presence of such findings as dyspnea, wheezing, cough, or sputum production or, in more severe cases, cyanosis; other key findings include edema, raised jugular-venous pressure suggesting the presence of cor pulmonale, or heart failure. Pulse oximetry to determine the resting oxygen saturation should be obtained as part of the routine examination. Such physical findings are important, as, in one study, abnormal findings on lung examination were the strongest predictors of PPC. The STOP questionnaire may be useful in identifying patients with possible OSA [13].

The laboratory may also add important information. An elevated hematocrit in patients with suspected pulmonary disease suggests chronic hypoxemia. Electrolytes are also helpful as bicarbonate elevations may be indicative of carbon dioxide retention. Less appreciated is the significance of a serum albumin as a low albumin level is not only a predictor of 30-day perioperative morbidity and mortality [14] but also a predictor of pulmonary complications. In one study, patients with levels of <36 g/L had a PPC rate of 27.6% vs. 7% in patients with normal levels [15]. An elevation of the blood urea nitrogen (BUN) greater than 30 mg/dL is also associated with elevated risk of PPC [16].

Arterial blood gases may be performed in conjunction with pulmonary function testing and help in the estimation of the severity of underlying pulmonary disease. Hypoxia confirms the need for supplemental oxygen, whereas an elevated CO_2 suggests respiratory insufficiency and the need for supportive measures (BiPAP, mechanical ventilation) postoperatively. As mentioned, a concomitant elevation in serum bicarbonate suggests chronic respiratory failure. Currently, arterial blood gas analysis is not recommended to stratify pulmonary complications.

An electrocardiogram should be evaluated for signs of right heart strain including *P*-pulmonale, right ventricular strain (dominant R waves in the septal leads), or right bundle branch block. Chest radiography may confirm hyperinflated lungs consistent with chronic obstructive lung disease and rule out other lung pathology. Spirometry of the lung is the procedure by which lung function is evaluated. In order to facilitate an understanding of the role of such testing, a brief summary of the relevant spirometric patterns is justified.

Measurement of the FEV_1 is the best single measure of pulmonary function, a low FEV_1/FVC ratio being diagnostic of chronic obstructive pulmonary disease (COPD). More formal evaluations such as flow-volume loops are also useful and may distinguish respiratory versus cardiac dyspnea and differentiate both obstructive versus restrictive lung diseases and reversible versus fixed pulmonary conditions (Figs. 14.1 and 14.2). The assessment of peak flow, a parameter analogous to the FEV_1, is easily measured using a simple, portable peak flow meter. It is useful both diagnostically and to follow the course of respiratory function in the postoperative setting.

While spirometric data can be helpful in planning for intrathoracic surgery, their benefit in extrathoracic surgery is not clear. Studies comparing spirometry to clinical data have not shown such testing to be diagnostically superior to the history and physical exam. However, McAlister found an FEV1 <1.0 L to be an adverse prognostic factor for PPC (OR 5.6) [3]. Spirometric assessment does not always predict PPC even in those with underlying lung disease [17]. As most patients identified as high risk by spirometry can be identified by clinical history, such testing should be performed mainly in patients with pulmonary symptoms but without a specific diagnosis. There is one orthopedic setting in which spirometric assessments are routinely employed, however: the patient undergoing complex spine surgery.

Exercise testing, whether formal treadmill or bicycle-based testing, or more simple measures such as the 6-min walk test, has been proposed for use in the preoperative environment. Nonetheless, the pain-related functional limitations in patients facing orthopedic surgery render these techniques of limited value.

With that background, this review now moves to a consideration of a number of chronic conditions known to contribute to the development of pulmonary complications

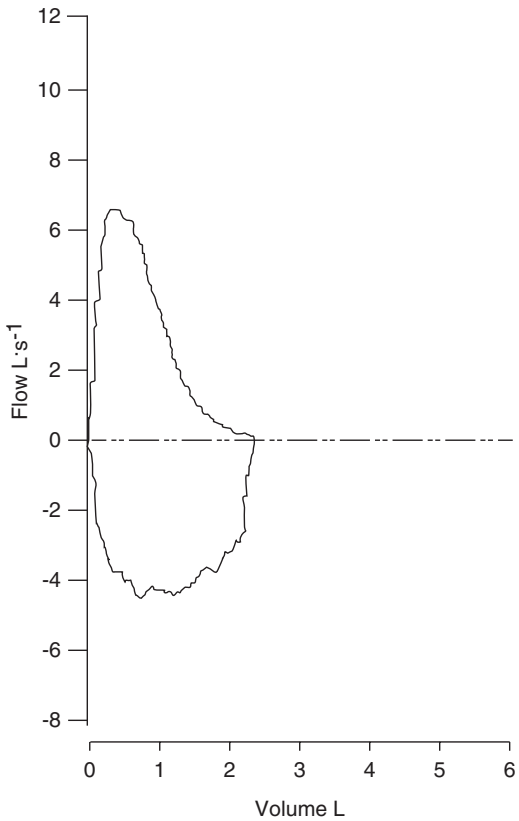

Fig. 14.1 Flow-volume loop of a normal subject with end expiratory curvilinearity, which can be seen with aging. (Used with permission of the ERS © 2019 from Miller et al. [104])

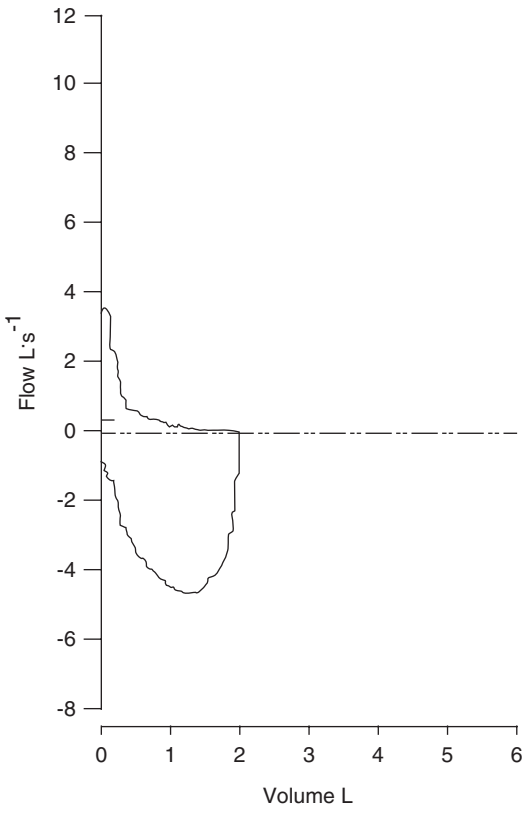

Fig. 14.2 Severe airflow limitation in a subject with chronic obstructive pulmonary disease. (Used with permission of the ERS © 2019 from Miller et al. [104])

after surgery (Box 14.2). These include chronic lung disease specifically emphysema, pulmonary arterial hypertension, and congestive heart failure. Further an impaired sensorium whether chronic or acute also contributes to an increased risk [18]. Although commonly implicated, conditions such as chronic stable asthma and obesity (even morbid obesity) do not increase the rate of pulmonary complications after noncardiac surgery.

Box 14.2 Risk Factors for PPCs

- Preoperative risk factors
- Chronic obstructive pulmonary disease (COPD)
- Age
- Inhaled tobacco use
- NYHA class II pulmonary hypertension
- Obstructive sleep apnea (OSA)
- Nutrition status
- Congestive heart failure
- ASA class
- Functional dependence

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Chronic Pulmonary Disease

Chronic forms of pulmonary disease are the most commonly identified comorbidities contributing to the likelihood of PPC [15, 16]. When conceptualized broadly, chronic pulmonary diseases are either reversible or irreversible.

Asthma is the prototypical reversible form and is a condition characterized by airway obstruction, inflammation, and hyperresponsiveness [19]. The severity of airway inflammation determines the degree of bronchial hyperresponsiveness and thus disease activity. Disease severity is assessed by the frequency and severity of attacks including hospital admissions, need for intubation, and drug history, especially the use of corticosteroids. In patients with well-controlled asthma, the postoperative complication rate is relatively low [20]. Previously higher complication rates were reported with asthma [21, 22]. In well-controlled asthmatic patients, pulmonary complications are not increased. Modern therapeutic strategies and anesthetic techniques have improved outcome. In asymptomatic patients with history of asthma, the frequency of perioperative bronchospasm may approach that of the non-asthmatic (1.2%) [20]. Patients with active disease may develop a higher incidence of bronchospasm. These patients may benefit from a course

of β2-agonists and systemic steroid pretreatment 5 days before surgery [23].

COPD is characterized by airflow limitation which is not fully reversible (Figs. 14.1 and 14.2). It is also associated with abnormal inflammatory response of the lungs to noxious stimuli, specifically cigarette smoking [24, 25]. This remains the major risk factor of chronic obstructive pulmonary disease (COPD). COPD is the most commonly identified risk factor for PPC with an odd ratio of 1.9 [18]. Patients with COPD have a 2.7- to 4.7-fold increased risk of PPC [18, 26]. It is associated with atelectasis and pneumonia postoperatively. In one study, prolonged ventilation and reintubation rates among COPD patients were 8.8 and 5.5%, respectively [27]. Studies have shown, however, that COPD alone does not predict the likelihood of PPC; other factors such as ASA physical status (Table 14.1), duration of surgery, and duration of anesthesia play a role [28]. In patients undergoing shoulder surgery, the potential for respiratory decompensation should be assessed prior to administering interscalene or supraclavicular block. Both these blocks can lead to diaphragmatic paralysis further compromising lung mechanics [29, 30].

One important pulmonary subgroup frequently seen in the orthopedic setting, specifically with spinal surgery, is the one with patients with spinal deformities who are undergoing major corrective surgery. While such spinal and chest wall deformities as kyphoscoliosis may result in severely restrictive lung physiology, the estimation of the incremental surgical risk is imprecise and not fully appreciated by many perioperative physicians. Physicians experienced in the perioperative care of these patients intuitively understand and recognize the challenge they present in the perioperative context, however. Such patients are discussed in detail in Chaps. 12 and 31.

Pulmonary Arterial Hypertension

Another important but less appreciated problem in the perioperative setting is the patient with pulmonary arterial hypertension (PAH). Defined as mean pulmonary arterial pressure >25 mmHg at rest or 30 mmHg during exercise, this pathophysiological state is characterized by elevated right heart afterload, decreased venous return, and reduced cardiac output. PAH is categorized according to its underlying etiology. Pulmonary hypertension may arise as a consequence of left heart disease, hypoxic pulmonary disorders (for instance OSA), or chronic thromboembolic phenomenon [31]. Owing to its association with a number of connective tissue diseases, this condition is well known not only to the pulmonologist but also to rheumatologists who frequently confront its consequences in patients with such diseases as scleroderma, mixed connective tissue disease, and systemic lupus erythematosus (Chap. 4).

Table 14.1 American Society of Anesthesiologists (ASA) classification

Class	Class definition
I	A normally healthy patient
II	A patient with mild systemic disease
III	A patient with systemic disease that is not incapacitating
IV	A patient with an incapacitating systemic disease that is a constant threat to life
V	A moribund patient who is not expected to survive for 24 h with or without operation

Table: Used with permission of Wolters Kluwer from Owens et al. [61] Rates of Postoperative Pulmonary Complication by Class: I: 1.2; II: 5.4; III: 11.4; IV: 10.9; V: N/A. (Data from: Qaseem et al. [18])

Obesity

In the obese patient, pulmonary physiology is characterized by a decrease in lung volume, ventilation perfusion mismatch, and relative hypoxemia, changes that may become more accentuated by anesthesia and surgery [32]. However, obesity is not considered to be a risk factor for PPC [33].

Congestive Heart Failure

Congestive heart failure (CHF) increases the risk for PPC; Smetana performed a MEDLINE search looking for studies on PPC [16]. There were a total of 10,960 pulmonary complication events among 324,648 patients. CHF increased the risk of PPC with an odds ratio of 2.93. Examining an array of pulmonary risk factors, Arozullah has reported that among potential predictors related to cardiac states, only CHF was a significant predictor, OR 1.3 (95% CI, 1.1–1.5) [34].

Impairment in Cognitive and Functional Capacity

Lastly, there is evidence suggesting that various nonpulmonary conditions also correlate with adverse postoperative pulmonary events. For example, an impaired sensorium, whether acute (delirium due to concomitant medical condition, alcohol withdrawal) or chronic (dementia), increases the rate of pulmonary complications after surgery [16, 34]. Such problems have other important and far-reaching consequences, interfering with the rehabilitative process and complicating discharge planning.

The Optimization of Conditions Relevant to Postoperative Pulmonary Outcome

Turan and associates evaluated 635,265 patients from the American College of Surgeons National Surgical Quality Improvement Program database and found higher mortality and serious postoperative complications in current smokers versus never smokers. The complications included pneumonia, higher intubation rates, cardiac arrest, myocardial infarction, and superficial and deep wound infection [35]. Of note, current smokers were defined as patients who reported smoking the year before admission, while never-smokers were patients who reported not smoking in the previous years and zero lifetime pack-years. Smokers with greater than 20 pack-year smoking history have a higher PPC rate compared to those with a less than 20 pack-year smoking history [36].

Some studies have implied a higher complication rate in patients who have stopped suddenly prior to surgery because of decreased cough and increased sputum production [37, 38]. In a meta-analysis of perioperative smoking cessation and outcomes, Myers and associates found no evidence that quitting smoking for less than 8 weeks before surgery had an impact on outcome [39]. Lindstrom in a group of patients undergoing general and orthopedic surgery found a statistically significant difference in complication rates in controls vs. an intervention group (41% vs. 21%) when smoking cessation started 4 weeks before surgery [40]. Complications were defined as any unexpected event that required treatment or prolonged care. A decreased need for postoperative ventilatory support has also been reported in a group of patients undergoing elective orthopedic surgery after enrolling in a smoking cessation program for 6–8 weeks [41]. Wong and associates, in a meta-analysis of 25 studies, concluded that at least 3–4 weeks of abstinence from smoking decreases respiratory and wound-healing complications [42]. In conclusion, the most effective time to stop smoking has not been well defined in the literature, but there is no evidence that quitting smoking less than 8 weeks prior to surgery leads to any harm.

Smoking is associated with hyperreactive airways and poor mucociliary clearance of secretions. Smokers are more prone to perioperative respiratory complications such as atelectasis or pneumonia even in the absence of underlying chronic lung disease [43, 44]. Besides pulmonary issues, smoking has many effects on bone health including an accelerated loss of bone mineral density, delayed fracture healing, and wound complications (through its effect on immune function), all relevant in the orthopedic setting [45, 46]. In addition, smoking is associated with higher hemoglobin concentration and platelet aggregation increasing the risk of thrombosis. Gronkjaer and associates in a meta-analysis of 9354 studies found that smoking is associated with increased risk of wound complications, infections, and higher ICU admission rates along with pulmonary and neurological complications [47].

Abstinence for 12 h before anesthesia allows time for nicotine clearance, a coronary vasoconstrictor. Nicotine also causes hypertension and tachycardia through its action on the sympathetic nervous system [48]. The presence of carbon monoxide leads to carboxyhemoglobin formation, shifting the oxygen-hemoglobin curve to the left and decreasing oxygen delivery to tissues [49]. Smoking cessation prior to surgery is usually recommended for improvement in ciliary action, macrophage activity, and small airway function, as well as a decrease in sputum production. The correct timing for smoking cessation prior to surgery has been debated. Although it takes about 6 months for recovery of antimicrobial and alveolar macrophage formation [50], smoking cessation for 6–8 weeks improves pulmonary function and diminishes cardiovascular complications [41, 50]. Wound healing improves after 3 weeks of abstinence [51]. Nicotine has a half-life of 1 hour, while carboxyhemoglobin has a half-life of 4 h. Therefore, one day of abstinence should result in much lower concentrations of these substances [51].

Prior to surgery, patients with COPD need to be assessed for quantity and quality of sputum production along with the frequency of their exacerbations. If a change in sputum is noted, the preoperative use of antibiotics may be helpful. A short course of preoperative steroids may also be indicated for severe COPD [52, 53].

Preoperative teaching focusing on techniques of lung expansion maneuvers and mobilization of secretions is imperative. After major surgery, hypoxia may persist postoperatively, especially for patients on opioids [54]. Oxygen supplementation should be given in that time period. Every patient who may be at risk for PPC should use incentive spirometer and undergo deep breathing exercises. Other techniques such as coughing, postural drainage, percussion, vibration, suctioning, and ambulation should be used when indicated. Therapy with any of them is superior to no prophylaxis [55] in terms of fewer abnormalities on chest radiograph and a tendency toward less complication. However, no specific treatment is better than the others [56]. Among the different modalities to maintain lung expansion postoperatively, continuous positive airway pressure (CPAP) may be helpful in the patient unable to perform deep breathing or incentive spirometry exercises [57]. The benefits of CPAP have included a decrease in intubation rates and a lower incidence of pneumonia in patients with postoperative hypoxemia after major abdominal surgery [58]. It has also been found to prevent pulmonary complications when used prophylactically [59, 60].

The Assessment of Perioperative Risk

With the exception of complex spine surgery and bilateral total joint arthroplasty, most orthopedic procedures are generally considered to be of low to intermediate risk. All patients undergoing noncardiac surgery, however, should be evaluated for possible COPD, age older than 60 years, American Society of Anesthesiologists (ASA) ≥ class II, functional dependency, and congestive heart failure all of which are known risk factors for PPC [18]. The higher the ASA class, the greater the risk [61]. Poor exercise tolerance and surgery lasting more than 3 hours carry a higher risk of pulmonary complications [34, 62]. Age also plays an important role especially above 60 years, even after adjustment for comorbid conditions [16]. Even the healthy elderly are at increased risk of pulmonary complication [34, 62] as the odds that a patient experiences pulmonary complications increase statistically with age. Functional dependence has also been identified as a risk factor with total dependence being worse than partial dependence (being able to perform some activities of daily living) (OR 2.51 vs. 1.65) [18, 34].

Several risk prediction tools have been proposed in order to estimate perioperative pulmonary complications by giving a numerical estimate. The ARISCAT tool uses readily available clinical information to arrive at overall incidence of PPC [7], while the Arozullah respiratory failure index helps predict the incidence of postoperative respiratory failure. It takes into account both clinical and laboratory data into their prediction model and is considered to be most useful for research purposes [34]. There are two Gupta calculators presently available; both can be easily found online. The first one uses several preoperative factors to predict postoperative respiratory failure including unplanned intubation/reintubation postoperatively based on information derived from the American College of Surgeons National Surgical Quality Improvement data set [63]. The other Gupta calculator predicts postoperative pneumonia [64].

Pulmonary Hypertension

In the surgical setting, PAH is especially perilous, challenging the medical consultant and anesthesiologist alike. It is important to know the etiology of PAH as it is divided into five categories: essential PAH from left heart disease, chronic lung disease, hypoxia, chronic thromboembolic disease, and multifactorial in origin. The approach to PAH may vary depending on the etiology. Rates of PPC are increased even in patients with mild to moderate disease regardless of etiology of PAH [65, 66]. In the setting of anesthesia, the sustained elevations in pulmonary vascular resistance and pulmonary arterial pressure, coupled with impaired vascular reactivity, may result in significant systemic hypotension. Further the negative inotropic effects of some anesthetic agents may exacerbate this tendency precipitating right heart failure. Simultaneously these adverse left-sided phenomena (systemic hypotension) are further exacerbated by concomitant right-sided responses resulting from hypoxia-mediated pulmonary vasoconstriction. In sum these events set in motion a cascade of adverse sequelae including hypercarbia, acidosis, and the release of catecholamines that, if allowed to progress too far, results in frank circulatory collapse. Reported experience supports these worrisome contentions. Ramakrishna and colleagues observed a 28% incidence of respiratory failure and 7% mortality in patients with PAH ($n = 145$). Factors found to be independent predictors of short-term morbidity in noncardiac surgery have been described (Table 14.2) [67]. In another study, the rate of respiratory failure was 21% in patients with PAH as compared to only 3% of matched controls; in-hospital mortality was also higher in the PAH group [68]. Emergency surgery, coronary artery disease, and systolic pulmonary artery pressure were independent predictors of morbidity. Kaw and colleagues in a cohort study of 173 patients with PAH found higher incidence of congestive heart failure and respiratory failure [69]. They were more likely to require longer periods of ventilatory support. In a retrospective study of 48 patients with PAH undergoing noncardiac emergency surgery, higher complication rates were noted. The rates of morbidity and mortality were 29% and 7%, respectively. In a study by Memtsoudis and colleagues of patients undergoing total hip or knee arthroplasty, using the national database, patients with PAH had a 4- to 4.5-fold index in the adjusted risk for mortality compared to those without PAH [70].

Another concern in patients with pulmonary hypertension is further elevation of pulmonary pressures by either thrombotic events with pulmonary embolism or fat embolism (FES) leading to acute right heart failure. Cardiac arrest due to FES occurring during joint replacement has been reported [10]. Manifestations of FES include respiratory failure, change in mental status, cardiovascular collapse, petechiae rash, pyrexia, and thrombocytopenia [71]. Acutely, however,

Table 14.2 Variables considered independent predictors in a multivariate logistic regression model of short-term morbidity after noncardiac surgery

Characteristic	*p* value	OR (95% CI)
History of pulmonary embolism	0.01	7.3 (1.9–38.3)
New York Heart Association functional class ≥II	0.02	2.9 (1.2–7.7)
Intermediate-/high-risk surgery	0.04	3.0 (1.1–9.4)
Duration of anesthesia >3 h	0.04	2.9 (1.03–4.6)

Used with permission of Elsevier from Ramakrishna et al. [67]
CI confidence interval, *OR* odds ratio

it may cause mechanical neurovascular obstruction further elevating pulmonary arterial pressures. This is followed by a chemical phase characterized by inflammatory damages in the lungs leading to acute respiratory distress syndrome [72].

In PAH, right heart afterload is elevated leading to decreased cardiac output, decreased venous return, and deficient oxygen saturation [73]. A preoperative echocardiogram may help evaluate the right ventricle (RV) which responds to elevated pulmonary pressures by hypertrophy initially followed by dilatation and reduced RV function. This is further complicated by the degree of tricuspid regurgitation. Intraoperatively, the vasodilating effects of anesthetics may help decrease the right ventricular preload and alleviate pulmonary pressures and ventricular ischemia. Postoperatively, however, anesthetic drugs are withdrawn and patients become more prone to decompensation due to surgical stress, pain, fluid shift increasing pulmonary vasculature, and compromising oxygenation and cardiac output [74]. There is an inverse relationship between survival and pulmonary arterial systolic arterial pressure [75, 76]. Anesthesia and surgery may lead to stress, pain, acidosis, and hypoxemia all causing further constriction of the pulmonary vasculature. Although there is no strong evidence to suggest that specific monitoring alters outcome, intraoperative transesophageal echocardiogram and/or pulmonary artery catheter should be considered in patients with severe PAH or in patients with right-sided heart failure. The risks and benefits to the insertion of a pulmonary artery catheter must be considered, however [77].

Patients with significant PAH should be evaluated for specific therapy prior to undergoing elective surgery. The need for therapeutic agents such as vasodilators, anticoagulants, anti-inflammatories, and vascular remodeling drugs should be considered [74]. Calcium channel blockers are first-line agents if the patient has had a positive response to vasoreactivity testing [78]. Prostanoids have also been used with improvement in exercise capacity and survival in patients with PAH. Phosphodiesterase inhibitors such as sildenafil and tadalafil are great vasodilators and have become first-line agents. They work via the nitric oxide cyclic guanylate monophosphate (No-cGMP) pathway, inhibiting the breakdown of phosphodiesterase. Riociguat has a dual mode of action. It works in synergy with endogenous nitric oxide (NO) and stimulates cyclic guanylate cyclase independent of NO. Endothelin receptor antagonists such as bosentan, ambrisentan, and macitentan have improved performance in patients with PAH. They have a vasodilatory and potentially antimitogenic effect on the vasculature. Many patients, however, will present for surgery without such therapy having been initiated. If surgery cannot be postponed, an oral dose of sildenafil may be given prior to surgery. This agent has significant effects on pulmonary pressures, while systemic pressures are not affected as much [79, 80]. Sildenafil can also be given intravenously. Other drugs such as inhaled nitric oxide or inhaled epoprostenol should be readily available. Phosphodiesterase inhibitors such as amrinone or milrinone should be in the operating room. They have an effect on both pulmonary and systemic pressures while increasing cardiac output [81]. In group II patients, with PAH due to left-sided systolic or diastolic heart disease, and left-sided valvular disease, vasodilator therapy may not be well tolerated. Consultation with cardiology may be helpful in the management of these patients. Vasopressin may be used to maintain systemic pressure [82]. It has less effect on pulmonary pressures when compared to other agents used for treatment of hypotension. Postoperatively, pain management with regional blocks and multimodal analgesia, oxygenation, and perfusion should be optimized. These patients should be monitored closely and respiratory acidosis avoided [83]. Careful attention to rapid volume administration should be given since this may compromise LV filling due to ventricular interdependence leading to decreased cardiac output.

Anesthesia Technique

General anesthesia may lead to decreased diaphragm activity from reflex inhibition of phrenic nerve and pain leading to decreased lung volume, alveolar collapse, airway closure, and ventilation/perfusion imbalance [84]. Regional anesthesia may avoid some of the pulmonary complications of general anesthesia, although a high spinal/epidural anesthetic may result in impaired intercostal muscle function leading to a decrease in FRC, perioperative basal atelectasis, and hypoxia [84]. At lower concentrations of bupivacaine 0.25%, however, ventilatory mechanics, inspiratory respiratory muscle strength, and airway flow are maintained even in patients with severe COPD [85, 86].

The use of neuraxial block may lead to fewer respiratory complications compared to general anesthesia. For upper abdominal and thoracic surgery, epidural analgesia has been found to be helpful in reducing the risk of PPC [85, 86]. Memtsoudis and colleagues compared perioperative outcome in patients undergoing joint arthroplasty under either general or neuraxial anesthesia [87]. Neuraxial anesthesia was associated with lower mortality rate at 30 days, decreased length of stay, and overall lower complication rates including PPC, such as pneumonia or the need for mechanical ventilation [88, 89]. Pedersen and colleagues found a higher incidence of PPC for orthopedic surgery performed under general anesthesia compared to regional anesthesia (11.5% vs. 3.6%) [90]. In a study looking at hip fracture repair, the rate of postoperative pneumonia was similar in the neuraxial group compared to the general group, 5.1% vs. 5.5% [91]. Haussman in a study of 2644 patients with severe COPD found a higher rate of pneumonia, 3.3 vs. 2.3% in patients undergoing general vs. neuraxial or regional anesthesia [92].

One of the major advantages of neuraxial block in orthopedic surgery, specifically after joint replacement surgery, is the reduction in the rate of DVT or pulmonary embolism (PE). In a meta-analysis by Hu, regional anesthesia decreased the incidence of thromboembolic disease (OR 0.45 DVT and OR 0.46 PE) in patients undergoing hip or knee arthroplasty [93]. In a meta-analysis of 141 trials of patients undergoing different types of surgery, neuraxial blockade reduced odds of DVT by 44% and PE by 55% [94].

Postoperative Considerations

Effective postoperative analgesia is important since it allows deep breathing, adequate coughing, and clearance of secretions. Epidural analgesia gives superior analgesia compared to intravenous patient-controlled analgesia and may improve recovery by reducing respiratory muscle dysfunction and pain-related hypoventilation [84]. Peripheral nerve blockade with or without catheter placement also adds to the analgesic regimen and reduces the need for opiate use [95–98]. They may be associated with superior perioperative population outcomes such as pulmonary complications [98], length of stay, and readmissions [99].

Multimodal analgesia using nonsteroidal analgesic agents, acetaminophen and ketamine which all act through nonopioid pathways, should be considered. They have all been shown to reduce pain scores and opioid-related side effects [100–102]. In addition, in a systematic review of perioperative use of gabapentinoids (pregabalin and gabapentin) by Tiippana and colleagues, they were shown to be effective at reducing postoperative pain, opioid-related adverse effects, and opioid use [103]. The optimal dose of these medications along with duration of treatment remains to be determined.

Summary

Chronic pulmonary disease is a potent contributor to problems of both a pulmonary and nonpulmonary nature in the postoperative setting. Although the perioperative literature has been highly focused, perhaps dominated, by concerns of a cardiac nature, pulmonary problems rival, if not exceed, the cardiac domain in their importance in this clinical setting. The assessment and management of patients with chronic pulmonary disease in its several variants have long been the focus of an extensive literature. Pulmonary hypertension, important because of its implication with respect to anesthesia, has been recently added to the discussion. This chapter reviews the role played by this panoply of conditions in the genesis of PPC. The mitigating role for such techniques as neuraxial is also introduced. See Box 14.3 for a summary of pulmonary risk reduction strategies in pre-, intra-, and postoperative settings.

Box 14.3 Pulmonary Risk Reduction Strategy

- *Preoperative*
  - Encourage smoking cessation.
  - Treat airflow obstruction.
  - Antibiotic administration and delay of surgery if respiratory infection or worsening symptoms present
  - Begin education on postoperative lung expansion.
  - If signs of RV strain and dysfunction on EKG occur, consider echocardiogram to rule out pulmonary hypertension.
- *Intraoperative*
  - Regional anesthesia.
  - Limit duration of surgery to <3 h.
- *Postoperative*
  - Deep breathing exercise or incentive spirometry
  - CPAP
  - Peripheral nerve block
  - Multimodal pain regimen

Summary Bullet Points

- Chronic pulmonary disease is frequently encountered in the perioperative setting and places patients at significant risk postoperatively. The magnitude of this risk is comparable to that of existing cardiac disease.
- Regional anesthesia, specifically neuraxial block, is often employed in orthopedic surgery and may avoid some pulmonary complications.
- A major advantage to regional anesthesia is the reduction in deep venous thrombosis after lower extremity joint replacement surgery.

Case Study

This is a 72-year-old woman presenting for left total hip replacement. Her past medical history is notable for mixed connective tissue disease (MCTD). She has a 24 pack-year smocking history. Upon questioning, she reports a chronic cough and dyspnea on exertion. On exam, she does have pedal edema and jugular venous distention. Laboratory values are notable for a hematocrit of 45. Preoperative evaluation included an echocardiogram which showed elevated pulmonary systolic pressure of 60.

This patient has several risk factors for pulmonary complications including age, smoking history, and pulmonary

hypertension (PHTN) which should lead to postponement of her surgery. The elevated hematocrit may represent chronic hypoxemia. Her exam reveals sign of fluid overload which may be due to congestive heart failure or cor pulmonale from her PHTN. The latter is especially worrisome in the setting of total hip replacement given the possibility of fat embolism. Chronic cough and dyspnea on exertion also suggest the possibility of chronic obstructive lung disease for which she should be referred for a pulmonary evaluation and possibly cardiac evaluation as well. Her clinical state needs to be optimized prior to surgery. Smoking cessation for at least 3–4 weeks prior to surgery would be recommended. Specific therapy for her PHTN needs to be addressed and left-sided heart disease ruled out.

Regional anesthesia would be recommended in such patient given the potential benefits seen with neuraxial block. Respiratory acidosis and hypoxemia are to be avoided in the perioperative setting. Intraoperative monitoring with an arterial line and possibly an echocardiogram should be considered. Effective postoperative analgesia using multimodal technique while minimizing opioid use should occur.

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Perioperative Care of the Orthopedic Patient with Renal Disease

15

James M. Chevalier

Objectives

- To realize the scope of chronic kidney disease in the United States
- To prepare patients with renal disease for orthopedic surgery
- To understand the perioperative needs of patients on dialysis or with a functioning renal transplant
- To evaluate, manage, and treat patients with acute kidney injury (AKI) and electrolyte disturbances, particularly hyponatremia
- To recognize medications known to be nephrotoxic, and in patients with kidney disease, medications and their dosages must be chosen carefully and administered in dosages adjusted based on renal function

Key Points

- During the preoperative evaluation, a patient's renal risk should be assessed, and the patient should be prepared in such a way to lower that risk to the lowest possible level.
- A patient's hemodialysis or peritoneal dialysis schedule needs to be coordinated with the timing of surgery; renal transplant patients should avoid interruption of their immunosuppressive medications.
- After surgery, AKI and hyponatremia are common in patients with kidney disease; when encountered, specific testing can determine the cause of the abnormality and allow for appropriate treatment.
- Several medications are known to be nephrotoxic, and many others are renally excreted; in a patient with kidney disease, medications and their dosages must be chosen carefully.

Introduction

Chronic kidney disease (CKD) is a pathological process encompassing a broad spectrum of conditions that adversely affect renal function. The hallmark of the condition, the progressive loss of nephrons, inevitably results in end-stage renal disease (ESRD). With a current prevalence of more than 30 million affected Americans (13% of the US adult population), the incidence of CKD is expected to rise in the future [1]. Thus the frequency of this problem, coupled with the centrality of the kidney to normal homeostasis, makes the management of impaired renal function a common and challenging problem in the perioperative setting. This chapter reviews the range of common renal problems that arise in this context.

Chronic Kidney Disease

CKD is defined by the National Kidney Foundation as either a glomerular filtration rate (GFR) <60 mL/min/1.73 m^2 or kidney damage for ≥3 months. The term kidney damage denotes either anatomic abnormalities of the kidney or other markers of kidney damage, including abnormalities seen in the blood and urine or by imaging studies [2]. CKD is further graded along a continuum of severity from stage I, the earliest period of deterioration, to stage V, the most severe (Table 15.1). ESRD is defined as the need to replace the native kidney function via dialysis or transplantation.

CKD develops from a number of conditions including diabetes mellitus, hypertension, glomerulonephritis, and

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Table 15.1 Stages of CKD

Stage	Estimated GFR (mL/min/1.73 m^2)
I	>90[a]
II	60–89[a]
III	30–59
IV	15–29
V	<15
VI[b]	ESRD

Data from National Kidney Foundation [2]
GFR <60 must be present for more than 3 months for a patient to be diagnosed with CKD
CKD chronic kidney disease, *GFR* glomerular filtration rate, *ESRD* end-stage renal disease. See text for details
[a]Patients with a GFR >60 have CKD if there is evidence of abnormal pathology, imaging, or renal laboratory tests such as proteinuria for more than 3 months
[b]Stage VI CKD is not part of the NKF guidelines but is used by many practicing nephrologists to distinguish patients with ESRD from patients with a GFR <15 who have not started dialysis or received a transplant (stage V)

polycystic kidney disease. Regardless of the cause, such patients often have coronary artery disease and, in fact, have a higher lifetime risk of death from cardiovascular disease than of ever-reaching ESRD [1]. Since a serum creatinine ≥2 mg/dL is considered to be a risk factor for poor cardiac outcome after surgery [3], appropriate perioperative care of renal patients undergoing orthopedic surgery takes on added importance.

The Preoperative Renal Evaluation

The patient with renal disease requires a comprehensive preoperative evaluation, one that often encompasses several organ systems. As such, the coordination of care between the orthopedic surgeon, nephrologist, anesthesiologist, and potentially other medical consultants is imperative. Management of preexisting renal disease may involve treating its underlying cause; managing the blood pressure, fluids, and volume status; correcting electrolyte abnormalities; choosing which medications to continue, add, or hold; optimizing nutrition; and providing dialysis or transplant care. The ultimate goal is the assessment of the patient's risk for renal impairment with a given procedure and to institute measures directed at minimizing that risk.

Renal Function and Postoperative Risk

During the preoperative evaluation, it is important to identify the risk factors for AKI and minimize them. Patients who suffer from an episode of AKI (regardless of whether they require dialysis) are at risk for a residual and progressive decline in kidney function, ESRD, and even death [4–6]. The greatest risk factor for such an outcome is preoperative CKD. Novis and colleagues in a systematic review of 28 heterogeneous studies have reported that preoperative CKD was the only consistent risk factor for postoperative AKI [7]. Several studies have also tried to define AKI predictors other than CKD in the setting of noncardiac (and sometimes specifically orthopedic) surgery [8–13]. Putative risk factors differ slightly depending on the type of surgery, but the overlap is significant. A composite list of these risk factors is provided in Box 15.1. Unfortunately, in patients undergoing orthopedic surgery, CKD patients often have multiple risk factors for AKI. These include advanced age, obesity, as well as dysfunction in other major organ systems. Once identified, modifiable risk factors should be addressed to the degree possible, since preventing AKI after surgery will improve the patient's short- and long-term outcomes [14]. Cardiac function should also be optimized in patients with congestive heart failure, as should lung function in patients with chronic obstructive pulmonary disease. Nephrotoxins, hypotension, hypovolemia, and hypervolemia should be avoided.

Box 15.1 Risk Factors for Perioperative Acute Kidney Injury

- **Advanced age**
- Anemia
- **Chronic kidney disease**
- Chronic obstructive pulmonary disease
- **Congestive heart failure**
- Coronary artery disease
- **Diabetes mellitus**
- Elevated BMI
- Emergent surgery
- **Hypertension**
- Liver disease
- Male gender
- Peripheral vascular disease
- **Use of nephrotoxic medications**: ACE, ARB, **NSAID**, **diuretic**
- Volume depletion
- **Worse American Society of Anesthesiologists score**

Bold items represent risk factors found in more than one study of orthopedic patients. *BMI* body mass index, *ACE* angiotensin-converting enzyme inhibitor, *ARB* angiotensin receptor blocker, *NSAID* nonsteroidal anti-inflammatory drug. See text for details.

Data from references [15–20].

The first step in establishing the patient's renal risk is to calculate the patient's estimated GFR. This allows for appropriate medication dosing and establishes the degree of risk for AKI, a risk that increases in step with a decreasing GFR. A 24-h urine collection is the traditional standard for the determination of the creatinine clearance; however, an acceptable and simple alternative is the Modification of Diet in Renal Disease (MDRD) formula for the estimation of GFR [15]. The formula can be found online at several websites including www.nkdep.nih.gov. This formula has not been validated in patients with stage I or II CKD and is applicable only when the serum creatinine is stable. In the setting of AKI, when the serum creatinine is rising, the estimated GFR is presumed to be <15 mL/min/1.73 m^2. Once the GFR has been established, recommendations are made to dose the patient's medications based on this value.

The preoperative creatinine relative to historical values is also important. Patients with stable renal disease are at lower risk for worsening serum creatinine after surgery. Thus, in the patient with a progressively rising serum creatinine, elective procedures should be delayed until the cause of deteriorating renal function is identified and has stabilized.

Medication Management

Choosing which medications to hold prior to surgery in order to decrease the chance of AKI remains controversial; however, several classes of medications are believed to be especially problematic, particularly in the patient with kidney disease. Nonsteroidal anti-inflammatory agents (NSAIDs) are a paradigmatic example. NSAIDs, even the cyclooxygenase-2 inhibitors, impair renal autoregulation by inhibiting prostaglandin-mediated dilation of the afferent arteriole in the glomerulus [16]. It is via this mechanism that these drugs are thought to produce their adverse influence on the kidney. Therefore, due to their nephrotoxic potential, all NSAIDs should be avoided in the perioperative setting, using alternative analgesics to control pain instead.

Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) diminish the ability of the efferent arteriole to constrict [16] and are reported to cause hypotension during induction of anesthesia [17, 18]. A meta-analysis confirmed this finding but found insufficient data to draw conclusions about other outcomes, such as AKI [19]. However, in one study [20], ACE inhibitor or ARB therapy combined with diuretics increased the risk of hypotension; in contrast similar rates of AKI in patients with and without the ACE inhibitor or ARB therapy have also been reported although in bariatric surgery the use of such medications increased the risk of AKI in one study [21]. Reasonable recommendations from a review on perioperative medication management [22] suggest holding ACE inhibitors and ARBs for patients who take these medications for hypertension and have acceptably controlled blood pressure. For patients who require the medication for congestive heart failure, an individualized approach may be needed.

In summary, prior to orthopedic surgery, CKD patients should generally hold NSAIDs, ACE inhibitors, ARBs, and diuretics on the morning of surgery. Patients who take such treatment for control of heart failure may need to continue their medication perioperatively, and in such circumstances the opinion of the patient's cardiologist should be sought. All medications held preoperatively should be considered for reinitiation postoperatively once hemodynamic stability and euvolemia are achieved.

Blood Pressure, Fluid, and Volume Management

Perioperative blood pressure management is discussed elsewhere, but it should be noted that most patients with CKD have volume-mediated hypertension and are often treated with diuretics. Volume status should be assessed during the preoperative evaluation. Hypovolemic and hypervolemic patients are treated with volume and diuresis, respectively, to achieve a euvolemic state. Some patients with long-standing congestive heart failure and kidney disease often have a "best" volume, i.e., a volume at which heart and kidney function have achieved balance, allowing the highest level of function. While this may not reflect true euvolemia, this is an assessment best left to physicians who care for the patient longitudinally.

Lactated Ringer's solution is generally avoided, given renal patients' propensity for hyperkalemia [23]. Patients with CKD also have difficulty excreting excess fluid and need lower intravenous (IV) fluid rates than patients without kidney disease. Similarly, patients currently on dialysis with no significant urine output require smaller volumes of IV fluid during surgery. Since CKD patients are at risk for both volume depletion and volume overload, maintenance IV fluid rate should account for insensible losses, residual urine output, and anticipated blood loss with additional IV fluid boluses as needed [23]. If central venous access is in place, central venous pressure (CVP) monitoring can guide fluid management, especially in dialysis patients who have little or no urine output [23].

Electrolyte Disturbances

Hyponatremia and hyperkalemia are sometimes encountered during preoperative lab testing. The cause should be determined and appropriate treatment administered, based on the

results of the workup. While there are no values of serum sodium or potassium that are considered totally "safe" prior to surgery, some observations can be made. The safety of any given serum sodium is likely related to the cause of the hyponatremia, its chronicity, and the patient's symptoms (if any). Clinical experience also suggests that patients with CKD, especially ESRD, tolerate hyperkalemia better than the general population. Indeed, in one study, electrocardiographic changes occurred only at a serum potassium level of >6.5 mmol/L [24]. The full evaluation, management, and treatment of hyponatremia and hyperkalemia are discussed in the postoperative section.

Hematologic Issues: Anemia

The kidneys are responsible for the production of erythropoietin, so as renal function declines, the prevalence of anemia increases [25]. Associated with an increased mortality in CKD [26], the presence of anemia also correlates with a higher mortality in patients undergoing cardiac [27, 28] and noncardiac surgery [29]. In one orthopedic study, however, the patients' comorbidities rather than their preoperative anemia correlated best with postoperative complications and mortality [30].

Prior to the widespread use of erythropoietin-stimulating agents (ESAs), patients with CKD required transfusions to treat their anemia. Such transfusions increase the risk of hyperkalemia and lead to antibody formation, ultimately decreasing the odds of successful kidney transplant in the future. For nearly two decades, ESAs were used freely to increase a patient's hematocrit, improve quality of life, and decrease the need for transfusion.

Three trials, CREATE [31], CHOIR [32], and TREAT [33], have called in to question the safety of such therapy as well as the concept of a target hematocrit when using ESAs. CREATE and CHOIR each randomized patients to a target hemoglobin of 11 g/dL versus 13 g/dL. In each study, normalization of the patient's hemoglobin failed to decrease cardiovascular events and suggested an increased risk of cardiovascular events and death. In contrast, TREAT randomized patients to a hemoglobin of 13 g/dL versus rescue therapy to prevent a hemoglobin <9 g/dL. Again no decrease in cardiovascular events resulted from a correction of anemia. Further, an increased incidence of stroke in the normalized hemoglobin group was noted, though the increased risk of other cardiovascular events and death seen in CREATE and CHOIR was not demonstrated. The National Kidney Foundation currently recommends a target hemoglobin of 10–11.5 g/dL [34], although this may change. The FDA, however, has already added a boxed warning to the package insert of all ESAs, warning of the risk of cardiovascular deaths and recommending individualized dosing to avoid transfusion, targeting a hemoglobin of 10–11 g/dL.

Besides anemia of CKD, the renal patient is often iron deficient. The evaluation of iron deficiency is more difficult in a patient with CKD due to the chronic inflammation associated with the disease. Accordingly, iron parameters have different targets in CKD: transferrin saturation >20% and ferritin >100 ng/mL are recommended thresholds in a CKD patient [34]. Because the ferritin may be elevated secondary to inflammation, the low transferrin saturation dictates treatment, despite an elevated ferritin. Patients with iron deficiency should still be referred for GI evaluation to rule out intestinal sources of bleeding. Iron can be supplemented orally or intravenously. Current formulations of IV iron can be a safe alternative to oral iron and have been used successfully prior to orthopedic surgery [35].

In summary, patients currently receiving peritoneal or hemodialysis should receive supplemental iron and ESAs according to their dialysis center protocols, usually to maintain a hematocrit of at least 30, especially if surgery is anticipated. Patients with CKD who are not yet on dialysis should be treated with iron to correct iron deficiency. ESAs can be added to achieve a hematocrit >30% prior to surgery if iron repletion alone did not achieve such a hematocrit. These recommendations are not dissimilar to those for the treatment of preoperative anemia before elective surgeries such as joint replacements [36]. Anticipatory planning is especially necessary in the patient with CKD. Postoperatively nonautologous blood transfusions should be limited or avoided since transfusions from other donors will increase antibody production and decrease the chances of a successful renal transplant in the future.

Hematologic Issues: Uremic Bleeding

Uremia causes platelet dysfunction and can increase the chance of perioperative bleeding. Desmopressin acetate can enhance hemostasis in general [37] and specifically improves the platelet dysfunction in uremia [38]. It has been studied widely from patients with CKD undergoing renal biopsy [39] to patients with normal renal function undergoing cardiac surgery [40]. Despite an extensive published record, the use of desmopressin for uremic patients undergoing surgery remains controversial. All of the randomized controlled trials were small. One review article [37] and a Cochrane review [41] did not support the use of desmopressin to reduce blood loss and decrease transfusion requirements. However, another meta-analysis [42] did find a small but statistically significant reduction in blood loss and blood transfusion requirement though the percentage of patients who received transfusions was not changed. Desmopressin acetate is not FDA approved for hemostasis; however, when given for this indication, the dose is usually 0.3 μg/kg IV, with a maximum of 20 μg. Side effects include flushing, hyponatremia, myocardial infarc-

tion or other thrombotic events, and hypotension; however, in the meta-analysis by Crescenzi and colleagues [42], only clinically insignificant hypotension occurred more often in patients receiving desmopressin as compared to the placebo group. It should be noted that in most studies patients were included regardless of severity of kidney disease, so it is possible that desmopressin may be more beneficial in the uremic patient. Therefore in order to mitigate the platelet dysfunction associated with the uremic state, patients with advanced CKD (GFR <20 mL/min/1.73 m^2) are often considered for treatment with desmopressin or are dialyzed prior to surgery.

Renal Replacement Therapy: Dialysis and Transplantation

Before discussing the preparation of ESRD patients for surgery, some statistics about the dialysis population are in order. The Medicare Payment Advisory Commission reports that as of 2014, there were more than 383,000 Americans receiving dialysis (mostly in-center hemodialysis (HD)) and more than 158,000 Americans with a functioning kidney transplant [43]. The 1-, 3-, and 5-year survival rate for an incident dialysis patient is only 79%, 52.8%, and 34.9%, respectively [44]. As of 2007, 36% of dialysis patients were aged 65 or over [43]. Given their age and background mortality rate, a few studies have analyzed the risk-benefit ratio of total hip arthroplasty in HD patients. Sakalkale and colleagues [45] reported a high short-term mortality rate (58%) and an average survival of 31 months. Further the success rate of total hip arthroplasty in HD patients has been mixed though most studies found a lower success in HD patients. Therefore it appears prudent to reserve joint replacement surgery for dialysis patients with a longer life expectancy, possibly those who qualify for renal transplant.

When preparing a patient with ESRD for a surgical procedure, special attention must be given to the patient's dialysis or transplant needs. A nephrologist must be involved in coordinating this care. For a comprehensive review of the perioperative management of the HD patient, the reader is referred to a review of the subject [46], the most pertinent aspects of which are reviewed here.

Hemodialysis Patients

Conventionally, an HD patient should receive dialysis the night before surgery, whether as an inpatient or an outpatient, even if this requires a change in the patient's regular three-times-per-week schedule. Doing so renders the blood as "clean" as possible for surgery. One session should be sufficient. Repeat labs should not be drawn within the first few hours following dialysis, as the electrolytes may be falsely low, having not yet re-equilibrated. For this reason, supplemental potassium should never be given based on labs drawn in the immediate post-dialysis period. The well-dialyzed patient should also experience fewer uremic complications such as poor platelet function and delayed wound healing. In addition, preoperative dialysis usually delays the need for dialysis after surgery. This is particularly beneficial in those patients who are not hemodynamically stable in the early postoperative period [23].

If a patient is well dialyzed and regularly attending his or her dialysis sessions three times per week, it is unclear if additional (daily) HD sessions prior to surgery will improve surgical outcome, unless the patient is significantly over his or her target weight and requires more fluid removal than can be achieved with the normal schedule. Sufficient fluid is generally removed to make the patient euvolemic and achieve the patient's dry weight (i.e., the patient's target weight at the end of dialysis). Traditionally, a dialysis prescription without heparin is used during the final presurgical HD session. The use of heparin with dialysis is also avoided for at least 1–2 days following major orthopedic surgery. However, many orthopedic procedures, particularly total joint arthroplasty, require anticoagulation after surgery and thus would require patients to receive heparin-free dialysis anyway.

Vascular access is required to perform HD. Examples of such access include an arteriovenous fistula (AVF), an arteriovenous graft (AVG), or a tunneled HD catheter. Since maintaining a functioning vascular access is critically important, special attention must be given to the access. All blood pressure readings, blood draws, and IVs should be performed in the extremity contralateral to the functioning AVF or AVG [46] as using the arm with the HD access risks thrombosis and loss of the fistula or graft. In fact, IV placement should be limited to only what is absolutely necessary in order to preserve the patient's other veins for future HD access placement.

Any required central venous catheter should be placed in the side contralateral to the HD access; otherwise, the HD access may not function as well [23]. The internal jugular location for catheters is preferred over the subclavian location due to the risk of subclavian stenosis and decreased function of the current (or future) access in the ipsilateral arm. Providers obtaining central venous access in an HD patient should be aware that patients with a long-standing history of HD may have one or more occluded central veins from current or previous central venous catheters, cardiac pacemakers, or other injuries and procedures.

An existing tunneled dialysis catheter should not be used during surgery unless no other IV access can be obtained. The catheter traditionally has an anticoagulant (usually heparin) dwelling in the tubing in order to decrease the chance of thrombosis. In patients with advanced CKD who are approaching ESRD and the need for dialysis, one should

avoid using the nondominant arm for blood pressure readings, blood draws, and IVs, if possible, as HD access will likely be created in this arm in the future.

Peritoneal Dialysis Patients

Peritoneal dialysis (PD) is a form of renal replacement therapy in which the clearance of toxins and ultrafiltration of water take place via the peritoneal membrane by exchanging substances from blood to PD fluid and vice versa. The patient either manually exchanges fluid in the peritoneal cavity an average of four times per day or uses a machine, called a cycler, to exchange the fluid at night while sleeping. When a PD patient undergoes a surgical procedure, alterations in the dialysis schedule are also needed. Some nephrologists recommend performing PD exchanges more frequently prior to surgery, but the beneficial effect of this strategy on surgical outcomes is not clear. PD patients should be advised to drain the fluid from their abdomen on the morning of surgery. A dry abdomen during surgery should be tolerated by a regularly dialyzed patient and will have only a small effect on electrolyte and fluid balance. In contrast, leaving PD fluid in the abdomen increases intra-abdominal pressure [23] and leads to the absorption of fluid during surgery, thus risking fluid overload. Assuming that the peritoneum was not compromised during surgery, PD can usually be resumed the morning after surgery (barring any emergent electrolyte or fluid issues requiring earlier initiation), when the patient is more alert and able to assist with the fluid exchanges. Nursing staff should feel comfortable with PD if performing the exchanges without the assistance of the patient. Patients on the cycler at home can be converted to manual PD postoperatively if the hospital does not have cycler machines available. PD patients do not have the same dietary restrictions as patients receiving hemodialysis. For example, while phosphorus and total fluid intake should be limited, potassium restriction is usually not necessary due to the nearly continuous removal of potassium provided by this form of dialysis. However, PD patients should still have their potassium level followed; if low, they can be encouraged to increase oral potassium intake or receive small doses of potassium repletion.

Renal Transplant Patients

Understandably, renal transplant patients have a keen interest in keeping their renal transplant functioning, as it is the sole buffer between their current lifestyle and a life of regular dialysis. Renal transplant patients should continue their regular immunosuppressive medications up to, and including, the morning of surgery. As soon as feasible after surgery, the patient should be allowed to continue taking his or her regular transplant medications by mouth. More tenuous transplant patients, who are unable to take their medications by mouth and are therefore at risk for missing their immunosuppressive medications, should be considered for administration via a nasogastric tube. If the transplant medication cannot be given enterally, IV formulations may be given, although the dosing conversion is not always 1:1 and it occasionally requires continuous infusion. A nephrologist or a pharmacist experienced with transplant medications should assist with the conversion of outpatient medications to an IV equivalent.

Calcineurin inhibitors, such as tacrolimus and cyclosporine, are common transplant medications that interact with many other medications. Care must be taken when starting or discontinuing any medication in a patient taking these agents, as the serum level may be affected. Levels should be monitored and appropriate dosage adjustments made. Of particular relevance to orthopedic surgery, especially total joint arthroplasty, is the concurrent use of warfarin and cyclosporine, as together these medications can lead to decreased anticoagulant and cyclosporine effectiveness [47]. In such circumstances, the levels of both warfarin and cyclosporine should be followed closely with dose adjustments made as needed. Many patients with a functioning kidney transplant also take low-dose prednisone chronically. These patients may require stress-dose steroids prior to surgery.

Finally, patients on chronic immunosuppression are at increased risk for infections, including opportunistic infections. Workup for the cause of fever should have a broader differential in the transplant patient. Those with a recent kidney transplant are at the highest risk. Should a transplant patient develop a life-threatening infection, the immunosuppressive agents may need to be held until the infection resolves, despite the risk of rejection and transplant failure.

Postoperative Renal Considerations

Postoperatively, patients with CKD are at risk for a broad range of complications including difficult-to-control hypertension, proteinuria, hematuria, volume overload, electrolyte disturbances, as well as AKI and thus may require nephrology consultation.

Acute Kidney Injury

AKI, formerly known as acute renal failure, is a potential complication of surgery, especially in the CKD population. AKI during hospitalization increases morbidity, mortality, length of stay, and cost of care [14]. Although the literature is difficult to interpret because of the wide-ranging defini-

tions of AKI in the past, efforts are being made to standardize the definition. Currently the most commonly used criteria are the RIFLE criteria [48], which stand for risk, injury, failure, loss, and end-stage kidney disease (ESKD). The severity of kidney dysfunction increases across the letters of the acronym, from risk to ESKD. The categorization of the patient's renal dysfunction is based on urine output and the change in serum creatinine/percent decrease in GFR from baseline.

In the general population, the incidence of AKI after noncardiac surgery is low, and after orthopedic surgery the incidence is even lower, with reported rates often <1% [8, 11, 49]. Risk scores exist to predict the risk of AKI after cardiac surgery [50], the risk of needing dialysis after cardiac surgery [51], the risk of AKI in patients undergoing general surgery [52], and the risk of AKI following liver resection [53]. Unfortunately, no such risk scores exist specifically for orthopedic surgeries.

A review by Thadhani and colleagues [54] discusses the rationale supporting the standard evaluation and management of AKI by nephrologists. After conducting a history and physical examination, the first parameter considered is the urine output as non-oliguric AKI has a better prognosis than the oliguric form. Further the differential diagnosis differs [54]. The placement of a Foley catheter is then considered, especially in patients with oliguric AKI, as this maneuver may be both diagnostic and therapeutic.

The cause of oliguric AKI is most often divided into prerenal, intrinsic renal, and post-renal (obstructive) causes [54]. Prerenal causes account for 60%, intrinsic renal for 30%, and post-renal for 10% of AKI [10]. Prerenal and post-renal causes are the most reversible, and prompt diagnosis leads to early intervention and attenuation of the effects of the AKI. Serum and urine electrolytes can help rule in or out a prerenal cause of AKI, while a renal ultrasound can help rule in or out a post-renal cause (Fig. 15.1).

To differentiate between these entities, a urinalysis and serum and urine electrolytes (specifically random urine sodium and creatinine) are ordered, and a fractional excretion of sodium (FeNa) is calculated. The FeNa is defined as the patient's urine sodium times the serum creatinine divided by the serum sodium times the urine creatinine (FeNa = UNa × SCr/SNa × UCr). When the FeNa is <1% and/or the urine sodium is <20 mmol/L, the patient is likely volume depleted. In contrast a FeNa >20 mmol/L and a FeNa >1% in the oliguric patient argue against intravascular volume depletion, suggesting intrinsic renal damage. If the patient has received diuretics, the FeNa may be inaccurate because of the sodium wasting effect of these medications. In such circumstances, a serum BUN and urine urea can be

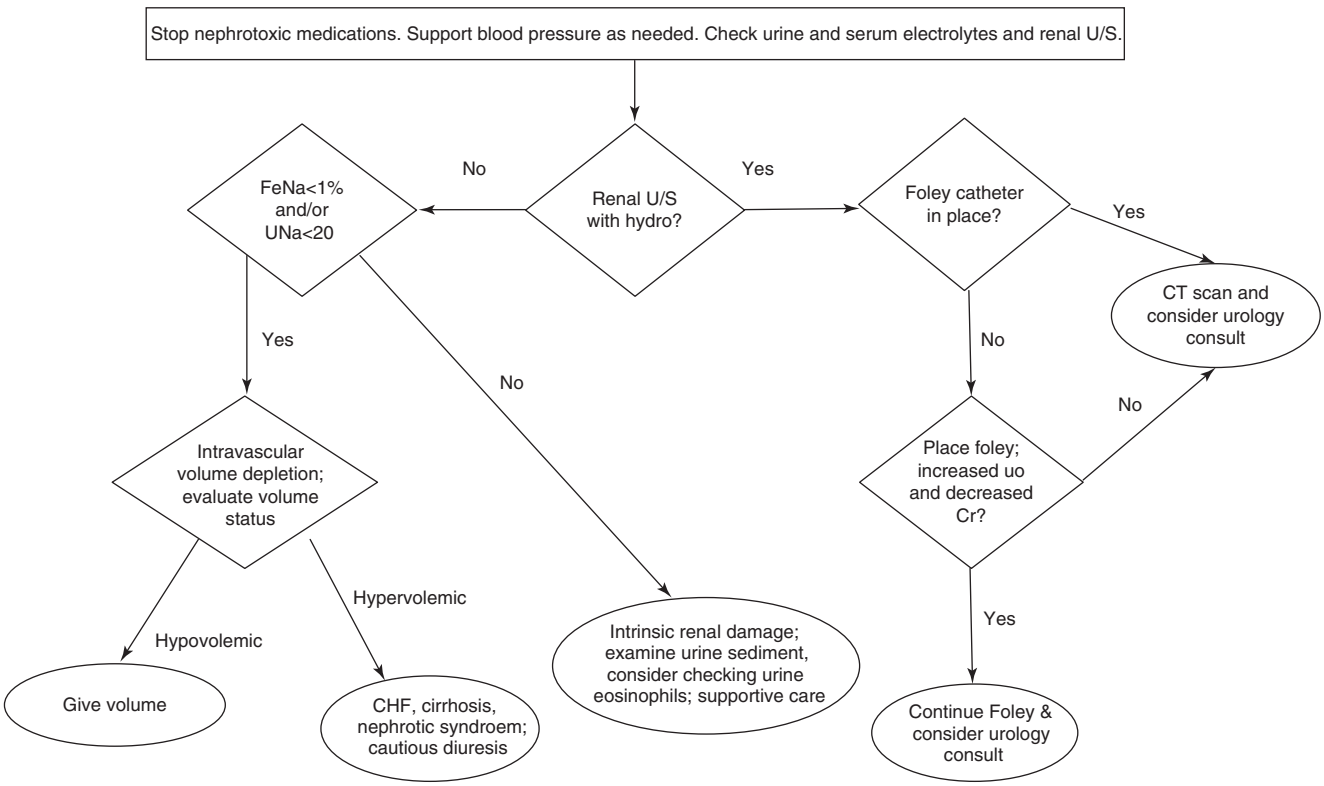

Fig. 15.1 Evaluation and management of oliguric acute kidney injury. *U/S* ultrasound, *FeNa* fractional excretion of sodium, *UNa* urine sodium, *uo* urine output, *Cr* creatinine, *CHF* congestive heart failure. See text for details

used to calculate a fractional excretion of urea (FeUrea), using the formula for FeNa, replacing sodium with urea. A FeUrea <30 (or 35) % suggests a prerenal cause. Patients with prerenal AKI are treated according to their volume status. Hypovolemic patients should receive volume. Hypervolemic patients should be diuresed.

A renal ultrasound is performed in order to determine whether or not hydronephrosis is present. Hydronephrosis denotes an obstruction along the course of the urinary tract, from the urethra to the kidneys, implying post-renal AKI. The likelihood of post-renal AKI increases in such circumstances as the older man with an enlarged prostate or any patient with a history of cancer, enlarged lymph nodes, scarring, or other abnormalities in the lower abdomen or the pelvis [54]. Inserting a Foley catheter in this clinical setting may improve both urine output and serum creatinine. If the AKI does improve after insertion of a Foley catheter, further urologic evaluation regarding treatment of the blockage and timing of catheter removal is warranted. If no improvement ensues, a CT scan of the abdomen and pelvis and urologic consultation are required. Of note, a renal ultrasound with Doppler may sometimes reveal a prerenal cause of AKI such as an abnormality in renal blood flow (aortic dissection) or bilateral renal vein thrombosis.

If the workup reveals neither a prerenal nor a post-renal cause of AKI, further testing for intrinsic renal causes of AKI should be sought. The differential diagnosis is based on the anatomic portion of the kidney affected, namely, the tubules, interstitium, glomeruli, or blood vessels [54]. Acute tubular injury (ATI), formerly known as acute tubular necrosis, accounts for 85% of the cases of intrinsic AKI. Ischemia, such as that seen after surgery, causes 50% of ATI cases, and toxins, such as iodinated IV contrast, cause the remaining 35% [54]. Examination of the urine sediment may reveal granular casts in ATI, white blood cell casts in allergic interstitial nephritis (AIN), or red blood cell casts in glomerulonephritis, all of which require different treatments. Checking the urine for eosinophils or cholesterol may also help establish the diagnosis of AIN or cholesterol emboli, although their absence does not rule out either diagnosis.

Unfortunately, there is no reliable way to reverse ATI, which is why prevention is so important. Treatment is merely supportive: decreasing the stress on the kidneys by avoiding hypotension and volume depletion, stopping nephrotoxic medications, correcting electrolyte imbalances and fluid overload, and monitoring for the need for dialysis.

Several preventive and therapeutic interventions for AKI have been studied, mostly in cardiac surgery and ICU patients, with mixed success. Dopamine, furosemide, and the combination of these two drugs failed to prevent AKI [55]. Indeed the group receiving furosemide may have had an increased risk of AKI. Neither has *N*-acetylcysteine been shown to prevent AKI in patients undergoing cardiac surgery [56]. Early treatment with erythropoietin after the development of AKI did not change the outcome [57]. In contrast, there is some evidence that fenoldopam decreases the incidence of AKI in patients undergoing cardiac surgery [58] and that natriuretic peptides may prevent and ameliorate the effects of AKI in patients undergoing cardiac surgery [59].

A significant loss of renal function must ensue before the serum creatinine rises. This late reaction to kidney injury may represent a point of "no return" and explain the lack of efficacy of treatments in recent trials. In the future, more sensitive biomarkers may replace serum creatinine in the diagnosis of AKI [16]. Biomarkers such as cystatin C, neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), and others are currently being studied and may eventually enter clinical practice [60].

Hyponatremia

Hyponatremia is relatively common after surgery, with 4–5% of patients developing a serum sodium <130 mmol/L [61, 62], and virtually all postoperative patients experience some drop in their serum sodium. Multiple mechanisms may be at play, including the release of antidiuretic hormone (ADH) secondary to postoperative intravascular volume depletion, nausea, and pain [61]; use of hypotonic IV fluids; poor oral intake; etc. ADH concentrates the urine and decreases urine volume by reabsorbing water from the urine back into the blood. During ordinary conditions, when ADH levels are appropriately suppressed by hypotonicity, a patient should be able to excrete up to 12–15 L of free water per day and prevent hyponatremia [63].

Hyponatremia is caused by an imbalance of several factors. Elevated ADH levels, increased free water intake, decreased free water excretion, and decreased intake of osmoles can all contribute to hyponatremia. Because patients with CKD have a decreased GFR, and therefore less water filtered for excretion, they are at higher risk for hyponatremia, especially when combined with a large intake (or administration) of free water [63].

Many medications may cause hyponatremia, so the patient's medication list should be reviewed and cross-referenced with a resource such as Micromedex [64], which lists more than 120 medications that can potentially cause hyponatremia. Liamis and colleagues provide a review of the mechanisms of drug-induced hyponatremia, including an extensive list of medications known to cause hyponatremia [65]. Any medication that may cause hyponatremia should be held or changed to another agent if possible. Hydrochlorothiazide should be held or switched to a loop diuretic if a patient is volume overloaded, especially in elderly female patients with a low body mass, since they are at increased risk for thiazide-induced hyponatremia

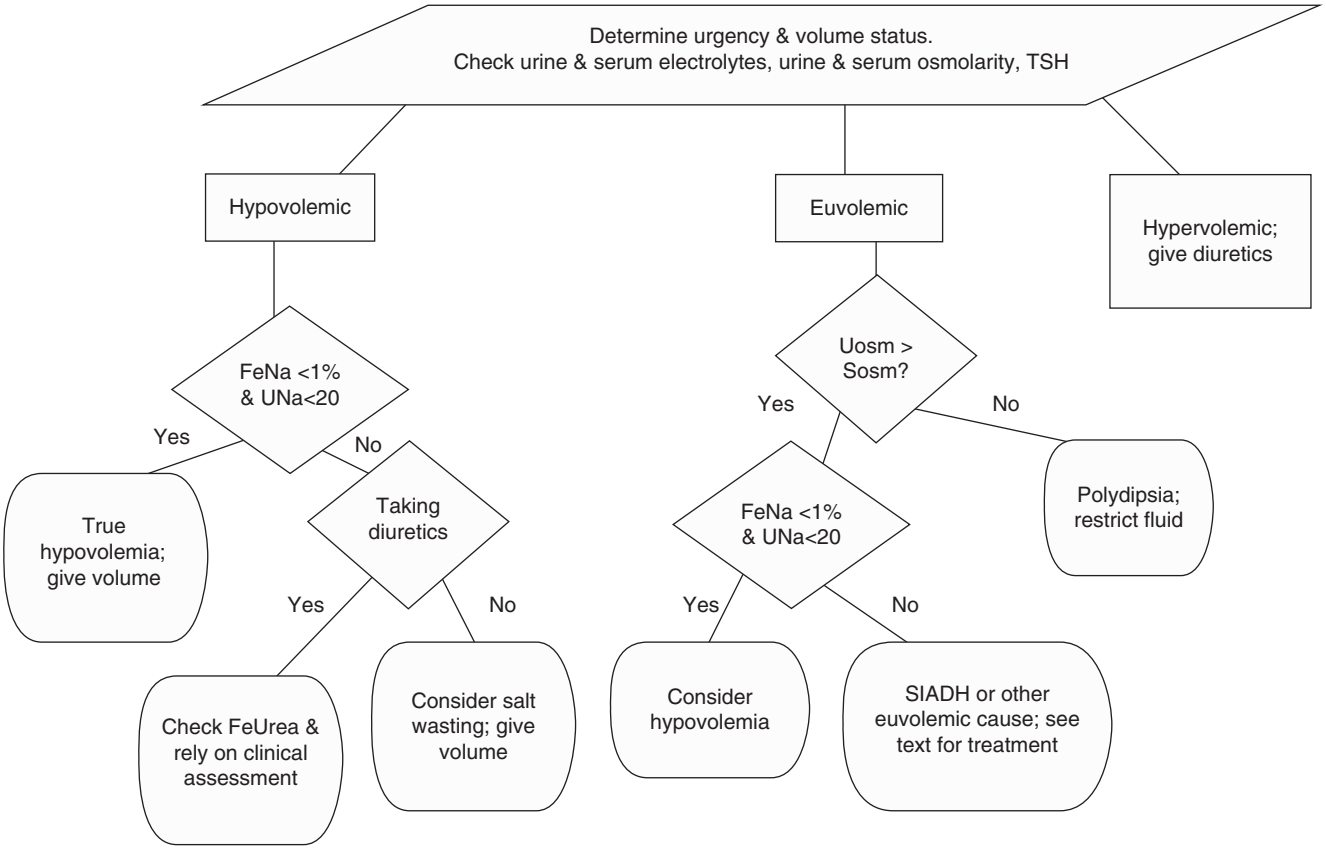

Fig. 15.2 Evaluation and management of hyponatremia. *TSH* thyroid-stimulating hormone, *FeNa* fractional excretion of sodium, *UNa* urine sodium, *FeUrea* fractional excretion of urea, *Uosm* urine osmolarity, *Sosm* serum osmolarity, *SIADH* syndrome of inappropriate antidiuretic hormone. See text for details

[66]. Selective serotonin reuptake inhibitors are also known to cause hyponatremia but may not be as easily discontinued because of potential side effects with discontinuation. Hypotonic IV fluids in the setting of little or no solid food intake can also lead to hyponatremia.

Whatever the cause, the urgency of the hyponatremia (i.e., symptoms) and the patient's volume status should be determined first, as the answer to these two factors will determine further diagnostic and treatment strategies. Symptoms can present at any serum sodium level. Mild hyponatremia (serum sodium 126–134), previously thought of as benign, is now recognized to be associated with decreased cognitive function, gait instability, falls, osteoporosis, fractures, and inpatient mortality [67]. More overt symptoms present at lower sodium levels or when the serum sodium falls quickly. Hyponatremic patients with neurologic symptoms need urgent treatment with hypertonic saline to quickly raise the serum sodium and resolve symptoms. Asymptomatic patients can undergo a more deliberate diagnostic evaluation followed by treatment directed at the underlying cause. Patients with postoperative hyponatremia should be monitored closely with frequent lab draws and evaluations for symptoms.

Determining the volume status and checking a few laboratory tests narrow the cause of the patient's hyponatremia (Fig. 15.2). Laboratory evaluation of hyponatremia includes serum and urine electrolytes, specifically sodium, potassium, and creatinine; urine and serum osmolarity; TSH; and possibly other endocrine tests depending on the clinical situation. Volume-depleted patients (see section on prerenal acute kidney injury) from any cause should increase solute and fluid intake. Hypervolemic patients should receive diuretics.

Euvolemic hyponatremia is most often due to an excess of free water and not a deficiency of sodium [68]; therefore, treatment is aimed at increasing the urine output so that it exceeds fluid intake. If urine osmolarity (Uosm) is less than serum osmolarity (Sosm), such as with primary polydipsia, then fluid restriction alone is usually sufficient. When Uosm is greater than Sosm and the urine sodium and fractional excretion of sodium (see section "Acute Kidney Injury") are elevated, the diagnosis of syndrome of inappropriate antidiuretic hormone (SIADH) is most likely. Treatments include restriction of total fluid intake to about 1 L per day, ideally avoiding free water as much as possible and choosing fluids with osmoles such as milk, oral supplements, and tomato soup; increasing the intake of osmoles

in the diet with sodium, including salt tablets, protein, and possibly potassium; and loop diuretics. If the hyponatremia remains refractory to these interventions, an AVP receptor antagonist or a hypertonic saline may be considered.

Hyperkalemia

Since the kidneys are responsible for the vast majority of potassium excretion, hyperkalemia is frequently seen in patients with renal disease. The serum potassium level generally increases postoperatively as a consequence of blood transfusions, cell death, certain medications, and certain IV fluids.

In patients with an elevated serum potassium but no obvious cause, ruling out "pseudohyperkalemia" by checking a concurrent plasma potassium is reasonable. Once confirmed, all patients with an elevated serum potassium level should be instructed to follow a strict low-potassium diet. A review of the patient's medication list and cross-referencing the list with a resource such as Micromedex [64] may reveal medications that can raise the patient's potassium. Such medications should be held or changed to another agent if possible.

Acutely, calcium gluconate is given if electrocardiogram changes are present. Agents to transiently shift potassium intracellularly include albuterol, bicarbonate, and dextrose with insulin. Use of a loop diuretic or a cation-exchange resin leads to potassium excretion.

Using a cation-exchange resin to lower potassium remains controversial. While frequently employed, data in support of the use of cation-exchange resins to lower the potassium are lacking, and reports of intestinal necrosis thought to be secondary to the sorbitol employed in the resin (or the resin itself) continue to accumulate, prompting a commentary about the use of such therapy [69, 70].

Medications and Nephrotoxins

Choosing a medication in patients with renal disease requires a consideration of two key principles: whether there is a potential for nephrotoxicity and whether the medication is renally excreted. While certain medications carry the potential for nephrotoxicity when used in the general population, most euvolemic patients with normal renal function do not develop AKI as a result of such medications. Nephrotoxicity increases in the presence of specific risk factors: advanced age, CKD, intravascular volume depletion, vascular disease, and number of concurrent nephrotoxic agents [54]. Medications with significant nephrotoxic potential in patients with CKD include ACE inhibitors, ARBs, NSAIDs, calcineurin inhibitors, aminoglycoside antibiotics, cisplatin, methotrexate, foscarnet, amphotericin B, and iodinated IV contrast agents, to name a few.

Because impaired renal function can alter the metabolism and excretion of numerous agents [71], renally excreted medications must be dosed according to the patient's estimated GFR or creatinine clearance in order to avoid supratherapeutic levels. Individual medications should be looked up on a case-by-case basis in references such as the medication's package inserts or a handbook of CKD [71], since the estimated GFR at which dose adjustments need to be made varies by medication. Drug levels should guide management whenever available.

The Use of Contrast When Imaging Patients with Renal Disease

Patients undergoing orthopedic surgery often require imaging prior to surgery or during hospitalization. In patients with normal renal function, the choice of the imaging modality is generally the technique providing the optimal diagnostic information. However, imaging a patient with renal disease often presents difficulty, particularly when the radiologic procedure requires contrast. Ultrasound, CT scan without IV contrast, and MRI without gadolinium are non-nephrotoxic. Dilemmas arise when a radiologic study with contrast is required in the patient with CKD. In such instances, the clinician must weigh the potential risk of contrast-induced nephrotoxicity (CIN) associated with the iodinated contrast of a CT scan versus the potential risk of nephrogenic systemic fibrosis (NSF) from gadolinium-enhanced MRI. This recently described systemic condition is characterized by fibrosis and thickening of the skin and other organs. Because of the risk and severity of these conditions, a serum creatinine and estimation of GFR should be determined in all patients undergoing radiologic studies with contrast. Two reviews discussing the risks of CIN and NSF in CKD patients [72, 73] are summarized below.

In addition to CKD, several other risk factors have been identified which increase the risk of CIN after interventional cardiac procedures [74]. These include advanced age, diabetes mellitus, congestive heart failure, hypotension, hypovolemia, and anemia. Since the adverse consequences appear to be a direct effect of the contrast agent itself, it can be inferred that these risk factors apply equally to CIN after CT scan with contrast. One method to mitigate CIN is the use of low-osmolar contrast media (<915 mOsm/kg) instead of high-osmolar (>1500 mOsm/kg) agents. Isoosmolar (290 mOsm/kg) contrast agents have also been studied, though it remains unclear if these agents reduce the risk further than that seen with the low-osmolar preparations [75, 76]. The dose of contrast should be minimized as much as possible [76, 77], and repeat doses should be avoided. The patient should receive IV fluid prior to contrast administration unless volume overloaded or other-

wise contraindicated [76]. The fluid should be isotonic, such as normal saline. According to the REMEDIAL I and REMEDIAL II trials, isotonic sodium bicarbonate-based fluids may or may not be superior to normal saline [78, 79], possibly depending on the patient's GFR and the precise therapy received by the control group. Results from studies describing the pericontrast treatment with *N*-acetylcysteine remain mixed. Given the relatively low cost and side effect profile of the oral preparation, many nephrologists previously used *N*-acetylcysteine as prophylaxis. The dose of 1200 mg rather than 600 mg twice daily on the day prior to and day of contrast may be more effective in preventing CIN [80]. The IV formulation of the medication has been used in patients who cannot tolerate oral administration but is more expensive and carries the risk of allergic reaction. The use of *N*-acetylcysteine as prophylaxis for IV contrast has fallen more out of favor since the last publication of this book, in favor of volume repletion with an isotonic solution without *N*-acetylcysteine.

The risk of NSF is highest with the use of gadolinium contrast agents that are nonionic and linear based [72, 81], and if possible these agents should be avoided in CKD patients. The dose of gadolinium should be limited to the smallest dose needed, and repeat gadolinium administration should be avoided. Patients with ESRD, AKI, or CKD stages IV and V (GFR < 30 mL/min/1.73 m^2) are at the highest risk, with only one reported case of NSF in a patient with a GFR >30 mL/min/1.73 m^2 (the GFR was 34 mL/min/1.73 m^2). Other putative risk factors include high-dose ESAs, IV iron, hypercalcemia, and hyperphosphatemia [81]. All potentially reversible risk factors should be corrected. Besides NSF, gadolinium also carries a small risk of AKI, much smaller than that of iodinated contrast with CT scans. Since the recognition of NSF, and the implementation of guidelines to decrease the chances of a patient developing NSF, the incidence of new cases has greatly decreased.

In summary, in patients with AKI, imaging with contrast should be delayed until renal function improves, if at all possible. In patients with stable CKD and a GFR >30 who require contrast to achieve adequate imaging, an MRI with gadolinium is preferred over a CT scan with contrast, as the risk of CIN with contrast-enhanced CT scan would be significantly higher than the risk of NSF with gadolinium. In patients on dialysis with no significant residual renal function, a CT scan with contrast is preferred over an MRI with gadolinium since the risk of NSF is significant and the risk of CIN is essentially nonexistent. In patients with a GFR <30 and who still have significant renal function, the risks and benefits of the imaging must be taken on a case-by-case basis; if non-contrast options are available, they should be used. Whenever a contrast modality must be used, steps should be taken to minimize the risk of complications, as noted previously. If a hemodialysis patient must receive gadolinium, then increased (daily) dialysis is often performed for at least three treatments after the gadolinium exposure. This usually means planning to give the gadolinium prior to a regularly scheduled HD session and the addition of at least one extra dialysis session to the usual three-times-per-week schedule. Repeat gadolinium should be avoided in any patient with a GFR <30. Peritoneal dialysis patients may have a higher risk of NSF [73], in addition to more reliance on their residual renal function, than their HD counterparts, so the risks and benefits of imaging with contrast in these patients must be carefully discussed with the patient's nephrologist. In any CKD patient whose risk of toxicity from the contrast outweighs the benefits of the radiologic study, contrast should be avoided.

Analgesia in Patients with Renal Disease

Ketorolac and other NSAIDs should be avoided in CKD patients, especially those with other risk factors for AKI. In circumstances where NSAIDs must be given, the dosage should be limited. Meperidine and propoxyphene should also be avoided due to the toxic effects of their metabolites which accumulate in CKD patients [82]. The pharmacologically active metabolites of morphine also have a prolonged half-life, and the dose of morphine required to achieve pain relief in CKD patients is usually lower than in patients with normal renal function. One source [83] has recommended fentanyl and methadone as the opiates of choice in CKD and dialysis patients, although these narcotics are the least dialyzable if a patient develops untoward side effects [84].

Anesthesia in Patients with Renal Disease

Choice of anesthetic agents is clearly important for any type of surgery, including orthopedics. The ideal anesthetic agent in the patient with renal disease should be one that is reliably cleared and non-nephrotoxic. Based on the experience during surgery in humans and animals, propofol [46, 85], sevoflurane [46, 85], possibly isoflurane [85], atracurium [23, 46], and cisatracurium [23, 46] have been successfully used in CKD and dialysis patients. Succinylcholine may raise the serum potassium and should generally be avoided in patients with preoperative hyperkalemia. Since the rise in serum potassium may be no worse in patients with ESRD than in patients with normal kidney function, it may be an acceptable choice in patients without preoperative hyperkalemia [23, 24]. The following agents are best avoided: ketamine, suxamethonium, mivacurium, vecuronium, rocuronium, gallamine, metocurine, pancuronium, pipecuronium, and tubocurarine [23, 46, 85].

Miscellaneous

Several laboratory tests are known to be abnormal in patients with CKD, especially patients on dialysis, despite a lack of pathology [86]. The abnormalities are assumed to be secondary to alterations in clearance of the substance from the circulation because of the patient's decreased renal function. While the aspartate aminotransferase (AST) can be decreased, most enzymes are elevated including troponin, amylase, lipase, lactate dehydrogenase, and alkaline phosphatase. If plans exist to follow one or more of these labs postoperatively, then baseline levels should be established at the time that the preoperative labs are drawn. Relative changes should still be considered significant.

Good nutrition, important for wound healing and overall good outcome after surgery, is discussed elsewhere. Renal patients should receive the renal formulation of oral supplements, with the exception of PD patients, who can usually get the regular formulation. Any patient receiving dialysis should be dialyzed sufficiently to meet adequacy goals in order to decrease the anorexia associated with uremia.

Preoperative antibiotics are generally given according to standard surgical protocol. Prophylaxis to prevent endocarditis should be given in certain dialysis patients [23]. Before epithelialization occurs, patients with newly placed synthetic AVG [87], and possibly peritoneal dialysis catheters [88], may have bacterial seeding of these foreign bodies without antibiotics.

Some patients require bowel cleansing prior to orthopedic surgery. Phosphate-based cleansing regimens should be avoided because of the potential for AKI from acute phosphate nephropathy [89], especially in older female patients with hypertension who are taking diuretics, ACE inhibitors, or ARBs. Likewise, during hospitalization, if enema is required for the treatment of constipation, tap water or mineral oil enemas are preferable to phosphate-based enemas.

Occasionally a patient develops supra-therapeutic levels of a medication that lead to unwanted clinical side effects. Some, but not all, medications can be removed from the blood by dialysis. For a determination of whether or not a given medication is dialyzable, the reader is referred to the *Dialysis of Drugs* handbook [84].

Summary

With the gradual aging of the US population, and the increasing number of patients with CKD and ESRD on dialysis or with a functioning kidney transplant, orthopedic surgeons will surely encounter renal patients in their practice. When evaluating and preparing a patient with renal disease for an orthopedic surgery, many factors are considered. With careful attention to the patient's degree of renal insufficiency/failure, need for renal replacement therapy, anemia, electrolytes, medications, etc., the patient can be appropriately assessed for risk, and recommendations can be made to reduce that risk.

The patient with renal disease may often appear to be quite ill and have numerous laboratory abnormalities, sometimes seeming quite overwhelming to manage. Careful preoperative evaluation and perioperative management reduce the risk of long-term renal complications after surgery. With appropriate care, most patients with renal disease can have a successful orthopedic procedure.

Summary Bullet Points

- As many as 40 million Americans may have CKD with over half a million Americans either receiving dialysis or living with a functioning kidney transplant.
- Preoperative evaluation and assessment of perioperative renal complications should include assessment of renal function, adjustment of medications, recommendations for volume status, and treatment of abnormalities in the labs, as needed.
- Patients who are currently receiving hemodialysis, receiving peritoneal dialysis, or living with a functioning renal transplant require coordination with a nephrologist to ensure continued delivery of their dialysis or transplant medications.
- Patients with AKI should have urine and serum electrolytes (including sodium and creatinine) and a renal ultrasound checked. Further management is then determined, based on whether the results suggest a prerenal, intrinsic renal, or post-renal cause of the AKI.
- Patients with hyponatremia should have serum and urine electrolytes (including sodium and creatinine) and serum and urine osmolarity checked; a TSH is often ordered as well. Based on the results of these tests and the patient's volume status, further management is determined.
- Check the patient's medication list to ensure that medications are appropriately dosed for the patient's estimated GFR; if a patient develops AKI, adjust renally excreted medications to prevent supra-therapeutic levels; in patients with preexisting renal disease, alternative medications which are less or non-nephrotoxic should be used in place of medications which are known to increase the risk of AKI.

Case Studies

Case 1

A 47-year-old woman, with a history of systemic lupus erythematosus since age 17, required a total hip replacement because of avascular necrosis and had scheduled the surgery for 2 months from the time of her office visit. She had stable chronic kidney disease secondary to diffuse proliferative lupus nephritis that had previously been treated with cyclophosphamide and prednisone.

Her medications included enalapril, sodium bicarbonate, twice monthly darbepoetin, and weekly vitamin D. Remarkably, she required almost no pain medications, using acetaminophen sparingly.

On exam, her blood pressure was 104/68, her heart rate was 64, and her weight was stable at 117 pounds. Her lungs were clear, heart sounds regular, and no lower extremity edema were present. The rest of her physical exam was also unremarkable.

Previous creatinine values had been in the 2.7–2.9 mg/dL range with an eGFR in the 20s. Laboratory results obtained at the most recent visit revealed the following values: HCT = 27%, Cr = 2.9 mg/dL (eGFR = 23), K = 4.7 mEq/L, HCO_3 = 21 mEq/L, Ca = 9 mg/dL, PO_4 = 4.6 mg/dL, Alb = 3.8 g/dL, unremarkable liver function tests, PTH = 26 pg/mL, and vitamin D 25 = 34 ng/mL.

The nephrologist was asked to counsel the patient on her renal risk from the surgery and to make recommendations for the surgery.

The patient was counseled that she was at risk for acute kidney injury (AKI) after the surgery, given her kidney disease, but that measures would be taken to decrease her risk of AKI, including the adjustment of her medications and use of other medications and intravenous (IV) fluids. Further, she was informed that there were no tests available that could determine if she, or any given patient, would develop AKI. In addition, she did not have risk factors commonly associated with an increased risk of AKI, including advanced age, diabetes mellitus, hypertension, congestive heart failure, peripheral vascular disease, liver disease, or chronic obstructive pulmonary disease.

The following preoperative recommendations were made:

- Renal dosing of medications, including antibiotics, for an estimated creatinine clearance of 20–29
- Avoidance of dehydration/hypotension and use of isotonic fluids such as normal saline during the procedure
- Avoidance of potassium-containing IV fluids, i.e., lactated Ringer's, in order to decrease the risk of hyperkalemia
- Continuation of sodium bicarbonate perioperatively
- Stopping of enalapril 24 h prior to surgery
- Avoidance of other nephrotoxins perioperatively, such as aminoglycosides, NSAIDs, ACE/ARB, IV contrast, etc.
- Treatment of iron deficiency and administration of darbepoetin continued to achieve a HCT > 30% prior to surgery

The patient received a course of IV iron in the kidney center and continued her darbepoetin with an improvement in her hematocrit to 34% prior to surgery. The use of desmopressin was not recommended; the patient did well without bleeding complications. She had an uneventful hip replacement and continued to remain dialysis independent 1 year later.

Case 2

An 82-year-old man was seen by nephrology in the hospital on postoperative day (POD) #2 for asymptomatic hyponatremia and acute kidney injury (AKI) which developed on the night of POD #1. The patient was status post a total knee replacement, secondary to osteoarthritis. He had a history of hypertension, chronic obstructive pulmonary disease (COPD), and gout. The patient had nothing by mouth the morning of surgery and had a late afternoon case. He reported not eating or drinking much on POD #1 but had been eating and drinking more on POD#2. He was receiving normal saline at a rate of 50 mL/h at the time of the renal consultation.

His medications included inhaled fluticasone/salmeterol, allopurinol, and ketorolac every 6 h for seven doses.

On exam, his blood pressure was 108/62 mmHg. His heart rate was 88 supine but increased to 112 beats per minute while sitting. The lungs were clear on auscultation, and his heart beat was regular. No lower extremity edema was noticed. The rest of the physical exam was unremarkable.

On POD #1 the serum Na was 132 mEq/L in the morning and 126 mEq/L in the evening. POD #2, the serum Na was 122 mEq/L. The serum osmolarity was 252 mOsm/kg, urine osmolarity was 630 mOsm/kg, and UNa was <10 mmol/L with a urine output of 480 mL on POD #1. The hourly rate of urine output increased slightly on POD #2. The serum creatinine was 2.4 mg/dL, up from 1.6 mg/dL preoperatively. Other laboratory data of note included a HCT = 33% (after transfusion), K = 4.3 mEq/L, HCO_3 = 24 mEq/L, Ca = 9.4 mg/dL, PO_4 = 2.6 mg/dL, Alb = 3.4 g/dL, and unremarkable liver function tests.

The nephrologist was asked to evaluate and make recommendations regarding the hyponatremia and AKI.

The patient was at risk for AKI, given his age, baseline chronic kidney disease, hypertension, COPD, volume depletion, and use of ketorolac. The cause of AKI was deemed to be prerenal because of the patient's low urine sodium, low fractional excretion of sodium, and physical examination consistent with volume depletion, most notably the low blood pressure for a patient with hypertension and the change in heart rate from the supine to the sitting position. It was concluded that this patient had hypovolemic hyponatremia, for the same reasons that the patient had prerenal AKI: the urine studies and the physical examination were consistent with volume depletion.

The ketorolac was held. The patient was treated with a slow bolus of normal saline: 1 L over 5 h, followed by an increase in the maintenance rate of the normal saline to 75 mL/h. The infusion was given slowly, given his age and history of COPD. The patient was also counseled to increase intake of solutes such as protein, salt, and potassium. He was encouraged to take fluids that had osmoles in them such as milk, soup, and oral supplements. He was encouraged to report any respiratory symptoms or lower extremity edema, at which time fluids were to be held.

Because the AKI had a reversible cause and because the hyponatremia had developed quickly, both were amenable to aggressive treatment. By the morning of POD #3, the patient's creatinine decreased to 1.7 mg/dL, and the sodium had increased to 131 mEq/L. The patient was eating and drinking well, and the IV fluids were stopped. On POD #4, the patient's creatinine was 1.5 mg/dL, and the sodium was 134 mEq/L. He was scheduled for discharge to a subacute rehabilitation center.

In this particular patient, a renal ultrasound was not ordered because the cause of both the AKI and the hyponatremia was apparent after physical examination and laboratory testing. A Foley catheter was not placed because the patient refused. It would, however, be reasonable to place a Foley catheter in an oliguric patient with AKI, especially if the urine output did not increase with fluid intake or if there were to be a suspicion for urethral obstruction.

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Perioperative Care of the Orthopedic Patient with Diabetes Mellitus

16

Naina Sinha Gregory and C. Ronald MacKenzie

Objectives

- To emphasize the challenge of caring for the patient with diabetes in the perioperative setting
- To present a stepwise approach to the preoperative assessment of the patient with diabetes
- To review the array of diabetes medications now used in the outpatient setting
- To present a physiologically based method for perioperative glucose control

Key Points

- Care of the patient with diabetes in the perioperative period is one of the most common and challenging problems of clinical medicine.
- This setting is marked by higher rates of infection, wound breakdown, and other adverse events.
- Management of these patients taxes all levels of medical and nursing care.
- Approaches to the evaluation and management of such patients warrant attention at all levels of inpatient and outpatient care.

Introduction

The number of people with diabetes continues to rise. In 2015 it was estimated that 30.3 million or 9.4% of the US population had diabetes [1]. This number is expected to rise with significant implications in both the inpatient and outpatient settings. Patients with diabetes have three times the risk of being hospitalized [2]. Evidence from several trials links inpatient hyperglycemia with poor outcomes including an increased risk of infection and higher mortality [3]. As the number of patients with diabetes increases, so does the number of patients with diabetes having surgical procedures. Infection and impaired healing are significant concerns. As such perioperative glucose management remains an important challenge. In this chapter the key considerations and current evidence guiding management of the patient with diabetes in the perioperative setting is presented.

The worldwide epidemic of type 2 diabetes continues unabated, its incidence and prevalence increasing hand in hand with the obesity epidemic. It remains the seventh leading cause of death in the USA and continues to be a leading cause of cardiovascular disease, end-stage renal disease, and vision loss [4]. It is estimated that one out of five patients that are discharged from hospital has a diagnosis of diabetes [3].

The outpatient management of diabetes has become even more complicated with the unrelenting development and introduction of new classes of medications, a complex pharmacology driven by new understanding concerning the pathogenesis of type 2 diabetes. No longer conceptualized as the dysfunction of a single organ (i.e., pancreas), diabetes is now understood to involve a convoluted interaction of the pancreas with muscle, fat, liver, brain, kidney, and gastrointestinal tract, a pathophysiology resulting in both insulin resistance and insulin deficiency. As the fourth most common reason for consulting a physician and a leading cause of mortality and disability in the US population, it follows that diabetes is frequently encountered in the perioperative setting where its management challenges the internist, anesthesiologist, and surgeon alike. Indeed in the orthopedic setting it has been estimated that more than 8% of patients undergoing

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primary and revision total hip and knee arthroplasty carry a diagnosis of diabetes and that these patients experience higher rates of postoperative complications and mortality [5]. Furthermore a substantial literature demonstrates that hyperglycemia in hospitalized patients is associated with multiple poor outcomes including infection, increased mortality, and prolonged length of hospital stay. Even patients with hyperglycemia but no history of diabetes fare more poorly [6–9]. Thus diabetes is destined to remain a major challenge to all involved in the care of patients undergoing surgery.

Box 16.1 Preoperative Evaluation of the Diabetic Patient

- Types of diabetes
- Complications of diabetes
- Glycemic control
- Hypoglycemia
- Diabetes therapy
- Other pharmacological therapies
- Surgical procedure
- Anesthetic

Preoperative Evaluation of the Patient with Diabetes

Given the higher prevalence of significant comorbidities in patients with diabetes, the history and physical examination must be broad though focused on a number of relevant organ systems, specifically the heart, kidney, and peripheral nervous system. As the preoperative evaluation of patients from the cardiac, renal, and neurological perspectives is dealt with in their organ-specific chapters in this book, this discussion focuses on an evaluation of glycemic control. Optimizing glycemic control is the main goal in the perioperative management of the diabetic patient. Moreover the high prevalence of coronary artery disease which includes a significant number of asymptomatic patients deserves specific attention, and thus the assessment of cardiac risk is essential in this population.

The key elements of the preoperative evaluation of the patients with diabetes are summarized in Box 16.1 [10]. The determination of the type of diabetes, specifically type 1 or 2, is important because in type 1 diabetes there is little to no endogenous insulin secretion. This places the type 1 patient at higher risk for ketoacidosis in the setting of insufficient insulin administration. They are also at higher risk for erratic glycemic control and hypoglycemic unawareness. For all patients with diabetes, a clear and thorough assessment of the patients' control, including the presence, frequency, and degree of hypoglycemia, is critical. A detailed history including the frequency of glucose monitoring, range of blood glucose values, recent HbA1c levels, and type of insulin or other diabetes medications should be obtained. Further relevant issues are the nature and type of surgical procedure the patient is to undergo, the time of day the surgery is to be performed, and its anticipated duration. The type of anesthesia to be employed is also important as the impact of anesthesia on glucose metabolism and insulin resistance varies with the technique employed. For instance, epidural anesthesia, so often employed in total joint arthroplasty, has minimal metabolic effects [11].

Preoperative investigations are justifiably broader when compared to the patient without diabetes and should include a baseline renal function, an ECG, and an assessment of the patient's glucose control. If not previously assessed within the past 2–3 months, a blood sugar and hemoglobin HbA1c should be obtained [12]. One study reported that a preoperative HbA1c > 8% was an independent risk factor for wound complications in diabetic patients having knee arthroplasty [13]. Another review of more than 700 patients with diabetes undergoing total joint arthroplasty found that an HbA1c of >7.4% resulted in a greater risk of postoperative hyperglycemia (BG > 200 mg/dL) [14]. Not only is there evidence suggesting that elevated blood sugars (>200 mg/dL) and HbA1c (>7.0%) correlate with postoperative complications including an increased mortality [15–18], but also the hemoglobin HbA1c informs decision-making, especially insulin dosing. There is convincing evidence that if the preoperative HbA1c is >9.0%, then basal insulin should be initiated and continued upon discharge if the patient was only on oral or GLP-1 agents prior to surgery [12]. Of particular relevance to the orthopedic population, one study of the risk of surgical site infection following spine surgery supports the view that poor diabetes control portends problems postoperatively [19].

Optimization of the Diabetic Patient

Surgery leads to a neuroendocrine stress response which results in hyperglycemia. This response is mediated by the release of many counter-regulatory hormones including epinephrine, glucagon, and cortisol and growth hormone. There are also inflammatory cytokines including interleukin-6 and tumor necrosis factor-alpha that are released. These hormones and cytokines together lead to a cascade of effects including increased peripheral insulin resistance, decreased glucose utilization, impaired insulin secretion, increased lipolysis, and protein catabolism with resultant hyperglycemia. Ketone production is possible in states of insulin deficiency and relative starvation. The magnitude of these changes varies with each patient and is also influenced by the

Box 16.2 Goals of Perioperative Diabetic Management

- Maintenance of fluid and electrolyte balance
- Prevention of ketoacidosis
- Avoidance of severe hyperglycemia
- Avoidance of hypoglycemia

type of anesthesia employed with general anesthesia resulting in larger metabolic effects. Other significant influences include the magnitude of the surgical procedure and other perioperative factors such as steroid use and the patient's nutritional status. Box 16.2 summarizes the primary goals of perioperative diabetes management.

Poorly controlled diabetes can lead to volume depletion and in severe circumstances such threatening conditions as diabetic ketoacidosis (DKA) or a nonketotic hyperosmolar state (NKH). The mechanism is largely due to the osmotic diuresis associated with hyperglycemia. The renal threshold of glucose reabsorption is exceeded at glucose levels greater than 215 mg/dL; therefore, at higher levels, glucosuria leads to polyuria and increased risk of dehydration [20]. Although rare, and usually a consequence of suboptimal management, these metabolic complications can be life threatening. Thus, in the preoperative phase of management of the diabetic patient, securing optimal control is important in warding off potential metabolic complications postoperatively. No prospective controlled trial demonstrating that controlling glucose or decreasing HbA1c improves the outcome before elective surgery has been reported. Further it is remarkable that many of the obvious questions concerning diabetes management remain unanswered [21]. These include such considerations as the following:

- Is there a preoperative glucose level (or HbA1c) above which surgery should be delayed?
- How should oral hypoglycemic agents be managed prior to surgery?
- How should insulin therapy be managed preoperatively?
- Should the insulin-naïve, poorly controlled patient be started on insulin preoperatively?

These are just a few of the unresolved but key management issues. In the absence of such information, generally accepted approaches to diabetes treatment in the perioperative hospital setting have been developed through consensus of the practicing community [22, 23].

Preoperatively, most patients with diabetes require limited laboratory testing, as a fasting blood sugar (supplemented with home glucose determinations if available), a HbA1c (an index of control over the preceding 3-month period), and a history of hypoglycemia will provide a sufficient picture of the patient's preoperative glycemic control. In patients with long-standing insulin-dependent disease, additional measures including renal function may be useful.

Given the known association between perioperative hyperglycemia and postoperative complications, measures should be taken in the preoperative period to decrease this risk. Time is often short, however, and there will be circumstances in which the prudent course of action is to cancel surgery to allow for the implementation or the modification of appropriate therapy. Defensible criteria for use in preoperative decision-making are as follows: A preoperative HbA1c of <7% is considered satisfactory diabetes control, while a level of >10% (correlates with an average blood sugar of 250 mg/dL) provides grounds for cancellation of elective surgery. For HbA1c levels of an intermediate degree, clinical judgment is required. Reasonable therapeutic responses include the institution of oral agents with quick action including sulfonylureas if daytime hyperglycemia is the patient's pattern or basal insulin if morning hyperglycemia is more the issue. Such therapy can be started 1 week before surgery. Efforts should be made to schedule the patient's surgery early in the day, thereby avoiding prolonged fasting periods. For patients who are on insulin pumps, the basal infusion rate should be maintained preoperatively and throughout the surgical procedure.

Once the decision is made to proceed with surgery, decision-making is then oriented around the patients' mode of therapy, mainly how to manage patients on oral and injectable non-insulin-based agents versus those treated with insulin.

Perioperative Care

Evidence supporting a specific perioperative approach to diabetes care is not strong. A Cochrane review found that intensive glucose control aimed at targets lower than 80–180 mg/dL was not associated with improved outcomes and was associated with more hypoglycemia [24]. Nonetheless the American Diabetes Association Standards of Care 2018 considers the following to be a reasonable approach [25]:

1. Target glucose range for the perioperative period should be 80–180 mg/dL.
2. Perform a preoperative risk assessment for patients at high risk for ischemic heart disease and those with autonomic neuropathy or renal failure.
3. Withhold metformin for 24–48 h before surgery.
4. Withhold any other oral agents the morning of surgery or procedure, and give half of NPH dose or 60–80% doses of a long-acting analog or pump basal insulin.

5. Monitor blood glucose at least every 4–6 h while NPO and dose with short-acting insulin as needed.

The concept of a "sliding-scale" insulin regimen for inpatient diabetes management has been replaced over the past decade by the more physiologic "basal-bolus" regimen. The traditional sliding scale was based on the correction of hyperglycemia once it had already occurred. There was no anticipation of hyperglycemia; therefore, there was no prevention. Basal-bolus regimens (i.e., basal insulin with q6 hours/pre-meal short-acting insulin) has been shown in numerous studies to improve overall glycemic control with less risk of hypoglycemia [26, 27]. A recent study in ambulatory surgery patients with diabetes found that a 25% reduction of the pre-admission insulin dose the night before surgery was more effective in producing a BG in the target range with less risk of hypoglycemia [28].

Non-insulin Hypoglycemic Agents

For the patient receiving non-insulin-based therapies, the topic has become much more complex in recent years with a substantially expanded list of available agents including agents that target the kidney and injectable non-insulin medications that target the gastrointestinal system. At least seven different classes of non-insulin hypoglycemic agents are now available, each differing in its mechanism of action. The list includes insulin secretagogues (sulfonylureas or glinides), biguanides, thiazoladinediones, alpha-glucosidase inhibitors, DPP-4 inhibitors, SGLT-2 inhibitors, and injectable GLP-1 receptor agonists. Despite their efficacy and safety in the outpatient setting, these are difficult agents to use in the hospital. The main reason is the rapidly changing clinical picture where patients are under stress, not eating well, or missing meals because of procedures and may be on new medications that temporarily impact glucose control. These medications cannot be withdrawn after daily dosing and can increase the risk for in-hospital hypoglycemia. It is for this reason that all oral agents are usually held preoperatively. Metformin particularly has been a focus of concern due to the small yet present risk of lactic acidosis, particularly in patients who have developed serious complications such as shock, hypoxemia, or renal failure. The validity of this apparent complication has been challenged, however [29]. Nevertheless metformin is generally held for 24 h preoperatively.

The newest class of diabetes medications, the sodium-glucose cotransporter-2 (SGLT-2) inhibitors, is also becoming a focus of concern. This class of medication improves glycemic control by blocking the reabsorption of glucose by the kidney – leading to glucosuria. This class of medication can increase the risk of dehydration and urinary tract infections. One serious concern is the possibility of "euglycemic" diabetic ketoacidosis that arises when ketoacidosis is not recognized early because of the resultant glucosuria (i.e., blood glucose readings remain normal despite the development of ketoacidosis) [30]. As such, experts in the field agree that this class of medication should be held 3–5 days before any elective surgeries or procedures.

For various reasons related to their specific pharmacology, the other classes of oral hypoglycemic agents are also held prior to surgery mainly to prevent hypoglycemia in patients whose oral intake has been temporarily held or decreased. Two injectable non-insulin medications, GLP-1 analogs and symlin, are now commonly employed in diabetes management. Although new, most clinicians approach these medications as they do the oral hypoglycemic agents, holding them on the day of surgery and restarting once the patient is tolerating oral intake postoperatively. An example of preoperative management guidelines for diabetes agents is shown in Table 16.1.

Table 16.1 Preoperative management of non-insulin hypoglycemic agents

Oral hypoglycemic agents	
Insulin secretagogues	
Sulfonylureasglyburide (Micronase®, Pfizer, NY, NY, USA) Glipizide (Glucotrol®, Pfizer, NY, NY, USA) glimepiride (Amaryl®, Sanofi, Paris, France)	Hold on the day of surgery and while patient is fasting Hypoglycemia may occur in the absence of carbohydrate intake
Glinidesrepaglinide (Prandin®, Novo Nordisk, Bagsvaerd, Denmark) Nateglinide (Starlix®, Novartis, Basel, Switzerland)	
Biguanides	
Metformin (Glucophage®, Merck, Kenilworth, NJ, USA)	Hold 24 h preoperatively
	Putative cause of lactic acidosis
Thiazolidinediones	
Pioglitazone (Actos®, Takeda, Tokyo, Japan)	Hold on the day of surgery and as long as the patient is fasting Minor concern due to slow onset of action and long half-life; these agents rarely cause hypoglycemia
α-Glucosidase inhibitors	

Table 16.1 (continued)

Oral hypoglycemic agents	
Acarbose (Precose®, Bayer, Leverkusen, Germany)	Hold on the day of surgery and as long as the patient is fasting
Miglitol (Glyset®, Pfizer, NY, NY, USA)	Only effective when the patient is eating carbohydrates
Dipeptidyl peptidase inhibitors	
Sitagliptin (Januvia®, Merck, Kenilworth, NJ, USA)	Hold on the day of surgery, restart when oral intake is resumed
Saxagliptin (Onglyza®, AstraZeneca, Cambridge, UK) Linagliptin (Tradjenta®, Boehringer Ingelheim, Ingelheim am Rhein, Germany)	Do not produce hypoglycemia Stop taking 3–5 days before surgery
Sodium-glucose cotransporter 2 inhibitors	
Dapagliflozin (Farxiga®, AstraZeneca, Cambridge, UK) Canagliflozin (Invokana®, Janssen, Horsham, PA, USA) Empagliflozin (Jardiance®, Boehringer Ingelheim, Ingelheim am Rhein, Germany)	Stop taking for 3–5 days
Injectable agents *Glucagon-like peptide inhibitors* *(daily or weekly dosing)*	
Exenatide (Byetta® or Bydureon®, AstraZeneca, Cambridge, UK) Liraglutide (Victoza®, Novo Nordisk, Bagsvaerd, Denmark) Albiglutide (Tanzeum®) Lixisenatide (Adlyxin®, Sanofi-Aventis, Bridgewater, NJ, USA) Dulaglutide (Trulicity®, Eli Lilly, Indianapolis, IN, USA) Semaglutide (Ozempic®, Novo Nordisk, Bagsvaerd, Denmark)	Hold on the day of surgery, restart when oral intake is resumed
Amylin mimetics	
Pramlintide (Symlin®, AstraZeneca, Cambridge, UK)	Hold on the day of surgery, restart when oral intake is resumed

NewYork Presbyterian Hospital-Weill Cornell Campus. (Updated October 11, 2017)

Insulin

In the absence of evidence concerning what constitutes appropriate preoperative insulin management, recommendations to patients should be based on safety considerations. The primary goal should be the avoidance of hypoglycemia with the secondary one being stability of blood glucose values. The glycemic targets in the hospital should be tailored to the individual clinical situation with generally more liberal control in the inpatient setting when compared to outpatient goals. The glycemic targets for inpatient non-ICU settings extended to the preoperative setting include a premeal glucose of 100–140 mg/dL or a random blood glucose level of <180 mg/dL. There are certain groups of patients, particularly the cardiac and surgical ICU patients, where there is evidence that even lower glycemic targets may provide morbidity and mortality benefit [8, 9].

The Assessment of Perioperative Risk in the Diabetic Patient

The reason that patients with diabetes are at higher risk for postoperative complications is not just a function of the hyperglycemia but also the increased risk of cardiovascular disease and immune dysfunction. Acute hyperglycemia has a number of adverse effects and contributes to poor postoperative outcome [31]. Figure 16.1 schematically depicts the relationship of surgical stress and hyperglycemia.

This hyperglycemia may suppress immune function via a number of mechanisms and increase the release of circulating inflammatory cytokines. Decreased nitrous oxide production and increased angiotensin II alter vascular resistance and reactivity. Finally the resulting osmotic diuresis may lead to dehydration and electrolyte and acid–base imbalances. In its most severe form, the resultant hyperosmolarity may result in central nervous system dysfunction and even cerebral edema.

Insulin resistance and its resultant hyperglycemia are directly related to the magnitude of the surgical procedure as well as concomitant therapies (i.e., steroids, epinephrine, and dextrose-containing IV fluids). Anesthetic technique is also of concern. With respect to procedures involving the lower regions of the body such as the spine, hip, and knee, the physiologic consequences of surgery are blunted by the use of epidural anesthesia and when feasible peripheral nerve blocks. Thus preoperative consultation with the anesthesiologist is often useful.

Most of the discourse concerning the diabetic patient undergoing noncardiac surgery focuses on the glycemic-related complications of infection and wound healing, both believed to be favorably influenced by better metabolic control. Indeed the current recommendation to maintain a perioperative glucose concentration of <180 mg/dL is mainly premised on the influence of serum glucose on postoperative infection [6]. Other

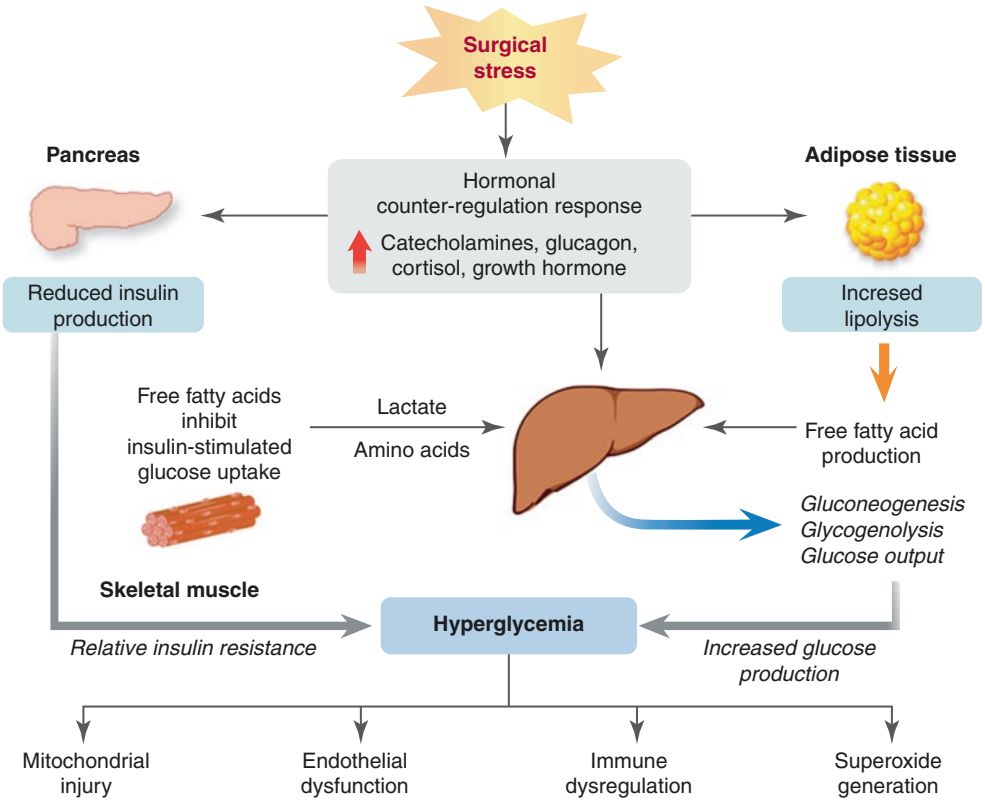

Fig. 16.1 The impact of surgery on stress response. (Used with permission of Wolters Kluwer from Duggan et al. [45])

complications are important, however, though the literature concerning outcomes in diabetic patients undergoing noncardiac surgery is limited. An increase in long-term mortality among patients with diabetes undergoing noncardiac surgery was noted in an early *beta*-blocker trial [32] as well as in another extensive retrospective review in which the overall postoperative mortality was 24% [33]. In the latter investigation, preoperative ischemic heart disease augmented the mortality significantly (44%) underscoring the importance of this prevalent comorbidity in the patient with diabetes. Indeed, of the evaluable preoperative comorbid diseases, coronary artery disease, often occult, should be investigated in this patient population. The evaluation of such cardiac disease follows the dictums and practices outlined in Chap. 13 of this book.

One further important complication relevant to the diabetic patient is that of cerebral injury. Hyperglycemia in the presence of cerebral ischemia may increase neuronal damage and worsen the severity of the neurologic injury incurred. A variety of mechanisms are responsible for this association including the development of lactic acidosis, hemorrhagic transformation of ischemic infarcts, and decreased cerebral blood flow to name a few. Of particular note in the noncardiac surgical setting are observations demonstrating a relationship with blood glucose levels and outcome of acute stroke. While not common after orthopedic surgery, such neurologic injury can have devastating and long-lasting consequences, fully undoing the usually positive impact of the surgical procedure. That elevated blood sugars may increase the severity of such injury should serve as a strong impetus for the optimization of the blood sugar in the perioperative period. Glucose levels >200 mg/dL appear to have unfavorable effects in the setting of cerebral injury, an observation that adds support for the setting of glycemic targets.

Patient Education and Preventive Practices

Patients with diabetes are often well informed and meticulous in their approach to their condition. As such they are important allies in achieving optimal management of their glycemic control. Further they have a good sense of their own system, including their responses to diet and to certain medications. Thus it is helpful to actively include them in the decision-making concerning their perioperative management. This discussion should begin at the preoperative visit when specific recommendations will be made regarding the medication protocol to be used prior to surgery.

As outlined earlier, a number of adjustments in the patient's medication regimen are usually necessary in the 24 h preceding the procedure. The specific nature of these adjustments, their rationale, the postoperative medication strategy, and estimates concerning when the patient is likely to return to his or her usual routine should be fully discussed and negotiated with the patient prior to admission.

Postoperative Management

Decision-making in the postoperative period requires consideration of a number of factors among which include the patient's general condition, their nutritional status, the magnitude of the surgical procedure, and the patient's type of diabetes and its control. The medically stable patient, undergoing surgery of a minor-to-intermediate magnitude, does not experience major surges in their counter-regulatory hormones and typically have their diet resumed soon after the procedure. In such circumstances, common in the orthopedic population, the usual medical regimen can be restarted almost immediately.

In those undergoing major procedures, more significant glycemic responses can occur and the management becomes more challenging. Indeed in such circumstances, oral and non-insulin injectable hypoglycemic agents are often avoided and patients are managed with insulin, usually via the subcutaneous route. Occasionally, in critical surgical settings, intravenous insulin infusions may be required although evidence of the safety and efficacy of such intensive glycemic control is lacking. Indeed meta-analyses of the major clinical trials addressing this issue failed to demonstrate benefit from such strategies [34, 35]. Further an increase of five- to six-fold in the incidence of significant hypoglycemia has been reported [36, 37]. Thus the value of tight glycemic control in the intra- and postoperative period has not been established nor generally advocated [38]. Expert opinion, however, does support achieving reasonable degrees of glycemic control in the perioperative setting. Several professional organizations have provided guidelines defining "glycemic targets" for the noncritically ill, hospitalized patient. These recommendations make clear that uncontrolled hyperglycemia is an unacceptable standard of care [39, 40]. Recommendations for inpatient (non-ICU) glycemic control are fasting and maximal glucoses of 110 mg/dL and 180 mg/dL, respectively. Recognizing the difficulty in achieving these goals consistently, coupled with the dangers of hypoglycemia, some leeway is generally accepted. How can these targets be consistently achieved in practice?

Postoperative Insulin Management

Diabetes management in the postoperative period can be challenging due to the variety of influences that can arise. As such the treatment regimen employed needs to be flexible and responsive to changes arising in the patient's clinical condition. Subcutaneous insulin is the drug of choice for the majority of hyperglycemic patients after surgery. Its advantages include its quick onset of action and its ability to be titrated immediately based on the patients' glucose control. Insulin therapy is indicated for all patients who are on insulin prior to surgery as well as those whose postoperative glucoses remain out of the desired range.

In the stable patient, with reasonable intake of nutrition and satisfactory blood sugars, simply resuming their usual diabetes regimen after surgery is appropriate. Nonetheless when such therapy proves unsatisfactory in the postoperative setting and insulin supplementation is required, employing a methodology that uses exogenous insulin to mimic normal physiologic insulin secretion is indicated. This regimen is built upon three distinct components: *basal* insulin, *nutritional* (prandial/meal) insulin, and *correction*-dose (supplemental) insulin [20, 21]. A patient's total daily insulin requirement (total daily dose, TDD) is the total of these and is the amount of insulin required in 24 h when taking adequate nutrition. Basal insulin is secreted continuously and suppresses hepatic glucose production and ketone production. Nutritional insulin is secreted in response to the ingestion of food and is responsible for the normalization of glucose following a meal. Correction insulin is that given to correct the hyperglycemia that can occur from the increase in counter-regulatory hormones during stress, illness, and surgery. Approximately one-half of the total daily insulin secreted is basal insulin, while the other half is a response to nutritional intake. Remembering this "50/50" rule is helpful in developing insulin regimens in the postoperative setting.

Basal insulin can be provided using a long-acting, low-peaking insulin that results in stable insulin levels, such as glargine or detemir. NPH insulin dosed twice daily can also serve as a basal insulin although the risk of hypoglycemia is higher because of its erratic peak; therefore, the dosage should be reduced by 30–50%. Nutritional insulin must be provided according to the postoperative nutritional program ordered for the patient. Thus patients receiving nutrition in a bolus fashion (regular meals, bolus tube feeding) should be given rapid-acting insulin at the time of their meal to cover the glycemic peak that will follow. Short-acting insulin analogs such as aspart, glulisine, and lispro are common examples. Regular insulin has fallen out of favor as it has an effect up to 6–8 h, and consecutive dosing can lead to accumulation of insulin and an increased risk of hypoglycemia, a phenomenon known as "insulin stacking."

Correction-dose insulin refers to the small supplemental dosages given to patients intermittently to correct hyperglycemia. Using similar insulin preparations as those used to meet nutritional requirements, the purpose of this additional therapy is to return the blood glucose back to the target range. Correction dosages are usually administered at the same time as the nutritional component or every 4–6 h in patients who are not eating. In patients requiring correction-dose insulin on a consistent basis, the basal and/or nutritional regimen will need to be modified. Estimates for the increase in dosing are based on the total number of units of correction insulin that was required in the preceding 24 h. This is then

divided up and added to the basal and nutritional components of the overall insulin coverage. Note that the previous, physiologically based, approach has replaced the familiar "sliding scale" methodology, a reactive generally ineffective strategy that was found to result in more erratic glycemic control with increased rates of both hypo- and hyperglycemia [41, 42].

In situations where correction dosages are required frequently or in high doses, the basal and nutritional insulin component may need to be increased. In these circumstances, the total daily corrective insulin is incorporated into the basal and nutritional insulin requirement for the next day. The goal of management is to achieve glycemic targets, without the need for large supplemental correction insulin. It is important to attempt to keep the 50:50 ratio of basal insulin to nutrition + correction insulin when adjusting the regimen; this will decrease the risk of hypoglycemia.

Having provided a physiologic framework for the approach to perioperative insulin therapy, certain dosing guidelines and rules are useful. Dosing estimates should take into account risk factors for hypoglycemia. These include various comorbidities including renal or hepatic dysfunction, low body weight, heart failure, adrenal insufficiency, alcoholism, and dialysis. Other considerations include elderly or thin patients, patients with poor nutritional intake, and a history of hypoglycemia. The following represents a basic approach:

- Estimate a patient's daily insulin requirement (TDD) when taking adequate nutrition, either using his or her outpatient TDD or employing a weight-based estimation of TDD (Table 16.2), dosing that may require adjustment according to certain patient characteristics.
- The TDD should then be divided into the basal and nutritional components, generally according to a 50:50 distribution. Note that nutritional insulin is held in patients not taking nutrition.
- Table 16.3 summarizes the recommended insulin regimens for varying nutritional situations.
- In order to cover periods of hyperglycemia, a correction-dose insulin scale using bedside glucose monitoring should be established.

Table 16.2 Weight-based insulin dosing

Patient characteristics	Dosing estimate (units/kg/day)
Insulin sensitivity (elderly, lean/malnourished, chronic kidney disease)	0.3
Clinically normal	0.4
Insulin resistance (obese, high-dose steroids)	≥0.5

Used with permission of the Society of Hospital Medicine from Wesorick et al. [23]

The last category of therapy has to do with patients who are managed with an insulin pump which continuously infuses subcutaneous insulin. This approach provides basal insulin at rates that have been adjusted to meet the 24-h needs of the patient. Insulin pumps are still not a common treatment but are more prevalent in the type 1 diabetes popu-

Table 16.3 Society of Hospital Medicine Glycemic Control Task Force recommendation-preferred insulin regimens for different nutritional situations

Nutritional situation	Necessary insulin components	Preferred regimen[a]
NPO (or clear liquids)	Basal insulin: 50% of TDD Nutritional insulin: None	Basal insulin: Glargine given once daily or detemir given twice daily. Nutritional insulin: None. Correctional insulin: Regular insulin q 6 h or RAA insulin q 4 h. Other comments: Dextrose infusion (e.g., D5 containing solution at 75–150 cc/h) recommended when nutrition is held. An IV insulin infusion is preferred for management of prolonged fasts or fasting type 1 diabetic patients
Eating meals	Basal insulin: 50% of TDD, Nutritional insulin: 50% of TDD divided equally before each meal	Basal insulin: Glargine given once daily or detemir given twice daily. Nutritional insulin: RAA insulin with meals. Correctional insulin: RAA insulin q AC and HS (reduced dose at HS)
Bolus tube feeds	Basal insulin: 40% of TDD. Nutritional insulin: 60% of the TDD, divided equally before each bolus feed	Basal insulin: Glargine given once daily or detemir given twice daily. Nutritional insulin: RAA insulin with each bolus. Correctional insulin: RAA insulin with each bolus
Continuous tube feeds	Basal insulin: 40% (conservative) of TDD. Nutritional insulin: 60% of the TDD in divided doses	Basal insulin: Glargine given once daily or detemir given twice daily. Nutritional insulin: RAA insulin q 4 h or regular insulin q 6 h. Correctional insulin: Should match nutritional insulin choice
Parenteral nutrition	Insulin is usually given parenterally with the nutrition	Initially, a separate insulin drip allows for accurate dose finding. Then, 80% of the amount determined as TDD using drip is added to subsequent TPN bags as regular insulin. Use correctional subcutaneous insulin doses cautiously, in addition

Used with permission from Maynard et al. [46]
HS at bedtime, *IV* intravenous, *NPO* nothing by mouth, *q 4 h* every 4 h, *q 6* h every 6 h, *q AC* before every meal, *RAA* rapid-acting analog, *TDD* total daily dose, *TPN* total parenteral nutrition

lation. Hospital staff, in contrast to the patients, is often not comfortable with the management of an insulin pump. Reaching an agreement with the patient to engage so directly in their own therapy (a unique form of comanagement) may be reasonable in some circumstances though it requires close communication with and oversight by the medical-nursing staff. Alternatively, if such conditions cannot be achieved, or the hospital personnel are not comfortable with this degree of patient therapeutic autonomy, patients on insulin pumps at home can be converted temporarily to the standard subcutaneous approaches just outlined. Other situations in which insulin pump therapy is not recommended include surgeries where fluid overload may occur as edema may interfere with the absorption of subcutaneous insulin or if patients may temporarily lose their ability either cognitively or physically to manage the pump postoperatively [43].

Finally, hospital discharge presents a challenging transition in care for the diabetic patient as their glycemic control may have been disrupted by the circumstances of their surgery. The Joint Commission recognizes this problem as an important quality domain citing the need for patient education with respect to finger-stick glucose monitoring, glycemic targets, and recognition and treatment of hyper- and hypoglycemia; communication with the patient's primary physician concerning any changes in diabetic care is also emphasized in their recommendations [44].

Summary

In conclusion, the care of the patient with diabetes in the perioperative period is one of the most common and challenging problems of clinical medicine. In addition to being plagued with higher rates of infection, wound breakdown, and other adverse events, the management of these patients taxes all levels of medical and nursing care. As such, approaches to the evaluation and management of such patients warrant attention at all levels of inpatient and outpatient care.

Summary Bullet Points

- Diabetes mellitus is a frequently encountered and challenging condition in the perioperative setting.
- Patients with diabetes are at additional risk after surgery due to their high prevalence of comorbidities, most importantly cardiovascular disease.
- A systematic approach to the preoperative assessment of the patient with diabetes is required emphasizing such considerations as the degree of glucose control, medications, and anticipation of postoperative insulin resistance.
- Postoperative "glycemic targets" should be established preoperatively.
- The concepts of basal, nutritional, and correction-dose insulin therapy must be appreciated.
- Glycemic-related postoperative complications, specifically infection and impaired wound healing, must be anticipated.

Case Study

A 58-year-old man with a history of type 2 diabetes, hypertension, and hyperlipidemia is scheduled to undergo a total knee arthroplasty and is seen for a preoperative visit to assess his diabetes control and to determine what adjustment in diabetes regimen should be done the night prior to surgery and postoperatively. His current diabetes regimen includes metformin 1000 mg po BID, exenatide 1.8 mg subcutaneously daily, and glargine insulin 18 units subcutaneously every evening. His HbA1c 1 week prior to the scheduled surgery is 7.8%. His renal and hepatic function is normal and his urine microalbumin is negative. His blood pressure is 132/84. Given his acceptable glycemic and blood pressure control, it is decided that he can proceed with the surgery. On review of his at home blood glucose (BG) monitoring, his fasting values are in the 100–120 mg/dL range, and his daytime postmeal values are generally less that 180 mg/dL with occasional values >220 mg/dL. The day before surgery, the metformin is held and the exenatide is given. The evening prior to surgery, his glargine dose of 18 units is given. The morning of surgery, his exenatide is held. In the hospital, he is placed on q6 hour finger sticks with an aspart insulin correction scale for values >150 mg/dL. Postoperatively, his BG is 220. He is given aspart insulin for correction. The evening of surgery, his BG is 185 and he is given 18 units of glargine. The morning following surgery, he is tolerating normal po intake and his correction insulin regimen is adjusted to start at 70–100 mg/dL to cover the carbohydrate intake of his meal. He is scheduled for discharge the following day. His BG values remain in the range of 100–180 mg/dL. He is discharged on his preadmission diabetes regimen with scheduled follow-up with his primary care doctor.

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Perioperative Care of the Orthopedic Patient with Gastrointestinal and Liver Issues

17

Charles Maltz

Objectives

- To present an approach to the perioperative evaluation and management of the patient with known or newly presenting gastrointestinal (GI)/liver diseases
- To explore approaches to the prevention and management of postoperative GI bleeding
- To present an approach to the diagnosis and treatment of postoperative abdominal distention

Key Points

- The most effective preoperative optimization of the patient with abnormal liver function tests/cirrhosis and GI disease is required.
- The evaluation of new postoperative liver function abnormalities is essential.
- The prevention and management of postoperative GI bleeding are critical.
- The evaluation and management of postoperative abdominal distention are critical.

Introduction

The majority of patients undergoing orthopedic surgery will have an uncomplicated postoperative course, experiencing no or only minor problems of a gastrointestinal or a hepatological nature. In circumstances when such clinical issues arise pre- or postoperatively, the gastroenterologist may be called for advice. Common problems such as postoperative nausea, vomiting, or constipation are most often managed by the general medical consultant. However, more threatening problems associated with significant morbidity and mortality do occur and constitute the primary emphasis of this chapter. Key to their management is early identification and preemptive treatment. Common examples range from the evaluation of abnormal liver function studies to more severe clinical challenges including the preoperative recognition of alcoholic liver disease, a condition that often portends alcohol withdrawal in the postoperative period; postoperative ileus, an often difficult problem arising as a consequence of bed rest and narcotics; infectious complications such as *Clostridium difficile* colitis; and gastrointestinal bleeding, all of which are reviewed herein.

Preoperative Evaluation

Identification of Conditions That Affect Postoperative Gastroenterological Outcome

As always, the preoperative evaluation begins with a thorough history, a physical examination, laboratory studies, and, if necessary, radiographic assessments. With a few important exceptions, the majority of gastroenterologic diseases do not require special consideration prior to surgery. Thus, the preoperative evaluation should primarily focus on conditions associated with actual mortality risk in the surgical patient, particularly liver disease. The other gastroenterologic conditions arising in the surgical setting tend to occur postoperatively and usually cannot be predicted prior to surgery.

Elevated Transaminases Without Cirrhosis

Due to the still widespread performance of routine laboratory studies prior to surgery, the finding of abnormal liver function tests (LFTs) in the preoperative setting is a common phenomenon. Indeed, broadly observed, such findings are

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seen in 9% of the US population [1]; thus, such abnormalities can be expected in a significant proportion of patients evaluated before surgery. The differential diagnosis of asymptomatic LFT elevations is broad and includes numerous, often benign, conditions (Box 17.1); the perioperative implications of such findings are dependent on their etiology and chronicity. The most common causes for chronically elevated LFTs are nonalcoholic fatty liver disease, alcoholic liver disease, chronic viral hepatitis (usually hepatitis C), and medications. Finally, one would be remiss in not considering alcoholism and the possibility of postoperative alcohol withdrawal in any patient with hepatic dysfunction [2]. In addition to the presence of liver disease, the history of unexplained multiple fractures or a history of head and neck cancer should raise the suspicion for alcoholism.

Box 17.1 Causes of Mild Increases in ALT or AST Levels

- *Hepatic: Predominantly ALT elevations*
  - Chronic hepatitis B
  - Chronic hepatitis C
  - Acute viral hepatitis (A–E, Epstein–Barr virus, cytomegalovirus)
  - Steatosis/steatohepatitis
  - Hemochromatosis
  - Medications
  - Toxins
  - Autoimmune hepatitis
  - Alpha-1-antitrypsin deficiency
  - Wilson's disease
  - Celiac sprue
- *Hepatic: Predominantly AST elevations*
  - Alcohol-related liver injury
  - Steatosis/steatohepatitis
  - Cirrhosis
- *Extrahepatic*
  - Gallstone disease
  - Thyroid disease
  - Hypernephroma
  - Hodgkin's lymphoma
  - Muscle injury
  - Anorexia nervosa
  - Adrenal insufficiency

Cirrhosis and Chronic Liver Disease

In the preoperative evaluation of the patient with potential hepatic dysfunction, one seeks to determine the severity of any chronic liver disease, as well as the degree of hepatic inflammation, and to consider how these processes might affect the ability of the patient to tolerate surgery and anesthesia. Clues regarding the presence of cirrhosis may be found in the patient's history, through physical exam or via ancillary testing. A history of alcoholism, prior illicit drug use, a history of hepatitis B or C, ascites, or prior variceal bleeding or encephalopathy has obvious meanings. The physical examination findings of cirrhosis include abdominal ascites, spider angioma on the chest, and gynecomastia in a male patient. Asterixis, altered sleep patterns, or slowing of mentation suggests encephalopathy.

The most common lab findings of cirrhosis are an elevated INR, low albumin, and decreased platelet count. If suspicion of cirrhosis exists, the most cost-effective test is a sonogram of the liver. Suggestive sonographic findings, coupled with the history and laboratory values, should be sufficient to alert the examiner to this diagnosis. The presence of cirrhosis results in an increased susceptibility to infections as well as decrease in liver reserve in the setting of perioperative circulatory changes. Such hepatic functional compromise may result in postoperative liver and/or renal failure. The stratification of the patient as to the risk of the procedure from a hepatic standpoint depends on the procedure under consideration, the elective or the emergent nature of the procedure, and the underlying condition of the liver.

Optimization of Gastroenterological and Hepatic Conditions That May Affect Postoperative Outcome

For virtually all of the benign conditions mentioned previously, surgery can proceed without delay. However, nonemergent surgery should be avoided in the patient with acute viral or alcoholic hepatitis, as such conditions are associated with a substantial mortality even in the absence of surgery [3]. Further, in other patients, who exhibit no evidence of cirrhosis, surgery can also be safely performed. In some instances such as with an offending medication or excessive alcohol ingestion, the etiology can be removed, surgery deferred, and the responsible factors eliminated so as to allow for improvement of liver function. In patients with chronic hepatitis C or nonalcoholic fatty liver disease, surgery can be safely performed if there is no cirrhosis.

As will be discussed later, postoperative outcome is closely linked to the optimization of hepatic processes in patients with more severe forms of liver disease. Thus in the cirrhotic patient, with clinical evidence of hepatic decompensation (elevated INR, low albumin, ascites, encephalopathy), surgery should be delayed with efforts directed at achieving better control of the hepatic dysfunction. Relevant treatment approaches may include platelet transfusions to correct severe thrombocytopenia (<50,000). The INR is not a good measure of bleeding diathesis and, indeed, most cir-

Table 17.1 The Child–Turcotte–Pugh (CTP) score

	1	2	3
Encephalopathy	None	Mild	Severe
Bilirubin	<2	2–4	>4
Ascites	None	Small	Large
Albumin	>3.5	2.8–3.4	<2.8
PT prolongation	<2 s	2–6 s	>6 s

CTP A5–6, CTP B6–9, CTP C10–15

rhotic patients tend to be hypercoagulable. Transfusions of plasma or blood should be avoided unless absolutely necessary so as not to increase portal pressure and provoke variceal bleeding. A high suspicion of infection postoperatively should be entertained in a deteriorating patient. This is particularly true of the cirrhotic with ascites as such patients are at risk for spontaneous bacterial peritonitis. Similarly, blood cultures should be drawn in the postoperative patient with clinical deterioration. In the advanced cirrhotic with ascites, albumin should be used rather than saline in an effort to increase renal perfusion and avoid hepatorenal syndrome. NSAIDS and other potentially nephrotoxic medications should be avoided perioperatively in these patients.

The Assessment of Postoperative Risk

In patients identified with acute or chronic hepatic disease, the Child–Turcotte–Pugh (CTP) score (Table 17.1) has traditionally been used to stratify patients as to the severity of their liver disease. Despite its long track record, weaknesses in the predictive capacity of the CTP methodology have been recognized and ascribed to two subjective components of the classification, namely, encephalopathy and ascites. Thus, recently an alternative approach employed in liver transplant allocation has been more broadly employed in surgical risk stratification [4, 5]. The formula, the so-called model for end-stage liver disease (MELD), uses only objective laboratory data and may be the best predictor of 30- and 90-day mortality (Table 17.2) which is calculated as follows:[1]

$$\text{MELD} = 3.78\left(\text{serum bilirubin}\left[\text{mg/dl}\right]\right) + 11.2\left(\ln \text{INR}\right) + 9.57\left(\text{creatinine}\left[\text{mg/dl}\right]\right) + 6.43.$$

In comparing the two systems, a CTP class A correlates with a MELD score of ≤8, CTP class B to a MELD score of 9–16, and CTP class C similar to a MELD score of >16 [4]. Using either a Child's score or the MELD reveals that worsening liver function results in increased perioperative mortality and morbidity [6]. The overall rates of significant complications were 14.3%, 28.6%, and 100% in cirrhotic patients with CTP classes A, B, and C; the associated mortality rates were 4.7%, 14.3%, and 100% for CTP classes A, B, and C, respectively [7]. A study from Korea reviewing hip arthroplasty in cirrhotic individuals found that a higher CTP score ($p = 0.0001$) and a high level of creatinine ($p = 0.0499$) were associated with significantly increased perioperative complications or death [8].

Table 17.2 Relationship between MELD score and postoperative mortality

Mortality, % (no. of patients at risk)						
MELD score	7 days	30 days	90 days	1 year	5 years	10 years
0–7 ($n = 351$)	1.9 (314)	5.7 (301)	9.7 (287)	19.2 (253)	50.7 (123)	72.6 (57)
8–11 ($n = 257$)	3.3 (236)	10.3 (219)	17.7 (200)	28.9 (170)	58.5 (83)	78.1 (35)
12–15 ($n = 106$)	7.7 (94)	25.4 (78)	32.3 (69)	45.0 (56)	69.5 (24)	87.2 (10)
16–20 ($n = 35$)	14.6 (29)	44.0 (19)	55.8 (15)	70.5 (10)	94.1 (2)	94.1 (2)
21–25 ($n = 13$)	23.0 (7)	53.8 (4)	66.7 (3)	84.6 (2)	92.3 (1)	100 (0)
≥26 ($n = 10$)	30.0 (6)	90.0 (1)	90.0 (1)	100 (0)	100 (0)	100 (0)

Used with permission of Elsevier from Teh et al. [4]
MELD model for end-stage liver disease

Elevated Liver Function Tests without Cirrhosis

As mentioned earlier, patients with elevated LFTs without evidence of cirrhosis may require further investigation to identify the etiology of their abnormal laboratory parameters. Typically, mild elevations in transaminases, such as those arising from chronic hepatitis or from nonalcoholic fatty liver disease, are not a contraindication to surgery. Patients with orthopedic issues often take non-steroidal medications; diclofenac is the biggest offender in causing a transaminitis. Alternatively, it would be unwise to proceed with non-emergent surgery in the setting of acute alcoholic or viral hepatitis. Elevations in transaminases from chronic alcohol abuse should prompt monitoring for alcohol withdrawal in the perioperative period. Not all patients who abuse alcohol suffer from alcohol withdrawal, and a thorough history should provide such details. A history of prior alcohol withdrawal is most worrisome. Symptoms include hypertension, tachycardia, tremors, nausea, and/or vomiting. If alcohol withdrawal is not addressed with administration of benzodiazepine therapy and hydration, patients can rapidly progress to a state of delirium tremens (DTs), a condition characterized by confusion, tachycardia, fever, and a mortality of 5%.

[1] Numerous internet sites which allow calculation of the MELD scores are available.

The Postoperative Period

The GI consultant often first becomes involved postoperatively, since the majority of gastroenterologic complications arise as a result of anesthesia, the surgery itself or from antibiotics, and/or narcotic therapy. The remainder of this chapter focuses on the common gastroenterologic complications in this setting.

Postoperative Nausea and Vomiting

Postoperative nausea and vomiting (PONV) is a frequent problem in the postoperative setting. Approximately one-third of surgical patients experience nausea and/or vomiting after general anesthesia [9]. An outcome rated by patients to be amongst the ten most undesirable consequences of surgery [10], PONV is believed to be multifactorial in etiology with such risk factors as female sex, nonsmoker status, and a previous history of postoperative nausea, vomiting, or motion sickness; postoperative opiate use is also a risk factor [11]. The presence of none, one, two, three, or four such risk factors is associated with an incidence of 10%, 21%, 61%, and 79%, respectively [12]. Such problems often herald the onset of more significant problems to come, specifically postoperative abdominal ileus.

When evaluating a patient with PONV, a thorough review of the medication list is important, since medications are often the culprit. Examples of medications used in the postoperative patient that may cause nausea and subsequent vomiting are analgesics, including aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), and opiates. Additionally, disorders of the gastrointestinal tract should be considered. Mechanical obstruction, such as a small bowel obstruction, can also cause acute-onset nausea and vomiting; similarly an intestinal pseudo-obstruction can bring about these symptoms. Other underlying conditions existing prior to surgery, such as gastroparesis and migraine headaches, can likewise manifest in this manner and should be considered as potential etiologies. Central nervous system causes, such as tumor, or meningitis may be considerations in the appropriate clinical setting but are uncommon.

Evaluation of the patient with new-onset postoperative nausea and vomiting involves a thorough history, addressing the previously mentioned issues, as well as a physical exam. If there is concern for obstruction or pseudo-obstruction, an abdominal X-ray or CT scan should be obtained and workup should proceed as discussed later in this chapter.

Treatment involves addressing both the presumed etiology and the use of antiemetics. If it becomes apparent that the nausea may be medication related, try to minimize or eliminate the use of that medication. Both antiemetic and pro-kinetic medications can be helpful. Given that postoperative nausea is felt to be associated with the neurotransmitter dopamine, metoclopramide, the dopamine antagonist can be used [13]. Metoclopramide, with its antiemetic and prokinetic properties, can also be associated with extrapyramidal side effects. Similarly, prochlorperazine, a dopamine antagonist, can be used for postoperative nausea and vomiting. Like metoclopramide, it is associated with extrapyramidal side effects. Ondansetron, a serotonin antagonist, can also be an effective antiemetic. One should be careful not to continue these medications at discharge, however.

If the nausea and vomiting persist, despite a thorough workup, elimination of offending medications, an unremarkable abdominal X-ray, and proper use of antiemetics, then one should consider an evaluation by a gastroenterologist. Endoscopy may need to be considered in order to rule out such conditions as partial outlet gastric obstruction due to peptic ulcer disease or erosive esophagitis.

Postoperative Abdominal Distention

Abdominal distention is not uncommon in the postoperative period. Usually this resolves as the patient is weaned from narcotic analgesia and becomes more ambulatory. Occasionally, however, it can persist or progress to marked distention, a condition referred to as postoperative ileus. Megacolon, arising from *Clostridium difficile* colitis, is also in the differential diagnosis, particularly when the diarrhea accompanies the distention. Acute intestinal pseudo-obstruction, called *Ogilvie's* syndrome, is an acute ileus occurring in the postoperative state after procedures that do not involve manipulation of the abdominal viscera [14]. This was originally described after the caesarean section and can be seen after cardiac surgery as well as after orthopedic procedures such as spine and hip surgery. Ileus was found to occur in 0.7–4.0% of patients after total joint arthroplasty and up to 5.6% in patients who underwent revision total hip arthroplasty [13]. This portion of the chapter focuses on the diagnosis and management of a postoperative distention.

Although there are no specific criteria for the diagnosis of *Ogilvie's* syndrome, the symptoms may include abdominal distention and bloating, diffuse abdominal pain, nausea and/or vomiting, obstipation, or delayed transit of flatus. This can be accompanied by the inability to tolerate any oral intake with symptoms persisting for more than 3–5 days after surgery. On physical exam, patients typically have abdominal distention, absence of or hypoactive bowel sounds, and tympani to percussion and may have abdominal tenderness.

Initial radiographic evaluation should include an abdominal X-ray, both supine and upright, to confirm that the symptoms can be attributed to a postoperative ileus and to rule out mechanical obstruction. A mechanical obstruction must be considered prior to proceeding with management of the

ileus. The differential for a mechanical obstruction includes volvulus (colonic torsion), diverticulitis, carcinoma, and a small bowel obstruction with the management of these depending on the diagnosis. A volvulus may be managed colonoscopically. The date of the last screening colonoscopy is vital when contemplating a colonic carcinoma. Similarly, the patient history is necessary, since a history of previous abdominal surgeries can suggest adhesions and thus small bowel obstruction. Feculent emesis, severe abdominal pain, and peritoneal signs are more suggestive of a small bowel obstruction than paralytic ileus, and management often involves surgery. Acute urinary retention may present with similar features, but a careful exam should be able to detect a distended bladder.

If a small bowel obstruction or other causes of mechanical obstruction cannot sufficiently be ruled out with the patient presentation and abdominal X-rays, then computed tomography (CT) scan of the abdomen and pelvis should be done for further evaluation. Prior studies have found CT to have high sensitivity and specificity for distinguishing paralytic ileus from small bowel obstruction. If there is concern for obstruction of the left colon, a gastrografin enema may be used as a diagnostic imaging modality. A closed loop obstruction can occur in patients who have Roux en Y bariatric surgery and may not be apparent on CT scan. In such a patient, a consultation with a bariatric surgeon should be sought.

Once a mechanical obstruction has been excluded and it has been determined that a postoperative paralytic ileus is the correct diagnosis, the initial management involves determining the etiology of the ileus since certain causes may be reversible. Laboratory tests including an electrolyte panel, including sodium, potassium, and magnesium, should be carried out. Hypokalemia and hypomagnesemia are easily correctable reversible causes of a paralytic ileus. The goal of repletion should be a potassium level of 4 mEq/L and a magnesium level of 2 mEq/L. Of note, the potassium should be repleted prior to the magnesium when both electrolytes are deficient. Another common, yet often reversible, cause of a paralytic ileus is one that is secondary to opiate use. It is not uncommon for patients to be on either intravenous or oral opiate regimens for pain control in the postoperative period. Opioids contribute to postoperative gastrointestinal dysmotility by decreasing the normally coordinated movement of the gastrointestinal tract. This may be prevented, or abated, by minimizing the use or stopping the use of narcotic medications or by substituting non-opiate medications for pain management, such as NSAIDs. Alternatively, the use of methylnaltrexone, a peripherally acting μ-opioid receptor antagonist, by subcutaneous injection, can mitigate the effects of opiates and help to promote a bowel movement. Further management techniques for postoperative paralytic ileus involve making the patient "nil per os" NPO or insertion of a nasogastric tube if the patient is suffering from vomiting. The use of rectal enemas and suppositories will also stimulate the bowel; the use of the rectal tube is controversial. If the patient is bed bound, frequent turning is necessary. Otherwise, the patient should be encouraged to get out of the bed to sit in a chair or ambulate, since movement will aid in the recovery of bowel motility.

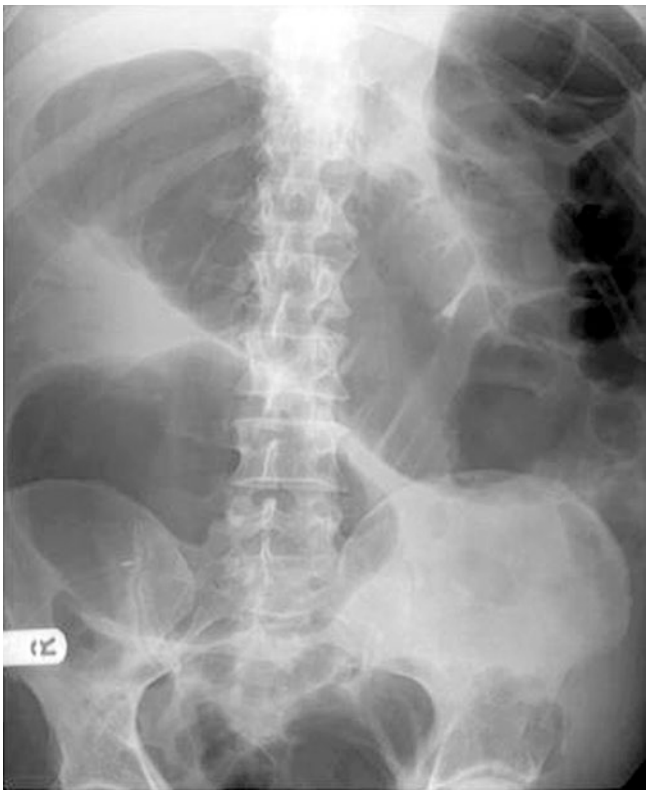

Fig. 17.1 Massive colonic distention

The abdominal X-rays should indicate the severity of the ileus. If there is massive colonic distention on the abdominal X-ray (Fig. 17.1), the differential includes acute intestinal pseudo-obstruction, or *Ogilvie's* syndrome (toxic megacolon), often secondary to *Clostridium difficile* infection. If *C. difficile* has been excluded with a stool sample, and if a mechanical obstruction has been ruled out with CT imaging, then one should proceed with management of the *Ogilvie's* syndrome as discussed previously. It should be noted that with *Ogilvie's* syndrome, there is a 3% perforation rate; 40% of such patients die [14]. Morbidity depends on both the diameter of the distended colon as well as the length of time the colon remains distended. The perforation risk increases with a cecal diameter of >10 cm, so that pharmaceutical or colonoscopic decompression should be considered in those cases. Similarly, decompression is often necessary in cases where the cecal diameter does not decrease with 72 h of conservative treatment.

If the patient has not responded to methylnatrexone and a mechanical obstruction has been excluded, then neostigmine,

a cholinesterase inhibitor, in a dose of 2.5 mg IV should be used in consultation with a gastroenterologist. Bradycardia is the most significant side effect of neostigmine, and thus the patient must be in a monitored setting and all electrolyte abnormalities should be corrected. More than 90% of patients respond within 4 min. If the patient fails to respond to an initial dose of neostigmine, a second dose may be given. Serial abdominal exams and follow-up abdominal X-rays should be obtained since the ileus may reoccur. Alternatively colonoscopic decompression using carbon dioxide and not air for insufflation may be attempted but is a second choice.

Clostridium difficile Colitis and Postoperative Diarrhea

As noted previously, infection with *Clostridium difficile* should be in the differential diagnosis in the postoperative patient with abdominal distention. In mild cases, *C. difficile* may present with diarrhea and an elevated white blood cell count; more severe cases, which tend to occur in elderly debilitated individuals, can progress to toxic megacolon requiring colectomy. In this setting, thickening of the colonic wall may be seen along with air in the wall of the colon (pneumatosis) on CT scanning (Fig. 17.2). If a colonoscopy or a flexible sigmoidoscopy is performed, the endoscopist may see pseudomembranes (Fig. 17.3).

Cases of *C. difficile* are most often seen in patients who have received antibiotics in the perioperative period or those who have had recent stays in a hospital or a rehabilitation facility. Although unusual, such infections can arise in patients who have received no antibiotics at all. Diagnosis is made via stool sampling. Several tests are available for the detection of *C. difficile*. The enzyme-linked immunosorbent assay (ELISA) for the glutamate dehydrogenase (GDH) antigen tests for the organism but not for the toxin. Thus, it cannot distinguish between toxin-producing and non-toxin-producing *C. difficile*. The PCR for the toxin producing genes is both sensitive and specific for the toxin and currently is the most common test used [15]. Patients with unexplained diarrhea of >3 unformed stools in 24 hours should be tested. One should be certain that the patient is not getting laxatives as is the case in many hospitalized patients.

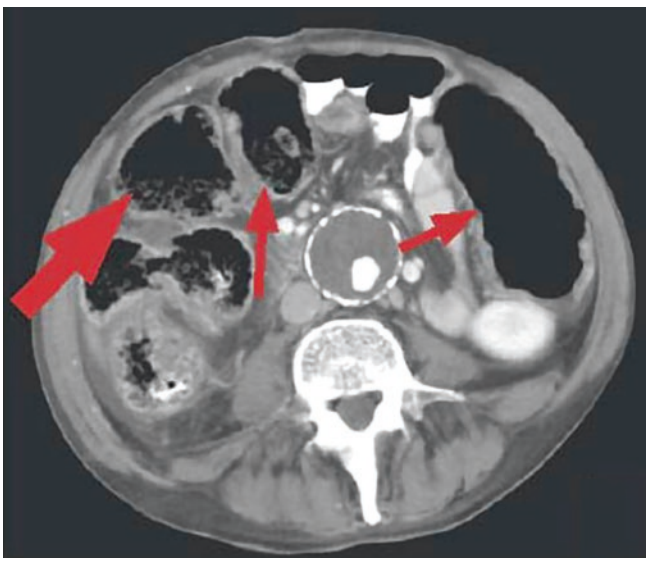

Fig. 17.2 Pneumatosis

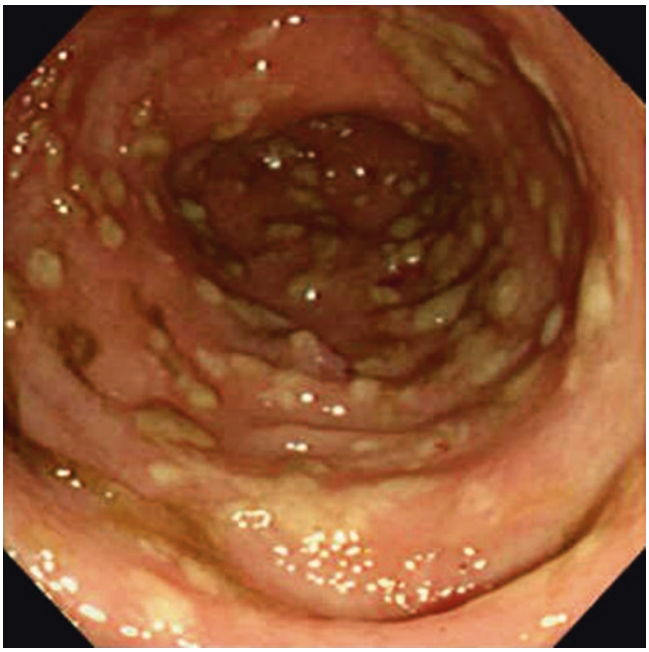

Fig. 17.3 Pseudomembranes

A single negative stool for *C. difficile* by PCR suffices to rule out *C. difficile* infection. With rare exception, there is no role for sending stool for ova and parasites since these are not acquired in hospital. Leukocytosis is often associated with a *C. difficile* infection. If the workup is negative for *C. difficile*, one should consider an antibiotic-associated diarrhea, non-*C. difficile* related. Mild cases may simply reflect carbohydrate malabsorption due to changed gut flora, but other pathogens such as *Staphylococcus aureus* [16] or *Klebsiella oxytoca* [17] have been implicated as causative agents in antibiotic-associated diarrhea.

Once a positive *C. difficile* toxin has been confirmed, or if it appears that the diarrhea is secondary to an non-*C. difficile* antibiotic-associated diarrhea, the first step is to discontinue the offending antibiotic. Antibiotics that are more likely to result in *C. difficile* infection are clindamycin, ampicillin, and quinolones. If an antibiotic is needed, then guided by sensitivities, sulfamethoxazole–trimethoprim is a good alternative.

Inpatient cases of *C. difficile* should be treated with vancomycin by mouth. The dose of 125 mg every 6 hours is adequate. More severe cases merit ICU admission and should be treated with the combination of oral vancomycin and intravenous metronidazole. Fecal transplant has most often been used for recurrent *C. difficile* but has also been employed for severe refractory cases. Stool may be obtained from *open biome* and administered either colonoscopically or from above by enteroscopy [18]. Anti-motility agents should be avoided. A general surgery consult is prudent if there is concern for toxicity or poor response to medical therapy. Surgery may be necessary if there is associated hypotension, an elevated lactate level, and worsening dilation of the colon on abdominal imaging. Of note, the toxin may remain positive for months so that follow-up stool studies are not indicated if the diarrhea has resolved. In the setting of an antibiotic-associated diarrhea with a negative *C. difficile* toxin, the diarrhea will often resolve without treatment. In an effort to prevent *C. difficile* infections, probiotics are commonly given along with antibiotics. The most frequently prescribed is the fungus *Saccharomyces boulardii*. Data for its efficacy are equivocal.

Postoperative Gastrointestinal Bleeding

Orthopedic patients, particularly those undergoing total joint arthroplasty, are almost universally placed on anticoagulation or antiplatelet agents for prophylaxis of deep vein thrombosis. Additionally, NSAIDs are often given for pain management postoperatively, and patients may also have been taking them regularly in the preoperative setting for joint discomfort. Thus, given the iatrogenic coagulopathic state of these patients, one must be attuned to the potential outcome of gastrointestinal bleeding in the postoperative state of an orthopedic patient.

The initial assessment of a GI bleed is focused on the location and determination of the characteristics of the bleeding. The history involves an assessment of a coagulopathic state, usually an active exposure to such medications as aspirin, Coumadin, NOACS (novel oral anticoagulents) NSAIDS, or clopidogrel. Additionally, if the patient has a history of cirrhosis, then portal hypertension with esophageal or gastric varices should be considered as a potential bleeding source. The type of bleeding, whether it is hematemesis, melena, or hematochezia, should be explored. A rectal exam with fecal occult blood testing is often necessary. As part of the physical examination, vital signs, noting specifically blood pressure and heart rate, should be measured to determine hemodynamic stability. Care should be taken to ensure that the patient has proper intravenous access. At this point, if the patient shows evidence of GI bleeding, it is prudent to prevent the patient from taking any food or water by mouth. Blood should be drawn in order to measure a complete blood count and coagulation profile as well as type and cross for possible transfusion. A GI consult should be called.

The nature of the bleeding helps to determine the source of the bleeding. If the patient presents with either hematemesis or melena, an upper gastrointestinal source of the bleeding is likely. The differential includes peptic ulcer disease, which can occur in the setting of aspirin, clopidogrel, and/or NSAID use, esophageal variceal bleeding with cirrhosis as mentioned previously, and also arteriovenous malformations, gastritis, esophagitis, or even underlying malignancy. A common scenario is the postoperative patient experiencing nausea and coffee ground emesis. In the setting of a suspected upper GI bleed, one should give bolus proton pump inhibitor followed by a q 12 hour regimen, a treatment shown to accelerate the resolution of ulcer bleeding and reduce the need for endoscopic therapy [19, 20]. These patients often require upper endoscopy for further evaluation and possible treatment. Patients placed on aspirin, coumadin, NOAC (novel oral anticoagulants), or NSAIDs after surgery may benefit from simultaneous proton pump inhibitor therapy by mouth daily, added for its gastro-protective effect against bleeding.

If a patient presents with hematochezia or frank bright red blood per rectum, a more distal bleeding source, such as the colon, is probable. The differential includes diverticulosis, ischemic colitis, or hemorrhoidal bleeding. Any of these conditions can be exacerbated by the medications listed previously. Depending on the clinical picture and the timing of the patient's bleeding, a colonoscopy may be indicated. A gastrointestinal consultant will dictate the remainder of the management.

Summary

There are several relatively frequent GI/liver issues that may arise in the perioperative management of orthopedic patients. Some, such as abnormal preoperative liver function studies, are often benign; however, other conditions, specifically cirrhosis, are important to define before surgery is performed. In addition, a number of gastrointestinal problems may arise postoperatively ranging from nausea and vomiting to more severe conditions such as abdominal ileus and *C. difficile* colitis. Physicians involved in postoperative care need to be attuned to these conditions, many of which may be subtle at first but quickly evolve and produce severe morbidity. This chapter reviews the most common and potentially severe of the postoperative gastrointestinal problems. The best strategies for avoiding and dealing successfully with these perioperative complications are prevention, anticipation, and early therapy.

Summary Bullet Points

- Abnormal liver tests noted preoperatively should be evaluated so that the presence or absence of cirrhosis can be determined, as well as the acuity, etiology, and severity of any hepatic inflammation.
- Postoperative distention may reflect simple constipation, mechanical obstruction, pseudo-obstruction (*Ogilvie's* syndrome), urinary retention, or megacolon from *C. difficile* colitis. The treatment differs depending on the cause, so a correct diagnosis is crucial to a good outcome.
- Postoperative bleeding is usually minor and will respond to acid reduction therapy. More significant bleeding will require a gastroenterologist for endoscopic evaluation.
- Postoperative nausea and vomiting are usually medication related and respond to appropriate change in medication and antiemetic treatment.

Case Studies

Case 1

A 72-year-old woman scheduled for total knee arthroplasty was seen preoperatively at which time elevated transaminases were noted on routine blood testing. There was no history of excessive alcoholic intake, she was not obese, and hepatitis serologies were negative. Her transaminases were normal in the past with the elevations developing coincident with the institution of diclofenac several months ago. An ultrasound of the liver was normal. A presumptive diagnosis of drug-induced hepatitis was made, diclofenac discontinued, and over the next few months the transaminases returned to normal. Subsequently, she underwent successful surgery.

Case 2

A 75-year-old woman was admitted for emergent surgery after sustaining a femur fracture from a fall. Preoperative blood work demonstrated elevated transaminases, an INR of 1.3, and an albumin of 2.9 g/dL. She had a history of variable transaminases in the past, was on no potentially hepatotoxic medications, and viral serologies were negative. The ANA was positive (3+). A hepatic sonogram demonstrated a cirrhotic liver. Autoimmune-induced cirrhosis (Child's class A) was diagnosed and the surgery was performed without complication. Gastroenterologic follow-up for her liver disease was advised.

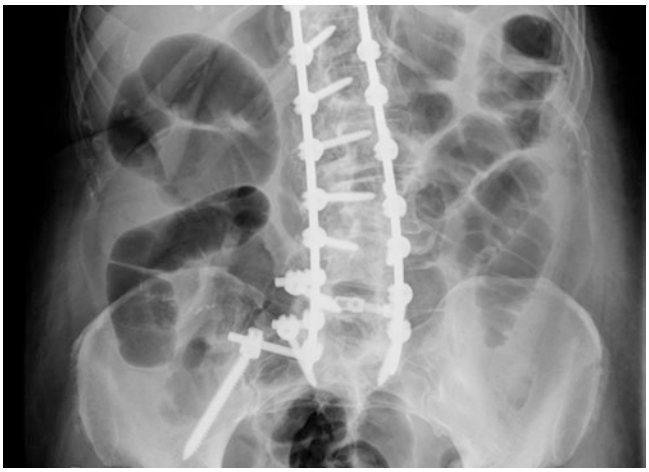

Fig. 17.4 Intestinal ileus

Case 3

A 65-year-old woman with a history of chronic constipation underwent spine surgery. Abdominal distension and no bowel movement were reported 1 week after surgery. On exam, she was mildly tender and distended without active bowel sounds. Laboratory testing demonstrated only mild anemia. An abdominal X-ray (Fig. 17.4) revealed an intestinal ileus.

Discontinuation of narcotics was advised and she was treated with enemas and methylnatrexone. One day after treatment her distention decreased, she developed active bowel sounds, and was put on standing dose of polyethylene glycol which resulted in the return of normal bowel function.

Case 4

67 year old S/P total hip and ankle surgery with subsequent infection on multiple antibiotics with diarrhea. Physical exam significant for distended abdomen with mild tenderness, white count 24.6 x10(3) /uL, creat 1.5 mg/dL and albumin of 2 g/L. A stool was positive for *C. difficile* toxin by PCR. He was initially placed on oral vancomycin along with intravenous metronidazole. His antibiotic coverage was narrowed to trimethoprim/sulfamethaxazole. He gradually improved with decrease in distention of his colon and solid stools.

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Perioperative Care of the Orthopedic Patient with Neurological Disease

18

Jonathan M. Goldstein, Alexander Shtilbans, Pantelis P. Pavlakis, and Erin Manning

Objectives

- To appreciate the variety of neurological conditions that may be seen in the perioperative period.
- To recognize the significant postoperative morbidity associated with these conditions.
- To appreciate the impact of these conditions and complications on postoperative functional recovery.
- To appreciate the antecedents and predictors of postoperative cognitive dysfunction particularly as it relates to surgery in the elderly.
- To understand the management of perioperative disorders such as stroke, Parkinson's disease, seizures, perioperative neuropathy, and confusion.

Key Points

- Neurologic conditions of a chronic nature as well as those arising in the perioperative period present important challenges to the orthopedic surgeon and perioperative team.
- An effective team approach to the preoperative assessment and postoperative management of neurological conditions is essential.
- Chronic neurologic conditions such as cerebrovascular disease, Parkinson's disease, multiple sclerosis, myasthenia gravis, muscular dystrophies, epileptogenic disorders, cerebral aneurysms, and arteriovenous malformations are challenging in the perioperative context.
- The postoperative complications of stroke, postoperative cognitive dysfunction, and the development of perioperative neuropathy are reviewed.

Introduction

Patients with chronic neurological conditions and those at risk for perioperative neurological complications tend to be older, have more comorbidities, and are more functionally compromised than the general surgical population. With the aging of the population, more patients of advanced age are undergoing surgery; furthermore, the number of patients with comorbid neurological diseases is also on the rise. Owing to these considerations, chronic neurological disease and a variety of postoperative neurological complications are increasingly encountered in the perioperative setting. Such problems involve a wide range of neurologic conditions including those of a neurovascular, neurodegenerative, and neuromuscular nature. This chapter reviews the implications of these conditions in the orthopedic setting.

The Preoperative Evaluation

The preoperative evaluation of the patient with preexisting neurological disease begins with a thorough clinical assessment, the intent of which is to clarify the etiology and severity of the underlying neurologic conditions and to ensure it is optimally controlled. This requires a thorough understanding of the pathophysiology of each patient's neurological condition, its treatment, and the patient's capacity to functionally recover from the surgical procedure. In light of the

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number of neurological comorbidities, preoperative decision-making involves such considerations as perioperative medication management, the anesthetic agents and techniques employed and, particularly in the orthopedic setting, the patient's capacity to rehabilitate from surgery.

Owing to the frequency of postoperative cognitive dysfunction (PCD) in elderly patients undergoing surgery, the patient and their family members should be asked about a history of ongoing medical conditions, prior cognitive problems in the postoperative or illness setting, prior medication reactions, subtle evidence of cognitive impairment, and remote neurologic issues, such as stroke, seizure, or head trauma. It is imperative to take an accurate history of alcohol and standing sedative use; the latter should generally be continued through the initial postoperative period. A full neurologic examination, including mental status, is indicated, especially in patients at risk. Useful screening tools for cognitive dysfunction include the mini-mental status examination and assessment of verbal fluency. Evidence of a subtle upper motor neuron lesion should be sought (facial asymmetry, pronator drift, tendon reflex asymmetry, Babinski sign). Abnormalities in gait, previous unprovoked falls, and problems with tremor are also important to identify preoperatively. Preoperative counseling concerning the possibility and natural history of PCD can spare much anguish later on.

Although the preoperative laboratory and general medical assessment also impart important information to the neurologist, these considerations are discussed in detail in other sections of this book. Usually the neurologist is consulted to provide advice regarding the presence of a specific neurological condition or a perceived heightened risk for problems of a neurological nature. Although falling within the general designation of neurological disease, the underlying pathophysiology, clinical manifestations, and treatment of these conditions are disparate. Thus, they are examined herein separately.

Assessment of Perioperative Risk

Cerebrovascular Diseases

Atherosclerotic cerebrovascular disease is among the most common phenomena of aging, a major consequence of which is stroke. Although the prevalence of stroke in the postoperative orthopedic setting is low, its consequences can be so serious such that stroke is still among the most feared potential complications of surgery.

The risk factors for postoperative stroke can be divided into three groups (Box 18.1): patient-related, intraoperative, and postoperative factors. Patient-related risk factors include age (≥62 years), chronic hypertension, myocardial infarction (<6 months of surgery), renal failure (acute or on dialysis), history of stroke or transient ischemic attack (TIA), history of peripheral vascular disease or carotid stenosis, COPD or current smoker, and abrupt discontinuation of antithrombotic therapy prior to surgery. The risk for perioperative stroke can be stratified based on these risk factors: patients ≤2 risk factors are at low risk, those with 3–4 risk factors are at moderate risk, and those with ≥5 risk factors are at high risk (OR = 21 of having a stroke compared with those with no risk factors). Not included in this list is untreated atrial fibrillation, a condition with a 15% annual risk of stroke.

Box 18.1 Risk Factors for Postoperative Stroke

- *Preoperative (patient-related) risk factors*
  - Advanced age (>70 years)
  - Female sex
  - History of hypertension, diabetes mellitus, renal insufficiency (creatine, >2 mg/dl [177 μmol/l]), smoking, chronic obstructive pulmonary disease, peripheral vascular disease, cardiac disease (coronary artery disease, arrhythmias, heart failure), and systolic dysfunction (ejection fraction, <40%)
  - History of stroke or transient ischemic attack
  - Carotid stenosis (especially if symptomatic)
  - Atherosclerosis of the ascending aorta (in patients undergoing cardiac surgery)
  - Abrupt discontinuation of antithrombotic therapy before surgery
- *Intraoperative (procedure-related) risk factors*
  - Type and nature of the surgical procedure
  - Type of anesthesia (general or local)
  - Duration of surgery and, in cardiac procedures, duration of cardiopulmonary bypass and aortic cross-clamp time
  - Manipulations of proximal aortic atherosclerotic lesions
  - Arrhythmias, hyperglycemia, hypotension, or hypertension
- *Postoperative risk factors*
  - Heart failure, low ejection fraction, myocardial infarction, or arrhythmias (atrial fibrillation)
  - Dehydration and blood loss
  - Hyperglycemia

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Table 18.1 Neurodegenerative, neuromuscular, and muscular dystrophy disorders

	Parkinson's disease	Myasthenia gravis	Multiple sclerosis	Muscular dystrophy
Classification	Movement disorder	Neuromuscular disease	Demyelinating disease	Myopathic disease
Pathophysiology	Cell death in midbrain (substantia nigra)	Autoimmune modulated disease by antibodies that block the acetylcholine receptor	Autoimmune-mediated damage to CNS and spinal cord	Inherited x-linked affecting skeletal muscle
Perioperative considerations	↓ Respiratory capacity ↑ Atelectasis ↑ Respiratory failure ↑ Aspiration ↑ Delirium ↓ Rehab capacity	↑ Respiratory failure Resistance to depolarizing muscle relaxants Sensitive to nondepolarizing muscle relaxant	Surgery may exacerbate Sensitivity to pyrexia (avoid) Diaphragmatic paralysis ↑ Aspiration Autonomic dysfunction (BP) Bowel, bladder dysfunction	↓ Respiratory capacity ↑ Respiratory failure Associated cardiomyopathy ↑ Malignant hyperthermia Muscle damage, hypercalcemia with volatile anesthesia and succinylcholine
Management considerations	Pulmonary function studies Initiate longer acting anti-Parkinson's therapy pre-op	PFTs/ABG in high-risk patients Steroids, intravenous immunoglobulin (IVIG), plasmapheresis Titrate anticholinesterase Rx Avoid drugs acting on neuromuscular junction Avoid respiratory depressants (barbiturates, benzodiazepines, opioids, propofol)	Treat pyrexia (ASA, Tylenol) Avoid warming devices PFTs/ABG if cervical/thoracic disease Avoid abrupt withdrawal of baclofen	PFTs, ABG EKG, echocardiogram Avoid volatile anesthetics, avoid succinylcholine

Adapted with permission of John Wiley and Sons from Kallas [69]
[a]Aminoglycosides, polymyxins, β-blockers, Ca^{2+} channel blockers, procainamide, phenytoin

Neurodegenerative and Neuromuscular Diseases

Among the significant diseases falling within these diagnostic categories are Parkinson's disease, multiple sclerosis, myasthenia gravis, and the muscular dystrophies. Table 18.1 summarizes perioperative risk by disease. Given the distinct underlying pathophysiologies involved across these disorders, surgical risk modification is distinct for each condition. If there is a common thread, it is the pulmonary risk conferred by these conditions, the mechanisms of which also vary according to the specific pathophysiology involved. Therefore, in addition to the involvement of the neurologist, pulmonary and preoperative anesthesiology consultation may be prudent in such patients.

Epileptogenic Disorders

Epilepsy, a disorder of recurring seizures, has a prevalence of 0.5–2.0% of the general population, and thus is not rare in the perioperative setting. Challenging to the anesthesiologist, the primary concern is the risk of aspiration, delayed awakening from anesthesia, and disruption of the wound, all potential postoperative complications of a seizure.

Interactions between the anesthetic agents and antiepileptic drugs, specifically the capacity of various anesthetics to modulate or potentiate seizure activity, are important management considerations [1]. Given the polypharmacy of the perioperative period, medication interactions can alter the concentration of antiepileptic drugs in unpredictable ways. Some may decrease seizure thresholds, while others alter the amount of circulating anticonvulsant available resulting in either insufficient or excessive anticonvulsant effects. Further suboptimal patient compliance preoperatively is common in epileptic patients augmenting their vulnerability.

Cerebral Aneurysms and Arteriovenous Malformations

Intracranial vascular anomalies such as aneurysms and arteriovenous malformations (AVMs) are relatively prevalent phenomena occurring in up to 6% and 0.01% of the population, respectively [2]. Although usually stable conditions, their risk of spontaneous bleeding varies according to a number of characteristics, namely the arterial systems in which the lesion arises as well as their size [3]. For instance, aneurysms <7 mm arising in the carotid artery are at low risk for bleeding [4]. Aneurysms in the anterior, middle, and posterior (noncavernous) internal carotid arterial systems, with no history of bleeding, exhibit similar risk for hemorrhage. However, the low risk status of these patients is based on their history of an absence of a prior hemorrhage. There is increased risk or rebleeding regardless of the size and location of the aneurysm.

Arterial vascular malformations similarly challenge decision-making, though owing to their low prevalence, they are encountered much less frequently. The risk they impose

remains significant and influenced by such characteristics as prior hemorrhage, age of the patient, and their location, because lesions deep within the brain are of the greatest concern [5].

Optimization of the Patient with Neurological Disease

Cerebrovascular Disease

Among the modifiable patient-related risk factors are diabetes, hypertension, peripheral vascular disease, smoking, and carotid stenosis, the latter constituting a common neurological dilemma in the perioperative context. As patients with symptomatic carotid stenosis have ipsilateral stroke risk of 26% over 2 years with medical therapy alone, carotid endarterectomy is recommended for those patients with high-grade (70–90%) symptomatic carotid stenosis prior to certain surgical procedures such as coronary artery bypass (CABG). Current data do not support a benefit from carotid stenting over carotid endarterectomy. For patients with asymptomatic carotid stenosis, the stroke rate from both carotid endarterectomy and general surgery is about 3%. As such, carotid endarterectomy is not recommended prior to the surgical procedure. There are no data regarding the relationship between asymptomatic carotid stenosis of any grade and the incidence of perioperative stroke in elective general surgery. However, in patients with known vascular disease such as coronary artery or peripheral arterial disease, it may be prudent to include imaging of the carotid arteries, either with carotid Doppler studies or magnetic resonance arteriography (MRA), as part of preoperative evaluation. If there is hemodynamically significant bilateral carotid stenosis (defined as 70–90%) using either modality, vascular consultation is advised as endarterectomy may be indicated.

Epileptogenic Disorders

In patients with a chronic seizure disorder, a careful history emphasizing the frequency and occurrence of breakthrough seizure should be obtained, medication compliance should be discussed and emphasized, and when possible drug levels should be obtained. Preoperatively, all anticonvulsants should be continued at their usual dosage, taken on the morning of the surgical procedure, and restarted immediately after surgery.

Cerebral Aneurysms and Arteriovenous Malformations

The decision to treat high-risk aneurysms or AVMs prior to surgery depends on the nature of the proposed surgery (coronary bypass, carotid surgery) and the attendant need for anticoagulant and antiplatelet therapy postoperatively. From the standpoint of risk associated with the procedures, orthopedic surgery is not especially hazardous in the setting of intracranial vascular pathology. Prophylactic anticoagulation is, however, standard practice after total joint arthroplasty. The use of low-molecular-weight heparins (LMWH), rather than Coumadin, may be preferable.

Neurodegenerative and Neuromuscular Diseases

Due to its prevalence and a number of important postoperative challenges presented by the disorder, the approach to the perioperative optimization and care of the patient with Parkinson's disease are discussed separately, later in this chapter. It is important to maintain patients on the treatment for their neurologic disease throughout the perioperative period.

Postoperative Complications

For the purposes of this review, selected postoperative complications are reviewed. These include stroke, Parkinson's disease, and the peripheral nerve injuries not infrequently seen after total joint arthroplasty. Although included elsewhere in this textbook, the problem of postoperative delirium is also reviewed here from the perspective of the consultant neurologist.

Stroke

Although the incidence of postoperative stroke is low, particularly in the orthopedic setting, the incidence of non-cardiac surgery-related subclinical stroke may be as high as 10% [6] and is among the most devastating of surgical complications. In addition to its disabling consequences, postoperative stroke is associated with an eightfold risk of (30 day) mortality. Indeed after total hip replacement, a 12% stroke-related mortality has been reported [7].

The etiology of stroke perioperatively is predominantly ischemia and embolic, accounting for 90% of strokes. A large study of patients with stroke after coronary artery bypass reported an embolic (from manipulation of the heart or aorta, atrial fibrillation) mechanism as the most common etiology (62%). Cerebral hypoperfusion, due to combination of arterial stenosis and hypotension, has been reported to be associated with about 9% of postoperative strokes in cardiac surgery patients [8]. While hemorrhagic stroke is seen in 10–15% of strokes in the general population, it is

reported in only 1% of patients with stroke after (CABG) surgery. However, other mechanisms of stroke include paroxysmal atrial fibrillation, systemic inflammatory/hypercoagulable state as a result of either bed rest/arterial stasis or withholding of antiplatelet/anticoagulants. Less common etiologies include air or fat embolism (not uncommon after total knee and hip replacement), paradoxical embolism in patients with patent foramen ovale, and extracranial carotid or vertebral artery dissection. Another more recently identified mechanism is tissue hypoxia due to anemia. The latter seems to be exacerbated by perioperative beta-blocker administration, which is now considered to increase stroke and mortality risk in non-cardiac surgery [9].

Perioperative stroke occurs in a bimodal distribution: half are identified within the first postoperative day and the remaining half occurs after the second postoperative day, even if there appears to be an uneventful recovery from surgery. Postoperatively, patients are at greatest risk for stroke within the first week.

Many older patients who undergo elective surgeries are on oral anticoagulants, and for those patients the risk of thromboembolic events when taken off anticoagulation must be balanced with the risk of bleeding perioperatively. Atherothrombotic events and stroke rates are lower in patients with atrial fibrillation who are on Coumadin but stopped prior to surgery compared with controls without prior anticoagulation; however, they also suffer more major bleeding events. The risk of severe bleeding with the novel oral anticoagulants dabigatran (Pradaxa), rivaroxaban (Xarelto), and apixaban (Eliquis) is reportedly similar to patients who used LMWH and similar to those patients with atrial fibrillation on Coumadin.

The incidence of antiplatelet use in the perioperative setting is high because of the high prevalence of cardiac disease in the elderly population. Aspirin is effective for primary prevention of cardiac disease, as well as secondary prevention of cardiac and cerebrovascular diseases, and also carries with it an increased bleeding risk during surgery. Studies have shown that patients taking aspirin have an increased risk of bleeding, but no increase in morbidity or mortality. Patients on clopidogrel (Plavix) who stopped the medication 5 days before surgery experienced more perioperative bleeding complications and strokes when compared with controls. Therefore, the discontinuation of antiplatelet therapy is not recommended because of associated rebound phenomena that promote thrombosis. Guidelines provided by the American College of Chest Physicians (ACCP) recommend that oral anticoagulants such as warfarin be stopped 5 days prior to major surgery, followed by the institution of shorter-acting heparin preparations. This so-called bridging anticoagulation employs either subcutaneous LMWH or IV unfractionated heparin. In the case of the former (LMWH), the last dose is given the morning of the day before surgery (that is, it should be stopped 24 h before the procedure); IV heparin is stopped 4–6 h before surgery. Pradaxa does not need to be stopped before minor surgery, but should be held 4–6 days before major surgery, depending on the bleeding risks and patient's renal function; it can be resumed 24 h after surgery if the wound is stable and an epidural catheter is not in place. Xarelto should be stopped for 3 days and Eliquis for 3–5 days before surgery, and both can be resumed 24 h after surgery. Patients on novel anticoagulants that are discontinued perioperatively do not require bridging with LMWH [10]. Perioperative discontinuation of aspirin therapy is discouraged, especially if it is used for secondary prevention, as abrupt discontinuation of aspirin can increase stroke risk. If ASA must be stopped for surgery, it is recommended to restart it 24 h after surgery. The Antiplatelet Agents in Perioperative Management of Patients (APAP) Trial, a randomized controlled trial of non-high-risk patients undergoing general or abdominal surgery in which ASA was held from 5 days before to 5 days postsurgery, showed no significant increase in bleeding risk in the aspirin group, as only 1 of 26 patients required reoperation due to postoperative bleeding [11].

Intraoperative risk factors for stroke have also been identified which include the type of surgery, with cardiovascular surgeries having higher risk, as well as duration of surgery, hypotension, hypertension, and cardiac arrhythmias. General anesthesia has been associated with more cerebrovascular complications than regional anesthesia. Patients undergoing CABG with higher mean arterial pressure (MAP) (80–100 mg) have fewer strokes compared to those with lower MAP (50–60 mg). Hypotension has been associated with increased stroke risk. In the POISE trial, extended-release metoprolol was given to patients with known atherosclerotic disease undergoing noncardiac surgery. The treatment group had fewer cardiac events but had more deaths overall. Further the stroke rate was doubled in the treatment group (1%) vs. placebo group (0.5%). In a study of patients undergoing noncardiac, non-neurosurgical procedures, a decrease in MAP >30% below baseline was associated with increased risk of postoperative stroke [12].

Intra- and postoperative hyperglycemia is associated with increased incidence of atrial fibrillation, stroke, and death, making tight control of glucose in the perioperative period essential. Atrial fibrillation peaks about 2–3 days postsurgery and can occur in up to 25–40% of patients with CABG as well as valvular surgeries. About half revert spontaneously to sinus rhythm within 24 h; 90% are in sinus rhythm by day 8. In cases of postoperative atrial fibrillation, treatment of underlying causes, if present, and rate control are required. In patients at high risk for stroke, unless otherwise contraindicated, anticoagulation is recommended with heparin, followed by warfarin or novel anticoagulants.

In patients who develop stroke perioperatively, emergent imaging of the brain to determine etiology (hemorrhagic or ischemic) is important. Patients who had major surgery within the preceding 14 days are not eligible for IV tissue plasminogen activator (t-PA); intra-arterial thrombolysis is a potential option and can be administered up to 6 h of post-stroke onset. Mechanical thrombectomy can be a useful alternative in the postoperative setting, as the time window for its application has been extended to 24 h in certain cases. Patients with intracerebral hemorrhage on warfarin will require treatment with vitamin K, fresh frozen plasma, or prothrombin complex concentrate. The effects of novel anticoagulant agents can be reversed with four factor prothrombin complex concentrate as well. Recombinant factor Xa was recently approved by the FDA for reversal of apixaban and rivaroxaban, while dabigatran can also be reversed by idarucizumab. Perioperative strokes and intracerebral hemorrhages should be further worked up to evaluate their underlying etiologies and managed in a similar manner to their non-perioperative counterparts.

Managing Patients with Parkinson Disease in the Hospital Setting

Parkinson's disease (PD) is the second most common neurodegenerative disease with disability ranging from mild to severe. Approximately 1% of the population over the age of 60 has PD with a male predominance of 3:2 [13]. While management issues related to PD itself do not typically necessitate hospital admission, patients with PD are hospitalized for a variety of other reasons including surgery. Managing PD in the in-patient medical and surgical setting can be challenging [14, 15]; the disruption of medication schedules, NPO status, reduced mobility, and use of certain medications can exacerbate the symptoms of this condition and lead to various complications [16–19] .

An important concern for PD patients in the perioperative setting is to maintain their previously prescribed medication schedule. Most patients take carbidopa/levodopa, or other dopaminergic therapy such as dopamine agonists (ropinirole and pramipexole) or MAO-B inhibitors (selegiline or rasagiline) [20, 21]. Delays and alterations in the PD medication regimen may increase morbidity, prolong recovery, and lengthen hospital stay. An abrupt cessation of dopaminergic drugs (especially levodopa) can be life threatening, leading to parkinsonism-hyperpyrexia syndrome. This presents in a fashion similar to neuroleptic malignant syndrome with altered mental status, rigidity, tremors, fevers, and autonomic dysfunction. The incidence of this condition is 4%; mortality is reported at 4% in treated patients and 20% for those who do not receive treatment [22].

The exact timing of drug administration is important and varies from one patient to another. If a patient cannot receive anti-Parkinsonian medications by mouth or via a feeding tube, one may consider using apomorphine subcutaneously or rotigotine transdermally [23]. However, these should be used as a temporary bridge until the patient can return to their home regimen. MAO-B inhibitors, in contrast, should be stopped 1–2 weeks prior to elective surgery. This will decrease the risk of perioperative hypertension and analgesia overdose [24].

Particular considerations should be made with regards to anesthesia medications perioperatively. Halothane should be avoided in those taking levodopa as it can increase cardiac sensitivity to catecholamines [25]. Propofol is commonly used in Parkinson's disease patients and can have antiparkinsonian effects; however, it may aggravate dyskinesias (a common side effect of levodopa) to the point of interfering with the procedure [25]. When treating intraoperative and perioperative pain, opioids, particularly fentanyl, may worsen rigidity and should thus be avoided [25]. Symptoms of dysphagia and excessive sialorrhea are important to note when evaluating the need for intubation in Parkinson's disease patients, as it puts them at an increased risk for aspiration. Intubation may be needed more readily than in non-Parkinson's disease patients.

Caution should be taken when using antiemetics and neuroleptics. Metoclopramide and prochlorperazine should be avoided, while domperidone, trimethobenzamide, and ondansetron may be used [23, 26]. Typical and some atypical antipsychotics may also worsen Parkinsonism, including haloperidol, risperidone, olanzapine, aripiprazole, and ziprasidone. If needed, quetiapine and clozapine can be used in PD patients [20].

Patients with Parkinson's disease are more prone to infections, particularly pneumonias and urinary tract infections, and should be closely monitored for such problems [12, 27]. They are also more likely to have autonomic disturbance as part of their underlying pathology or as a side effect of PD medications (orthostatic dysregulation), which can be exacerbated by dehydration [28]. Thus adequate hydration is essential and should be provided before adjusting PD medications.

Psychiatric disturbances are also common in advanced PD, as well as other Parkinsonian syndromes and Lewy body dementia. Symptoms may include agitation, hallucinations, paranoia, delusions, and sundowning. A rapid worsening of PD symptoms with alterations in mental status is most commonly due to a toxic-metabolic cause including infectious and metabolic derangements which should be investigated [29]. If found, the underlying cause should be treated before making any adjustments to PD medications. Finally, physical therapy is essential in all PD patients and will help to increase mobility and decrease recovery time.

Peripheral Nerve Injury

Leg weakness after hip or knee surgery is a common cause for neurological consultation in the postoperative setting. Weakness of the ankle (foot drop) is a common complaint or finding. Foot drop is associated with a variety of surgical procedures, including cervical and lumbar spine surgery [30] as well as knee [31] and hip [32] replacement. Simply having surgery is thought to be a rare cause of an autoimmune inflammatory neuropathy [33].

Foot drop occurs most often after hip surgery with a prevalence of 0.17–1.9% of patients undergoing total hip arthroplasty (THA) [34, 35]. The nerves affected include the sciatic (71–100%), femoral (0–20%), and obturator (rare but one series reported 7% involvement). When the sciatic nerve is involved, the peroneal division is most often affected [36]. Risk factors include revision surgery [34], coexisting lumbar spinal stenosis [37], preexisting peripheral neuropathy, younger age, and smoking. Femoral neuropathy also occurs after THA. The incidence after primary THA is 0.1–2.4% and it is higher after revision procedures (0.3–3%) [38]. It may also occur after hip arthroscopy. Causes include iatrogenic/mechanical factors (trauma, cement, heat) [39], hip dysplasia [37], difficulty of the surgery and positioning, leg lengthening, surgical approach (anterior) [40], and compression from hematoma [41–43]. The reason why neuropathy occurs more often after revisions is uncertain but it may be related to the more extensive dissection through scar tissue required in these procedures as well as possible tethering of the nerve by scar tissue. Obturator and superior gluteal nerve injuries rarely occur in association with THA but have been reported. Gluteal nerve injuries may occur in association with the direct lateral approach. Obturator nerve injuries are often undiagnosed and cause inguinal or groin pain.

Nerve injuries after total knee arthroplasty (TKA) are also rare (0.3–1.3%). Risk factors include preoperative valgus deformity, postoperative epidural anesthesia, rheumatoid arthritis, preexisting neuropathy, use of tourniquet, and hematoma formation at the wound site [44]. Patients usually have weakness immediately after surgery, although the weakness can be delayed by a day or two due to possible injury from edema or masking by peripheral nerve blocks. The peronal division of the sciatic nerve or the common peroneal nerve is the most common nerve affected. This typically causes a foot drop and numbness or neuropathic pain in the lateral lower leg and dorsum of the foot. The reason why the peroneal division is more affected than the tibial division is not known. There are a few proposed mechanisms including less connective tissue in the peroneal nerve making it more prone to traction injuries, the relatively fixed nature of the peroneal nerve at the sciatic notch, and the natural course of the nerve being superficial and more lateral than the tibial nerve. Nevertheless, muscles innervated by the tibial nerve are often affected to a lesser extent [45]. Femoral and obturator nerve dysfunction occur in 0.1–2.4% of cases and are often detected slightly later in the postoperative period as the subjective awareness of problems with knee movement may not be realized until the patient resumes mobility [35, 46].

Once weakness is detected, a diagnostic search for the cause is necessary. The blood work should be reviewed for evidence of diabetes, inflammatory disease, connective tissue disease, or vasculitis. Inflammatory neuropathy triggered by the surgery, though not common, is a recognized cause of the postoperative weakness [33]. When it occurs, it typically involves the lumbosacral plexus or the brachial plexus. Additional blood work may be needed depending on the clinical situation. An MRI of the site of surgery is necessary to determine if a hematoma is responsible for the nerve dysfunction. If detected, there is uncertainty as to how best to manage this. Some studies suggest that hematoma evacuation is associated with a better prognosis. However, there are situations where close monitoring while allowing the hematoma to resolve on its own, is appropriate. Alternatively, the MRI may demonstrate hyperintensity or edema, indicative of nerve injury, although a lack of these findings does not rule out such an injury. The MRI can also be limited by expected postsurgical changes. An MRI of the lumbar spine is an important consideration as the patient may not have had preoperative indicators of lumbar stenosis or radiculopathy. Nerve conduction studies (NCS) and needle EMG are useful in confirming the clinical examination, excluding an underlying neuropathy, estimating severity of the nerve damage, and estimating prognosis. However, the full extent of such changes can take 2–4 weeks to be seen on nerve conduction studies except for early conduction block. Sensory nerve responses in the distribution of the sensory loss are usually lost within 7 days after the axons are severed. Denervation potentials (positive sharp waves and fibrillation potentials) occur within 2–3 weeks. For these reasons, an early NCS/EMG is better for determining preexisting conditions than assessing the full extent of the nerve injury before 2–4 weeks. Retained sensory potentials and paucity of denervation after these time periods may be harbingers of good prognosis, especially if these findings are replicated on serial studies.

Recovery from sciatic distribution weakness associated with THA is poor and may be only as high as 50% [45]. However, recovery is good for sciatic neuropathies after TKA or femoral neuropathies from any cause. Recovery time periods can vary from days to weeks to months depending on the situation and the degree of nerve injury. Intensive rehabilitation for strengthening combined with gait and balance training and sometimes brace support is essential.

Postoperative Delirium

Alteration of mental status is a common complication of surgery. The etiology can be difficult to determine as most cases are multifactorial. However, it is important to try to determine causes as many factors are potentially treatable or modifiable. It is crucial to properly examine and evaluate every patient who develops a mental status change. At the very least, education of the patient and family about the commonness of this complication and the expected course can greatly ease the stress associated with it.

Best defined as a "global impairment of upper brain functions that involves consciousness, attention, cognition and perception" [47], delirium is by definition transient and fluctuating. It results from the "interaction of vulnerability on the part of the patient… and hospital-related insults" [48]. Typical incidence in noncardiac surgery is in the range of 15–25% [49].

Causes

It is helpful to divide the causes of postoperative delirum (POD) into three separate categories, which correlate roughly to the time course of surgery: (1) risk factors including demographic and other variables predating the surgery, (2) perioperative factors which are those related to the surgery itself or immediate perioperative care, and (3) aggravating factors or those modifiable medical or environmental conditions arising following surgery.

Risk factors include older age, medication use, and multiple systemic medical conditions. The most common systemic medical conditions causing postoperative delirium are preexisting brain disorders, including dementia, Parkinson's disease, and prior stroke. Other important risk factors are impaired sensorium (vision, hearing), multiple medications, specific psychoactive medications, and chronic alcohol or sedative use. Aggravating factors include sleep deprivation and sleep cycle disturbance, unfamiliar environment, immobility, hypovolemia, metabolic derangements, and inadequate analgesia.

Intraoperative factors include type of surgery, type and duration of anesthesia, and degree of blood loss and/or hypotension. Outside of cardiothoracic surgery, the highest rates of delirium are seen in vascular and orthopedic procedures (particularly after hip fracture) [50]. The duration of anesthesia seems to have a mild effect [51, 52]. General anesthesia confers no increase in risk over regional anesthesia [53]. Data on specific agents are difficult to come by. While avoidance of N_2O led to fewer major complications in one study [54], there is no clear effect on the incidence of postoperative delirium [51]. Controlled hypotension is a commonly used technique to limit intraoperative blood loss. Two studies [52, 55] found no significant effect on POD, whereas another did not find hypotension to be a risk factor in spine surgery [56]. A large study randomizing primary hip replacement patients to high- and low-mean-arterial pressure groups found a difference in incidence (9 vs. 4%) that was not statistically significant [57].

Although less common as causes of acute confusional episodes, primary neurologic conditions should be a consideration. Stroke usually does not present as a pure confusional syndrome without focal deficits unless it is related to a shower of emboli. However, it may be difficult for the nonspecialist to distinguish severe aphasia clinically from a global confusional state [58]. One important distinction is that the mental status in a stroke patient does not typically change at different times. Nonconvulsive status epilepticus should be considered whenever there are abrupt changes in consciousness or attentiveness, or in the presence of automatisms. Subtle twitching of the face or extremities may be seen with eye or head deviation.

Postoperative analgesic use is frequently blamed for POD, but this is a controversial subject. The use of patient-controlled analgesia (PCA) has been correlated with an increased rate of delirium, and a pilot study of gabapentin preoperatively reduced both postoperative opiate use and POD [51, 59]. Higher pain scores are associated with an increased POD rate [60]. However, a large prospective study found that the pain effect was primary and that in cognitively intact patients, higher rates of POD correlated with lower rates of opiate use [61]. It is likely that both excessive and inadequate analgesic use can be a contributing factor in different patients and considering both possibilities is important. The medications that are implicated in a higher rate of POD include those with anticholinergic (e.g., tricyclic antidepressants, amantadine, and diphenhydramine) and dopaminergic properties. Corticosteroid and opiate use are also of concern. Benzodiazepines are well known to cause paradoxical agitation, especially in the elderly, and therefore to increase the risk of POD. However, in some series, a potential preventive effect has been suggested [52, 62].

Presentation

Onset is usually between the first and fifth postoperative days, but it may occasionally develop preoperatively [47]. Prodromal symptoms of incoherence and mild disorientation may precede frank delirium by 1–4 days. The level of consciousness can range from normal to severely impaired. Patients often have a reduced awareness of their environment with impaired attention. There is often disruption of the sleep–wake cycle and "sundowning" is common. This is important to manage as getting less sleep at night can worsen the POD. Disorientation to time and place is common. Language is typically normal in form, which helps to distinguish this from aphasia. Perceptual disorders include delusions and paranoia and, in more severe cases, hallucinations. The hallucinations are usually benign and involve

people or animals. These symptoms usually fluctuate over the course of the day. The prognosis is excellent for typical toxic-metabolic and withdrawal cases with recovery within 10–12 days [47]. However, the course may be more prolonged in the elderly and in those with superimposed medical problems or neurodegenerative disease. Moreover, it is not uncommon for POD to "unmask" previously unrecognized dementia. Compared to patients without POD, there is an increase in average recovery time, morbidity, and mortality. However, the latter may be an epiphenomenon of the underlying medical factors, and it is not clear that treatment of the delirium alters these complications.

Evaluation

Patients and their family members should be asked about a history of prior difficulties after surgery, prior medication reactions, alcohol and standing sedative use, subtle evidence of cognitive impairment, and remote neurologic issues, such as stroke, seizure, or head trauma. This can be part of the preoperative evaluation, but repeating the history at the time of presentation may uncover factors that were not previously recognized. A full neurologic examination, including mental status, is indicated, especially in patients at risk. Useful screening tools for dementia include the mini-mental status examination and clock face drawing. Evidence of a subtle upper motor neuron lesion should be sought (facial asymmetry, pronator drift, tendon reflex asymmetry, Babinski sign). Frontal release signs, such as the glabellar reflex, offer a clue to central nerve system degenerative disease. Preoperative counseling about the possibility and natural history of POD can be helpful for patients and their families to understand that the symptoms may occur but that they usually resolve.

It is important to identify treatable factors. The neurologic examination is directed at ruling out a focal lesion suggestive of stroke, post-ictal state, or another structural disorder. Mental status testing may be limited by the attentional deficit, but a prominent disturbance of language, despite normal attention, is suspicious for a focal syndrome. Asterixis or tremor may be present but these are nonspecific findings. The level of pain control and the extent and type of opiate and nonopiate pain control should be assessed. Among the most common complicating metabolic disturbances are hypovolemia, hyponatremia, and hyperglycemia. The laboratory examination should include an electrolyte and metabolic panel, TSH, B12 and folate levels, CBC, and ammonia. In appropriate cases, blood alcohol level, toxicology screen, Lyme serology, and RPR may be ordered. Routine search for infection includes chest X-ray, urinalysis, blood cultures, and assessment of wound infection. Lumbar puncture is rarely indicated. Arterial blood gas and screen for thrombosis may be indicated when clinical suspicion warrants. EEG should be considered when there is a fluctuating level of consciousness or attention in brief episodes, staring spells, abnormal eye movements, or subtle facial or hand twitching [63]. Brain imaging is not always critical on initial evaluation when stroke is not suspected, when the delirium is mild, and when there is a likely alternative explanation.

Treatment

Although most cases of POD run their course naturally requiring only supportive measures, more proactive intervention is recommended in order to lessen patient discomfort and anxiety, to enhance the patient's capacity to engage in physical therapy, and hopefully to reduce the length of stay. Treatment can be divided into prevention, symptomatic treatment, and treatment of underlying disorders. The latter is the most direct and includes correction of metabolic abnormalities, such as hyponatremia and hyperglycemia. Blood pressure and oxygenation should be maintained, and treatment of other conditions such as suspected infection should be conducted as needed. Suspicion for focal neurologic etiologies should involve treatment in conjunction with neurologists. As measurement of a thiamine level is impractical, and frank or borderline thiamine deficiency may be more common than realized, we recommend that all POD patients presumptively receive thiamine 100 mg for 3 days [64]. Symptomatic treatment of agitation can be accomplished with nonpharmacologic methods including one to one observation and frequent reorientation. These methods are preferred over medications [65]. If medication is needed, antipsychotics, either traditional (e.g., haloperidol) or second-generation formulations (e.g., quetiapine, olanzapine) can be considered, although these should be used sparingly in the older patient due to the associated increased mortality. Benzodiazepines are generally discouraged, particularly in the elderly, as they can cause oversedation that may confound the lack of responsiveness due to the delirium itself, as well as potentially causing paradoxical agitation. The exception is in the patient with standing sedative use, in whom sudden discontinuation could cause a withdrawal syndrome.

Prevention is complex and multifaceted. Excessive opiate use is generally considered to contribute to many cases of POD, although, as mentioned, inadequate analgesia can also play a role. It is generally best to convert from patient-controlled parenteral analgesia to oral opiates as early in the course as possible. There is preliminary evidence that preoperative treatment with either alternative analgesics (e.g., gabapentin) [66] or ketamine [67] may reduce the incidence of POD. Antipsychotics are not currently recommended to prevent POD due to contradictory studies and risk of harm [65]. Prophylaxis should be initiated for potential alcohol withdrawal, and standing sedatives should be continued. Anticholinergic medications should be avoided. Bowel and urinary retention should be minimized. Modification of the environment includes normalization of sleep pattern, increasing mobility, correction of visual and

hearing impairment, regular orientation of the patient to time and place, cognitive engagement, and optimization of environmental stimulation [48].

Summary

Neurologic conditions, including those of a chronic nature as well as those arising as complications of surgery, present a challenge to the surgical and medical team. This chapter reviews the span of such conditions and presents an approach to their assessment and management pre- and postoperatively.

Summary Bullet Points

- The preoperative evaluation of chronic neurological disease requires a thorough understanding of the pathophysiology of the condition.
- Chronic neurological disease encompasses a variety of conditions that require a thorough understanding for proper management at all stages in the surgical process.
- Postoperative cognitive dysfunction arising most commonly in the elderly after surgery is an important disorder to recognize and promptly treat.
- Postoperative neuropathy is an important complication that needs to be recognized rapidly to provide timely treatment that can improve outcome.

Case Studies

Case 1

A 70-year-old man has an 8-year history of low back pain radiating down both legs into the feet. The patient notes numbness in his feet and has a limp walking on the right that has been present over the past 6 months. The patient has been followed by pain management and has received epidural steroid injections over the past year, treatments that are no longer working in terms of pain relief. Indeed, he currently rates his pain at 8/10. The patient is referred to a spine surgeon. An MRI of the lumbar spine demonstrates severe lumbar stenosis with nerve root compression at L4 and L5 bilaterally.

After discussion with the surgeon, the patient decides to undergo a lumbar laminectomy. He is informed of the risk of neurologic and other complications. The surgery is seemingly uneventful. However, when the patient wakes up he is noted to have a foot drop on the right with numbness in the right lateral leg and dorsum of the foot. When an MRI demonstrates expected postoperative changes (mild edema), the patient is started on dexamethasone and pregabalin though experiences no benefit and is fitted with an ankle-foot-orthosis. On follow-up weeks later, the foot drop has almost completely resolved as has the associated numbness.

In conclusion, the patient experienced a postoperative nerve root neuropraxia at the L5 level, a problem that typically improves over 2–4 weeks.

Case 2

A 75-year-old woman with a history of old right hemisphere stroke undergoes a complex hip reconstruction under general anesthesia. The surgery appears to have been uneventful until the patient is taken off anesthesia and is noted to have jerking movements of the arms and legs. The patient is maintained intubated and propofol is turned up. The shaking stops and vital signs are stable. The patient is transferred to the recovery room where jerking movement recurs after turning down the propofol. Neurologic consultation is called and the patient is given 1 mg IV lorazepam with the jerking stopping. A CT scan of the head is negative except for the old right hemisphere stroke. A loading dose of IV phenytoin is administered achieving therapeutic levels 2 hours later. The patient is maintained on phenytoin and successfully extubated and stable. An EEG shows intermittent spikes discharged from the right hemisphere. The patient is switched to oral Keppra and has no further seizure activity.

In this case, the patient had a seizure after general anesthesia. In patients with a previous structural lesion such as stroke, there is a lowered seizure threshold with seizures presenting in the postoperative setting.

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Perioperative Care of the Orthopedic Patient with Sleep-Disordered Breathing: Obstructive Sleep Apnea

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Objectives

- To discuss current evidence, existing guideline recommendations, and critical knowledge gaps with regard to the perioperative management of patients with OSA

Key Points

- OSA is a driver of perioperative complications.
- OSA-related perioperative complications are often deemed to be preventable with a systematic and cautious approach to perioperative care planning.
- Preoperative evaluation and risk stratification: OSA screening enables the implementation of measures of precaution.
- Intraoperative OSA management: readiness for possible difficult airway management; consideration of the compounding impact of anesthetics, sedatives, and analgesics on a compromised cardiorespiratory system; regional anesthesia as a strategy to potentially improve outcomes and increase patient safety.
- Postoperative OSA management: subsequent to surgery and anesthesia, a heightened level of vigilance, and if feasible a monitored environment for the treatment of possible respiratory deterioration may be useful in order to prevent complications.

Introduction

Obstructive sleep apnea (OSA) is the most frequent sleep-related breathing disorder, characterized by periodic upper airway collapse during sleep. In patients with OSA, airway narrowing and increased airway resistance is often promoted by fatty deposits in the pharyngeal walls [1]. Obstructive events lead to recurrent hypopnea or apnea, subsequently causing hypoxia [2]. Clinically, patients suffer from chronic sleep disruption and deprivation due to recurrent activation of the sympathetic nervous system in response to hypoxia, which eventually causes chronic cardiovascular and respiratory disease [3, 4].

In the adult surgical population, the prevalence of OSA has been estimated to be 10–20% [5, 6], while specific risk populations, such as bariatric patients, may exhibit rates of 70% and higher [7]. Currently, more than 80% of affected patients are undiagnosed and therefore untreated [3, 8]. This is in part due to the laborious and costly nature of polysomnography examination, which constitutes the current gold standard for OSA diagnosis. As a consequence, profound perioperative implications arise on a public healthcare level, because patients featuring higher perioperative vulnerability present to surgery unrecognized [2, 6]. Clinically, obesity is the single most important risk factor for OSA, especially when fat builds up in the upper portion of the abdomen and the neck region [9]. Other factors contributing to OSA risk include male gender and age [10]. The identification of undiagnosed OSA is a particular issue in orthopedic surgery because many arthroplasty patients are obese [11]. This is of particular concern because the demand for orthopedic surgery is increasing, given the demographic shift and the increasing prevalence of obesity [11, 12].

Obesity Hypoventilation Syndrome

In the context of managing perioperative sleep-disordered breathing, the prevalence of obesity hypoventilation syndrome (OHS) should also be considered. While OHS is

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estimated to be relatively uncommon, approximately 90% of patients with OHS have concomitant OSA [13, 14]. While OHS should be suspected in very obese patients, clinical predictors include the concurrent presence of increased serum bicarbonate levels, room air hypoxemia while resting, persistent hypoxemia during polysomnography, and the presence of a restrictive ventilatory defect [14, 15]. For a diagnosis of OHS, the patient should have a body mass index of 30 kg/m^2 or greater and an arterial pressure of carbon dioxide of 45 mmHg or greater during wakefulness, while other causes of hypercarbia should be excluded [16]. An elevated serum bicarbonate or base excess may offer a superior marker of prolonged hypoventilation compared to daytime arterial blood gases, because patients may hyperventilate during the sampling [17]. Furthermore, the use of serum bicarbonate in addition to the STOP-Bang questionnaire may identify potential patients with OHS [16, 18].

Compared to patients with OSA alone, patients with OHS have an increased risk of cardiorespiratory failure, prolonged intubation, critical care requirement, and extended hospitalization [19]. Given that OHS patients present a particularly high-risk group in the perioperative period, more evidence is needed to provide specific clinical guidance. However, similar to OSA, this condition requires careful consideration of possible cardiorespiratory deterioration and a high level of vigilance for the prevention of perioperative complications [16, 20].

Perioperative Implications

Based on the pathophysiology of OSA, affected patients commonly exhibit a number of comorbidities, including hypertension, coronary artery disease and atherosclerosis, arrhythmias, congestive heart failure, diabetes, cerebral vascular events, pulmonary hypertension, and impaired quality of life [2, 21]. Naturally, these factors also constitute drivers of perioperative morbidity and may present confounders in scientific research investigating the independent risk conferred by OSA [16].

A growing body of evidence has established OSA as a significant driver for perioperative morbidity and mortality [22–24]. The pathophysiological implications of OSA are compounded by the surgical insult and the impact of anesthetics, analgesics, and sedatives that deteriorate alertness and respiratory drive and affect the sympathetic response to hypoventilation and apnea. The risk for cardiorespiratory failure, emergent intubation, and critical care requirement is therefore significantly increased in the presence of OSA [22, 25]. In particular, respiratory failure presents a significant patient safety indicator given its association with mortality [22, 26]. On the other hand, minor adverse events such as postoperative desaturations are typical in OSA and of questionable clinical significance. The classification of desaturation thresholds that predict further respiratory deterioration and increased resource utilization are yet to be determined [16].

Evidence shows that critical, life-threatening, and fatal postoperative events in OSA may be preventable with adequate measures of precaution [27–29]. Therefore, the development of a perioperative action plan for this patient population, including adequate patient surveillance, is warranted.

Preoperative Evaluation, Risk Assessment, and Clinical Management

Despite growing evidence regarding the perioperative detriment associated with OSA, general consensus on best clinical practices that facilitate preoperative risk stratification and assure improved outcome remain lacking.

The American Society of Anesthesiologists (ASA) recommends the implementation of protocols for the preoperative evaluation and identification of patients at risk for OSA based on medical history and physical examination [30]. Routine preoperative polysomnography is neither feasible due to limited resources nor is current evidence sufficient to support such practice in every patient undergoing surgery. In particular, there is a lack of evidence to justify the delay or cancellation of surgery for formal OSA diagnosis in the absence of significant comorbidities or respiratory disease [23]. Therefore, OSA screening by questionnaire is increasingly being implemented into standard preanesthetic evaluation [23]. The most common perioperative screening tools include the STOP-Bang score, the perioperative sleep apnea prediction score, the Berlin questionnaire, and the ASA checklist [16, 23, 31]. These tools are validated for the surgical setting and easy to administer and feature comparable accuracy for the identification of patients at high risk for OSA [23]. While such approaches cannot replace diagnostic polysomnography, they allow for feasible preanesthetic risk stratification. Their predictive values have been established studies demonstrating associations between higher preoperative screening test scores and worse postoperative outcome [32]. Caregivers should be especially alert to basic clinical predictors of OSA including increased BMI, increased neck circumference (>43 cm in male and >40.5 cm in female), history of snoring and breathing cessations, reported choking during sleep, daytime somnolence, uncontrolled hypertension, cardiovascular comorbidities, hyperglycemia, male gender, age higher than 65 years, and increased tonsil size and tongue volume [30, 33]. Furthermore, other clinical

aspects such as surgical invasiveness, intra- and postoperative opioid and analgesic requirement, the presence of other comorbidities, and drivers such as alcohol use and smoking demand cautious consideration [3, 30].

Recent guidelines by the Society of Anesthesia and Sleep Medicine recommend that patients with diagnosed or suspected OSA may proceed to surgery, given that present comorbidities are taken into account or optimized and perioperative measures of precaution are in place to mitigate the risk for postoperative complications [23]. In cases of severe OSA or where associated perioperative risk is deemed as high, the preoperative optimization of the patient's condition may be considered. This may include formal testing, the initiation of continuous positive airway pressure (CPAP) or noninvasive positive pressure therapy, the preoperative use of mandibular or oral appliances, and potentially preoperative weight loss measures [23, 30].

Intraoperative Considerations

With regard to the intraoperative setting, the presence of OSA requires a cautious approach when it comes to airway management, anesthetic drug utilization, and the selection of the most appropriate anesthesia technique.

Airway Management Complications

Intraoperative anesthetic management often involves airway interventions, particularly when general anesthesia is administered. According to recent recommendations by the Society of Anesthesia and Sleep Medicine, known or suspected OSA should be considered as an independent risk factor for pre- and postoperative difficult airway management, including intubation and mask ventilation. This is consistent with the underlying pathophysiology of OSA, featuring impaired airway patency with recurrent airway obstruction [34, 35].

A number of prospective and retrospective cohort studies demonstrate an association between OSA and difficult airway management [35]. Kim and colleagues observed that with an increasing apnea-hypopnea index (AHI) there was an increasing trend for difficult intubation [36]. Furthermore, OSA-related complications are increasingly recognized in the legal field with prevalent litigation cases involving death and anoxic brain injury due to airway management complications or failure of postoperative intubation [24].

Given the increased risk for the occurrence of critical airway management events, the ASA recommends that patients with known or suspected OSA should be managed according to the practice management guidelines for a difficult airway [30, 37]

Medications

Upper airway obstruction occurs when negative pressure, generated by inspiratory muscles, exceeds the capacity of upper airway dilatator muscles to maintain airway patency [2, 38]. Usually, negative pressure generated by inspiration is counterbalanced by the contraction of pharyngeal muscles. Medications, however, can impair the ability of upper airway muscles to overcome the negative forces of inspiration and thereby further promote airway obstruction. This is of particular concern in patients with OSA and obesity as they may present with a reduced diameter of the upper airway from baseline [2, 39, 40].

Thus, patients with OSA are especially receptive to the effects of sedatives, anesthetics, opioids, and other analgesics which can further suppress alertness and respiratory function by modulating the chemical, metabolic, or behavioral control of breathing. Evidence shows that all anesthetic and sedative agents, including propofol, dexmedetomidine, midazolam, phenobarbital, sevoflurane, desflurane, ketamine, and opioids, cause at least some degree of airway collapse. However, anesthetic drug agents differ with regard to margins of safety, therefore causing varying levels of respiratory depression [2]. Furthermore, the dose-dependent depression of upper airway muscle activity by the use of general anesthesia is well established [41, 42]. Studies investigating the effects of anesthetics, sedatives, and analgesics have exposed the pharynx as the primary site of obstruction after anesthesia [2, 43, 44]. Specifically, it appears that airway obstruction caused by sedation and anesthesia follows a pattern similar to obstructive apneic events during sleep. This includes increased airway collapsibility, loss of pharyngeal muscle tone, and insufficient activation of upper airway muscles [2, 41, 45]. Careful consideration is therefore warranted in the selection of perioperative anesthetic drug agents and their dosing when managing patients with OSA. The utilization of regional anesthesia and multimodal pain management strategies may facilitate a reduction in opioid use, improve pain relief, and increase patient safety [46]. Furthermore, the use of short-acting anesthetic regimens has been shown to result in rapid postoperative recovery, improved oxygen saturation, and shorter length of stay [2, 47]. Intraoperatively, continuous monitoring of ventilation is required. This applies to procedures under sedation as well, while intraoperative CPAP therapy or oral appliances may be appropriate in patients accustomed to these modalities [30]. The selection of the optimal intraoperative anesthetic drug agents should also account for residual drug effects in the postoperative setting, where patients readjust to independent spontaneous breathing at a scaled level of monitoring and surveillance.

Despite the lack of evidence to specifically delineate the impact of individual drug agents, it is recommended to reduce the use of opioids and other drugs with central respiratory depressant effects [34].

Inhalational Agents and Propofol

General anesthesia confers a dose-dependent depression of upper airway muscle activity [41, 42]. For instance, an increasing depth of propofol anesthesia is associated with increased upper airway collapsibility [41]. This is similar for inhalational agents, which also promote upper airway collapse by suppressing responses to tracheal stimulation [48]. In this context, the immediate emergence from anesthesia with the onset of spontaneous breathing is a critical period given the residual impact of hypnotics that may confer respiratory complications [48].

There is a lack of studies specifically addressing differential effects of hypnotic agents between patients with OSA and the general population. Nevertheless, in the closely associated obese population, two meta-analyses, investigating the comparative effectiveness of desflurane, isoflurane, sevoflurane, and IV propofol anesthesia, have established desflurane as the agent featuring the most favorable recovery profile [49, 50]. Patients who received desflurane required less time to respond to commands such as eye opening, hand squeezing, and name stating and were extubated earlier. Moreover, desflurane was associated with reduced sedation levels and conferred higher postoperative blood oxygen saturation [49, 50]. As also shown in the general population, desflurane, followed by sevoflurane, may therefore enable faster anesthesia recovery and improved respiratory and hemodynamic and stability, which appears clinically significant in the management of OSA. Some authors have further recommended the practice of intraoperative monitoring and titration of levels of inhalational agents to reduce anesthetic drug consumption and improve postanesthetic recovery [51, 52].

Neuromuscular Blocking Agents

Neuromuscular blocking drugs are commonly utilized intraoperatively to facilitate endotracheal intubation and surgical relaxation. However, problems may occur in the immediate postoperative setting due to incomplete reversal [53]. This poses a high risk for critical respiratory complications [54]. Although evidence is scarce, current literature suggests that OSA patients who receive intraoperative neuromuscular blockade may be at higher risk for postoperative hypoxemia, respiratory failure, and residual neuromuscular blockade compared to non-OSA patients [55]. Xara and colleagues reported that patients with OSA had a higher incidence of residual neuromuscular blockade and a nearly fourfold increased incidence of respiratory compromise immediately after emergence from general anesthesia [56]. In particular, the authors observed an impairment in the patients' ability to conduct deep breathing [56]. The Society of Anesthesia and Sleep Medicine therefore recommends that patients with OSA receiving neuromuscular blocking agents should be considered at increased risk for the effects of incomplete reversal of neuromuscular blockade and therefore respiratory compromise [34]. Importantly, the full reversal of neuromuscular blockade should always be verified before extubation, particularly as effects may persist even after the use of reversal agents [30, 34, 55].

Opioids

Given their high analgesic efficacy, opioids remain a basic element of perioperative pain management. Opioids, however, also interfere with chemical, behavioral, and motor control of respiration, causing a depression of central ventilatory drive and pharyngeal neuromotor tone. This subsequently leads to impaired airway patency, obstructive apnea events, oxygen desaturation, and elevated blood CO_2 levels [27, 48, 57, 58]. During sleep, adverse respiratory opioid effects may be enhanced, due to the natural depression of the upper airway muscle tone [2, 58]. The decline in electromyographic activity of the pharyngeal dilator muscles at sleep onset is much greater in OSA patients compared to the general population [2, 59]. While postoperative hypoxemia due to opioids is relatively common, the major threat is posed by the risk for opioid-induced respiratory depression (OIRD) [16, 60]. A national closed-claim analysis demonstrated that OSA was highly prevalent among patients who suffered brain damage or death in the context of postoperative OIRD [28]. Furthermore, among postoperative death and near-death events in patients with OSA, Subramani and colleagues recently identified opioids and sedatives as causative drivers [27]. Based on the effect mechanism opioids exert, it is conceivable that respiratory function may be further deteriorated in OSA [16]. The sensitivity to develop OIRD and respiratory effects may, however, vary among individual OSA phenotypes [16, 61–63]. Some OSA patients have a high arousal threshold to oxygen desaturation, while others wake up frequently to minimal reductions in oxygen levels based on a low arousal threshold. These individual differences may be clinically significant, because opioids may delay arousal reactions, which could subsequently promote the occurrence of unexpected death from respiratory failure [27, 64]. Furthermore, evidence indicates that basic features of OSA, such as chronic sleep fragmentation and recurrent hypoxia, may confer increased pain perception and enhanced opioid sensitivity in patients with OSA [65]. These developments could therefore increase the risk for OIRD, even in the absence of opioid overdosing, demonstrating the importance of OSA phenotype and disease severity in the context of perioperative complication risk [66, 67]. While more high-quality evidence with specific focus on optimal opioid dosing in patients with OSA is clearly needed, a growing body

of evidence consistently supports a detrimental impact of opioids in OSA, thus raising concerns regarding postoperative OIRD [67]. Strategies to reduce the risk for OIRD in patients with OSA include the use of short-acting anesthetics with the goal to reduce postoperative sedation and somnolence. Furthermore, the implementation of opioid-sparing multimodal strategies, as well as the avoidance of basal opioid infusions and concurrent sedative drug utilization, may also be useful in achieving this goal [3, 16]. In this context, recent studies suggest that the utilization of centrally acting α-2 agonists may – because of their sedative, analgesic, and sympatholytic properties – facilitate a reduction of opioids [34, 68]. Notably, appropriate monitoring may reduce the risk for complications during periods that OSA patients are exposed to opioid medication, at least until a steady state of consumption and effect can be assessed [3].

Benzodiazepines

Evidence with regard to the differential impact of benzodiazepines in patients with OSA is scarce. According to the Society of Anesthesia and Sleep Medicine, patients with OSA should be considered at increased risk for adverse respiratory events from benzodiazepine use [34]. Intravenous sedation with benzodiazepines is commonly utilized to induce airway collapse for diagnostic purposes, thus indicating that this drug class may enhance a compromised airway [34, 69, 70]. Deflandre and colleagues established the use of benzodiazepines as a predictive factor for nocturnal hypoxemia in patients with OSA [71]. This was supported by evidence showing that upper airway obstruction during recovery from general anesthesia can be induced by benzodiazepines [45]. Overall, benzodiazepines used as sedatives have been identified as main cause of upper airway obstruction during recovery from general anesthesia, which emphasizes an appropriate risk-benefit analysis before use in patients with OSA [45].

Anesthesia Technique

Numerous studies demonstrate improved outcomes with regional anesthesia as an adjunct or substitute to general anesthesia [72]. While evidence specifically addressing patients with OSA is scarce, observational studies of comparative effectiveness supporting the use of regional anesthesia in OSA patients exist [73]. A recent population-based analysis showed that among 30,024 major orthopedic surgery patients with OSA, the risk for major complications, including postoperative mechanical ventilation and critical care admission, prolonged hospitalization, and increased cost, was significantly lower with neuraxial versus general anesthesia [74]. Moreover, the use of peripheral nerve blocks was associated with decreased odds for respiratory failure. The favorable impact of regional anesthesia in OSA patients was also confirmed by others, with reported benefits including reduced mortality [34, 75]. Notably, Liu and colleagues found that general versus regional anesthesia was associated with hypoxemia, even among OSA patients receiving postoperative continuous supplemental oxygen therapy [76]. Moreover, a recent prospective study demonstrated that general anesthesia was associated with an increased postoperative central apnea index, suggesting that residual effects of general anesthesia may affect postoperative sleep architecture and promote sleep-disordered breathing [77].

Disadvantages of general anesthesia also include the necessity of airway manipulation and neuromuscular blockade, which take a compounding effect considering the underlying features of OSA [55]. Furthermore, OSA-related chronic intermittent hypoxia and sleep fragmentation have been suggested to cause altered opioid potency and pain perception, thus supporting the use of regional anesthetic techniques, rather than systemic opioid use to achieve optimal pain management [78]. Another argument in favor of regional anesthesia is the systemic catabolic stress response, which follows surgical injury. This systemic reaction is initiated by neural stimulation and can worsen postoperative outcome, particularly in patients at higher perioperative risk. Regional anesthesia can efficiently block or diminish this detrimental effect [79, 80].

The Society of Anesthesia and Sleep Medicine and the ASA, therefore, strongly recommend the preference and implementation of regional anesthesia techniques, whenever feasible, in surgical patients with OSA [30, 34].

OSA in the Postoperative Setting

Primary drivers of postoperative complications include the effects of anesthetic and sedative agents on upper airway muscle tone and ventilation responsiveness, the postoperative increase in rapid eye movement (REM) sleep, and postoperative supine positioning. Furthermore, anesthetic drugs, including hypnotics, sedatives, and analgesics, appear to negatively affect postoperative sleep architecture and aggravate OSA, thereby causing an exacerbation of nocturnal hypoxia and hypercapnia and promoting postoperative complications [27, 81]. The initial 24 hours after opioid administration mark the period of highest risk for acute respiratory insufficiency [67]. Postoperative respiratory complications range from difficult airway challenges associated with extubation to postoperative deterioration of ventilation with hypoxemia, respiratory failure, and potentially death [27, 77]. The worsening of sleep-disordered breathing, however, usually reaches its peak in terms of apnea-hypopnea index and blood oxygen desaturation on postoperative day three and typically recovers after 7 days [82].

OSA-related perioperative complications are increasingly recognized in the legal arena and progressively reported as the central contention of medical malpractice lawsuits in courts [16, 24, 83]. A recent review of legal literature on catastrophic perioperative complications in OSA demonstrated that the most frequently reported cases are cardiorespiratory arrests in unmonitored settings and cases of difficult airway management. These outcomes resulted in permanent brain damage and death, while deadly outcomes appeared to be most likely associated with opioid use. Although the medicolegal burden of OSA is likely underestimated due to settlement out of court, such evidence emphasizes the importance of postoperative monitoring, cautious drug utilization, and the avoidance of premature extubation [24, 83]. Moreover, the perioperative management of sleep-disordered breathing is now considered an important patient safety initiative [16, 84].

Literature on interventions for the postoperative management of OSA relate to the immediate postoperative care, including extubation, continuous monitoring, oxygen therapy, and pain management as well as the postoperative sleep phase with interventions of sleep positioning, respiratory monitoring, and the use of CPAP therapy [3]. Nevertheless, there appears to be substantial variability with regard to clinical practice across hospitals, while most institutions seem to lack respective policies [16, 24].

Patient Extubation

Following general anesthesia, the postoperative period is usually initiated by patient extubation [3]. This intervention, however, is not without significant risk in patients with OSA. The risk for life-threatening post-extubation airway obstruction in OSA is estimated at 5% [85]. This risk is most commonly precipitated by premature extubation in the absence of physiological readiness to sustain adequate spontaneous ventilation. In this period, OSA patients are vulnerable to airway collapse due to residual effects of anesthetics, analgesics, or sedative medications. The assessment of readiness to effective spontaneous ventilation without assistance is therefore critical before extubation is attempted. Moreover, the probability of post-extubation apnea in patients with OSA is significantly reduced when patients are fully awake and neuromuscular blockade has resolved. To maintain upper airway patency during extubation and assure efficient consecutive spontaneous ventilation, it is therefore recommended that full reversal of neuromuscular blockade and patient alertness be verified before extubation. While avoiding supine positioning during this period, the following extubation criteria can provide guidance regarding patient readiness. Patients should be able to follow commands, such as eye opening in response to name. Furthermore, they should have attained the ability to accomplish sustained head lifting for more than 5 seconds, sufficient cough strength, feature a vital capacity greater than 15 cc/kg, and a minimum spontaneous respiratory rate of 12 breaths per minute [2, 30, 86]. During or immediately after extubation, patient positioning in semi-upright or 30° reverse Trendelenburg is favorable [3].

Patient Positioning

Following and during extubation, patients at increased risk from OSA should be placed in a non-supine position throughout the entire postoperative recovery period [3, 30]. This is based on the fact that structural properties of the passive pharynx change by changing body position from supine to lateral [87]. Notably, the collapsibility of the upper airway is strongly influenced by body positioning, rather than mediated by sleep stages [2, 88]. Especially after the administration of anesthetics, sedatives, and opioids, the soft palate of the upper airway is highly susceptible to collapse in the supine position [3]. Lateral position structurally improves maintenance of the passive pharyngeal airway in patients with OSA [87]. Furthermore, upper body elevation, or 30° reverse Trendelenburg position, significantly improves upper airway stability during sleep and may allow therapeutic levels of CPAP to be substantially reduced, because the compression of the abdomen against the diaphragm is minimized [89]. The ASA therefore recommends a semi-upright position during extubation and recovery as well as non-supine positioning postoperatively if not restricted based on surgical grounds [2, 3, 30].

Patient Monitoring

Postoperative patient monitoring facilitates the detection of early signs of potentially morbid or fatal events [90]. Therefore, many clinicians prefer for patients with confirmed or suspected OSA to be admitted to a monitored care environment after surgery for continuous surveillance of ventilatory parameters (e.g., respiratory rate, oxygenation, tidal volume, end-tidal carbon dioxide) until baseline oxygen saturation is maintained on room air [3, 30, 91]. Although more research is needed, observational data indicate that the implementation of postoperative monitoring may improve outcomes in patients with OSA [24, 92]. In particular, evidence from cases of critical OIRD further emphasizes the importance of repeated and careful assessment of sedation levels and the potential correlation to ventilatory depression [28]. The ASA recommends that patients remain under continuous monitoring until the postoperative respiratory function is sufficient to maintain baseline oxygen saturation

while breathing room air. Surveillance can be maintained in critical care units, step-down units, or on hospital wards or by utilizing telemetry and observation [30].

Nevertheless, the large variability in clinical OSA severity and the frequency of undetected OSA have increasingly raised controversies regarding the appropriate level and duration of postoperative patient surveillance [16]. Monitoring algorithms, enabling early postoperative risk stratification and the identification of patients who require advanced and prolonged surveillance, are currently lacking [16]. Gali and coauthors [93] showed that in OSA patients, recurrent adverse events in the PACU, related to ventilation and sedation, were predictive of subsequent major postoperative respiratory complications, including critical care requirement, requirement for ventilation support, and postoperative pneumonia.

Evidence shows that the lack of postoperative patient monitoring presents a significant driver of adverse postoperative outcome, including death or near-death events in patients with OSA [27]. In this context, OSA patients featuring a high arousal threshold to hypoxia are especially prone to adverse sedative effects of anesthetics, including OIRD and respiratory arrest in unmonitored environments [16, 27, 64]. This can be further compounded by a postoperative decrease in pain severity and increased rapid eye movement (REM) sleep, causing loss of upper airway tone during this period [27]. Lapses in monitoring are therefore often implicated in the occurrence of preventable postoperative catastrophic complications, including hypoxic brain injuries and deaths [27].

As healthcare institutions seek to avoid patient harm in the continuously growing OSA population, the utilization of resources is increasingly emerging as a crucial factor. While harm can be associated with substantial cost, strategies of reducing OSA-related complications involve the surveillance and early detection of potential deterioration. Although resource constraints pose a major obstacle to more uniform surveillance in many institutions, it should be noted that prevention is usually economically more advantageous per patient than rescue after complication [16]. Complicating this issue is that current preoperative OSA screening tools have high false positive rates, leading to waste of resources, particularly when enhanced monitoring and treatment is not allocated to patients who are truly at increased risk for OSA- or OHS-related complications [16].

Probable OSA patients are therefore particularly challenging in the perioperative setting, as healthcare providers must work with heightened vigilance to detect symptoms of OSA while implementing additional monitoring interventions [3]. In this context, understanding the different endotypes underlying the phenotype of OSA is a desirable goal for the future as it may result in more personalized screening and monitoring [16, 94].

Further unintended consequences of monitoring interventions include false positive alarms resulting from poor specificity or technical alarms due to poor signaling. False alarms can lead to alarm fatigue, clerical burden, patient sleep loss, and waste of resources [16].

Oximetry

Currently, pulse oximetry monitoring presents the most common technique for the postoperative surveillance of respiratory function. The ASA and the Anaesthesia Patient Safety Foundation recommend that patients at increased perioperative risk from OSA should receive continuous monitoring with pulse oximetry and possibly capnography for the early detection of desaturation and ventilation compromise. This in particular applies to patients consuming significant amounts of opioids in the postoperative setting and should be continued until patients achieve baseline oxygen saturation levels while breathing room air. Respiratory function may be observed in an unstimulated environment, preferably during sleep [27, 30, 64].

Although pulse oximetry monitoring is widely established, end-tidal carbon dioxide monitoring provides a more sensitive indicator of hypoventilation and can deliver advanced warning [3, 95]. The implementation of capnography is therefore increasingly supported, although not typically utilized postoperatively, due to the requirement of advanced training skills for the accurate interpretation of signals during spontaneous breathing [95, 96]. Traditionally, continuous capnography required patients to be intubated, and only recent advancements have enabled this approach in non-intubated patients [3, 95]. Given the ability of capnography to provide early warning of postoperative respiratory depression, even before oxygen desaturation, this technology may progressively become more commonplace [97].

Among other evolving technologies for the prediction of postoperative respiratory depression are the FDA-approved impedance-based noninvasive respiratory volume monitors. These deliver continuous, real-time measurements of minute ventilation, tidal volume, and respiratory rate in spontaneously breathing patients. It remains to be seen how useful such monitors will be for the management of postoperative OSA patients [98].

Supplemental Oxygen

The administration of supplemental oxygen in the postoperative care of patients with OSA is common. To prevent hypoxia in the postoperative setting, the ASA recommends the maintenance of postoperative supplemental oxygen administration until baseline oxygen saturation can be

achieved while breathing room air [30]. In practice, oxygen administration can be titrated until an oxygen saturation level of 90–95% is achieved [3]. This intervention has shown to significantly improve oxygen saturation in patients with OSA [99]. Moreover, in a randomized controlled trial, Liao and colleagues demonstrated that it decreased the AHI and the central apnea index and shortened the longest apnea-hypopnea event duration [100]. While generally recommended in OSA, postoperative oxygen therapy seems particularly favorable in patients not adherent to CPAP and in newly diagnosed patients without adequate time for CPAP initiation. Caution is nevertheless warranted, as a subset of patients retain carbon dioxide with the use of oxygen therapy [100]. This is based on the role of hypoxemia in triggering respiratory arousal in patients with OSA. Thus, when supplemental oxygen abolishes hypoxemia, the apnea duration may increase, causing hypoventilation and hypercarbia, which subsequently bears the risk for life-threatening respiratory depression [99, 100]. These complications can be managed and prevented with additional monitoring of respiratory rate or PCO_2 during oxygen therapy [16, 100]. The general recommendation is therefore to suspend continuous postoperative oxygen therapy as soon as patients can maintain baseline oxygen saturation while breathing room air, to reduce the risk for prolonged apneic episodes, atelectasis, transient apnea, and hypoventilation which may remain undetected by pulse oximetry [2].

CPAP

As a pneumatic splint, CPAP treatment can prevent airway collapse during sleep and thereby diminish the incidence of apneas, hypopneas, and resulting hypoxic and hypercapnic events [2]. Based on this airway-stabilizing effect, CPAP has emerged as the gold standard of OSA therapy and proved to mitigate OSA symptoms and increase quality of life [101]. Besides long-term use, however, more high-quality evidence on the impact of CPAP implementation in the perioperative setting is currently needed. Despite evidence indicating that CPAP can mitigate opioid-related ventilatory impairment postoperatively, the usefulness of CPAP as a secure preventive measure against OIRD, particularly when considering opioid-induced central apnea, or the emergence of central apnea in CPAP-naïve patients, requires further research [3, 102].

Other current questions pertain to the optimal duration of pre- and postoperative CPAP administration and the impact of OSA severity [103]. Furthermore, the low patient compliance with CPAP presents a general challenge [2]. Nevertheless, recent evidence indicates that CPAP may alleviate postoperative airway obstruction, reduce postoperative AHI, modulate opioid-related respiratory depression, and decrease the incidence of major complications [2, 102, 104, 105]. Currently, CPAP administration is widely recommended in the immediate postoperative period for patients with known or high risk for OSA, preferably in semi-upright position [3, 16]. ASA guidelines specifically suggest that if severe airway obstruction or hypoxemia is observed, perioperative caregivers should consider the initiation of nasal CPAP or noninvasive positive airway pressure ventilation [30]. Alternatively, in postoperative OSA patients who do not respond to CPAP or have not previously received CPAP therapy, the American Society of Sleep Medicine suggests that oral appliances may be trialed [3, 106]. The efficacy of latter devices in that setting remains to be determined. In patients with prior CPAP therapy, the intervention should be sustained in the postoperative setting, while patients may be encouraged to provide and utilize their own equipment [3].

Pain Management

In patients at increased perioperative risk for OSA, postoperative pain management should be provided by targeting different pain signaling pathways in the context of a multimodal analgesic approach. This includes the administration of various non-opioid analgesics, such as NSAIDs, COX-2 inhibitors, and acetaminophen, as well as the use of regional anesthesia techniques to reduce the consumption of systemic opioids and other potentially sedating drugs [30, 86]. Notably, the concurrent administration of patient-controlled systemic opioids with continuous background opioid infusions, or the combination of sedative and opioid analgesic drugs, increases the risk for respiratory depression and airway obstruction and thus warrants caution [2, 30].

Healthcare Challenges

To date, despite numerous published recommendations on perioperative quality improvement in patients with OSA, no standard protocol has been universally accepted into clinical practice [3]. Currently, most institutions do not appear to have policies in place [24]. As healthcare institutions seek to avoid harm, pressures to reduce healthcare expenditure dictate that perioperative care be optimized to prevent unnecessary monitoring and use of limited resources [2, 16]. This reality often stands at odds with the perioperative management of OSA and OHS [16]. While adverse perioperative outcomes in OSA and OHS can be catastrophic, evidence shows that life-threatening or deadly events are rare but often preventable [24]. Nevertheless, patients at greatest risk for complications related to OSA and OHS are currently not well defined, and accurate risk stratification requires further development [16]. To resolve these important research questions, large sample sizes will likely be needed, requiring collaborative research networks [16].

Summary

In summary, OSA is becoming increasingly prevalent in our society, making surgical procedures and postoperative care increasingly more challenging [3]. The perioperative risk of OSA is defined by disease severity, individual comorbidity burden, invasiveness of the surgical insult, and the anesthetic management [30]. Although the vulnerability of OSA patients to sedation, anesthesia, and analgesia is well established, the prevalence of undetected cases of OSA in the perioperative setting remains high. More research is needed to increase patient safety and assure a cost-efficient allocation of resources. In the meantime, however, institutional pathways for the perioperative management of OSA and OHS should be developed and implemented based on the current body of scientific evidence, provided guideline recommendations and the availability of resources.

Summary Bullet Points

- OSA is a driver of adverse postoperative outcome.
- The prevalence of OSA is continuously increasing, while the majority of patients remains undiagnosed.
- Institutional protocols for the perioperative management of OSA should assure the following:
  - Preoperative patient evaluation and risk stratification
  - Intraoperative anesthetic management pathways, including airway management and risk-adapted anesthetic strategies
  - Postoperative monitoring and pain management taking postoperative cardiorespiratory risk into account

Case Report

A 64-year-old white male patient was admitted for an elective unilateral total arthroplasty of the left knee. The patient had no prior medical or surgical history when presenting for surgery. Physical examination revealed obesity with a BMI of 34 kg/m^2, a blood pressure of 155/95 mmHg, and a heart rate of 97 bpm. Electrocardiographic examination and blood laboratory values showed no abnormalities. While not on any medications, the patient disclosed the consumption of one beer per day and denied the use of any other drugs or cigarettes. The patient reported discomfort due to chronic daytime sleepiness, prompting him to regular napping. Regular loud snoring and occasional choking during sleep were confirmed by his wife. In the absence of a prior sleep study, the STOP-Bang questionnaire was instantly administered and yielded a score of 6. Head neck examination revealed an enlarged neck circumference as well as redundant posterior pharyngeal tissue. A perioperative risk management strategy was implemented. The patient received no preoperative sedative medications. Intraoperatively, the patient received neuraxial anesthesia and an adductor canal block. The patient was extubated in upright position and after neuromuscular blockade was fully resolved. Subsequently, the patient was transferred to a 24-hour monitoring environment with cardiac and respiratory surveillance. Postoperative analgesia included epidural anesthesia with the addition of NSAIDs and acetaminophen. After two oxygen desaturation episodes below 75%, CPAP therapy including supplemental oxygen was administered throughout the night. The next morning, the patient was able to maintain baseline oxygen saturation while breathing room air and was ready for transfer to a general ward with scaled surveillance. After the third postoperative night, the patient was deemed ready for home discharge, given that he was not living alone. The patient was referred to his primary physician for urgent further investigation and sleep testing based on his clinical symptoms of OSA.

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Perioperative Care of the Patient with Psychiatric Disease

20

John W. Barnhill

Objectives

- To better understand the preoperative assessments that can reduce perioperative morbidity
- To better understand the diagnosis and treatment of perioperative psychiatric complications
- To better understand how to make use of a psychosocial team and the psychiatric consultant

Key Points

- Delirium, substance use disorders, and the "difficult patient" are robust predictors of hospital complications and delayed discharges.
- Brief psychiatric assessments and interventions can reduce the likelihood of these complications.
- The consulting psychiatrist and/or psychosocial team can help the primary surgical team retain its focus on the patient.

Introduction

Psychiatric and behavioral problems can delay surgery and discharge, complicate the hospitalization, and undermine rehabilitation. Further, the evaluation and treatment of psychiatric issues require a perspective and fund of knowledge that is different from that which goes into orthopedic surgery.

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Fortunately, the majority of psychiatric issues encountered in the perioperative period fall into one of the three basic categories: drugs and alcohol, delirium, and the psychiatrically "difficult" patient. These three categories can overlap but are useful to distinguish. Two additional topics that are of particular concern to the surgical team are capacity to provide informed consent and how to best work with a psychosocial team during the perioperative period.

Withdrawal and intoxication can occur from illicit substances and alcohol as well as from medications prescribed by physicians. Withdrawal leads to the most difficulty in the perioperative period, while intoxication is most likely to be involved in orthopedic trauma. Withdrawal can be subtle and cause mild physical and psychological symptoms, but it can also be potentially life threatening. Alcohol and opioids are of particular importance in the orthopedic patient population.

Delirium may be the single most robust predictor of perioperative delays and complications. Also known as encephalopathy and ICU psychosis, delirium is commonly encountered after all types of surgery. Delirium is especially typical in patients who combine multiple risk factors such as advanced age and cognitive decline (e.g., patients at high risk for hip fracture). Early recognition and intervention can reduce the incidence and severity of delirium and can reduce the resulting complications and extended lengths of stay [1].

Psychiatrically difficult patients have a range of psychiatric diagnoses, including personality disorders, depression, anxiety, and chronic psychosis, that may be lifelong or be precipitated by the stress of hospitalization and/or surgery. From a psychiatrist's perspective, this category is overly broad, but, from the perspective of an orthopedist or perioperative medical consultant, these patients are presenting with behavioral and psychological difficulties that impede treatment. Regardless of the specific diagnosis and degree of severity or chronicity, the vast majority of these "difficult" patients can be efficiently identified and managed so that the necessary surgery can be successfully performed.

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Capacity to provide informed consent is evaluated routinely by surgeons prior to doing a procedure. In most circumstances, patients provide informed consent without difficulty. When concerns do arise, surgeons are expected to follow their hospital's guidelines for an independent capacity evaluation. Generally done by either the psychiatric consultation-liaison service or a member of the hospital's ethics committee, the "capacity consult" can pave the way for an efficient hospital course or can contribute to ongoing delays and miscommunications.

The psychiatric consultant and psychosocial team may include psychiatrists, psychologists, social workers, nurse practitioners, and a variety of allied health personnel. These colleagues can be helpful for two basic reasons. First, psychosocial issues are their area of expertise. Second, as members of the hospital team, they apply this expertise to psychosocial assessments and interventions that directly improve surgical outcome, reduce complications, and enhance patient satisfaction.

This chapter focuses on common psychiatric complications of the perioperative period by dividing them into the pre- and postoperative periods.

Preoperative Assessment

The preoperative assessment already includes a psychological assessment. Not always explicit and not requiring the patient to even be conscious, the evaluation includes the team's own reaction to the patient as well as some consideration of whether the patient is liable to cause some sort of trouble. "Trouble" can be almost anything but is most often related to a psychiatric diagnosis such as substance abuse or dementia or it can relate to issues related to informed consent or excessive worries about the surgery. Such patients are disproportionally represented among patients whose perioperative course is marked by delays, cancellations, and complications.

As surgical teams and hospitals look more attentively at preoperative conditions that diminish outcome, increased attention is being paid to mental distress. For example, rates of anxiety and depression are elevated in orthopedic populations, tend to be systematically underdiagnosed [2], and lead to relatively poor outcomes and diminished patient satisfaction scores [3].

Psychiatric involvement can be useful preoperatively by helping to provide an assessment structure that clarifies risks, provides useful interventions, and reduces later morbidity. Most initial "screens" take just a few minutes and are done by the surgeon or a member of the surgical team. One study found, for example, that anxiety is best reduced by the surgeon clearly explaining the surgery [4], while another demonstrated that a 60 second video exercise on mindfulness could reduce pain, anxiety, depression, and anger in an orthopedic population [5]. One important principle that underlies such screens is that their primary task is to streamline the surgical intervention and *not* to diagnose and treat every psychiatric diagnosis.

No simple algorithm or roster of questions can replace a tactful and sensitive psychiatric interview, but a handful of straightforward questions will identify most people at risk. Figure 20.1 lists a typical preoperative psychiatric screen.

A psychiatric screen is not without consequences. Some patients may get offended by personal questions, while others may provide far more information than is necessary for a pre-op evaluation. Most problematic, however, is that some patients will reveal information about their substance abuse, memory deficits, and suicidal thoughts that will require a response from the surgical team [6]. Without an intact psychosocial team or psychiatric consultant, this will require additional work from the orthopedic team. For this reason, many orthopedic services have employed people whose specific role is to handle typical psychosocial problems.

Preoperative Assessment of Psychiatric Medications

Psychiatric medications are widely used, and almost all can be safely given on the day of surgery. While some surgeons routinely take patients off as many medications as possible during the perioperative period, it is likely that far more morbidity has ensued from unnecessary medication discontinuation than from actual drug interactions.

Discontinuation of psychiatric medications can lead to withdrawal symptoms. For example, sedating medications tend to have withdrawal effects. Opiate withdrawal is especially uncomfortable, while benzodiazepine withdrawal can be life threatening. Acute withdrawal from antidepressants—especially paroxetine (Paxil® (GlaxoSmithKline, Brentford, UK) and venlafaxine (Effexor® (Pfizer, NY, NY, USA))—can be highly unpleasant.

Withdrawal of psychiatric medications can also lead to a recurrence of a primary psychiatric condition. A brief period of insomnia can, for example, induce a manic episode in a bipolar patient, while some patients with schizophrenia and anxiety are very sensitive to even a few days away from their psychiatric medication. On the other hand, a brief break from antidepressants is unlikely to induce a depression, which is fortunate since all of the currently available antidepressant medications must be given by mouth.

Two of the older classes of antidepressant medication, the monoamine oxidase inhibitors (MAOIs) and the tricyclic antidepressants (TCAs), have potential anesthetic interactions.

- How are you feeling about the upcoming surgery?
  - Any particular concerns?
- Do you have any particular psychiatric conditions we should know about?
- How has your mood been?
  - Have you been depressed? Have you been suicidal?
- Are you on any psychiatric medications?
- What other medications are you on?
- Do you use health food supplements?
- How much alcohol do you drink?
  - It's useful for us to get a clear view of your drinking since people often have symptoms when they stop drinking for surgery. Have you had difficulties before? Any withdrawal problems?
- How has your memory been?
  - What's today's date?
  - Where are we?
  - If any concerns: Would you draw a clock with all the numbers that indicates 10 after 10?

Fig. 20.1 Sample of preoperative psychiatric screen

While neither class of medication is currently used extensively by psychiatrists, the TCAs are often used to help manage pain. More dramatically, one of the MAOIs, phenelzine (Nardil®, Pfizer, NY, NY, USA), has been famously implicated in sudden death when combined with opiates, particularly meperidine [7]. By and large, however, psychiatric medications do *not* interact with pain medications or with anesthesia, and they need not be discontinued prior to surgery [8].

Preoperative Assessment of Substances of Abuse

It can be a challenge to assess for substances of abuse. Many patients do not spontaneously report the use of illicit drugs and prescribed psychoactive medications, and so a tactful but skeptical history is essential [9–11]. All substances of abuse should be considered, especially the sedating ones that can cause severe withdrawal symptoms: alcohol, benzodiazepines, and opioids. History should include a focus on withdrawal complications that accompanied prior hospitalizations, since they are likely to recur.

Many patients will be relatively frank about their substance use if the clinical approach is matter of fact and motivated by a desire to prevent complications. A central credo of substance abuse treatments is that many people are "pre-contemplative" and may not consciously realize that they have a problem and, even if they do, that they do not feel ready to quit. The goal of a perioperative evaluator is not, however, the same as that of a substance abuse

counselor. The first goal is to prevent surgical and medical complications; a secondary goal is long-term remission. Once that is clarified in the interviewer's mind, exploration of possible substance abuse needs to be no more tense than a discussion of other elements of the patient's history.

Pertinent labs may assist the evaluation. An elevated or high–normal mean corpuscular volume (MCV) is suggestive of chronic alcohol use, for example, as is an elevated aspartate transaminase (AST) with an AST/ALT ratio of approximately 2:1. There are other causes besides alcohol for an elevated MCV and a transaminitis, but in at-risk populations, they are definitely suggestive of alcohol dependence and likelihood for withdrawal symptoms.

A toxicology screen and a blood alcohol level can help identify a particular substance of abuse; these tests will only reveal recent use, and neither will reveal whether someone is likely to go into withdrawal. These lab screens can, however, point the clinician in useful directions. If a known alcohol-dependent patient is admitted with an alcohol level of 0, the clinician should anticipate that alcohol withdrawal symptoms might develop on the first hospital day. If a patient is admitted with an alcohol level of 0.220 and does not appear impaired, then the clinician should anticipate withdrawal regardless of the patient's claims of only "social drinking." On the other hand, if a trauma patient is stumbling and slurred with a relatively low alcohol level, the clinician might be inclined to believe that the patient is not a regular heavy drinker, though the altered mental status could also indicate head trauma or cirrhosis.

The nation-wide opiate crisis has led to a dramatic reevaluation of the overall management of chronic pain. In regards to the preoperative assessment, surgical teams are increasingly screening for chronic opioid use and deferring elective surgery in patients whose opiate use is deemed too high. One particular concern is that chronic use of opiates leads to a generalized sensitivity to pain (i.e., opioid-induced hyperalgesia, or OIH) [12]. A surgical approach to chronic pain can, therefore, lead to acute-on-chronic pain and an intensified cycle of opiate use. In such instances, a slow taper of opiates often allows the planned procedure to go forward [13]. In one study of patients undergoing a total joint arthroplasty, a 50% reduction in preoperative opioids led to postoperative results that resembled the opioid-naïve population [14]. See Box 20.1 for postoperative complications of chronic opioid use.

Box 20.1 Anticipated Postoperative Complications of Chronic Opiate Use

- Increased risk of infection
- Ileus and new-onset chronic constipation
- Respiratory suppression with atelectasis and pneumonia
- Compromised wound healing
- Reduced arthroplasty or intervertebral fusion success
- Opioid-induced hyperalgesia
- Increased readmissions and ED visits

Data from: Sayal et al. [38] and Jain et al. [39]

Preoperative Assessment of Capacity

Patients have the right to provide informed consent for all surgical procedures unless they are deemed to lack capacity by a physician. The capacity to provide informed consent can be determined by any physician, and almost all pre-op capacity assessments are done informally by the primary surgeon in the course of discussing the proposed intervention. Occasionally, however, patients appear to be making unwise or idiosyncratic decisions, recurrently changing their minds, demonstrating cognitive impairment, or being psychotic or severely depressed. In these situations, the surgeon tends to look elsewhere for help in deciding the patient's capacity to provide informed consent.

The laws that underlie capacity vary between countries and between states within the United States. The laws tend to be patchwork and incomplete even within a particular state so that the de facto rules and procedures tend to vary between adjacent hospitals and sometimes between services within the same hospital. In addition, there is no single definition of capacity and no agreed-upon tool for measuring capacity. These multiple layers of uncertainty can lead to the involvement of psychiatrists, ethicists, lawyers, and administrators, and the path to surgical efficiency can get frustrated.

It is important, therefore, for the orthopedic team to understand the definition of capacity and to have a working knowledge of the principles of *specificity*, *the sliding scale*, and the use of *proxies*. Capacity refers to the ability to understand the pertinent medical information and to make a reasonable, consistent decision. For example, an elderly patient may lack the ability to process information related to a hip fracture because of dementia, while other patients might have questionable capacity because of the confusion related to an alcohol withdrawal delirium; the paranoid mistrust of schizophrenia; or the waffling uncertainty brought about by depression, anxiety, and panic.

All capacity decisions are *situation specific* in that a particular capacity decision relates to a specific question. In other words, capacity to provide surgical consent does not necessarily mean they can refuse nursing home placement

(i.e., dispositional capacity). The *sliding scale of capacity* refers to the concept that it requires a higher degree of cognitive and emotional capacity to consent to an intervention that is deemed to be high risk/low benefit or to refuse an intervention that is low risk/high benefit. This concept explains why a patient may have the capacity to consent to the repair of a hip fracture but lack the capacity to refuse the same procedure. Some ethicists have argued that the sliding scale creates a Catch-22 for patients: if they accept the physician's recommendations, they are deemed to have capacity, but if they disagree, they lack capacity. In general, however, hospital-based ethics committees tend to abide by the sliding scale at least partly because it seems both fair and pragmatic.

Patients who are deemed to lack capacity do not immediately lose their rights or their ability to obtain necessary treatment. Specific laws vary from state to state, but, in general, the aim is to abide by what the patients would have wanted if they did have capacity. Some patients will have spelled out their intentions in an *advance directive*. Since medical and surgical circumstances are often complex and specific, even a well-designed advance directive may be inadequate to spell out an exact course of action. When the advance directive is not adequate or available, the goal is to identify the person, or the *proxy*, who is best able to stand in for what that particular patient would have chosen if he or she did have capacity. The proxy may have been previously identified by the patient, may be chosen as next of kin, or may be a member of the hospital administration who functions as an independent advocate for the patient's wishes. Virtually the only adults excluded from serving as health care proxies are members of the treatment team, since they may be viewed as having a conflict of interest in regard to the medical and surgical care.

To speed the process of assessing capacity, the orthopedic team can help clarify the medical and surgical issues: the specific procedure being proposed, its likely risks and benefits, reasons that the procedure might be specifically useful or problematic to this particular patient, reasonable alternative treatments that might be more acceptable to the patient, and any disorders whose treatment might improve his or her judgment (e.g., pain, fear, depression, dementia, or withdrawal).

Preoperative Prevention of Delirium

Perioperative confusion predicts morbidity, mortality, and delayed discharge in orthopedic patients [15–19]. While often unrecognized, delirium develops in about 30–40% of at-risk patients following orthopedic surgery. Often viewed as a postoperative condition, delirium has also been found in as many as 21% of hip fracture patients *prior* to surgery [20]. Recent studies have tried to identify which patients are at greatest risk for post-op delirium. Among a population of patients undergoing hip fracture repair, pre-op risks include advanced age, dementia, reduced ability to care for self, and being white (i.e., African Americans had lowered rates of delirium). Anticipation of delirium is potentially useful since delirium is associated with prolonged lengths of stay, discharge outside the home, higher odds of 30-day readmissions, and 30-day mortality [21].

The most robust interventions to reduce the incidence of delirium in at-risk hospitalized patients include adequate hydration, optimization of analgesia, reducing sleep deprivation, reduction in polypharmacy, aggressive physiotherapy, reorientation, and letting the patients wear their glasses and hearing aids [22–24]. Pre-op prophylaxing with low doses of antipsychotic medication appears to modestly reduce the incidence of delirium in at-risk patients [25]. On the other hand, reducing the depth of anesthesia in hip fracture repair did not lead to a reduction in the incidence of delirium in at-risk patients [26]. Other interventions have focused on such delirium contributors as infection, anemia, pulmonary edema, and pulmonary embolus.

A more extensive discussion of delirium can be found later in this chapter.

Postoperative Psychiatric Issues

The psychiatric issues that most commonly complicate the postoperative course include delirium, withdrawal, mood disorders, behavioral disturbances, and a reluctance to progress with physical therapy and/or transfer to a rehabilitation center.

Postoperative Delirium

Delirium can sometimes be predicted, but it generally develops quietly during the day or two following surgery. Also called metabolic encephalopathy and ICU psychosis, delirium is marked by acute and fluctuating disturbances in cognition, behavior, and mood. While alcohol withdrawal delirium is generally hyperactive and accompanied by agitation and obvious confusion, most postoperative patients with delirium appear subdued and depressed. When interviewed, quietly delirious patients will reveal some combination of confusion, inattention, diminished memory, anxiety, paranoia, and depression [27, 28].

While common, delirium is generally ignored. When delirium is noticed, a common response is to normalize (e.g., "Who wouldn't be a little confused?" or "they are better off not knowing what is going on").

There are several problems with not aggressively diagnosing delirium. The first is that delirium often reflects an underlying

medical problem that warrants attention; in fact, delirium is the only psychiatric diagnosis that must be accompanied by a medical diagnosis that is the presumed trigger. The second problem with not identifying delirium is that patients and loved ones are often frightened by the change in mental status, often worrying that the patient has acutely developed an untreatable dementia. An encouraging explanation can reduce their family members' worry and improve the quality of the subsequent hospitalization. A third reason is more pragmatic. Delirium may be the most robust predictor of a prolonged hospital stay, and so hospitals, administrators, and medical teams are increasingly motivated to prevent and treat delirium.

Risk factors for delirium include age, cognitive impairment, low body mass index, and anything that increases metabolism (e.g., infection) or decreases physiologic efficiency (e.g., anemia or electrolyte abnormality). Hundreds of medications have also been implicated in delirium, but the classes that appear most risky include opioids, benzodiazepines, and calcium channel blockers [29].

Once identified, treatment of delirium is problematic [30]. The single best medication appears to be a low-dose antipsychotic, generally given in the evening [31, 32], but all of the antipsychotic medications have been implicated in elevated rates of sudden death in elderly patients with dementia [33]. Nevertheless, antipsychotic medications are frequently used to help with sleep and paranoia. Benzodiazepines are generally reserved for alcohol and benzodiazepine withdrawal since they tend to cause a paradoxical disinhibition in the elderly and cognitively impaired. Coaching the family can be crucial. By defining delirium and underlining its frequency and transience, family members can be both reassured and enlisted to help ensure the patient's safety. Further, informed family members are more likely to effectively participate in treatment and discharge planning.

Postoperative Withdrawal and Intoxication

It is useful to try to anticipate which patients are likely to go into withdrawal (see discussion earlier in this chapter). Psychiatric issues often remain hidden until the hospitalized patient's symptoms become acutely problematic, and this is particularly true for substance abuse, which is often noticed only when the patient goes into withdrawal [34].

The most common and potentially most dangerous type of acute withdrawal is from alcohol. Because of the potential catastrophe of delirium tremens (DTs), surgical teams should have a low threshold for beginning alcohol withdrawal precautions. These precautions generally include frequent vital signs and a brief neurological exam looking for objective signs of alcohol withdrawal. When alcohol withdrawal is detected, the response varies significantly between hospitals and between units at the same hospital, but they generally include the use of benzodiazepines at doses adequate to induce a light sedation and maintenance of normal vital signs. Most people who abuse alcohol can be discharged in comfort and without delay. It is possible to overmedicate, but the greater likelihood is under - treatment, which helps create—at best—an edgy, unhappy, and potentially nonadherent patient. In addition, early detection and treatment help identify those patients who are at risk of going into the sort of frank withdrawal that can lead to delirium, delayed discharge, and serious medical complications.

Assessment for opioid abuse and dependence is complicated by the reality that many orthopedic patients have considerable pain and a legitimate need for pain relief. Opioids are well known to induce dependence, a tolerance for increasing doses of the medication, and diminishing tolerance of pain. Many orthopedic surgeons are familiar with the former athlete whose previously high pain threshold has melted under years of opioid medication and who presents in middle age with a variety of orthopedic complaints, low tolerance of pain, and a robust dependence on high doses of opioids. Such a constellation is especially difficult in the perioperative period. That particular patient will likely need increased opioid dosages during and after surgery in order to control pain. That same patient is also likely to present with a worrisome triad: detailed knowledge of opiate dosages and delivery methods, high dosage requirements, and desperation. The average-expectable staff reaction to this triad is to identify possible substance abuse and then *reduce* pain medications. The patient, meanwhile, has often been taking his opioids as prescribed and finds himself in serious postoperative pain. This staff/patient interaction can lead to an unhappy cycle of mutual hostility and mistrust. Such situations are difficult, but in general, it is reasonable to treat the pain commensurate with the need and defer opioid detoxification until after discharge.

Psychiatrically Difficult Patients

"Difficult" patients are those people whose behaviors interfere with the perioperative process. In addition to the delirium, substance abuse, and capacity questions that have been discussed, many other psychiatric conditions can complicate surgical treatments. These include anxiety, depression, agitation, interpersonal conflict, nonadherence, and/or some type of oddity. Sometimes, these characteristics are accompanied by a formal psychiatric diagnosis. At

other times, the patient presents without a psychiatric diagnosis but with a clear history of bumpy hospitalizations. Often, however, the primary team has no such guideposts. In most instances, tactful professionalism from the surgical team allows for the smooth performance of the planned intervention.

The anxious or depressed patient may need additional reassurance, for example, while the highly critical patient might soften with extra attention to his or her concerns. The unusually entitled patient may be calmed by getting to spend a few extra minutes with the senior surgeon. It is useful to recall that the average expectable staff response to needy or critical patients might be avoidance or overt skepticism and that such typical responses might worsen the situation.

In working with a particularly difficult patient, it is useful for the surgical team to take its own pulse. Some patients are unusually difficult for almost anyone, but certain types of difficult patients can be specifically difficult for particular healthcare providers. Nonadherence may be difficult for some surgeons, for example, while alcohol, entitlement, or low health literacy might trigger a negative reaction in others.

Some patients have psychiatric symptoms that are explicitly situational to the orthopedic procedure. For example, many people are intensely worried about surgery and anesthesia. This can lead to apprehension and resistance to surgery. Many of these people function well in the outside world and lack a psychiatric diagnosis, but, as soon as their anxiety interferes with the surgical process, they fit the "difficult" definition. If a patient appears nervous or admits to anxiety, it is very useful for at least one member of the surgical team to tactfully discuss the concern. It is also useful to recall that some people will be just as reluctant to reveal a needle phobia as other patients might be of revealing substance abuse. Most concerns can be remedied by a simple explanation, while others might warrant such interventions as exposure to the surgical suite, an instructional video, or exercises to enhance calm (e.g., breathing, muscle relaxation, mindfulness meditation, visualization). At other times, a single low dose of an antianxiety medication can allow the surgery to proceed smoothly.

Psychotic patients are an example of a potentially difficult psychiatric patient. Generally, however, the difficulty is not the psychosis. The predominant psychotic disorder is schizophrenia, and most people with schizophrenia are more disabled not by hallucinations or delusions but by the "negative" symptoms such as apathy and cognitive difficulties. These latter impairments can reduce their ability to understand the informed consent process as well as the ensuing need for rehabilitation. At the same time, people with schizophrenia are often model, dutiful patients who will respond well to the stress of surgery—especially if their psychiatric medications are continued during the perioperative period.

Another common type of difficult orthopedic patient is one who presents with a cluster of seemingly unrelated symptoms following a trauma. Anxiety, irritability, and substance abuse may be present, but a careful history may reveal a characteristic cluster of stress-related symptoms: reexperiencing of the trauma through dreams and memories, avoidance of reminders of the trauma, and autonomic hyperarousal. Early psychiatric intervention can reduce the likelihood of the development of a full-blown posttraumatic stress disorder (PTSD) and can also bring clarity to what can be a bewildering array of symptoms.

Such psychological treatments are likely to be difficult for a solo surgeon, but large programs often have a designated nurse or patient educator to work with such patients before and after their procedures. Larger programs also tend to employ psychiatric consultants who can focus on psychiatric disorders that are outside the realm of the patient educator. As with consultants from neurology and the pain service, psychiatric consultants should not preempt the orthopedist's role as the patient's primary physician but rather make it more straightforward for the surgeon to focus on the care of the patient.

Summary

While psychiatric issues are some of the most common complications of the perioperative period, they are routinely underdiagnosed on surgical services. Systematic evaluations and straightforward interventions can significantly reduce the burden of psychiatric issues, while the judicious use of psychiatric consultants and a psychosocial team can allow the surgical and anesthesiology teams to focus more fully on their work with patients.

The preoperative period allows the surgical and anesthesiology teams to anticipate problems. These can vary dramatically, from issues related to informed consent to virtually any psychiatric or behavioral condition. The best preoperative assessment combines the surgical team's intuition and clinical acumen with a set of relatively routine questions that can be asked by a selected member of the team. Evidence indicates that a single question is adequate to elicit useful information about many different psychiatric conditions. These can range from "Do you have worries about the surgery?" to "Have you ever had difficulties with alcohol or alcohol withdrawal?" Since people are not always forthcoming about their psychiatric issues, it can also be useful to search for additional information through lab results, old surgical/medical records, and family members.

Perhaps the biggest concern with searching for problems is that they may require an intervention. If a cognitive problem is elicited, for example, it may become necessary to formally assess capacity, to try to reduce the likelihood of delirium, and to anticipate that they may need postoperative placement in a subacute rehab or nursing facility. It is useful to recall that elicited problems are liable to cause complications even if they are ignored preoperatively and that the bulk of the intervention can be done by ancillary members of the team.

The day of surgery can be psychiatrically complicated for several predictable reasons. Anxiety about the surgery and/or the anesthesia is a common problem; if anticipated, such concerns can often be easily addressed. Problems with capacity and informed consent can stall surgery, so it is best to anticipate the problems prior to surgery by having someone available to make rapid capacity assessments (generally a psychiatrist or a member of the ethics committee) as well as someone who can become a proxy if no friends or family members are available and willing to serve as proxies (generally an administrator from patient services and specifically someone not from the primary surgical team).

The postoperative period generally goes smoothly for patients with psychiatric disorders. Nevertheless, several problems are common. Abuse of alcohol and illicit substances can complicate all aspects of the perioperative period and is particularly common in the orthopedic trauma population. The use of opioids is very common in patients with chronic pain, and opioids can affect both the anesthesia needs and postoperative pain management. "Difficult" patients are defined here as any patients who complicate the perioperative period because of behavioral or interpersonal conflicts. These include a wide array of psychiatric disorders, including people with substance abuse, personality disorders, and PTSD. For most of these patients, their acute symptoms can dissipate with brief, tactful interventions [35, 36].

Regardless of whether or not they are recognized or addressed, psychiatric issues routinely affect orthopedic surgery. Anticipation can reduce disruption to the perioperative period. Ideally, the process of recognition and treatment of psychiatric issues is informed by psychiatric specialists while the orthopedic team can maintain its focus on surgery and the patient.

Summary Bullet Points

- Psychiatric issues commonly complicate the perioperative period.
- Psychiatric medications should generally be given throughout the perioperative period.
- Informed consent is routinely assessed by the surgery team. Psychiatrists, ethicists, and hospital administrators may get involved in complex capacity questions.
- The psychiatric consultant often works within a context of a psychosocial team composed of professionals with a range of relevant expertise.

Case Studies

Case 1

An 84-year-old man was brought to the emergency room following a hip fracture. In preparation for surgical repair, the orthopedic team noted that he seemed confused, distracted, and unable to pay attention to the conversation. His wife confirmed that he had been alert and oriented prior to the accident but that he had experienced some mild cognitive decline in recent years.

A psychiatric consultation was called. The patient was diagnosed with mild dementia. The psychiatrist noted that he lacked capacity to provide informed consent and had signs of delirium, so consent for surgery was provided by his wife. In addition, the psychiatrist elicited the fact that the patient had a prolonged period of confusion the prior year when he had a cardiac bypass procedure. The primary team evaluated him specifically for dehydration, polypharmacy, insomnia, and pain complaints. After discussion with the surgical team and the patient's wife, and a normal QT interval on an EKG, the patient was offered a low dose of olanzapine the night before and after surgery. His postoperative course was marked by some nighttime confusion, but he quickly stabilized and was ready for transfer to a subacute rehabilitation center by postoperative day four.

Case 2

A 38-year-old former professional skier suffered a femoral fracture in a snowmobile accident. He was admitted for surgery to a specialty orthopedic hospital after a 4-day hospitalization at a community hospital near the site of the accident. By the time he arrived, the patient was agitated, hostile, and mildly confused. A psychiatric consultation was solicited to help manage the agitated behavior and streamline efforts to repair the fracture.

The patient was able to provide some history to the psychiatrist, but he appeared agitated, anxious, and tremulous. He was hypertensive and tachycardic. The psychiatrist elicited multiple pertinent historical issues: the patient drank approxi-

mately half a liter of vodka per day; long-standing pain from prior sports injuries had led to chronic use of opioids; and, while he denied interpersonal issues, his wife insisted that he was an entitled, difficult man who responded to adversity with hostility and rage attacks.

This cluster of symptoms and history suggested that he was at risk for serious alcohol withdrawal. His laboratory data were pertinent for an MCV of 104 and liver function tests with a characteristically elevated AST. A review of his suitcase uncovered a half-full bottle of vodka, and, while he had never been treated for alcohol abuse, his wife indicated that he had twice been arrested for driving under the influence. The patient was more focused on his pain, which he believed was being vastly undertreated, and he was threatening to leave against medical advice.

The psychiatric intervention was multifold. First, a long-acting benzodiazepine was prescribed with the goal to reduce his somatic complaints of shakes and anxiety and to reduce his heart rate and blood pressure. Secondly, the psychiatrist worked with the pain service to increase his pain medications with the recognition that his tolerance to opioids was increased because of his chronic use of pain medications. By adding methadone to the standing pain regimen, he was able to tolerate his pain before and after surgery.

The patient's agitation and confusion had diminished by the second day of hospitalization. By that time, the psychiatrist identified that the patient had been chronically depressed since the end of his athletic career. Recognizing the importance of identifying and treating co-occurring psychiatric disorders [37], the psychiatrist diagnosed depression with prominent anxiety which the patient had been partly "self-medicating" with pain medications and alcohol. She also explicitly told the patient that his recovery would depend on some of his long-standing character traits: a competitive spirit, discipline, a need to be seen as in charge, and a desire to regain satisfaction in his marriage and at work. She discussed the use of an antidepressant medication for the depression and anxiety, non-opioid strategies to reduce pain; the use of naltrexone to reduce the craving for opioids and alcohol, psychotherapy to reduce marital and interpersonal conflicts, and an outpatient neuropsychiatric evaluation for possible sports-related traumatic brain injury. None of these discussions slowed the discharge, and the patient went home without delay.

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Perioperative Care of the Orthopedic Patient with Chronic Pain

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Faye Rim and Seth A. Waldman

Objectives

- To present an approach to the preoperative evaluation and management of the patient with chronic pain, opioid use, substance use disorder, and behavioral comorbidities
- To explore approaches to the management of postoperative pain in patients with chronic pain
- To discuss characteristics of the patient with long-term opioid use which are relevant to perioperative optimization
- To understand the safest ways to use opioid pain medications when they are necessary

Key Points

- Postoperative pain management begins with preoperative assessment.
- Psychological state, substance abuse, and high-dose opioid therapy pose significant challenges to postoperative pain management.
- Multimodal analgesia for postoperative pain control is essential.
- Consultation with specialists in psychiatry, addiction medicine, and chronic pain may be required.
- During and after surgery, treatment should focus on reducing the patient's exposure to pain *and* opioids.
- Whenever opioids are initiated, a plan for when and how they will be tapered and discontinued must be established.

Introduction

Chronic pain-related conditions represent a significant economic burden, estimated to carry an annual cost of $560–635 billion in the United States alone [1]. In the setting of chronic pain, the addition of acute postoperative pain increases associated disability and can have additional negative secondary effects [2]. Inadequately controlled acute pain causes unnecessary and excessive opioid use, delayed recovery, and increased length of hospital stay following many surgeries [3, 4]. The use of a larger amount of opioid pain medication in this setting is associated with unintended ethical and public health consequences. These include increased professional risk for clinicians who are obligated to treat electively induced acute pain in the setting of unrecognized substance use disorder or other aberrant behavior and an increased volume of unnecessary opioids available for diversion. Substance use disorder, high intensity pain, negative affect, and catastrophizing are all risks factors for opioid misuse or abuse in patients with chronic pain [5–7]. Preoperative screening for these conditions allows caregivers to devise action plans to treat these patients.

Further, the opioid epidemic poses challenges to treating acute and chronic pain. Increased availability of opioid medications prescribed for surgical pain has been an associated contributor to the opioid epidemic. In this context, it has been suggested that a significant number of surgeries may be performed due to the magnification of preoperative pain com-

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plaints by opioid-induced hyperalgesia [8]. For the individual, sustained use of opioids can lead to tolerance, hyperalgesia, and adverse outcomes. Public health issues include inappropriate use, crimes related to drug diversion, addiction, and unintentional overdose. The Centers for Disease Control (CDC) guidelines for opioid prescribing published in 2016 recommend that the volume of prescribed opioids be reduced on the basis of individual and public safety [9]. There has been an increase in the number of state mandates which limit opioid prescribing and in the number of states which operate prescription monitoring programs (PMPs). Prescribing recommendations which limit the use of opioids even for acute pain recognize that dependence on opioids can occur even after a few days of exposure [10]. While this has led to the development of new opioid-free pathways and surgical regimens, it does not specifically address the needs of patients with chronic pain on chronic opioid therapy, patients on opioids for medication-assisted treatment (MAT) of substance abuse, or those with an expectation of being treated with opioids.

Chronic Pain

The intensity and duration of preoperative pain is a strong predictor of outcome [11]. Preoperative chronic pain is often treated with opioids and has been suggested to increase postoperative pain levels and opioid consumption [12]. Patients who reported chronic opioid use before orthopedic surgery experienced an increased severity of acute pain and prolonged pain resolution [13]. In addition, preoperative opioid exposure has been associated with increased length of stay, risk of complications, and the need for additional surgical procedures, likely due to higher and more sustained postoperative opioid dose requirements [14, 15]. Postoperative opioid prescription patterns are also reflective of preoperative comorbid conditions. The risk of persistent postoperative pain has been associated with higher levels of preoperative opioid use [16, 17].

There is evidence that chronic pain patients – even without the use of opioids – have slower rates of postoperative pain resolution. Those not using opioids have been reported to have similar levels of pain after surgery as patients without chronic pain, however, pain resolution seems to be protracted. In patients with chronic pain using opioids, initial levels of pain are markedly higher and resolve at the same slow rate as in other chronic pain patients. It is therefore not surprising that this group reports substantially more postoperative pain over time than chronic pain surgical patients who have not been treated with opioids [18]. These concepts underline the importance of reducing opioid consumption preoperatively as much as possible.

Strategies for Perioperative Pain Control

Preoperative education and planning for perioperative pain management is of primary importance in all patients undergoing surgery, but it is critical in patients with chronic pain or those at risk for increased opioid needs due to other comorbidities. This should include tailored education for the patient and, when necessary, their caregiver. Information given should include treatment options, necessary preoperative interventions, and evaluation. Further, it is important to set reasonable goals for postoperative pain management for all involved [19]. Documentation and communication of a care plan to the patient, surgeon, and other perioperative staff, as well as to the postoperative prescribers is essential to its success.

Preoperative stratification can help to identify patients at risk for poor pain control or prolonged postoperative pain. While chronic preoperative exposure to opioids, SUD, and mental health comorbidities are the most common concerns, central sensitization, genetic, and personality-related risk factors may also put patients at higher risk. Specific perioperative management such as reduction in preoperative opioid use, perioperative use of medications such as ketamine and gabapentinoids, and close postoperative follow-up may help reduce postoperative opioid use, the development of chronic pain, and the worsening of chronic pain.

The effect of chronic opioid use on surgical outcomes is likely multifactorial. One potential cause is opioid-induced hyperalgesia (OIH), which is defined as a heightened expression of pain because of nociceptive sensitization from exposure to opioids [20]. While this effect may appear paradoxical, evidence suggests that opioid tolerance and OIH limit the long-term clinical utility of opioids. OIH can develop rapidly and be difficult to recognize. It can develop as early as 1 week after the initiation of opioid therapy and be expressed as an increased verbalization of otherwise expected pain [21]. When a patient on opioids has escalating pain without an evident cause, or reports repeated escalations in the dose of their medication, tolerance and OIH should be considered and a pain management consultation initiated. This consultation should focus on evaluating possible causes of the patient's increased pain, such as complex regional pain syndrome or other less common but potentially overlapping conditions. Behavioral reasons which might alter the expression of pain should be considered. Toxicology screening and evaluation of prior prescribing records is an important step and helps guide treatment. Consideration must be given to evaluation by a behavioral or addiction specialist if after careful assessment there is no apparent physiologic cause and evidence of addictive or other aberrant behavior is lacking.

When possible, a reduction in the dose of opioid pain medication prior to surgery is advised. In patients who use opioids chronically, a taper of at least 50% in the preoperative dose has been demonstrated to reduce the risk of abuse and improve functional outcomes after surgery [22]. During and after surgery, treatment should focus on reducing the patient's exposure to pain and opioids by concentrating on multimodal analgesia featuring regional anesthetic techniques and non-opioid adjuvant medications.

While data regarding optimal perioperative analgesic techniques are lacking, extended duration regional anesthetics are likely to benefit the opioid-tolerant patient. Additional short-acting opioid medications are often introduced as needed for postoperative pain. However, in most circumstances, long-acting opioids should be avoided. After a functional postoperative analgesic regimen has been developed, a plan for tapering and discontinuing opioids is essential. Without a tapering plan, there is an increased risk that patients will remain on opioids chronically secondary to tolerance, OIH, and at times addiction. An unprepared patient left with insufficient instructions on the best way to taper opioids may simply remain on this medication indefinitely, or be forced to stop them suddenly, leading to an abrupt, painful, and unnecessary withdrawal.

A comprehensive perioperative pain program should assess and treat patients at every stage of the surgical process. Without preoperative recognition of patients at increased risk, however, it is not possible to provide the best care in subsequent phases. Given the large volume of elective surgeries, the most effective way to screen patients who would benefit most from early intervention is to develop tools which can be employed at the time of initial surgical consultation. In addition to a routine query of the state prescription monitoring program, questions should be asked about any preoperative use of opioids as well as a history of any prior substance use or SUD treatment. Patients who are identified in this initial screening phase should have a formal pain management consultation, which involves reviewing the detailed history of opioid treatment, contacting the prescribing clinician, and performing a toxicology screen. Subsequently, a plan for treatment is developed. When necessary, this may include referral for psychological or addiction evaluation and treatment or development of a reduction schedule. The latter should involve the patient's prescriber in cases in which excessively high opioid morphine milligram equivalent (MME) doses are used. The preoperative pain evaluation is an ideal time at which to counsel the patient regarding issues related to OIH, establish an agreed-upon plan for perioperative pain treatment, and when possible postoperative weaning. For these patients close postoperative follow-up is required, with the goal of adjusting medications to safe levels which manage pain and improve daily function [23–25].

Substance Use Disorder

Chronic pain often coexists with SUD, and patients with this diagnosis appear to be at a greater risk for aberrant medication-related behaviors. These individuals are more likely to be prescribed opioid medications at higher doses than patients without a history of SUD [26]. Failure to recognize and evaluate SUD prior to elective surgery not only exposes the patient to increased risk, but creates an unnecessary risk to the postoperative prescribing clinician, who will have to consider the likelihood of opioid misuse, diversion, and overdose.

There is a growing number of patients on chronic opioid therapy for medication-assisted treatment (MAT) of opioid addiction. While there are physiologic similarities between patients prescribed maintenance methadone or buprenorphine for opioid addiction and those who use other opioids for chronic pain, there are important behavioral and legal differences. In the United States, it is illegal to prescribe an opioid addict the medication to which they are addicted, except under very narrowly defined circumstances, such as acute trauma or for end of life care. The only opioid medications approved for use in the treatment of addiction are methadone and buprenorphine, and their use requires special training on the part of the clinician. The pharmacodynamics of these medications make them well suited to managing opioid addiction; however, they can produce problems when they are used in proximity to surgery, and understanding their mechanism of action is essential for anyone involved in perioperative pain management.

Methadone is a synthetic long-acting opioid that has been used since the 1960s for maintenance of patients with addictive disorders and is routinely prescribed for chronic pain as well. It has a biphasic elimination pattern with an alpha-elimination phase of 8–12 hours and a beta-elimination phase of 30–60 hours. The alpha-elimination correlates to the long duration of its analgesic effect, but accounts for some of the life-threatening complications. In general, when a patient is prescribed methadone for MAT, it is not advisable to adjust the dose of methadone. Alternative opioids should be used for pain control in addition to methadone and then tapered as soon as clinically feasible. Patients with SUD may have persistently high pain scores despite interventions. As a result, non-opioid analgesics, complementary and alternative techniques should be considered. If methadone needs to be converted to different opioid, the prescriber should consider that there may be incomplete tolerance and the fact that conversion ratios are not bidirectional [27].

Buprenorphine-naloxone is approved for outpatient addiction treatment. However, it also has been used off label for chronic pain management. Current data suggest that

buprenorphine-naloxone may provide pain relief in chronic pain patients with opioid dependence or addiction. However, since it is a weak analgesic, this may not be the case in patients without opioid dependence. Buprenorphine is a semi-synthetic opioid. It has a high binding affinity for the mu-opioid receptor, however, it functions as a partial agonist, has a slow rate of dissociation, and a half-life of 20–70 hours. Because of its mu opioid receptor affinity, it can block other opioids from exerting their effect at the same site. As a result, patients on buprenorphine therapy will likely require higher doses of opioids in the perioperative period, and it is recommended to eliminate this medication prior to scheduling elective surgery [28].

For surgery with anticipated minimal postoperative pain or emergent surgeries, buprenorphine may be continued while maximizing non-opioid analgesia, including regional anesthetic techniques. For elective surgeries with anticipated intermediate to high-opioid requirements, buprenorphine should be discontinued 3–5 days prior. Even with the medication held, however, perioperative opioid management will likely require higher doses of direct agonist therapy. Close supervision, maximization of non-opioid adjuvants, and regional anesthetic techniques are recommended [29].

A particular challenge in patients with SUD is the risk of relapse. It is imperative to take a detailed history of their substance use disorder, including information regarding their treating clinician and social support system. Utilization of social supports, consult to addiction medicine or psychiatry, and coordination with buprenorphine prescriber are recommended to improve safety and improve compliance with the perioperative tapering plan. Short-acting opioid medications should be limited to a minimum in terms of potency and duration of use. If there is likely to be a sustained need for opioid treatment, frequent visits with low volume prescribed at more frequent intervals is recommended. It is also wise to avoid the use of any opioids that were previously problematic for the patient. Patients with a history of SUD may need more intensive and ancillary treatment options than usual in order to have the best chance at long-term improvements in pain-related function. Although the specific interventions may vary, it is recommended that patients with a history of SUD will be best served by a multidisciplinary team, including a specialist in addiction medicine [30].

Mental Health Problems

The relationship among pain, anxiety, and depression is well established, but the mechanisms are unclear. Several studies have demonstrated that elevated levels of anxiety and depression predict poor surgical outcomes. Preoperative depression has also been correlated with higher levels of pain and reduced postoperative function. Preoperative anxiety has been associated with higher levels of disability, pain, and dissatisfaction with quality of life [31, 32]. Preoperative negative affect states such as posttraumatic stress disorder, depression, anxiety, and pain catastrophizing are all risk factors for intense acute postoperative pain and high-dose opioid use [33]. Inadequately controlled acute pain and excessive opioid use have been reported to delay recovery and hospital discharge. In addition, this group has associated risk factors for opioid misuse and abuse [34] [7].

Effective communication with the patients about their mental health condition is imperative. Reassurance is central, but in many cases of little value in isolation. Depression carries risk of morbidity and mortality from suicidal behavior. Untreated anxiety may lead to hypertension and cardiac adverse effects. It is not uncommon that patients are on benzodiazepines to treat this disorder. Given the interaction with opioids, there is increased risks for overdose or impairment of cognitive function as well as psychomotor skills. Further, there is an increased risk of addiction and dependence associated with these conditions, which must be addressed as components of perioperative care. Non-pharmacologic treatments such as cognitive behavioral therapy (CBT) or other mind–body programs should be considered in addition to pharmacologic treatments [35, 36].

Summary

Chronic pain and opioid use, SUD, and OIH present challenges in perioperative pain management which require recognition, planning, and treatment. For elective surgery, this is best initiated as early as possible during the preoperative assessment process. Clinicians involved in all aspects of perioperative care must be prepared to recognize patients who might be at risk, perform a comprehensive pain history and examination, and evaluate common comorbidities for substance abuse, including psychiatric disorders. Despite the current emphasis on minimizing their use, opioids are very effective analgesics and will likely remain an important element of acute postoperative care for some time. Early interventions such as tapering the dose of opioids preoperatively, psychotherapy, or substance use treatment are essential as is a multidisciplinary, multimodal approach to postoperative pain management.

Integrated treatments which reduce pain *and* opioid exposure can result in significant benefit to the patient in terms of pain, pain-related surgical outcomes, mental health, and the risk and severity of substance use. These same treatments can also result in a significant benefit on a public health level. Consequently, good perioperative practices can reduce availability of opioids for diversion, healthcare costs, and disability.

Summary Bullet Points

- During preoperative pain assessment, patients who are at risk for increased expression of pain and elevated opioid requirements should be identified. This includes patients who use opioids chronically or have behavioral disorders such as SUD, depression, and anxiety.
- The presence of psychological and other risk factors for the development of SUD is important, even when there is no prior history of SUD.
- Elective surgery should be deferred in the presence of SUD or OIH, until the patient has been assessed, treated, and a plan for postoperative management has been designed.
- During and after surgery, treatment should focus on reducing the patient's exposure to pain *and* opioids by concentrating on multimodal analgesia featuring regional anesthetic techniques and non-opioid adjuvant medication.
- Whenever opioids are initiated, a plan for when and how they will be tapered and discontinued must be established.
- The best way to improve pain-related surgical outcomes is to address the plan for postoperative pain control preoperatively.

Case Studies

Case 1

A 78-year-old woman with a history of diabetes, hypertension, systemic lupus, and rheumatoid arthritis scheduled electively for reverse total shoulder replacement and was treated for chronic multifocal joint pain with a fentanyl transdermal patch 50 mcg/hr q 72 hours and oxycodone 30 mg TID as needed. The patient's MME dose was calculated to be 255, and she was felt to be at high risk for opioid-related complications. This risk was also increased secondary to her age. Over a 6-month period, the opioid dose was reduced to fentanyl 25 mcg/hr q 72 hrs and oxycodone 10 mg TID as needed. Her MME dose was 105, which, while still greater than the CDC guideline, was significantly improved. She underwent the procedure under general anesthesia and a supraclavicular nerve block with local anesthetic and dexamethasone to prolong the nerve block. Postoperatively, the patient was maintained on a fentanyl patch at 25 mcg/hr and given increased doses of oxycodone. She was discharged 3 days later with oxycodone 10–20 mg daily as needed to a subacute rehabilitation facility.

Case 2

A 42-year-old man presented for elective lumbar fusion. He had a known history of substance use disorder from heroin and was on buprenorphine-naloxone 8 mg–2 mg sublingual strips TID. He was tapered off this medication 72 hours prior to surgery and given a fentanyl patch 25 mcg during that time. The surgery was performed under general anesthesia, and postoperatively he was given a low dose intravenous (IV) infusion of ketamine with IV fentanyl PCA. He was then taken off the parenteral medication, the fentanyl patch was continued, and oxycodone 15–30 mg was used as needed. While an inpatient, he was also followed by a psychologist for counseling and offered a virtual reality (VR) headset. He was discharged from the hospital after 4 days and was followed by the pain service for 2 weeks after discharge, for maintenance of the fentanyl patch and oral oxycodone. The patient was subsequently transitioned back to his psychiatrist and restarted on buprenorphine-naloxone.

Case 3

A 60-year-old woman presented for urgent open reduction and internal fixation of a fracture of the proximal humerus after a fall. She was on 30 mg methadone daily as MAT for substance abuse disorder, with comorbid depression, anxiety, and borderline personality disorder. For these, she was prescribed duloxetine 60 mg daily and clonazepam 2 mg at night, which were continued through her hospitalization. She underwent the procedure using a peripheral nerve block and intravenous sedation. Methadone 30 mg daily was continued as part of her MAT to prevent withdrawal, and the patient was given IV ketorolac and acetaminophen postoperatively, with oxycodone 5 mg as needed. Gabapentin 100 mg TID was started, with the goal of titrating up to 300 mg TID. She was followed by psychology and psychiatry services as an inpatient and discharged home 1 week later on a pain regimen which included her baseline level of methadone.

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Jonathan T. L. Cheah and Theodore R. Fields

Abbreviations

ACR	American College of Rheumatology
IL-1	Interleukin 1
NSAID	Non-steroidal anti-inflammatory drug
ULT	Urate-lowering therapy
US	United States

Objectives

- Understand the burden of gout in the perioperative setting.
- Be aware of when to continue or discontinue prophylactic and/or urate-lowering therapy perioperatively.
- Understand the principles of managing gout flares postoperatively.
- Understand the role of ensuring continuing care for gout post discharge.

Key Points

- Gout is an important comorbidity to consider in the perioperative setting.
- Preoperative continuation of gout prophylaxis reduces postoperative flares.
- Rapid identification and management of postoperative gout flares improves participation in postoperative rehabilitation and may shorten length of stay.
- Ensuring post-discharge management for patients with gout, especially those on urate-lowering therapy, avoids significant ongoing morbidity.

Introduction

Gout is characterized by the chronic deposition of monosodium urate crystals in synovial fluid and other tissues in the presence of an increased concentration of uric acid [1]. Clinically, this manifests as an inflammatory arthritis which is often recurrent and can lead to damage of the affected structures. Other clinical manifestations include the subcutaneous deposition of urate crystals (tophi) and the development of renal stones. Affecting almost 4% of the United States (US) population [2], gout is the most common form of inflammatory arthritis. As such, it is frequently seen in surgical populations.

Gout in the Perioperative Context

A number of risk factors contribute to the incidence and prevalence of gout [3] and its implications in the perioperative context. These include hyperuricemia, older age, renal disease and concurrent medications, all of which are important when considering an individual's suitability for orthopedic surgery (Box 22.1). Recent data suggest that the incidence of gout continues to rise in the US and individuals diagnosed with gout have a higher prevalence of comorbidities such as hypertension, renal disease, atrial fibrillation and obesity, conditions that in themselves are of significance in the perioperative setting [4, 5]. Furthermore, data have

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indicated that individuals with a diagnosis of gout are up to 1.56 times more likely to undergo either total hip or knee replacement surgery compared to individuals without a diagnosis of gout [6]; thus, gout may be an independent risk factor for total joint replacement. In addition, owing to the initiation or cessation of certain medications, the use of intravenous fluids and changes in renal function, fluctuations in the serum urate level may arise in the perioperative period increasing the risk for acute gout. As a result, gout itself (as well as its disease associations) is an important comorbidity to consider in those anticipating and undergoing orthopedic procedures.

Box 22.1 Risk Factors for the Development of Gout

- Male sex (risk increases in women after menopause)
- Obesity and the metabolic syndrome
- Purine-rich diet (e.g., shellfish, red meat)
- Medications (e.g., loop or thiazide diuretics, cyclosporine, tacrolimus, pyrazinamide, angiotensin II receptor antagonists other than losartan)
- Older age
- Alcohol (especially beer and spirits)
- Fructose-sweetened beverages
- Chronic kidney disease
- Obstructive sleep apnea
- Certain inherited genetic risk variants

The essential role of urate in the pathophysiology of gout is well-established. Despite the availability of effective and generally well-tolerated urate-lowering therapy (ULT), gout remains a poorly managed condition worldwide. Suggested reasons for this circumstance include poor adherence to medications, inadequate knowledge and misconceptions amongst both practitioners and patients and a perception that gout is not an important condition (does not often evolve into chronic or recurrent disease) [7, 8]. Evidence suggests that such therapeutic inadequacy not only has significant economic consequences but results in a decrease in quality of life for gout sufferers [8–10]. For example, Lim et al. [11] described that over the period 1993–2011, the annual hospitalization rate in the United States where gout was the primary diagnosis rose from 4.4 to 8.8 per 100,000 adults, with the inflation-adjusted gout-related hospital costs per 100,000 adults rising from $34,457 to $58,003.

Individuals admitted to hospital are at increased risk for acute gout during their admission. An online survey of 724 individuals with gout reported an adjusted odds ratio of 4.05 for the development of an acute flare when hospitalized for any reason compared with no hospitalization [12]. Additionally, based upon unified records from one region in the US, hospital admission for any reason in an individual with known gout increased the risk of an acute flare ten-fold compared to individuals in the outpatient setting (85 flares per 100 inpatient patient years vs. 8.5 per 100 outpatient patient years). Those experiencing an acute flare while admitted had a length of stay on average 1.8 days longer [13]. In the orthopedic patient, such increased length of stay may be further exacerbated due to the inability to participate in postoperative physical therapy due to the superimposition of gout-related pain.

Few studies have investigated the incidence and risk factors associated with acute gout in the postoperative setting. A 10-year single center retrospective chart review reported a 17% incidence rate of postoperative gout [14]. Of note, for 13% of those who developed an acute gout flare postoperatively, this was their first such episode. In a retrospective series of individuals undergoing bariatric surgery, a population at increased risk for gout, of 411 individuals in the cohort, 5% had a prior history of gout [15]. Post surgery (bariatric), 33% of those with gout had an acute flare, the majority monoarticular. More recently, a single center study from South Korea compared 67 individuals with known gout who developed a postoperative flare with 67 individuals with known gout who did not experience a flare [16]. The procedure involved was musculoskeletal in approximately 12% of patients in each group. Preoperatively, those patients who developed a postoperative flare tended to have higher mean serum urate levels (8.5 mg/dL vs. 7.1 mg/dL) and were less likely to have received colchicine prophylaxis or to be on ULT with allopurinol (1.5% vs. 1.9% and 19.4% vs. 44.6%, respectively). Gout flares occurred at a mean of 4.2 days after surgery; 51% of the postoperative flares were polyarticular.

Based upon the above, the ensuing discussion will address the following issues regarding gout in the perioperative setting:

1. The principles of gout management
2. What to do in the preoperative setting in individuals who already have a diagnosis of gout and are already receiving medical management
3. Approach to preventing acute gout flares in the postoperative period
4. Approach to safely and effectively treating acute gout flares postoperatively
5. Arranging appropriate follow-up on discharge to ensure continuity of care regarding long-term management of gout

General Principles of Gout Management

A number of specialty associations worldwide have released guidelines concerning the management of gout [17, 18]. Those recently published by the American College of Rheumatology (ACR) are herein reviewed [19, 20]. All individuals with a diagnosis of gout should receive education on the disease and treatments, including dietary and lifestyle recommendations. Furthermore, consideration should be given to the secondary causes of hyperuricemia (obesity, excessive alcohol intake, medications known to elevate serum urate), with modifiable risks addressed. With regard to pharmacologic measures to lower serum urate, it is recommended to start ULT with a xanthine-oxidase inhibitor, most commonly allopurinol, starting at 100 mg orally daily (50 mg orally daily if stage 4 chronic kidney disease or worse). An alternative ULT is febuxostat 40 mg orally daily. ULT is indicated in the following situations: (1) tophus or tophi by clinical exam or imaging study, (2) >/=2 flares of acute gout per year, (3) gout with stage 2 chronic kidney disease or worse or (4) gout with a history of urolithiasis. Concomitant pharmacologic anti-inflammatory gout flare prophylaxis should also be initiated, given the increased risk of inducing flares soon after the introduction of ULT. Options for prophylaxis include oral colchicine (0.6 mg orally once or twice a day), which is the best-studied option, or low-dose non-steroidal anti-inflammatory drugs (NSAIDs) (e.g., naproxen 250 mg orally twice a day). If neither of these options are appropriate, tolerated or effective, then prednisone at once daily doses of </=10 mg can be considered. Once ULT is begun, serum urate should be monitored every 2–5 weeks with dosing adjusted to achieve the serum urate target of <6 mg/dL (<5 mg/dL if tophi are present).

For acute flares of gout, the general treatment principles involve pharmacologic therapy starting ideally within 24 hours of symptom onset; ongoing pharmacologic ULT should not be interrupted during the acute flare. For flares of mild to moderate severity involving 1 or a few small joints or 1–2 large joints, monotherapy with NSAIDs (full approved dose until the acute flare has resolved), oral colchicine (1.2 mg, then 0.6 mg 1 hour later, followed by 0.6 mg twice a day starting 12 hours later, until the acute phase has resolved) or alternatively intraarticular or systemic corticosteroids (prednisone 0.5 mg/kg per day for 5–10 days at full dose or 2–5 days at full dose before tapering over the subsequent 7–10 days) is recommended. For more severe flares involving multiple joints, combination therapy is indicated. Several approaches can be considered: (1) NSAIDs and oral colchicine; (2) oral colchicine and oral corticosteroids or (3) intraarticular corticosteroids with either NSAIDs, oral colchicine or systemic corticosteroids. In cases of inadequate response to initial therapy, consideration to switching monotherapy, stepping up to combination therapy or the possible use of interlukin-1 (IL-1) inhibitors (anakinra) can be considered.

Although the majority of gout is managed in the primary care setting, referral to a rheumatologist should be considered in the following circumstances: (1) unclear etiology for hyperuricemia, (2) refractory signs and symptoms of gout, (3) difficulty in reaching the target serum urate level and (4) multiple and/or serious adverse events from pharmacologic ULT.

At present, although the ACR in conjunction with the American Association of Hip and Knee Surgeons have released guidelines regarding the use of antirheumatic medications in individuals undergoing elective hip and knee surgery, gout was specifically not included in the scope of this guidance [21]. There are no current society guidelines regarding the perioperative management of gout nor controlled trials assessing optimal perioperative gout management.

Approach to Preoperative Management of Gout

Given that a history of preexisting gout is a risk factor for the development of acute flares while hospitalized, ascertaining this history during the preoperative medical assessment is imperative. Additional information such as the frequency of flares, current or past medication regimen, prior postoperative gout flares and recent serum urate level are also important as potential markers indicating a heightened risk for a postoperative gout flare.

For individuals with a known history of gout and currently on ULT and/or anti-inflammatory gout prophylaxis (such as colchicine), we recommend the continuation of these medications pre- and postoperatively at their preoperative dose. ULT such as allopurinol can be given on the morning of surgery. Colchicine may also be given on the morning of surgery, but some may prefer to hold it that morning. Both should be restarted as soon as is practical postoperatively. For those patients using low-dose prednisone or its equivalent for anti-inflammatory prophylaxis, in line with recent evidence and guidance from the ACR in other rheumatic diseases, we would not recommend the use of supra-physiologic (stress-dose) glucocorticoid doses [21, 22]. However, if the individual is currently using low dose NSAIDs as anti-inflammatory prophylaxis, there may be center-specific guidance regarding the preoperative cessation of the NSAID based on concerns regarding the effect of NSAIDs on platelet function and hemostasis. As a general rule, given that

platelet function normalizes within 3 days of discontinuation of most NSAIDs [23], stopping these medications at least 3 days prior to surgery seems prudent. Additionally, presurgical planning in elective cases should include efforts to optimize the ULT so as to reach the goal serum urate level of <6 mg/dL preoperatively.

For those patients with a known history of gout but not currently taking ULT or acute flare prophylaxis such as NSAIDs or colchicine, management should be individualized. Since starting ULT can precipitate gout flares, the initiation of such medication in proximity to surgery is discouraged. However, in patients with a history of frequent flares, starting colchicine preoperatively and maintaining it after surgery should be strongly considered.

The prevention of acute gout after surgery is thus premised on a number of practices. These include the continuation of preoperative ULT in conjunction with prophylactic therapy, most commonly colchicine. Ensuring adequate hydration postoperatively, coupled with the perioperative caution in the use of medications that raise serum urate levels (e.g., loop or thiazide diuretics), is an additional measure relevant to the prevention of acute gout flares postoperatively.

Approach to Postoperative Gout Flares

An acute arthritis with pain, swelling, warmth, erythema and loss of function of the affected joint will suggest gout. Pain is generally maximal within 24 hours and has a predilection for onset at night. The most common site for acute gout is the first metatarsophalangeal joint (podagra), although other areas of the foot as well as the knee and ankle are also often involved [24]. Systemic features can involve fever and chills. Clinical clues include the finding of tophi, subcutaneous urate deposits which are typically found over the helix of the ear, bursae, tendons and joints. The challenge in the postoperative setting is to distinguish an acute gout flare from infection or other diagnoses presenting as an acute arthritis as many of the clinical and laboratory features will be shared. Of note, although rare, acute gout flares in a prosthetic joint, occurring as soon as 4 days postoperatively, have been reported [25, 26]. In addition, the concomitant finding of both an acute crystal arthritis and septic arthritis affecting the same joint is also well described [27]. At times it may be difficult to separate cellulitis from a gout flare, since erythema over a joint with a gout flare can extend proximally and distally. When two contiguous joints are involved in a gout flare, erythema commonly will extend between them, making it hard to rule out cellulitis. When there is a "clear area" between involved erythematous joints, however (Fig. 22.1), this can help to diagnose two joints with gouty inflammation and exclude cellulitis. The intensity of erythema seen with most gout flares is of a level rarely seen with most types of arthritis, such as rheumatoid or psoriatic arthritis. Additionally, the intensity of erythema and pain in a severe gout flare suggests a relatively small differential diagnostic group of options in the postoperative setting, infection being the major concern. In cases not definitive for gout, aspiration for cell count, culture and crystals should be considered.

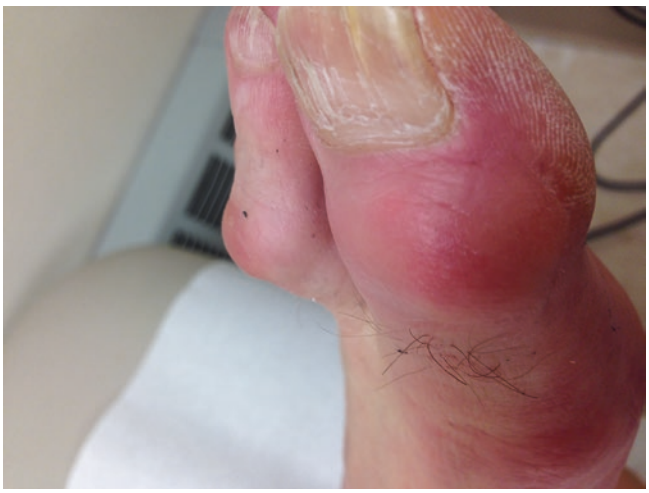

Fig. 22.1 Acute gout flare of the first metatarsophalangeal and first interphalangeal joint of the left foot. Note the relative lack of erythema in the area between the two joints, making an overlying cellulitis less likely in this case

Serum urate, although usually elevated in individuals with gout, may be low during a flare due to frequent drops in urate level during flares [28]. Laboratory markers of inflammation such as the C-reactive protein, erythrocyte sedimentation rate and white cell count are usually increased during an acute flare; however, these are also expected to be elevated in the immediate postoperative period due to the surgery itself [29] or may be a consequence of postoperative infection. These markers, although helpful, are therefore less useful during this period. Furthermore, plain radiographs are also not helpful in the diagnosis of an acute gout flare as they are generally normal except for non-specific soft tissue swelling. Even in cases of chronic gout, where long standing urate deposits have produced the typical radiographic changes of this condition (erosions with an overhanging edge and sclerotic rim), a superimposed infection cannot be ruled out. Other imaging modalities used in gout include ultrasound, which can identify joint effusions, tophi (demonstrated via the double contour sign) as well as dual-energy computed tomography, which is able to detect and color-code urate deposits [30]. However, while these modalities are excellent for confirming the presence of gouty arthritis, they are unable to identify whether the acute flare is due to gout, infection, or other causes.

Therefore, if possible, synovial fluid examination of the affected joint in the postoperative setting is recommended. This remains the definitive way to diagnose gout by identify-

ing the presence of intracellular monosodium urate crystals by polarizing light microscopy, where the crystals are needle-shaped and negatively birefringent (Fig. 22.2). Synovial fluid cell count in both acute gout and septic arthritis will be inflammatory with a neutrophilic leukocytosis. Therefore, culture and Gram stain of the synovial fluid is important to obtain to assess for infection. Depending on the clinical situation, blood cultures and empiric antibiotic therapy may be warranted pending culture results if infection remains high on the differential.

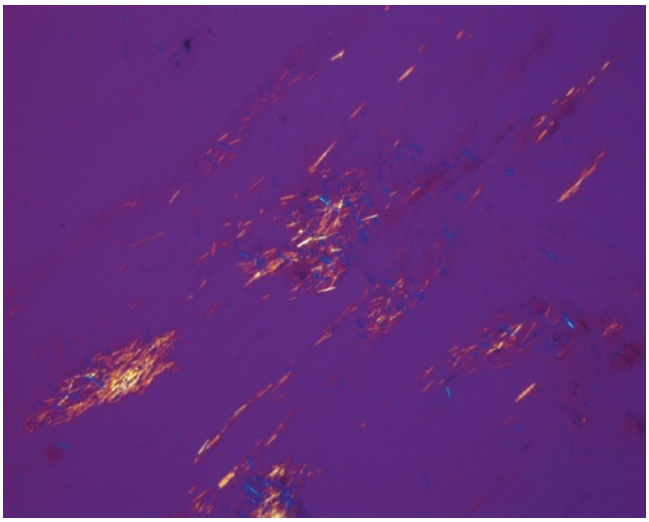

Fig. 22.2 Aspirated joint fluid, seen under polarizing microscopy, shows negatively birefringent needle-shaped monosodium urate crystals, which are seen as either yellow or blue, depending on their axis of orientation

Once acute gout has been diagnosed, the options for treatment of the acute flare follow the same general principles as previously outlined, with a number of caveats due to the nature of the postoperative period as well as individual comorbidities that may be present. Non-pharmacological therapies such as ice and rest are useful adjuncts. An overview of pharmacological options is presented in Table 22.1. For acute gout flares only affecting one or two joints, intraarticular glucocorticoid injections are often effective and may have less systemic effects than other options.

NSAIDs are generally less favored in this setting due to the older patient population that often undergoes orthopedic intervention, as well as the risk of renal and gastrointestinal complications. Additionally, postoperative joint replacement procedures may be followed by anticoagulation, and combining anticoagulation and NSAIDs has been demonstrated to increase bleeding risk [31, 32].

Colchicine is recommended for flares with onset </=36 hours prior to the onset of treatment. Dosing and precautions are reviewed in Table 22.1. In those who develop polyarticular gout, particularly patients with the comorbidities listed above, systemic glucocorticoids may be the most appropriate option. A recent systematic review analyzing trials comparing corticosteroids with NSAIDs in the treatment of acute gout found no difference in efficacy and lower risk of gastrointestinal adverse effects with the corticosteroids [33]. Elevations in blood sugar should be monitored in those with co-existing diabetes. Suggested dosing is reviewed in Table 22.1. There are a number of glucocorticoid regimens described for gout flare, but we recommend attempting a rapid taper in the postoperative patient to minimize glucocorticoid exposure and infection risk, when possible. The

Table 22.1 Therapies for acute flares of gout in the postoperative setting

Drug	Dose	Duration	Route of administration	Notes
NSAIDs	Full approved dose	Until flare has resolved	Oral	Caution in the elderly, those with renal impairment, or on concurrent anticoagulant therapy
Colchicine	1.2 mg, then 0.6 mg 1 hour later, followed by 0.6 mg twice a day starting 12 hours later	Until flare has resolved	Oral	Caution/dose adjustment in those with severe levels of renal or hepatic impairment. Caution with interactions (e.g., clarithromycin, atorvastatin)
Oral corticosteroids	Prednisone: tapering regimen starting at 30–60 mg daily and tapering by 10 mg daily as long as improvement continues; dose escalation for worsening	Until flare has resolved	Oral	Since special concern to avoid postoperative infection, best to attempt rapid taper and only escalate dose for failure to respond
Intramuscular or intravenous corticosteroids	40 mg or 80 mg methylprednisolone	Once	Intramuscular or intravenous	
Intraarticular corticosteroids	Depends on size of affected joint but generally in the range of 20–80 mg methylprednisolone	Once	Intraarticular	
Anakinra	100 mg daily	3 days	Subcutaneously	Significantly more expensive than other options

NSAIDs non-steroidal anti-inflammatory drugs

hospitalized patient provides the opportunity for daily observation and individualized glucocorticoid dose adjustment. Intramuscular or intravenous glucocorticoids may also be an option where the individual is unable to tolerate or receive oral medications.

In situations where traditional colchicine, NSAID and glucocorticoid regimens are contraindicated or ineffective, IL-1 inhibition can be considered. Given potential concerns about risk of infection with IL-1 antagonists especially in the postoperative setting, anakinra, a short acting IL-1 receptor antagonist, appears optimal. IL-1 blockade has been demonstrated to be effective in acute gouty arthritis and appears safe when used for short periods of time. The initial recommended dose is 100 mg subcutaneously daily for 3 days [34].

In individuals with a known history of gout who develop an acute flare while taking ULT, such therapy should not be discontinued. For individuals for whom the postoperative gout flare is their first presentation of gout or if they were not previously on ULT, traditional teaching has been to wait at least 2 weeks after the resolution of the acute flare to initiate ULT. However, recent studies have indicated that concurrent initiation of ULT during an acute flare does not prolong the flare as long as the flare is adequately treated [35]. While not yet adopted in guidelines for gout management, if this strategy is adopted, then ongoing anti-inflammatory prophylaxis as discussed above should be maintained.

Using Discharge Planning to Improve Long-Term Gout Management

For individuals who experience an acute gout flare while hospitalized, the event provides an important opportunity for patient education and for assuring that ongoing outpatient care will follow, via a primary care provider or rheumatologist. A recent single center retrospective chart review demonstrated that of all admissions where gout was listed as a primary or secondary diagnosis, only 26% of individuals were receiving ULT at the time of admission and only 40% had their ULT dosing adjusted upon discharge [36]. Furthermore, a systematic review of 20 studies identified a number of barriers to optimal gout care [37]. Providers demonstrated gaps in gout knowledge, which the authors felt was likely to decrease appropriate patient education. Other barriers such as time constraints and a lack of incentives for optimal gout management were also felt to be important contributors. Patients too contributed having knowledge gaps and a reluctance to take medications over a long period of time.

Patient education from a variety of different providers, including pharmacists, nurses and physicians, has been shown to improve knowledge and understanding of gout, as well as increased likelihood of achieving target serum urate levels and reduction in the frequency of acute flares [38–40]. Such published patient education strategies are unable to target all the previously noted barriers and have been limited to the outpatient setting. However, gout flares are common in the hospital and inpatients are a "captured audience" for educational intervention. Gout education programs that include inpatients would likely provide valuable direction for patients. These could be modeled along the lines of other chronic medical conditions such as heart failure [41].

Areas of focus for patient education would address risk factors, especially opportunities for diet and lifestyle modification; emphasize the rationale and need for long-term medication adherence and empower self-management strategies and medication use during acute episodes. Additionally, a plan for follow-up in the community in order to insure patient adherence should be arranged prior to discharge. Box 22.2 summarizes the factors to consider in the discharge planning for a patient with gout.

Box 22.2 Discharge Checklist for an Individual with Gout

- Arrange appropriate follow-up (primary care provider or rheumatologist).
- Patient education including diet/lifestyle factors and medication management (both chronic urate-lowering therapy and management of acute flares).
- Consider initiation of colchicine prior to discharge in an individual not currently on urate-lowering therapy but with a plan to start ULT in the outpatient setting.

Summary

Gout is the most common inflammatory arthritis. Acute flares in the postoperative setting occur frequently and may result in significant morbidity with delays in rehabilitation and discharge planning. Although specific guidelines have not been developed for the perioperative management of gout, the overarching principles which underlie general gout management can be adapted and applied in this clinical setting. Through identification of preexisting disease, careful attention to physiologic and medication changes in the postoperative period and knowledge of target serum urate levels, the incidence of acute flares of gout can be reduced. Finally, ongoing patient education during the perioperative period should be undertaken to reinforce key aspects of management of this chronic disease.

Summary Bullet Points

- Gout flares are not uncommon in the postoperative setting and can prolong hospital stay.
- In individuals with known gout on urate-lowering therapy and/or colchicine undergoing an orthopedic procedure, their preexisting therapy should be continued throughout the perioperative period.
- The management of a postoperative acute gout flare should be tailored according to the individual's comorbidities and concurrent medications.
- The opportunity for gout patient education and arrangement of ongoing care in the community to address this chronic condition should not be lost.

Case Study

A 66-year-old man develops a hot, red and swollen left first metatarsophalangeal joint on post-operative day #1 after right total knee replacement. He has a long history of gout and takes 300 mg allopurinol daily, but has not had a serum urate level checked in several years. Over the preceding year, he has had 2 flares of gout identical to the present episode. He also has a history of insulin-dependent diabetes, his creatinine is 1.65 (eGFR 49) and he has received his first dose of warfarin after surgery. He is afebrile.

What are the options for acute management? NSAIDs are not optimal in view of his creatinine elevation and having started warfarin. Systemic corticosteroids are also not ideal in view of his diabetes. Colchicine is an option here, and his eGFR permits its use at a standard dose of colchicine for gout flare: 1.2 mg PO followed in an hour by 0.6 mg PO after which 0.6 mg PO BID is continued until resolution. An alternative would be a corticosteroid injection of the involved joint with betamethasone a reasonable choice given its fewer local reactions when compared to crystalline methylprednisolone. Colchicine was started and the patient did well.

What instructions should he be given at discharge? Given the frequency of this patient's flares, it is reasonable to discharge him on colchicine (0.6 mg daily) while continuing the 300 mg daily of allopurinol. The episode provides an excellent opportunity to impress on him the importance of regular follow-up for his gout. Since serum uric acid levels often drop during acute flares, the optimal time to follow-up his serum urate is at least 2 weeks post flare and he should be advised to arrange this with his internist. His frequent flares suggest that the serum urate is probably above the desired therapeutic level (>6.0 mg/dL). Since we know, that over time, the propensity to acute flares will abate in the majority of patients who keep their urate levels below 6.0 mg/dL, patients should be educated about the importance of monitoring their urate level with dosing adjustments then made by their physicians as needed. Further, the patient should also be educated about weight loss and key dietary issues, such as the limitation of alcohol and red meat.

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Part IV

Specific Perioperative Problems in Orthopedic Surgery

Perioperative Care of the Elderly Orthopedic Patient

23

C. Ronald MacKenzie and Charles N. Cornell

Objectives

- To define the perioperative risks associated with advanced age
- To provide strategies for optimizing the surgical risk for the elderly patient
- To describe modifications of the surgical approach that benefit the elderly patient
- To explore proven pathways of care and rehabilitation of the elderly patient

Key Points

- Changing demographics of our society insure that elderly patients will dominate much of orthopedic practice in the future. The special needs and conditions of these patients must be anticipated (cognitive impairment, frailty, immobility and functional dependency, poor nutrition, among others).
- Elderly patients have the same potential to benefit from orthopedic reconstructive procedures as the nonelderly, and they have the potential to greatly improve their overall health and quality of life with orthopedic reconstruction.
- Chronological age is not an independent risk factor for surgery; rather it is the patient's overall health. The concepts of "homeostenosis" and frailty are useful in understanding the special risks associated with surgery in patients of advanced age. The elderly should be assessed as "fit" or "frail" and their care plan adjusted accordingly.
- When elective surgery is planned, the special needs of the elderly patient should be anticipated with preoperative medical optimization, preoperative physical conditioning, preoperative education, postoperative pain management, and planning for a prolonged recovery, physical therapy, and rehabilitation process.

Introduction

It is projected that patients older than 65 years will become the largest segment of the surgical population by 2020 [1]. Further, it is known that in the surgical setting older patients have longer lengths of stay, account for greater costs of care, and experience more adverse outcomes related to surgery [2]. Among all surgery performed on older persons, the fractured hip makes a large contribution to the problem of surgery in the elderly. As such, the perioperative care of those latter in life is highly relevant to the orthopedic surgeon. This chapter introduces the topic of surgery in the elderly, exploring what makes the elderly "different." Important age-related risk factors for postoperative complications will be discussed. The chapter concludes with a review of current approaches to the fractured hip, the orthopedic condition most associated with surgery on the elderly.

Age-Related Perioperative Risk Factors

The significant patient-associated risk factors in elderly patients that correlate with postoperative adverse outcome [3] include the problems of cognitive impairment and

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delirium, frailty, immobility and functional dependency, poor nutritional status, and the challenges of discharge (transitions) (Box 23.1).

Box 23.1 Age-Related Perioperative Risk Factors
- Cognitive impairment
- Frailty
- Immobility/functional dependency
- Poor nutrition
- Challenges of discharge (transitions)

Cognitive Impairment

Cognitive decline and memory dysfunction is a leading cause of functional impairment in the population at large, a problem that increases with age and is heightened by hospitalization for critical illness and surgery [4]. That patients >65 years are projected to become the largest segment of the surgical population by the year 2020 underscores the importance of this problem for the health-care system at large [1]. Indeed, state-of-the-art symposia have been held concerning this problem, forecasting an "epidemic" of postoperative cognitive dysfunction projecting forward [5]. The incidence of this problem is already high in some surgical populations. For example, in the orthopedic realm, patients undergoing emergent surgical repair of a fractured hip experience a 37% rate of postoperative cognitive dysfunction among the non-demented fraction of this cohort [6]. The significance of this observation is highlighted by the observation that among patients who experience delirium after surgery, 69% (vs. 20%) developed frank dementia over a five-year postoperative follow-up. Monk et al. have reported that patients with postoperative cognitive dysfunction at discharge were more likely to die within the first year after surgery as compared to those without such postoperative cognitive problems [7].

Numerous studies have sought to identify patient attributes and clinical factors that contribute to the development of postoperative cognitive dysfunction. These have included the exposure to anesthesia and various perioperative phenomena (hypoxemia, hypotension, hyperventilation, specific medications), the effects of aging, comorbidities (cancer, neurodegenerative, and cerebrovascular disease), and even genetic considerations (*APOE4* polymorphisms). Indeed, a basic science pertaining to this clinical problem is emerging focused on the role of inflammation and the activation of the immune system, both of which are associated with cognitive decline [5]. Animal models as well as preclinical studies suggest a causative role for various pro-inflammatory cytokines, specifically interleukin 1*B* [8–10]. These observations have parallels to a related syndrome known as *sickness behavior*. Arising as a consequence of acute illness, sickness behavior is a constellation of signs and symptoms—fever, anorexia, somnolence, hyperalgesia, fatigue—accompanied by a decline in cognitive function, mimicking what is often seen after surgery [11, 12].

Another putative mechanistic domain links the types of nervous system changes seen in neurodegenerative diseases (i.e., Alzheimer's) in which the accumulation of abnormal proteins is believed to be responsible for the cognitive decline and disruption of memory [13]. In this regard, relationships between anesthesia, *B*-amyloid, and tau protein phosphorylation have been suggested as potential mechanisms [14–16]. In addition, evidence suggests that anesthetics may affect memory and behavior, effects that may persist beyond the dissipation of the medications from the body [17]. Nonetheless, the literature in support of such neurotoxic effects of anesthesia is complex, in evolution, and challenged by the results of clinical trials involving older patients undergoing major noncardiac surgery. In these clinical studies, the rates of postoperative cognitive dysfunction after regional as compared to after general anesthesia were comparable [18, 19].

Many of the predictors of delirium both for hospitalized patients [20, 21] and for patients in the postoperative setting have been studied [22]. Patients are at an increased risk for the development of delirium after surgery due to a confluence of factors that arise in this clinical setting. Indeed a pneumonic has been described that enumerates the common causes of delirium (DELIRIUMS SPAC): *D*rugs, *E*motional/*D*epression, *L*ow pO2 states, *I*nfection, *R*etention of urine or feces, *I*mmobile, *I*ctal states, *U*ndernourished/or dehydrated states, *M*etabolic, *S*urgery-specific (hip, cardiac, vascular, thoracic) factors and *S*ensory/Sleep deprivation, *P*ain, *A*ge, *C*ognitively impaired baseline [23].

Various interventions, the purpose of which is the reduction of risk for postoperative delirium, have been suggested and include supplemental O2, the restoration of electrolyte imbalances, the discontinuation of high-risk medication, the assurance of adequate nutrition, early mobilization, and aggressive pain management [3].

Frailty

Frailty as a core concept of geriatric medicine has proven compelling for a number of reasons [24]. These include the perception that frail individuals, usually the elderly, constitute an assemblage of individuals at high risk for disability and dependency, falls and injury (fracture), and slow and incomplete recovery after acute illness and hospitalization. As a group, they disproportionately require health-care-related and support services, often community based. In addition, a consideration well known to clinicians is their

increased susceptibility to multiple chronic diseases, conditions that accompany the aging process and contribute to (or are possibly a consequence of) the problem of frailty. Further complicating these circumstances is evidence suggesting that disease-mediated determinants alone do not sufficiently explain the functional consequences of the aging process. Finally, given the high (and increasing) prevalence of frailty in the population (10–25% >65 years, 30–45% >85 years), the medical and social consequences of this clinical problem will present challenges to families and the health-care system in general in perpetuity. These considerations have high relevance in the setting of caring for patients with an important geriatric syndrome—the patient who suffers hip fracture—a problem that begs for a redesign of care and reimbursement.

A simple, useful frailty scale has been developed that serves in the identification of such patients [25]. The scale employs a four-level classification across the spectrum of fitness to frailty: (0) able to walk without help, perform activities of daily living (eating, dressing, bathing, bed transfers), are continent of bowel and bladder, and are not cognitively impaired; (1) bladder incontinence only; (2) one (two if incontinent) or more of needing assistance with mobility or activities of daily living, have cognitive impairment (but not dementia), or have bowel or bladder incontinence; and (3) two (three if incontinent) or more of totally dependent for transfers or one or more activities of daily living, incontinent of bowel and bladder, and a diagnosis of dementia.

Those involved in the care of the elderly have long recognized the constellation of weakness, immobility, and poor tolerance to stress, accompanied by multiple comorbid conditions, as prevalent in older patient groups. This, the syndrome of frailty, results in a progressive decline in general function, a loss of physiologic reserve, and an increased vulnerability to disease and death; in addition, it predisposes to falls, disability, social isolation, and the need for institutionalization. Although as a concept it has proven challenging to define [26], frailty is not difficult to recognize as its markers are easily identified. Relevant characteristics include such age-associated declines in lean body mass, strength, endurance, balance, walking performance, and low levels of activity. Multiple components must be present in order to constitute frailty.

The progressive restriction of physiologic reserve that occurs as a function of aging is captured in the concept of "homeostenosis." A model well known to geriatricians, homeostenosis is a reduction in the maintenance of homeostasis resulting from even mild perturbations to the system at large. Figure 23.1 provides a schematic representation of this concept. In this depiction, younger individuals are on the left while the older are on the right. Homeostasis corresponds to the line separating physiologic reserves already in use from those still available to meet health challenges; the "precipice" is the point of inflexion where adverse outcomes begin to occur. Thus, according to this conception, the object of medical care is to avoid reaching the precipice. According to recent interpretations, younger individuals deal with challenge readily owing to the physiological reserves conferred by their youth and overall good health. With aging, however, greater proportions of our physiological reserve are siphoned off, directed to the maintenance of homeostasis, leaving less capacity to address health challenges. It is therefore self-evident that extraneous perturbations such as surgery may impel individuals, particularly the frail elderly, away from optimal homeostasis toward a state of vulnerability (the precipice).

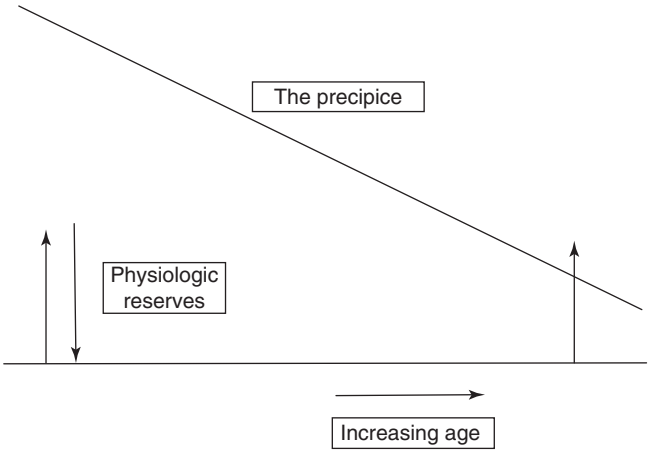

Fig. 23.1 Standard schematic of homeostenosis. As the individual ages, there is no change in homeostasis, but the amount of physiologic reserves available to counter any challenge to homeostasis decreases with aging. Challenges to homeostasis are depicted as *arrows* moving away from the baseline. The precipice may be any clinically evident marker such as death, confusion, or cardiac arrest. (Used with permission of Springer Nature from Taffert [72])

Immobility and Functional Dependency

Inextricably connected to the concept of frailty, the problem of immobility and functional dependency is a common characteristic of the elderly. This is especially true of the patient with chronic orthopedic and rheumatic disease, conditions that independently produce such compromise. Thus, prior to surgery, patients may be struggling to ambulate and perform activities of daily living. Thus, significant postoperative difficulty related to such challenges as weight-bearing, transfers, and independent ambulation can be anticipated.

Poor Nutrition

Elderly patients are often determined to be at high nutritional risk for numerous reasons. Some elderly patients may be

diagnosed with malnutrition due to inadequate food intake or may present with physical/functional impairments. Conditions affecting patients' functional capacity to effectively chew and swallow food, prepare meals, and independently feed themselves can greatly impact nutritional status. As a result of declining physical and cognitive function, poorly fitting dentures, missing teeth, alterations in taste sensation, and reduced salivary flow, elderly patients may find it difficult to meet nutritional needs via oral intake.

Such patients should be identified immediately upon admission so that proper nutritional care can be initiated as early as possible. Additionally, elderly patients may need assistive devices to overcome difficulty grasping utensils or cups, they may require assistance with meals, or their conditions may necessitate the use of altered food and beverage consistencies to reduce risk of aspiration in the hospital.

As a result of the physiologic stress response brought about by physical trauma, the nutrient needs of a trauma patient presenting for orthopedic surgery may be greatly increased. Caloric needs postoperatively can be as high as two times the amount normally required for weight maintenance and the support of basic physical functioning. The greatly increased needs for protein and calories to support healing postoperatively and following trauma are often difficult for patients to achieve.

Furthermore, the perioperative fasting regimen as well as the side effects that are commonly experienced from medications may result in a negative net nutrient balance in the patient. Additionally, there has been considerable research to suggest that nutrition is closely linked with health outcomes of the trauma patient. Malnutrition is not only frequently found among trauma patients, but it has also been identified as an independent risk factor for morbidity, mortality, and length of hospitalization. See Chap. 26 on Nutrition.

Transitions

With the increasing pressures to shorten hospital length of stay, it has become uncommon for patients to receive the entire care for their major illnesses and surgery in the acute care hospital setting. This is particularly true of the elderly with whom the complexities of care often include transfers from one team of providers to another, often to other health-care setting. One recent study of Medicare beneficiaries found that over the 30-day period following hospital discharge, 60% of such patients made a single transfer, 18% two transfers, 9% three transfers, and 4% made four or more. This pattern is particularly common in the orthopedic setting, as the rehabilitative requirement of this population after surgery often outstrips the capacity of the acute care hospital to provide the necessary physical therapy needs.

Risk factors for unsuccessful transitions of care have been identified, among which are advanced age, serious illness, various psychosocial considerations such as insufficient support, and a history of prior hospitalizations [27]. Recognizing the implications associated with poor health-care transitions, Coleman et al. have published a patient-focused instrument for the assessment of this clinical domain. Developed as a quality improvement measure, the specific domains of care employed in the Care Transitions Measure (CTM) are instructive as they identify the broad areas of concern. They include the reliability and timeliness of the information transferred; the preparation of the patient, family, and the caregiver; the support to insure successful patient self-management; and the need to empower patients to define and assert their individual goals and preferences. Lower scores on the CTM at discharge predict subsequent emergency room use and rehospitalization.

Inferred from this discussion, the attention to transitional care has evolved from the convergence of two contemporary health-care movements—patient safety and patient-centered care [28]. The recognition of the adverse consequences of poorly executed care transitions (Box 23.2) has led to a considerable body of work directed at improving this domain of health-care delivery. Many approaches have been studied, all of which emphasize the role of patient education (often provided by nurses), the provision of home care follow-up (social worker), dietary intervention, medication review (often involving pharmacists), and prompt follow-up with the patient's primary care physician. Regardless of the extent and nature of the systems employed, efficient information transfer remains a key component of successful transitional care. Managing the transfer of relevant information is challenging as a well-coordinated and orderly transfer of responsibility of care involves the provision of information to multiple health-care settings as well as various providers, including physicians, nurses, physician assistants, physical therapists, social workers and ultimately, the patient and their family.

Box 23.2 Transitions of Care: Consequence of Poor Execution

- Adverse events in the peri-discharge period
- Recidivism to the emergency room or hospital
- Reduced patient, family, and provider satisfaction
- Increased cost of care

Specific Clinical Problems

Postoperative Delirium

Postoperative cognitive decline (POCD) generally follows two disparate patterns: acute cognitive dysfunction, known as early postoperative delirium, and a later onset and more persistent form [29]. Delirium is often seen in older patients developing once hospitalized or after surgery and presents as an acute change in mental status, inattention, disorganized thinking, and altered consciousness [30]. Behaviors range from a placid inactivity to frank agitation. Although generally a transient phenomenon, delirium is associated with increased mortality [31], higher costs [32], and prolonged hospitalization [33]. In the surgical setting, risk factors [34] and scoring systems [22, 35] have been developed and validated for the prediction of delirium after surgery. In elective noncardiac, nonorthopedic surgery, the reported incidence of postoperative delirium is 9%; this incidence increases to 41% after orthopedic procedures [36].

As compared to delirium after surgery, postoperative cognitive dysfunction is a more subtle and prolonged alteration in cognition [5]. Vaguely defined as a "more than expected" deterioration in cognitive function, the syndrome may involve a range of impairments including memory (short and long term), mood, consciousness, and circadian rhythm (often manifested by a severe disturbance in the normal sleep-wake cycle) [37]. First noted after cardiac surgery (so-called pump-brain), such declines in cognitive function may arise after noncardiac procedures as well. As with delirium, postoperative cognitive dysfunction is associated with longer hospitalizations and higher mortality [38]. Further, there appear to be prolonged, even permanent, consequences with several studies demonstrating cognitive difficulties for months, even a year after surgery [39–41]. There are additional implications as patients with postoperative cognitive dysfunction at discharge appear more likely to die within a year of the surgery [7].

In the realm of orthopedic surgery, the implication of postoperative cognitive dysfunction has been studied extensively in the hip fracture setting. In this surgical setting, the incidence of cognitive decline is as high as 37% in nondemented patients; further, one study has reported that 69% of such patients developed frank dementia over a subsequent five-year period (as compared with a 20% incidence in those without postoperative delirium) [42]. Thus, the implications of this problem are profound.

Hip Fracture

Hip fracture is a major public health-care problem with far-reaching consequences [43]. Worldwide over 1.6 million older adults sustain hip fractures annually, with over 300,000 of these in the United States; the prevalence will certainly increase in the years to come owing to the aging of the population. Indeed, adults over the age of 85 years are 10 times more likely to sustain a fractured hip as compared to younger cohorts. Risk factors are well defined and include osteoporosis and falls, problems particularly common in elderly women. Older adults who experience hip fracture have poor outcomes, including permanent functional declines, higher rates of institutionalization, and death. In older cohorts, 13.5% of hip fracture patients die within 6 months of the event, and 24% within a year [44, 45]. Further, following hip fracture, older patients are five times more likely to be institutionalized at 1 year [46]. These statistics are well known to orthopedic surgeons and geriatricians and serve to underscore the seriousness of this problem at both the patient and the health-care systems level.

The goal of hip fracture surgery is to return patients to their prefracture level of functional status, the achievement of which produces daunting challenges. As such, surgery should proceed as soon as the patient's clinical status is regarded as optimized as the beneficial effects of early surgery have been well documented. These include decreased pain, fewer postoperative complications, and shortened lengths of acute hospital stay [47]. For example, in one large cohort study (367 patients), a delay in surgery of >2 days resulted in a doubling of the 1-year mortality, especially in those patients with comorbid conditions [48, 49].

Surgical Management

The 2000 population census confirmed that the predicted graying of the US population is occurring. The evolving demographics of our society will have an important impact on the practice of orthopedic surgery and related musculoskeletal specialties. By the year 2040, 20% of the population or approximately 77.2 million citizens will be >65 years of age. The current estimate of the demand for joint replacement surgery in citizens older than 65 is 15 per 10,000. In the year 2000, approximately 500,000 total knee replacements were performed and 375,000 hip fractures were repaired. With the projected growth of the elderly population, the demand for these procedures will increase sevenfold. Thus, by 2040, 3.5 million citizens will seek total knee replacement. Such developments will require a shift in the focus of the orthopedic workforce as well as efforts to improve the delivery of care to the elderly population. Of additional interest is the fact that the oldest segment of the population is the part expanding most rapidly. By 2040, the over-85-year-old population will double in size to 3% of

the overall population. While recent studies are informing guidelines and principles for treatment in this age group, the results of surgical intervention in this population remain largely uncharted territory.

Much of what has been learned concerning the perioperative care of the elderly patient has been gained from the study of surgical outcomes of fractures of the hip over the past 20 years. Through this study, a new paradigm for the approach to care and the evaluation of outcomes has emerged. Traditional reports of hip fracture treatment focused largely on surgical aspects of care and emphasized traditional wisdom. For instance, it was widely held that preservation of the femoral head was the most desirable outcome of treatment. This was because it seemed logical that in the absence of visible arthritic change, the patient's own femoral head, the native bone, would be a better bearing surface than an artificial or metallic prosthetic replacement. Most of the studies viewed the hip fracture population as homogeneous, stratifying outcomes according to age and sex. Since then, clear evidence has emerged suggesting that the most important predictor of outcome in the elderly hip fracture patient is their preinjury overall health status [50]. As such, hip fracture patients should be stratified according to preinjury health status and that the choice of surgical procedure should largely be based on this stratification. Past and recent studies all conclude that although overall perioperative mortality has improved, an increased mortality risk during the first year after hip fracture persists. This mortality rate ranges from 12% to 25%. Further, for those surviving the first postfracture year, mortality predictably returns to that of the age-matched general population. After the first year, the 5-year predicted survival is 50% [50]. Indeed, there appears to be two distinct groups: those that die within the first year after surgery versus those that recover and experience a life expectancy similar to aged match citizens (who have not sustained a hip fracture). The best predictor for which group a patient will fall is their overall prefracture health status [50].

This new understanding has helped to clarify what was considered contradictory findings of past studies. For instance, it has been observed that the outcome of hip fracture surgery can be predicted from the nutritional status of patients on admission [51, 52]. In our own experience, one-third of our patients admitted with hip fractures had clear evidence of acute and chronic protein malnutrition and that this group of patients predictably suffered more complications and an increased risk of one-year mortality. The data clearly demonstrate two populations: one group was malnourished while the other was not. Of great frustration, however, has been the disappointing observation that nutritional supplementation fails to alter the outcomes in these two populations [53, 54]. It would therefore appear that nutritional deficiency per se is not a predictor of outcome. It is, however, associated with poorer overall health status and physical function, both of which can act as independent predictors of outcome. Analyzing this population for their nutritional status reveals nutrition to be a vital element of overall health status, and it is through this linkage that malnutrition exerts its negative influences. One-third of our patients present with poor overall health and suffer poor outcomes of treatment. Therefore, it is now clear that elderly patient populations are not homogeneous but rather should be categorized as falling into a fit versus an unfit group. Nutritional status is an important indicator of preinjury fitness.

In the elderly, it is clear that fitness cannot be judged by chronological age. Rather it is judged based on several factors. Fit elderly patients have fewer than three medical comorbidities, are competent community ambulators, routinely engage in sports or other social activity, and participate in the management of their social and financial affairs. Also comorbidity, as measured by the Charlson Comorbidity Index, is a consistent indicator of recovery from the hip fracture experience. Since recent studies analyzing the outcome of hip fracture care confirm the inhomogeneity of this population, surgical management must take into account the "fitness" of the patient, not just their chronological age or fracture classification [50, 52, 55]. The two procedures once felt to be the gold standard for displaced femoral neck fractures (closed pinning and hemiarthroplasty) have now been shown to carry a higher risk for reoperation and ultimately higher morbidity and cost as compared to total hip replacement (THR) in the active and "fit" elderly patient. A prospective, randomized study has now shown that for patients with displaced femoral neck fractures, total hip replacement – traditionally considered "overkill" – is actually the ideal procedure [56]. Compared to hip pinning and partial hip replacement, THR patients subsequently require fewer revisions surgeries, have better function, and superior overall perceived health status. The fitter or more active the patient, the greater the advantage for THR.

This experience points out that the elderly need surgical procedures that minimize the risk of reoperation, result in excellent pain relief, and restore anatomy sufficiently to permit return of function and ambulation. This approach has led to a new evidence-based algorithm for treatment of femoral neck fractures in the elderly. Nondisplaced fractures are treated by pinning in situ in both fit and unfit patients as the results of this procedure are excellent. However, for displaced fractures, fit elderly patients are best treated with THR. Unfit patients, typically the nursing home patient or those limited to household ambulation, can be most safely treated by hemiarthroplasty.

The principles outlined previously also pertain to total joint arthroplasty in the elderly population. The demand for arthroplasty in the oldest portion of the population is growing rapidly. Among nonagenarians, the demand for total hip

replacement is approximately 136 per 10,000 population. In 1995, 33,000 were performed in the United States. The perioperative mortality was 2.3% [57].

There are several reported studies examining the outcome of total joint replacement in this oldest population. Berend et al. [58] reviewed their experience with hip and knee replacement and found a higher incidence of post-op complications and longer hospital stays but low perioperative mortality and excellent outcomes. L'Insalata [59] examined results for total knee replacement (TKR) in the above 80 population and had similar findings. Shah et al. [60] looked specifically at frail elderly patients undergoing THR and found excellent outcomes with low mortality. Several key findings are consistent in these three studies:

1. Elderly patients with adequate preparation can safely undergo arthroplasty and achieve improvements in hip and knee scores that are comparable to younger patients.
2. There is an increased risk of perioperative complication, including post-op delirium, pneumonia, UTIs, and decubitus ulcers.
3. Aseptic loosening did not occur in any of these series suggesting that the prostheses outlive the patients. This justifies the routine use of constrained prostheses in this population to reduce the risk of instability and dislocation.

In spite of the higher risk of morbidity, perioperative mortality was low and the successful elimination of pain and restoration of mobility justify the procedures.

Postoperative Pain Management in Elderly Patients

Orthopedic procedures are painful unless appropriate and adequate pain management is employed. The elderly present a particular challenge in that poorly controlled pain can result in a delirious, immobile uncooperative patient that is prone to venous thromboembolism, pressure sores, decubitus ulceration, abdominal ileus, and poor response to mobilization. On the other hand, the elderly are especially sensitive to the side effects of narcotic medications that can produce delirium, constipation, and respiratory depression. The current approach to pain management in the elderly attempts to minimize reliance on narcotics while avoiding medications that predictably result in delirium or somnolence as well as those that are prone to produce harmful side effects or adverse drug reactions. Demerol and benzodiazepines are particularly to be avoided. Nonsteroidal and COX-2 inhibitors are useful for pain management but their dose must be adjusted to each patient's renal function or risk from GI complications. Multimodal strategies are especially useful in the elderly as they attack pain through multiple pathways and allow lower doses of narcotics but predictably good pain relief.

The multimodal approach to pain management has been enthusiastically embraced in hopes that the undesirable side effects and consequences of traditional reliance on narcotic medications can be overcome. In the past two decades, techniques of continuous infusion of narcotics, partially controlled by the patient (PCA), either by an intravenous route or through the continuation of the epidural route after surgery, have been very successful in helping to manage postoperative pain. Epidural PCA is especially attractive for lower extremity surgery because narcotics can be mixed with local anesthetics lowering the dose and toxicity of the narcotic while achieving very dramatic pain control. Unfortunately, this excellent control of pain has unwanted consequences. Patients who are comfortable on epidural PCA often require a urinary catheter, suffer nausea presumably from the epidural narcotic, and experience significant postural hypotension limiting their ability to mobilize optimally while their pain is being controlled. The unintended consequence is an acceptable level of pain but discomfort from nausea and an in-hospital stay lengthened by relative immobility in the immediate postoperative period.

Multimodal and preemptive strategies to prevent postoperative pain have benefitted from recent advances in the understanding of neuronal plasticity and how undertreated acute pain can lead to chronic pain. Also, clarifying the role that inflammation plays in the injured tissue that is increasing the sensitization of nociceptors has led to drug therapies incorporating NSAIDs and COX-2 agents in preemptively controlling post-op pain. Blocking the pain signal by a variety of methods including perioperative administration of narcotics, anti-inflammatories, and peripheral nerve blockade (multimodal) has improved postoperative pain management and has improved the overall quality and efficiency of care [61–63]. One drug that may be underutilized in the elderly is acetaminophen. Intravenous acetaminophen has been widely used in Europe with great success and its recent approval for use in the United States has made perioperative use of this drug a new tool in pain management of the elderly patient. At Hospital for Special Surgery, multimodal pain management strategies have also been dramatically effective in helping elderly patients' recovery from total knee replacement. Our protocol is based on the successful experience using intra-articular continuous infusion of local anesthetic rather than reliance on epidural analgesia in total knee replacement patients [64]. In this protocol, patients are pretreated with a COX-2 inhibitor and decadron. Intraoperatively spinal or epidural anesthesia is augmented with a peripheral nerve block and additional NSAID or acetaminophen. Prior to wound closure, an indwelling catheter is placed in the knee or a high volume local infiltration of a pain cocktail is given.

If a catheter is placed, continuous infusion of local anesthetic (ropivacaine) is administered for 48 h after surgery. Further, patient-controlled analgesia is avoided and usually only small doses of oral narcotics are required for the first several weeks following surgery. We remain enthusiastic about this approach, which moves the target of the pain intervention from central to the peripheral site of pain, thereby decreasing the centrally mediated side effects which are so counterproductive in the elderly patient.

Physical Therapy and Rehabilitation of the Elderly

Rehabilitation of the elderly patient following major orthopedic surgery should be aimed to optimize physical, intellectual, psychological, and social function. A multidisciplinary approach involving physical and occupational therapy is needed, and the rehabilitation process should be expected to take 6–12 months depending on the type of surgery performed. Expectations for recovery must assess the presurgical health of the patient, again emphasizing that the relative fitness or frailty of the patient is more important than their chronological age.

Rehabilitation following hip fracture repair is an especially complex task. It is well recognized that prompt surgical treatment of the hip fracture patient is usually associated with improved survival with fewer postoperative complications. The benefit of early surgery is attributed to relief of pain and restoration of mobility [47–49]. It follows that prompt surgery leads to prompt rehabilitation. Early mobilization and gait training are the early goal but later physical therapy should target the restoration of joint mobility and muscle strength and improvement in balance, the aim of which is to prevent falls. Ultimately, every effort should be made to help train the elderly hip fracture patient to regain their preinjury level of function so that they can once again enjoy life and resume their preinjury lifestyle.

Elderly hip fracture patients face many challenges in the rehab process (Box 23.3). Nonetheless, it is well established that elderly patients respond well to the rehabilitation effort. Frailty and sarcopenia result in reduced muscle strength and contribute to poor balance and physical function in the elderly. Indeed, these phenomena are often the root cause of the fall that produced the hip fracture, and such deficits must be addressed in order to maximize recovery following hip fracture surgery. Following the initial period of healing, which usually takes 6–12 weeks, a physical therapy program directed at improvement in muscle strength, endurance, coordination, and balance should be instituted. Improvement in function is usually evident for at least 6 months after fracture [50], justifying a prolonged and progressive program. Although no specific regimen has been documented to be superior [65], combinations of exercises incorporating strength and endurance training are the most effective. Several recent studies clearly document the benefit of aggressive and prolonged training programs for the elderly as they result in better muscle strength, endurance, and improved balance [66–68].

Box 23.3 Special Considerations for the Rehabilitation of Elderly, Hip Fracture Patients

- High likelihood of multiple medical comorbidities that must be addressed.
- Cognitive and sensory impairments must be assessed.
- Reduced muscle mass and strength, decreased joint mobility, and reduced aerobic capacity may be present.
- There is usually an increased risk for falls and future injury.
- Many elderly live alone with inadequate social support.

Rehabilitation following total joint arthroplasty (THA) is also needed for patients to achieve the optimal benefits of these procedures. Because THA is elective, the process of rehabilitation should be multidisciplinary, structured, and should address all the contextual factors of these patients. These factors include coping skills, the home environment, social supports, and self-efficacy of these elderly patients. Education and preoperative training programs are effective, and structured goals for the recovery period should be well defined. Milestones for recovery have been used to document the important aspects of post-THA rehabilitation programs [69, 70]. When patients and their families are educated as to these goals during their preoperative preparation for surgery, they can perform preoperative fitness training, undertake adjustments to their living environment in anticipation of the post-op recovery, and become overall more engaged in the rehabilitation process.

The lessons learned from rehabilitation of the elderly hip fracture patient also apply to the elderly joint replacement patient. Age-related musculoskeletal, cognitive, and sensory impairments should be taken into account. As opposed to the hip fracture setting, the elective aspect of THA allows prospective planning along the continuum of postoperative recovery and should include factors which aim to improve

enjoyment of quality of life, activities that promote mobility, leisure time, and sports. Resistance exercises, endurance, and falls prevention training should all be included. Recovery following THA, especially TKR, is prolonged, with improvement possible over the entire first year. Patients should be fully aware of the slow nature of this recovery, and their rehabilitation program should be designed with this in mind [71].

Summary

The changing demographics of our society make it clear that elderly patients will predominate much of orthopedic practice in the future. As such, the special needs of these patients must be anticipated. The concept of "homeostenosis" is useful in understanding the special risks associated with surgery in patients of advanced age. Also important, however, is the understanding that chronological age by itself is not an appreciable risk; rather it is overall health. The elderly should be assessed as "fit" or "frail" and their care plan adjusted accordingly. Elderly patients have the same potential to benefit from orthopedic reconstructive procedures, and they have the potential to greatly improve their overall health and quality of life with orthopedic reconstruction. When elective surgery is planned, the special needs of the elderly patient should be anticipated with preoperative medical optimization, preoperative physical conditioning, preoperative education, and planning for a prolonged recovery process. Current evidence strongly suggests that with appropriate care the elderly benefit from orthopedic reconstruction to the same degree as younger counterparts.

Summary Bullet Points

- Special considerations related to aging (homeostenosis) must be addressed when elderly patients require orthopedic surgery.
- Assessment of risk and surgical planning should be based on the elderly patient's "fitness" as opposed to their chronological age.
- Modifications of surgical technique which take into account the lower demands of the elderly can help eliminate potential postoperative risks. An example of this would include use of constrained THR components, which prevent postoperative dislocation.
- The elderly patient has the potential to benefit as much from orthopedic reconstruction as younger counterparts, but special rehabilitation strategies should be incorporated into their treatment plans.

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Venous Thromboembolism and Orthopedic Surgery

24

Anne R. Bass

Objectives

- To review the problem of venous thromboembolism in orthopedic surgery.
- To review risk factors and screening strategies for venous thromboembolism.
- To review prevention strategies for venous thromboembolism.
- To review current treatment options in various orthopedic surgical settings.

Key Points

- Thromboembolism is an important perioperative consideration in orthopedic surgery.
- Well-established strategies have been developed for the prevention, detection, and treatment of these complications.
- There are an evolving range of anticoagulants that can be employed both for the prevention and treatment of thromboembolic events.

Introduction

Venous stasis, endothelial injury, and hypercoagulability (Virchow's triad) can all contribute to thrombosis, and all three are often present in orthopedic patients. It should come as no surprise then that venous thromboembolism (VTE) is a frequent complication of orthopedic surgery. Risk factors for VTE can be separated into those that are patient-related and those that are procedure-related. Patient-related factors can include the inherited and acquired thrombophilias listed in Box 24.1, and a variety of other genetic variants have been identified in genome-wide association studies [1, 2]. While genetic thrombophilias can be associated with a greatly increased risk of thrombosis, they are present in only a small percentage of the population (0.1–5%) [1, 3–5]. Therefore, although thrombophilic allelic variants are enriched in arthroplasty patients experiencing pulmonary embolism (PE) [6], they do not explain most cases of postoperative VTE. Patient-related risk factors for VTE are listed in Box 24.2. While these factors carry less risk than the inherited thrombophilias, they are far more prevalent in the general population [3, 7–13].

Box 24.1 Thrombophilias

- Factor V Leiden
- Prothrombin *G20210A* mutation
- Methyltetrahydrofolate reductase mutation
- Plasminogen activator inhibitor-1 mutation
- Protein S deficiency
- Protein C deficiency
- Antithrombin III deficiency
- Antiphospholipid antibody syndrome (acquired)

Box 24.2 Patient-Related Risk Factors for Venous Thromboembolism

- Advanced age
- African American race
- Cancer
- Central venous access (IV or pacemaker)
- Chronic lung disease
- Congestive heart failure

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- Estrogen
- History of venous thromboembolism
- Immobility
- Inflammatory bowel disease
- Myeloproliferative diseases
- Non-O ABO(H) blood type
- Obesity
- Rheumatic disease
- Sleep apnea
- Smoking
- Venous insufficiency

Protective: Asian or Pacific Islander race, statin therapy

Although patient-related risk factors are important in the genesis of thrombosis, it is the procedure itself that places orthopedic patients at high risk for VTE; rates of VTE are in fact higher after orthopedic surgery than other procedures [14, 15]. Bone and joint surgery strongly activate the coagulation cascade, and, in hip arthroplasty, peak prothrombin fragment levels are seen at the time of femoral bone preparation [16, 17]. Intraoperative limb positioning and the use of tourniquets also contribute to VTE risk by inducing venous stasis and endothelial injury [18]. Other arthroplasty-related VTE risk factors are listed in Box 24.3 [19–22].

Box 24.3 Arthroplasty-Related Risk Factors for Venous Thromboembolism

- General anesthesia
- Bilateral
- Revision
- Fracture indication

Protective: Autologous blood donation

Diagnosis of Venous Thromboembolism

Symptoms of deep vein thrombosis (DVT) include calf or thigh pain and swelling, symptoms that can be difficult to interpret in patients who have undergone lower extremity surgery. D-dimer levels are elevated in most patients following orthopedic surgery making them of limited utility in this setting [23, 24]. Ultrasound (US) of the lower extremities has supplanted venography for the diagnosis of DVT because it is noninvasive and less expensive. Although US is less sensitive (83%) than venography particularly for distal clots [25], over 85% of patients with symptomatic DVT have proximal vein thrombosis [26]. Color Doppler US is more sensitive than compression US for the detection of calf clots, but is more expensive [27].

Symptoms of pulmonary embolism (PE) include shortness of breath, hypoxemia, tachycardia, chest pain, syncope, or in rare cases sudden death. The diagnosis can be made by ventilation perfusion scan, computed tomography angiography (CTA), or angiography. CTA has largely supplanted ventilation perfusion scanning because it is easier to perform and provides additional clinical information to treating physicians, such as the presence or absence of pneumonia or fluid overload. It should be noted that in a study of 109 total knee arthroplasty patients who all underwent CTA 3–7 days after surgery, the incidence of *asymptomatic* PE was 1.8% [28]. This suggests that if more imaging is done, more PE will be detected. Clinical diagnostic tools together with D-dimer testing can be used to identify patients in most need of CTA, and the recently developed "YEARS" algorithm seems to perform well even in hospitalized patients [29].

Subsegmental Pulmonary Embolism

CTA detects more clots than ventilation perfusion scanning; however, the significance of isolated subsegmental PE (SSPE) that can be detected by CTA has been questioned. Studies suggest that there is low inter-reader agreement in the diagnosis of SSPE among radiologists reading CTA [30]. In addition, a 2010 meta-analysis demonstrated that while the rate of PE detection using single- vs multidetector CT is 4.7% vs 9.4%, the rate of VTE events during 3 months of follow is no different between these two groups [31]. This suggests that ascertaining more PE may not improve outcomes and may subject some patients to unnecessary anticoagulation. Some point out that, although the incidence of diagnosed PE after surgery is increasing, PE case fatality rates have declined and mortality rates are unchanged suggesting that greater detection of small SSPE is not clinically meaningful [31]. Conversely others argue that SSPE are clinically significant and should be treated. For example, in an analysis of 3769 patients with suspected PE, the rate of recurrent PE and death was actually *higher* in the treated patients with SSPE compared to those with larger clots, suggesting that SSPE are not a benign phenomenon [32]. There are no prospective trials testing the hypothesis that isolated SSPE in the absence of DVT can safely go untreated, although one such trial is under way (NCT01455818 PI: Carrier). Nonetheless, the most recent guidelines from the American College of Chest Physicians recommend that patients with isolated SSPE and no proximal DVT undergo surveillance rather than anticoagulation [33]. The rate of proximal DVT in patients with SSPE on CTA is 7.1%, demonstrating the importance of performing

bilateral lower extremity ultrasound in patients with isolated SSPE if withholding of anticoagulation is being considered [31].

Screening for Venous Thromboembolism in Asymptomatic Patients

Historically, studies of hip and knee arthroplasty in which mandatory venography was performed demonstrated DVT in well over half of patients in the absence of prophylaxis; the rate of clinically apparent DVT is much lower, however [34]. Clinically apparent PE also represents only a subset of all PE. In studies in which imaging is performed in all patients undergoing hip or knee arthroplasty, PE is found in 5–19% but only 1–3% of them are symptomatic [28, 35, 36]. The rationale for radiographic screening for DVT in clinical trials (as distinct from clinical practice) is to increase the number of patients achieving the trial endpoint, thus lessening the number of patients needed to power the study. The rate of subclinical DVT serves as a surrogate marker for the outcome of interest, that is, clinically apparent VTE. It would be impractical to design a prospective orthopedic trial using PE or death as its endpoint, although these are the outcomes of interest to clinicians, because the number of patients needed to treat (to demonstrate a difference in the two study arms) would be prohibitively large. This is important to recognize when interpreting the results of clinical trials. Some prophylaxis studies are quoted as demonstrating "equal" rates of PE or death in two study arms when in fact the studies are inadequately powered to do so [37]. In future, studies using large orthopedic registries and administrative databases may allow for analyses of these important outcomes.

Neither the American College of Chest Physicians nor the American Academy of Orthopedic Surgeons recommends screening asymptomatic patients postoperatively for DVT in clinical practice [38, 39]. The sensitivity of lower extremity US in asymptomatic patients is only 47%, far lower than in symptomatic patients [40]. This may relate to the localization and quality of clots in asymptomatic versus symptomatic patients. In asymptomatic patients, 66% of DVT are in the calf in comparison to 15% in symptomatic patients. In addition, when a proximal DVT is present in an asymptomatic patient, it is often less extensive than in symptomatic patients. Finally, asymptomatic thrombi tend to be more recent in onset and less organized, which makes them harder to image.

Two studies have suggested that the use of screening US at the time of discharge after arthroplasty does not predict who will develop future VTE. In one study of almost 2000 hip and knee arthroplasty patients who received low-molecular-weight heparin postoperatively, pre-discharge US demonstrated clots in only 0.15% of patients [41]. Nonetheless, VTE occurred in 2% of patients after discharge (and one patient died of a PE despite a negative pre-discharge US). In another study, 1026 hip and knee arthroplasty patients who received warfarin postoperatively were randomized to pre-discharge US or sham US [42]. There were asymptomatic DVT in 3.7% of the screened group (they were treated). After discharge, symptomatic VTE occurred in 0.87% of the US group, and 1% of the sham US group, suggesting no benefit to screening.

Prevention of Venous Thromboembolism

Advances in surgical and anesthetic technique as well as early mobilization in the postoperative period have helped to reduce the risk of postoperative VTE following orthopedic surgery. This has forced a reappraisal of the true risk of VTE in the absence of prophylaxis. Current prophylaxis trials typically lack a placebo arm and instead use low-molecular-weight heparin (LMWH) as the "gold standard" against which newer agents are compared. In order to estimate the risk of VTE in the absence of prophylaxis, some recommend doubling VTE rates seen in patients assigned to LMWH in contemporary randomized controlled trials [39].

Although the risk of VTE is highest in patients with hip fractures and undergoing hip or knee arthroplasty, patients undergoing other orthopedic procedures can also experience VTE, particularly if they have additional thrombosis risk factors.

Nonpharmacological Approaches

There are a variety of nonpharmacological approaches to VTE prophylaxis. Intermittent pneumatic compression can prevent VTE without causing bleeding [43–45], but patients may not comply with mobile devices after discharge from the hospital due to discomfort and inconvenience [46]. Pneumatic compression can be used in the hospital as an adjunct to pharmacological prophylaxis, however [47]. Neuraxial anesthesia may also reduce VTE risk as compared to general anesthesia. For example, an analysis of the American College of Surgeons-National Surgical Quality Improvement Program (NSQIP) 2011–2015 database demonstrated a 15% reduction in the odds of 30-day VTE with neuraxial anesthesia compared to propensity-matched patients who underwent general anesthesia [19]. However, a recent observational study in Japanese arthroplasty patients demonstrated a higher rate of VTE in patients undergoing spinal anesthesia compared to combined epidural/general anesthesia (commonly used in Japan) after propensity matching although less than half of the patients in this study were on anticoagulants [48]. A large phase IV study of rivaroxaban compared to standard of care prophylaxis in patients undergoing major orthopedic surgery suggested that

the efficacy of rivaroxaban was not impacted by pneumatic compression or choice of anesthesia [49], and a secondary analysis of dabigatran trials in orthopedic patients also suggested that anesthesia type did not impact VTE rates [50]. This suggests that nonpharmacological approaches to VTE prophylaxis may demonstrate the greatest benefit when added to less potent anticoagulants such as aspirin, which is more commonly used in the United States than in Europe or Asia.

Inferior Vena Cava Filters

Inferior vena cava (IVC) filter placement is a nonpharmacological approach that is indicated for VTE *treatment* in patients with a contraindication to anticoagulation or who have recurrent thromboembolism despite adequate anticoagulation [51], not for VTE prophylaxis or treatment if anticoagulation can be given [39, 52]. Nonetheless, one study demonstrated that IVC filters are placed in almost 1% of orthopedic surgery patients and that in over 60% of cases they are placed for VTE *prophylaxis* [53]. This was confirmed in a recent single-institution study of 589 IVC filters placed over a 2-year period demonstrating that 46% were placed prophylactically (67% for orthopedic surgery) and only 27% were later removed [54]. IVC filter placement can be associated with vena cava perforation, filter migration, and filter thrombosis [55]. Although they reduce the risk of PE, IVC filters increase the risk of DVT [55, 56]. Although retrievable filters can obviate some of these risks, only 40% of patients with retrievable filters have them removed, and filter removal is associated with complications in 11% of patients [53, 57]. After a period of high IVC filter utilization in the United States between 2005 and 2008, utilization fell by 27% from 2009 to 2012 [57], likely due to recognition of these hazards. Although well-designed studies are lacking, there may be some instances where placing a prophylactic IVC filter makes sense, such as in patients with hip fractures or multiple trauma who have a contraindication to pharmacological anticoagulation. Retrievable filters should be used whenever possible and plans put in place to assure later filter removal. Patients with a retained filter will benefit from lifelong anticoagulation (unless contraindicated) to reduce the risk of filter thrombosis and DVT.

Pharmacological Options

Aspirin (acetylsalicylic acid) irreversibly inactivates cyclooxygenase and blocks the formation of thromboxane A2, a mediator of platelet aggregation and vasoconstriction. After a single dose of aspirin, platelet function remains impaired for 4–7 days, but bleeding times generally returns to normal within 24–48 hours because new, unaffected platelets are released from the bone marrow.

Warfarin inhibits the synthesis of vitamin K-dependent clotting factors, which include Factors II, VII, IX, and X and the anticoagulant proteins C and S. Although there is an anticoagulant effect by 24 hours after warfarin initiation, peak effect is usually delayed 72–96 hours. In the immediate postoperative period, this has the advantage of lowering the rate of hemorrhage, as compared to more rapidly acting agents such as LMWH, and warfarin remains popular among US orthopedic surgeons [58, 59]. A variety of factors influence patient responsiveness to warfarin including age, nutritional status, concomitant medication, and genetic polymorphisms in cytochrome P450 enzymes (CYP2C9) and the vitamin K receptor (VKORC1). Warfarin, like other potent anticoagulants, can be associated with bleeding and is responsible for 15% of emergency department visits for adverse drug reactions [60]. However, warfarin use can be made safer through the use of a dosing nomogram [61, 62] and through the use of genetic testing, as recently shown in large prospective randomized controlled trial of pharmacogenetics warfarin dosing [63]. A dosing algorithm that incorporates clinical factors and patient genotype is available at www.warfarindosing.org. In preoperative patients, already on warfarin for atrial fibrillation, bridging anticoagulation with low-molecular-weight heparin is not recommended because it increases the risk of bleeding without reducing the risk of stroke [64]. When warfarin is used for VTE prophylaxis, the first dose can be given either the night before or the night of surgery.

Heparin potentiates antithrombin's inhibition of activated factor X (factor Xa) and thrombin. Thus, it is an "indirect factor Xa inhibitor." LMWH, such as enoxaparin, is expensive and must be given by subcutaneous injection, but does not require daily blood test monitoring, greatly simplifying its use in the perioperative period. Maximum anticoagulant effect occurs 3–5 hours after subcutaneous injection of enoxaparin. Because LMWH is 30% excreted through the kidneys, its dose should be modified in the presence of renal insufficiency and it should be used with great caution, if at all, in patients with renal failure. LMWH is generally started 12–24 hours postoperatively assuming adequate surgical hemostasis. LMWH can, however, be started as early as 6 hours after minor procedures, and in Europe LMWH is started at half-dose preoperatively. The use of LMWH in conjunction with an epidural catheter has been associated with epidural and spinal hematomas. Therefore, LMWH should not be used in the 24 hours prior to epidural catheter placement or with an epidural catheter in place and should not be instituted until 4 hours after removal of an epidural catheter [65]

Fondaparinux is a synthetic pentasaccharide that, like heparin, binds to antithrombin and potentiates its inhibition of factor Xa. Thus, it is also an indirect factor Xa inhibitor. Because it is comprised of a very short polysaccharide chain it does not inhibit thrombin, it does not bind to platelets, and it is generally not associated with heparin-induced thrombo-

cytopenia. Fondaprinux is excreted by the kidneys and should not be used in patients with significant renal impairment. Fondaparinux should also be avoided in patients with an epidural catheter in place [66].

Two direct factor Xa inhibitors, rivaroxaban (Xarelto®, Janssen Pharmaceuticals, Raritan, NJ, USA) and apixaban (Eliquis®, Bristol-Myers-Squibb, NY, NY, USA) are FDA-approved for VTE prophylaxis in orthopedic surgery patients. These agents have the advantage of being administered orally and at a fixed dose without need for blood test monitoring. Rivaroxaban has a half-life of 7–11 hours and is 33% cleared by the kidneys. The dose for VTE prophylaxis is 10 mg nightly. Apixaban has a half-life of 8–13 hours and is 25% excreted by the kidneys. The dose for VTE prophylaxis is 2.5 mg twice daily. Both drugs should be avoided in patients with significant renal impairment.

Three other oral anticoagulants, edoxaban (Savaysa® (Daiichi Sankyo, Tokyo, Japan), a direct factor Xa inhibitor), betrixaban (Bevyxxa® (Portola Pharmaceuticals, South San Francisco, CA, USA), a direct factor Xa inhibitor), and dabigatran (Pradaxa® (Boehringer Ingelheim, Ingelheim am Rhein, Germany), a thrombin inhibitor) are FDA-approved, but not for use in orthopedic patients. Dabigatran binds directly to the catalytic site of thrombin, blocking its function. Dabigatran can be associated with dyspepsia and may increase the risk of myocardial infarction [67, 68]. Dabigatran's half-life is normally 12–17 hours, but is much longer in the presence of renal impairment because the drug is 80% excreted by the kidneys. Dose reduction should be strongly considered in patients with even mild renal disease, and the drug should be avoided in patients with significant renal impairment. Several reversal agents have been developed for use in patients on direct oral anticoagulants who experience severe uncontrolled bleeding [69–71] (Table 24.1).

Table 24.1 New anticoagulation reversal agents

Anticoagulant	Reversal agent	Mechanism of action	FDA approval
Dabigatran	Idarucizumab	Monoclonal antibody fragment binds free and thrombin-bound dabigatran	2015
Enoxaparin, rivaroxaban, apixaban, edoxaban, betrixaban	Andexanet alfa	Inactive FXa decoy protein that binds direct and indirect FXa inhibitors' active site	2018
Heparin, dabigatran, rivaroxaban, apixaban, edoxaban, betrixaban	Aripazine	Binds to and inhibits heparins, direct factor Xa, and thrombin inhibitors	Not approved

Venous Thromboembolism Prophylaxis in Orthopedic Patients

Hip and Knee Arthroplasty

Rates of VTE following hip and knee arthroplasty are far lower than they were historically due to contemporary surgical and anesthetic techniques, and some argue that this obviates the need for potent anticoagulants [72]. In the absence of pharmacological prophylaxis, it is now estimated that the rate of PE and DVT would be 1.50% and 2.80%, respectively [39]. Nonetheless, PE remains an important cause of death following arthroplasty [73]. Many arthroplasty surgeons risk stratify their patients and prescribe aspirin to low-risk patients and warfarin or LMWH to higher-risk patients. A prospective randomized controlled trial demonstrated comparable rates of VTE and lower rates of bleeding when risk stratification was compared to routine administration of LMWH to all patients [74].

There are many prospective randomized controlled trials of pharmacological VTE prophylaxis in patients undergoing hip and knee arthroplasty, some examples of which are shown in Table 24.2. Although LMWH is more effective than warfarin in preventing VTE in this setting, particularly following TKR, many orthopedists prefer to avoid it because of its rapid onset of action and a concern that it may increase wound hematomas [75, 76]. In the United States, warfarin is still commonly prescribed to arthroplasty patients because of its low cost, oral bioavailability, and effectiveness [59], and the use of pharmacogenetics dosing can increase its safety further [63]. When either warfarin or LMWH is used, the duration of prophylaxis should be at least 10–14 days, but prolongation of therapy to 4–6 weeks will further reduce the risk of VTE [77].

Although aspirin is less efficacious than warfarin or LMWH [39], it was shown to reduce the risk of PE by 30% in 4088 arthroplasty patients randomized to aspirin or placebo (in addition to standard of care, which could include heparin) [78]. In that study, however, and in an earlier study comparing aspirin to warfarin prophylaxis [35], aspirin therapy was associated with an increased risk of bleeding complications. Very small studies in knee arthroplasty patients have shown aspirin to be as effective as enoxaparin when used in conjunction with IPC [79, 80]. More recent studies have demonstrated that aspirin can be a safe approach to extended prophylaxis in arthroplasty patients initially treated with low-molecular-weight heparin or direct factor Xa inhibitors [81, 82].

Direct oral anticoagulants have greatly expanded available approaches to VTE prophylaxis in arthroplasty patients. Rivaroxaban, for example, has greater efficacy than enoxaparin in preventing postoperative VTE [83, 84] although bleeding risk may be higher than with LMWH [85–88]. Dabigatran had an efficacy and safety profile comparable to that of enoxaparin in preclinical orthopedic trials [88, 89] but is not approved in the United States for this indication.

Table 24.2 Venous thromboembolism prophylaxis in hip arthroplasty, knee arthroplasty, and hip fracture

Study	Reference	Patients	Drug	Total VTE and mortality	Symptomatic VTE	Major bleeding
Lotke 1996	[35]	338 TKR and THR	Aspirin vs low-dose warfarin	56.6% vs 53.4%	Not noted	3.6% vs 0.7%
Westrich 2006	[79]	275 TKR	Aspirin vs enoxaparin 30 mg bid started 48 h postoperatively, plus IPC	17.8% vs 14.1%	Not noted	None
Hull 1993	[106]	1436 TKR and THR	Warfarin vs logiparin (LMWH) 10 days	44.4% vs 38.4% $P = 0.03$	0.4% vs 1%	1.2% vs 2.8% $P = 0.04$
PENTA-THALON	[107]	2275 THR	Fondaparinux 2.5qd vs enpoxaparin 30 mg bid 5–10 days	6.5% vs 8.2%	1% vs 0.1% $P = 0.006$	2.2% vs 0.9%
PENTA-SACCHA-RIDE hip fracture trial	[108]	1711 Hip fracture	Fondaparinux 2.5qd vs enpoxaparin 40 mg qd 5–10 days	8.3% vs 19.1% (VTE only) $P < 0.001$	0.5% vs 0.5%	2.2% vs 2.1%
RE-MODEL	[88]	2076 TKR	Dabigatran 150 mg qd vs enoxaparin 40 mg qd 6–10 days	40.5% vs 37.7%	0.5% vs 1.3%	1.3% vs 1.3%
RE-NOVATE	[89]	3494 THR	Dabigatran 150 mg qd vs enoxaparin 40 mg qd 28–35 days	8.6% vs 6.7%	0.9% vs 0.4%	1.3% vs 1.6%
RECORD-3	[13]	2531 TKR	Rivaroxiban 10 mg qd vs enoxaparin 40 mg qd 10–14 days	9.6% vs 18.9% $P < 0.001$	0.7% vs 2% $P = 0.005$	0.6% vs 0.5%
RECORD-1	[83]	4433 THR	Rivaroxiban 10 mg qd vs enoxaparin 40 mg qd 35 days	1.1% vs 3.7% $P < 0.001$	0.3% vs 0.7%	0.3% vs 0.1%
ADVANCE	[109]	3195 TKR	Apixiban 2.5 mg bid vs enoxaparin 30 mg bid 10–14 days	9.0% vs 8.8%	1.2% vs 0.8%	0.7% vs 1.4%
ADVANCE-3	[84]	5407 THR	Apixiban 2.5 mg bid vs enoxaparin 40 mg qd 35 days	1.4% vs 3.9% $P < 0.001$	0.1% vs 0.4%	0.8% vs 0.7%

Hip Fracture Surgery

The Mortality in the 90 days following hip fracture is 10–16% [90, 91]. Elderly patients with hip fracture represent a particularly debilitated cohort; many are admitted from nursing facilities, and many suffer from dementia. As a consequence, some physicians consider them poor candidates for anticoagulation. Unfortunately, these same patients are at high risk for VTE by virtue of their age and comorbidities. Most debilitated elderly patients are discharged to a supervised facility where they can continue to be monitored closely while receiving anticoagulants. LMWH, warfarin, fondaparinux, or a direct factor Xa inhibitor is preferred over aspirin for VTE prophylaxis in hip fracture patients. Aspirin did reduce the risk of clinical VTE by 30% in a study of 13,356 hip fracture patients randomized to aspirin or placebo in addition to usual care (which included heparin in 44% of patients), but this came at the price of more wound and gastrointestinal bleeding complications [78]. Although aspirin reduced the rate of fatal PE by 50% in this trial, other vascular deaths were higher in aspirin-treated patients so overall mortality was not reduced. Preoperative treatment with LMWH or a direct factor Xa inhibitor can further reduce the risk of VTE in patients with hip fracture [92, 93].

Spine Surgery

The rate of symptomatic VTE following spine surgery is approximately 1% among patients with degenerative arthritis, with higher rates among those with infection, trauma, or cancer and those undergoing anterior thoracolumbar fusion, especially with corpectomy [94, 95]. The risk of VTE can be lowered with the use of pharmacological prophylaxis, but this may increase the risk of epidural hematoma [96, 97]. There is no consensus as to the best approach to VTE prophylaxis in spine surgery patients and neurosurgeons are twice as likely as orthopedic surgeons to use LMWH in addition to nonpharmacologic measures [98]. Given the risk of epidural hematoma with pharmacological prophylaxis, we recommend early ambulation and the use of mechanical devices such as IPC in spine surgery patients, unless they are at extremely high risk for VTE, such as those with cancer or

infection. In patients who undergo complex anterior thoracolumbar spine fusions and have a prolonged hospital stay, unfractionated heparin can be considered after postoperative day 5, when the risk of epidural hematoma has diminished.

Knee Arthroscopy

The term "knee arthroscopy" encompasses a wide variety of surgical procedures ranging from simple knee "washout" or meniscectomy to ligament repairs and other procedures involving bone drilling. These differences in surgical invasiveness as well as differences in tourniquet use and duration, type of anesthesia, and duration of postoperative immobility are important procedure-related risk factors to consider, in addition to patient-related risk factors, in assessing the likelihood of postoperative VTE. With regard to pharmacological prophylaxis, two large prospective randomized controlled trials studying the effect of a 1-week course of LMWH after arthroscopy came to opposite conclusions regarding its benefit. The first demonstrated a two-thirds reduction in VTE with prophylaxis [99], while the second found no difference between the treatment and placebo groups [100]. A recent meta-analysis of 8 clinical trials ($n = 4148$) did suggest that pharmacological prophylaxis significantly reduces the risk of VTE (RR 0.42; 95% CI 0.23–0.76) without a significant increase in the risk of major bleeding [93]. However, the absolute rate of VTE was low in these studies (mean 4.8% with ultrasound surveillance), and LMWH treatment did not benefit patients undergoing "non-major" arthroscopy. Given the low absolute risk of VTE following knee arthroscopy, we do not recommend routine prophylaxis. However, in patients undergoing major arthroscopic procedures who have additional VTE risk factors, a 7–10 course of LMWH may be warranted.

Shoulder Arthroplasty

A large prospective shoulder surgery registry, which included 1378 consecutive patients (72% arthroscopy, 17% hemiarthroplasty, 9% total replacement, 2% humeral fracture), demonstrated a 90-day symptomatic VTE rate of 0.66% (95 CI% 0.2–1.12) [101]. One-third of the patients in this study received LMWH prophylaxis. In multivariable analysis, duration of surgery >60 minutes increased the odds of VTE 11-fold. A second study used a large national database and examined VTE rates in shoulder surgery patients over a 1 year period [102]. Rates of DVT, PE and death were 0%, 0.20%, and 0.22% for total shoulder replacement ($n = 4061$), and 0.01%, 0.01%, and 0.03% for shoulder arthroscopy ($n = 65{,}302$). Finally, a retrospective study of 2574 patients who underwent shoulder arthroplasty in an integrated health care system suggested a trend toward higher VTE risk in those with a traumatic rather than elective indications (1.71% vs 0.8%; $p = 0.055$) [103]. All these real-world studies include a mix of patients who did and did not received prophylaxis. In the absence of prospective randomized trials of VTE prophylaxis in shoulder surgery patients, we recommend LMWH prophylaxis for those whose surgery lasts longer than 1 hour or who have significant VTE risk factors such as a history of PE or DVT.

Foot and Ankle Procedures

A retrospective analysis of 23,212 foot and ankle procedures in the NSQIP database demonstrated VTE in 0.6% [104]. The most common procedures included in this cohort were bimalleolar fracture (24%), distal fibular fracture (21%), and foot amputation (17%). The risk of VTE was higher in older patients and in those with non-elective surgical indications. A large retrospective study analyzing foot and ankle surgeries in the English National Health Service database demonstrated rates of DVT, PE, and death to be, respectively, 0.12%, 0.17% and 0.37% for ankle fracture ($n = 45{,}949$); 0.01%, 0.02%, and 0.04% for metatarsal osteotomy ($n = 33{,}626$); and 0.03%, 0.11%, and 0.11% for hindfoot fusion ($n = 7033$). PE occurred in 1/1633 (0.06%) total ankle replacement patients [102]. VTE rates were significantly higher in older patients and in those with a Charlson comorbidity index score ≥2. There are no prospective randomized controlled trials of VTE prophylaxis in patients undergoing elective foot and ankle surgery. Although the risk of postoperative VTE is low following standard podiatric procedures, it is higher following more complex procedures performed by orthopedic surgeons, especially when prolonged casting is needed. The American College of Foot and Ankle Surgeons' Clinical Consensus Statement recommends risk stratification to determine which foot and ankle patients should receive prophylaxis, with a focus on those with a history of VTE, active cancer, and known hypercoagulablity and those requiring prolonged casting [105].

Conclusions and Summary

VTE is a common and potentially lethal complication of orthopedic surgery, particularly hip and knee arthroplasty and hip fracture surgery, although rates have declined as a consequence of modern surgical and anesthetic techniques, early postoperative mobilization, and the use of pneumatic

compression devices. For patients who require pharmacological prophylaxis, there is now a wide array of anticoagulants to choose from and newly developed antidotes for use in the rare cases of severe hemorrhage. Procedure- and patient-specific factors impact both VTE and bleeding risk. Hospitals should develop standardized risk stratification protocols and service/procedure-specific treatment algorithms to guide VTE prophylaxis in orthopedic patients.

Summary Bullet Points

- Venous thromboembolism is one of the most common and feared complications of orthopedic surgery.
- Clinical strategies directed at the prevention, surveillance, and treatment of such complications are supported by a prodigious literature.
- The pharmacology for the prevention and treatment of postoperative thromboembolism is evolving with newer agents recently added to the armamentarium.
- Multimodal approaches to prophylaxis are often employed in the setting of lower extremity arthroplasty.

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Coagulation Disorders and Orthopedic Surgery

25

C. Ronald MacKenzie and Raymond D. Pastore

Objectives

- To recognize the importance of coagulation problems in the perioperative setting.
- To develop an approach to the assessment of bleeding risk that emphasizes information obtained for the medical history, reducing the role of laboratory testing.
- To describe the physiological processes underlying hemostasis.
- To develop an orderly method for the detection of coagulation disorders preoperatively.
- To review the hematological basis for the disorders of primary and secondary hemostasis.

Key Points

- Bleeding problems are among the greatest fears of the surgeon.
- Hemostasis as a physiological process is well defined.
- Disorders of hemostasis can be due to platelet dysfunction (primary hemostasis) or clotting factor deficiency (secondary hemostasis).
- Patients at increased risk can be identified based on the patient's history, deemphasizing the reliance on the laboratory.

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Introduction

Hematological problems are common in the perioperative setting. Indeed, the bleeding complications of surgery are among the greatest of a surgeon's concerns threatening not only the health of the patient but also the success of the surgical procedure. Conversely, thrombosis is a particular fear postoperatively. Commanding a prodigious literature, thromboembolic complications of orthopedic surgery are reviewed separately in Chap. 24. This chapter will focus on disorders and processes that enhance the risk of bleeding. A practical method for their detection prior to surgery will be developed utilizing information derived from the patient's history and deemphasizing a reliance on the laboratory. As such, the content of this chapter complements the preceding discussion on venous thrombosis. Taken together, they represent a relatively comprehensive review of the range of hematological issues that may be seen in the orthopedic surgical setting.

The Preoperative Evaluation

The methodologies currently employed for the preoperative identification of patients at risk for bleeding in the setting of surgery have followed two distinct strategies [1]. The traditional approach has been to rely on the laboratory, utilizing routine testing such as the platelet count (primary hemostasis) and the prothrombin (PT) and activated thromboplastin times (aPTT) for the secondary disorders of hemostasis. Despite the persistence of this practice, its shortcomings in predicting postoperative bleeding are well recognized and expected based on the complex physiology of hemostasis. Indeed, these laboratory studies were not developed to determine the risk of postoperative bleeding but rather for the detection of clotting factor deficiencies.

When a blood vessel is injured, the vascular, platelet, coagulation, and fibrinolytic systems react in concert to mitigate

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the loss of blood. Simultaneously, thrombus forms, localizing to the site of injury. Bleeding may arise from a disruption in any of these hemostatic mechanisms, operating alone or in combination. The physiology is multifaceted and how such physiological processes play out in the clinical setting is not well-assessed by the commonly employed in vivo assessments [2]. Indeed, a recent extensive review of the literature, from which practical guidelines have been derived, recommends the discontinuation of such indiscriminate testing favoring a more selective approach in which patients are selected for further evaluation based on their bleeding history. Nonetheless, despite these challenges, the laboratory approach to the assessment of bleeding risk remains a remarkably enduring practice.

The second, more modern method for the assessment of bleeding risk involves the identification of patients based on their medical history and physical examination with targeted laboratory testing performed only on those with specific risk factors. Supported by the observations of Girolami and colleagues stressing the role of the clinical examination [3], Koscielny and colleagues have enhanced and systematized this view with the development of a bleeding risk questionnaire (Box 25.1) used to identify patients who should undergo further laboratory testing of their coagulation [4]. The questionnaire, developed retrospectively, has been validated in a large prospective study [5]. Using this methodology, 88% of patients (5021/5649) possessed no risk factors for bleeding. Contemporaneous laboratory studies revealed a prolonged aPTT in nine of these patients, all the result of a lupus anticoagulant (which typically increases the risk of thrombosis, not hemorrhage). No other laboratory test (prothrombin time, platelet count, platelet function study, and von Willebrand factor assay) uncovered any bleeding disorder. With respect to the questionnaire, the most reliable (sensitive) questions are related to bleeding of minor wounds (85%), frequent bruising (73%), and use of nonsteroidal anti-inflammatory agents (62%). If any four of the questions were answered in the affirmative, the positive predictive value for the presence of a bleeding diathesis was 99%.

Box 25.1 Questionnaire for Detection of Bleeding Risk

- Have you ever experienced strong nose bleeding without prior reason?
- Did you ever have—without trauma—"blue spots" (hematoma) or "small bleedings" (at the torso or other unusual regions of the body)?
- Did you ever have bleeding of the gums without apparent reason?
- How often do you have bleedings or "blue spots": more than 1–2 times a week or 1–2 times a week?
- Do you have the impression that you have prolonged bleedings after minor wounds (e.g., razor cuts)?
- Did you have prolonged or grave bleedings during or after operations (e.g., tonsillectomy, appendectomy, or during labor)?
- Did you have prolonged or grave bleedings after a tooth extraction?
- Did you ever receive blood packs or blood products during an operation? If so, please define the operation?
- Is there a history of bleeding disorders in your family?
- Do you take analgesic drugs or drugs against rheumatic disease? If so, please specify?
- Do you take other drugs? If so, please specify?
- Do you have the impression that you have prolonged menstruation (>7 days) or a high frequency of tampon change?

Used with permission of SAGE Publications from Koscielny et al. [4]

The clinical history is helpful in distinguishing between acquired and hereditary bleeding disorders [1, 3]. Table 25.1 summarizes these considerations emphasizing the presence or absence of a family history of bleeding, the age of onset of bleeding, the pattern of bleeding, comorbidities, and a history of transfusion as historically important factors. Physical findings also provide important clues to diagnosis (Table 25.2). Various etiologies are implicated depending upon the site of bleeding, although, as Girolami describes, there is considerable overlap [3]. A distinct differential diagnosis can be structured around the organ system involved in the bleeding. While imprecision in terminology and semantics may cloud the discussion, certain bleeding patterns are generally appreciated by clinicians and are of some importance in diagnosis.

Whether identified by history, physical examination, or screening laboratory tests concerns about a patient's hemostatic capacity warrants further evaluation. Hemostasis is

Table 25.1 Distinguishing characteristics of bleeding disorders

Acquired	Hereditary
Negative family history	≥1 family member affected
Presence of associated diseases	Hereditary pattern
Variable in time	Fixed pattern of bleeding
Variable in aspect and type	History of blood transfusion
Onset in middle age or later	Early onset

Adapted with permission of John Wiley and Sons from Girolami et al. [3]

Table 25.2 Differential diagnosis based on physical findings

Cutaneous	
Purpura	Coagulation disorders, cryoglobulinemia, steroids vasculitis, Henoch–Schonlein, systemic infection
Petechiae	Thrombocytopenia
Ecchymosis	Thrombocytopenia, steroids, senile, trauma
Mucosal	Osler-weber-Rendu, von Willebrand's
Hematomas	Coagulation factor deficiencies
	Circulating anticoagulants
	Trauma
Hemarthrosis	Hemophilias
	Factor II, VII, X deficiencies

conceptualized as primary (platelet related) or secondary (coagulation factors), and its investigation can be developed according to these distinctions.

Hemostasis

When a blood vessel is damaged, hemostasis is activated in order to arrest bleeding. The process has three phases:

1. Vascular phase: involves a transient, localized vasoconstrictor response in the damaged blood vessel thus stopping the flow of blood.
2. Platelet phase: damaged endothelial cells release von Willebrand's factor resulting in "sticky" endothelial cells, a process known as platelet *adhesion*. Platelets that adhere to the blood vessel wall in this manner secrete adenosine diphosphate (ADP), a chemical that causes nearby free platelets to attach to each other and to those already fixed to the vessel wall, thereby forming a platelet plug. This "clumping" phenomenon served a number of important functions: the plug may seal the defect in the vessel wall; aggregated platelets release platelet thromboplastin (Factor III) which activates the clotting process; further the clumped platelets secrete thromboxane, a potent vasoconstrictor.
3. Coagulation phase (Fig. 25.1): begins within minutes of the initiation of the vascular and platelet phases and involves the formation of insoluble protein fibrin (from fibrinogen via the action of the enzyme thrombin). Once formed, fibrin produces a network of fibers that traps blood cells and platelets, thereby forming the clot. This process depends on the presence of 11 different clotting factors and calcium, all of which are required to generate the production of prothrombin activator (Factor X). Two distinct pathways with different triggers may be activated.

   The extrinsic pathway is initiated by tissue thromboplastin (Factor III) which is released by injured tissue, hence "outside" (extrinsic) the blood. The process is rapid and provides a shortcut to the clotting process. The resultant clot is small is considered a "quick patch." Alternatively, there is the second intrinsic pathway which is initiated when the blood itself comes in contact with the exposed collagen of the damaged blood vessel. Although a slower (5–10 min) process, it results in the formation of much larger amounts of thrombin and thus more robust clots. This process involves the sequential activation of multiple clotting factors: Factor XI, activated by contact with the exposed endothelium, activates IX leading to the production of Factor VIII which, when coupled with calcium and Factor II (derived from platelets), ultimately activates Factor X (prothrombin activator). This is the point in the hemostatic process where the two pathways converge: a composite of clotting factors (Factor V, Ca^{2+}, and platelet-derived phospholipids) engage Factor X creating the Factor V Complex which initiates the conversion of prothrombin to the active enzyme thrombin which completes the cascade by accelerating the formation of fibrin thread from fibrinogen (Factor I).
4. Clot retraction: this process occurs several days later mediated by contractile proteins contained in the platelets pulling the edges of the wound together and assisting in the reparative process.
5. Fibrinolysis: this refers to the dissolution of the clot a process driven by the proteolytic enzyme plasmin.

Evaluation and Approach of Primary Hemostasis: Platelet Deficiency

The assessment of primary hemostasis focuses on the platelet. While the platelet count is a dependable test, it does not provide information concerning platelet function and thus is not a sufficient assessment of the bleeding risk attributable to platelet-mediated problems. The normal platelet count is in the 140,000–400,000/mm^3, although bleeding problems do not occur until substantial reductions are reached (i.e., <50,000/mm^3). However, there is one important caveat. Anesthesiologists require higher platelet counts (at least 70,000/mm^3) in order to employ neuraxial blockage, an important consideration in the orthopedic setting where such techniques are often employed. Indeed, the American Society of Regional Anesthesia (ASRA) has published recommendations (Box 25.2) concerning such blocks in order to reduce the risk of paraspinal hematomas which can lead to serious neurologic sequelae [6].

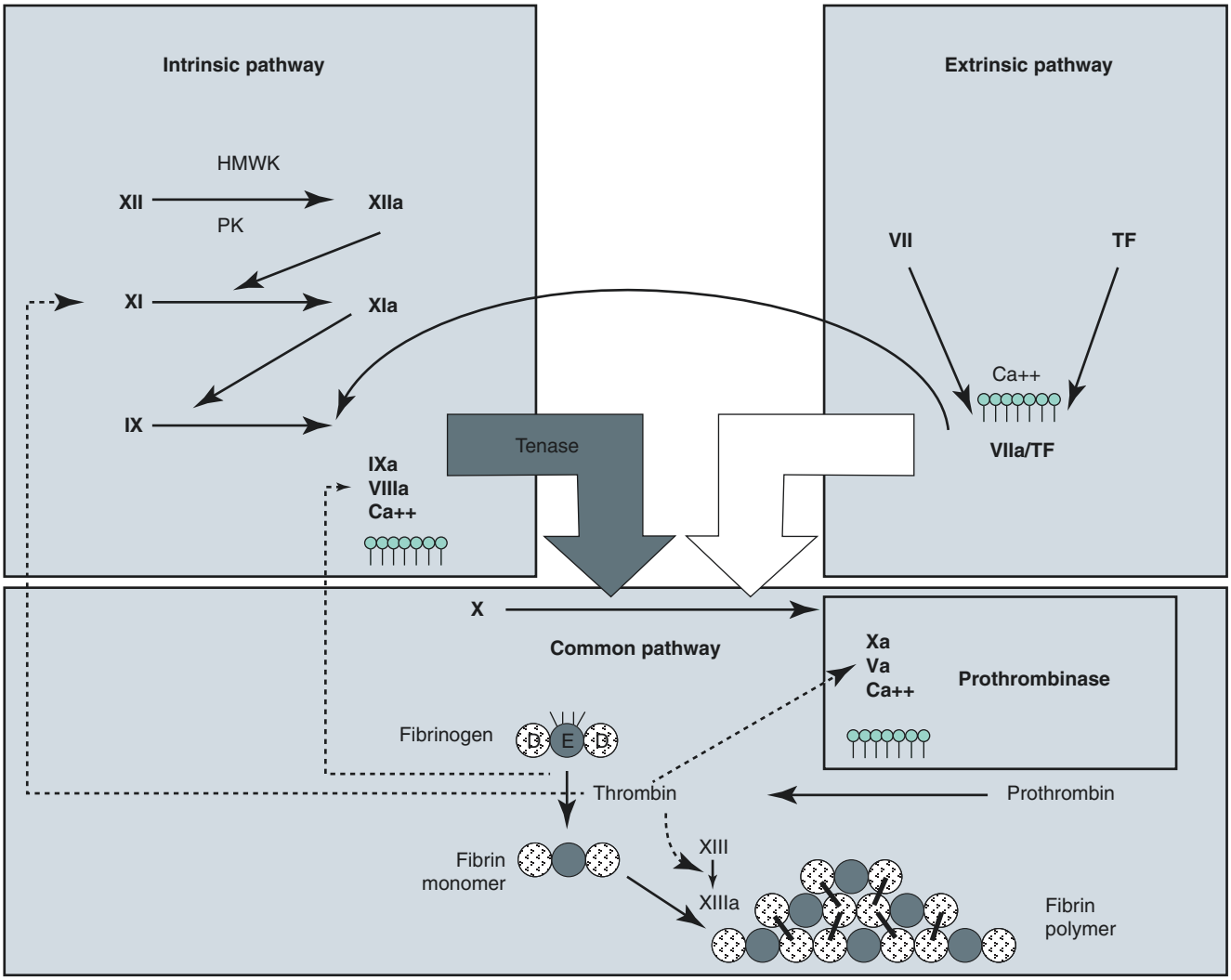

Fig. 25.1 Diagram of the coagulation cascade, depicting the intrinsic and extrinsic pathways of activation. The extrinsic pathway of activation is started with exposure of tissue factor (TF), coupled with Factor VIIa that leads to the activation of Factor X. The intrinsic pathway is started by the contact activation factors (Factor XII, high-molecular-weight kininogen (HMWK), and prekallikrein (PK)) with eventual activation of Factor X by the tenase complex (Factors IXa, VIIIa, calcium (Ca^{2+}), and phospholipid). Activated Factor X (Xa) participates in the prothrombinase complex (Factor Xa, Va, Ca^{2+}, phospholipids) for the conversion of prothrombin to thrombin, which converts fibrinogen to fibrin monomer. Fibrin then polymerizes and is cross-linked by Factor XIIIa. Further activation of coagulation is fostered by thrombin's activation of Factors V, VIII, and XI. (Used with permission of Springer Nature from Kottke-Marchant [13])

Box 25.2 ASRA Recommendations Concerning Neuraxial Blockade

- Coadministration of antiplatelet and anticoagulant medication is contraindicated with indwelling epidural catheters. Clopidogrel must be held for 7 days before neuraxial block
- Spinal or epidural anesthesia should occur at least 12 h after the last thromboprophylaxis dose of LMWH and at least 12 h after the last full dose of LMWH
- An epidural catheter should not be removed no sooner that 2 h after the last prophylactic dose of LMWH
- The first dose of LMWH should be administered no sooner that 2 h after the catheter is removed
- Delay LMWH administration if the patient experienced excessive trauma during attempted epidural or spinal anesthesia

Data from www.asra.com

The mechanisms of thrombocytopenia can be categorized broadly: impaired production, increased consumption, and redistribution/dilution (Box 25.3). In addition, pseudothrombocytopenia, a relatively common laboratory phenomenon occurring in approximately 1.9% of hospitalized patients [7, 8], results from the ethylenediaminetetraacetic acid or EDTA, a chelating agent used in blood collection tubes for CBC determinations. The in vitro agglutination of platelets produced by the EDTA results in low platelet counts but no bleeding tendency. Lastly, congenital thrombocytopenia represents a rare array of inherited disorders characterized by reduced platelet number and function.

Box 25.3 Etiology of Thrombocytopenia

- *Impaired platelet production*
- Congenital
- Acute leukemia, myelodysplasia
- Osteopetrosis
- Toxins (chemotherapy, alcohol)
- Infection (HIV)
- *Peripheral destruction*
- Autoimmune disease
  - Primary (idiopathic thrombocytopenia purpura, ITP)
  - Secondary
- Disseminated intravascular coagulation (DIC)
- Thrombotic thrombocytopenic purpura (TTP)
- Hemolytic-uremic syndrome
- *Redistribution and dilution*
- Massive transfusion
- Splenomegaly
- *Pseudothrombocytopenia*

Adapted with permission of Elsevier from Marcucci et al. [1]

Asymptomatic thrombocytopenia is often caused by the presence of antibodies to circulating platelets resulting in a condition known as idiopathic thrombocytopenic purpura (ITP) which typically arises from autoimmune platelet destruction. In contrast, secondary ITP may arise as autoimmune sequelae of viral infection (including hepatitis and HIV), connective tissue disease (including systemic lupus erythematosus (SLE) and rheumatoid arthritis), antiphospholipid antibody syndrome, and B-cell malignancies [3].

Medications are an important cause of thrombocytopenia and virtually any agent may be culpable. Heparin-induced thrombocytopenia (HIT) is caused by antibodies that bind to complexes of heparin and platelet Factor 4 (PF4), thereby activating platelets and leading to a prothrombic state. Serious thrombotic phenomena may occur in both the arterial and venous circulations resulting in loss of limb and life. Most patients have had prior heparin exposure since this is an amnestic response. More frequently associated with unfractionated heparin than with low-molecular-weight heparin, it should be suspected in patients who experience a drop of >50% in their platelet count within 5–10 days after the initiation of heparin therapy [9].

Due to their widespread use in the primary and secondary prevention of cardiac and cerebrovascular disease, the most common cause of qualitative platelet dysfunction in the perioperative setting is the use of antiplatelet agents. Aspirin (ASA) and thienopyridine agents (primarily clopidogrel) are among the most commonly employed. The former, ASA, irreversibly acetylates platelet cyclooxygenase-1 (COX-1) inhibiting thromboxane A_2 thus impairing platelet function (for the 7-day lifespan of the platelet). The more potent clopidogrel permanently inhibits platelet aggregation; the recovery time for its effect is also approximately 7 days although active metabolites potentiate its effect. The impact of ASA on bleeding risk in association with surgery appears mild and outweighed by its influence on graft patency in patients with known coronary artery and cerebrovascular disease. Further, the continuation of ASA in patients undergoing neuraxial block is not associated with bleeding risk [10]. The perioperative management of these agents is fully discussed in Chap. 13. Algorithms for the perioperative management of patients receiving antiplatelet agents have been published. One useful decision tree is shown in Fig. 25.2.

Lastly, another important disorder of platelet function occasionally encountered in the perioperative setting is *von Willebrand's disease* (*vWD*). Being the most common of the inherited bleeding disorders, its prevalence in the general population is approximately 1% [11]. The hallmark of this condition is a deficiency of von Willebrand factor which is important for platelet adhesion and aggregation. Patients typically present with mucosal bleeding including epistaxis. However, bleeding after surgery can be brisk. Diagnosis relies on measurement of von Willebrand factor antigen, ristocetin cofactor activity, and Factor VIII activity along with platelet function. Several subtypes exist ranging from quantitative deficiency in VWF antigen to qualitative reduction of VWF function. Treatment involves administration of desmopressin (DDAVP) which increases release of endogenous von Willebrand factor from the Weibel-Palade bodies in the endothelium. Purified plasma factor concentrates are necessary for more severe forms of the condition.

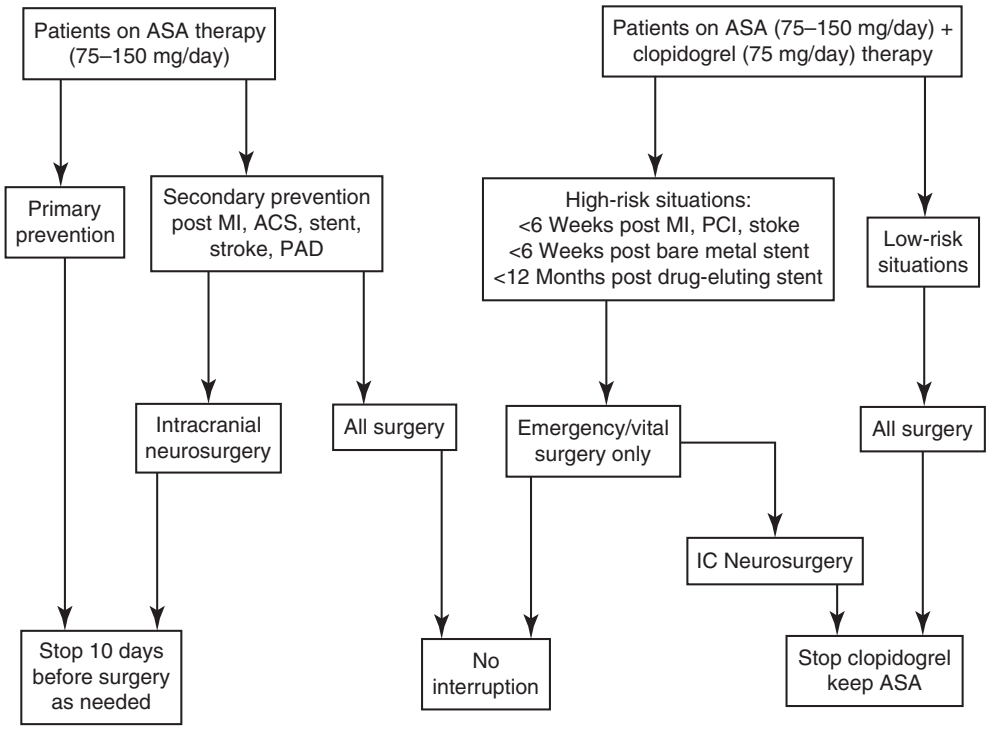

Fig. 25.2 Algorithm for patients receiving antiplatelet agents. *ASC* acute coronary syndrome, *ASA* acetylsalicylic acid, *IC* intracranial, *MI* myocardial infarction, *PAD* peripheral arterial disease, *PCI* percutaneous coronary intervention. (Used with permission of Elsevier from Marcucci et al [1])

Evaluation and Approach to Secondary Hemostasis: Clotting Factor Deficiency

The prothrombin time (PT) and partial thromboplastin time (aPTT) are the most commonly employed tests of secondary hemostasis preoperatively in spite of a prodigious literature demonstrating their poor predictive value for the development of postoperative bleeding [3] in the absence of a concerning history. As implied by the Koscielny algorithm, an unsuspected bleeding diathesis is unlikely to be discovered by such testing preoperatively in patients with a negative bleeding history [4, 5]. In this extensive study, none of the commonly employed screening studies (platelet count, PT, aPTT) identified a single patient without a suspicion of a preexisting bleeding problem based on their history. Further, with respect to the aPTT specifically, the prolongation of this parameter is a fairly common circumstance resulting from either a mild Factor XII deficiency or the presence of a lupus anticoagulant. In the Koscielny study, all patients with this laboratory abnormality (and negative bleeding history) were found to have of a lupus inhibitor. A phenomenon known to increase the risk of thrombosis not the risk of bleeding, the lupus anticoagulant is relatively common and found in 1.2–3.8% of healthy individuals, although its incidence increases with age and chronic disease, most significantly in patients with systemic lupus erythematosus [12].

The hemophilias are important hereditary disorders of coagulation. Hemophilia A (Factor VIII deficiency) and hemophilia B (Factor IX deficiency) are both X-linked and manifest early in life. Due to their propensity for intra-articular hemorrhage and ultimately joint destruction, these conditions have been relevant to the orthopedist. Modern clotting factor replacement therapy has significantly mitigated the chronic joint destruction formerly experienced by these patients. Treatment paradigms for the perioperative management of these conditions are well established and involve factor replacement via a continuous infusion pump to keep pace with consumption. Hemophilia C (Factor XI deficiency) is autosomal and prevalent among Ashkenazi Jews (its incidence outside that population is about 1 per one million). The condition typically causes delayed postoperative bleeding since Factor XI can be important for clot stabilization. Treatment involves transfusion of fresh frozen plasma since Factor XI concentrates are not routinely available.

Other specific clotting factor deficiencies do exist. In those rare patients, the risk of surgery-related bleeding may be significantly increased. Deficiencies of Factors I (fibrinogen), II, V, VII, and XII are well known to hematologists. Factor VII deficiency is the only hereditary clotting factor deficiency with a prolonged PT and normal aPTT. Factor XII (Hageman) deficiency results in an elevated aPTT but not a bleeding diathesis. Rather, such patients experience thromboembolic phenomenon.

One of the more common acquired coagulopathies is vitamin K deficiency which results in decreased synthesis of Factors II, VII, IX, and X. Typically seen with malnutrition (including fasting), hospitalization, and antibiotic use, vitamin K deficiency can result in prolongation of the PT and the

aPTT. Oral repletion is sufficient although parenteral administration is more effective in patients with ileus and malabsorption. Intravenous vitamin K can result in anaphylaxis and thrombosis.

Specific Chronic Diseases

The contributions of kidney and liver disease should not be overlooked in the peri-operative orthopedic setting.

Patients with chronic renal failure (including end-stage renal disease) have qualitative platelet dysfunction which results from the uremic state. Platelet transfusions have limited utility. Dialysis may be appropriate in certain settings along with the administration of DDAVP. Estrogens mitigate uremic thrombocytopathy but potentiate thrombosis as well and present a risk to orthopedic patients.

In contrast, patients with chronic hepatic failure have clotting factor deficiency and portal venous insufficiency which contribute to increased bleeding risk. All of the clotting factors are synthesized by the liver, except for Factor VIII. Liver impairment results in a coagulopathy typically identified by a prolonged prothrombin time (PT), although the aPTT can be prolonged as well. Vitamin K may be helpful in those patients who are also malnourished. However, most patients require repletion of clotting factors with fresh frozen plasma (FFP) or specific factor concentrates. Large dosages of FFP are often required; near normalization of the PT is the desired outcome.

Summary

In conclusion, problems of coagulation are important considerations to the orthopedic surgeon, to the anesthesiologist, and particularly to the medical consultant who serves as the first line of defense in the recognition of such conditions. Suspicions concerning their presence can generally be gleaned from the patient's history though a general understanding of the processes underlying normal hemostasis is also necessary and forms the basis upon which a logical approach to the detection, characterization, and treatment of these conditions is formulated.

Summary Bullet Points

- Coagulation problems are among the surgeons' most feared complications of surgery.
- The presence of disordered coagulation can be determined with a targeted medical history.
- Available preoperative laboratory assessments of coagulation do not predict postoperative bleeding complications and should be deemphasized in practice.
- Disordered coagulation can be divided into primary and secondary forms.
- Diseases of the kidney and liver contribute significantly to the risk of postoperative bleeding.

Case Study

The patient is a 78-year-old man with osteoarthritis who is scheduled to undergo total knee replacement surgery. He notes easy bruising with minimal trauma which he attributes to aspirin that he takes daily for coronary artery disease. On further probing, the patient states that he had an episode of brisk gastrointestinal bleeding which required double-balloon enteroscopy with clipping. In addition, he bled for days following a vascular procedure requiring transfusion and transfer to a tertiary care facility.

Preoperative laboratory testing demonstrated a normal platelet count with normal creatinine and hepatic function. The prothrombin time was prolonged at 13.9 seconds with a normal APTT and fibrinogen. The patient was referred to hematology for additional evaluation.

The PT corrected with mixing suggesting a factor deficiency. Factor II activity was reduced at 52% (the lower limit of normal was 79%.) The remaining clotting factors were within normal limits except for Factor VIII activity which was increased at 160%.

The patient received fresh frozen plasma preoperatively and again on the first postoperative day. Surgery was accomplished successfully without significant bleeding complications. Low-dose warfarin was employed as pharmacologic VTE prophylaxis and was titrated carefully to an INR of approximately 2.

This case illustrates the importance of the bleeding history, establishing the need for additional testing. Likewise, it demonstrates the role of a laboratory evaluation when appropriate and the impact that it can have on management.

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Perioperative Nutrition in the Orthopedic Surgical Patient

26

Barbara J. Chin

Objectives

- Recognize the role of nutrition in orthopedic surgical patients
  - Optimizing preoperative nutrition status
  - Importance of early feeding postoperatively
  - Nutrition during recovery
- Understand how undernutrition and malnutrition affects orthopedic surgery
- Understand how diabetes mellitus affects orthopedic surgery
- Understand how obesity affects orthopedic surgery
  - Role of weight reduction prior to orthopedic surgery
- Recognize nutrition-related complications to surgery

Key Points

- Surgery of any kind creates a metabolic stress and shifts the body into a catabolic state. The goal of nutrition before, during, and after surgery is to optimize a patient's nutrition status to minimize catabolism and promote anabolism and healing.
- Orthopedic patients should be referred to a registered dietitian as early as possible if they are suspected to be malnourished, be undernourished, be obese, have uncontrolled diabetes mellitus, or have any other conditions that may compromise recovery from surgery.
- Enhanced Recovery After Surgery (ERAS) protocols that include minimal time NPO prior to surgery, carbohydrate-loading with a carbohydrate beverage consumed up to 2 hours before surgery, and early feeding postoperatively can minimize the postoperative catabolic state and promote recovery.
- Malnourished and undernourished patients are at particularly increased risk of postoperative complications, infection, poor wound healing, and longer hospital stay. Such patients require intensive nutrition intervention to improve nutrition status for improved post-surgical outcomes.
- Identifying malnutrition should be done using the established criteria for malnutrition diagnosis that includes weight loss, energy intake, subcutaneous fat depletion, muscle mass depletion, fluid accumulation, and functional assessment. Traditional use of serum markers for malnutrition such as albumin, prealbumin, transferrin, and total lymphocyte count are unreliable indicators of malnutrition.
- Obesity creates a low-grade inflammatory state, comorbid conditions, and technical challenges in the operating room that can increase risk for postoperative infection, complications, and readmission.
- Patients with diabetes mellitus as well as patients with hyperglycemia and glycemic variability even without prior diagnosis of diabetes mellitus are at increased risk for postoperative complications and poorer outcomes. Improving glycemic control before and after surgery is key to decreasing these risks.
- Early feeding after surgery, minimizing use of narcotic medications, and careful administration of intravenous fluids can help reduce the risk of postoperative ileus.

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- Adequate nutrition and fluids can help reduce the risk of skin breakdown. Patients with compromised skin integrity require additional calories, protein, fluids, and key micronutrients to support wound healing.
- Enteral and, when feeding through the gut is not feasible, parenteral nutrition support is sometimes crucial to help patients meet nutritional needs when they are unable to do so on their own by mouth.

Introduction

Nutrition plays a key role in the success and overall health of the patient undergoing orthopedic surgery. Because of the metabolic changes as a result of surgery, patients should be encouraged and allowed to optimize their nutrition status in the preoperative, perioperative, and postoperative periods. This will aid in wound healing, promote return to normal mobility and function, prevent losses in lean body mass, maintain immune function, and minimize the risk of complications after surgery.

Surgery of any kind is a trauma to the body. Regardless of the type of procedure, both endocrine and inflammatory systems are involved in the stress response [1]. The hypothalamic-pituitary-adrenal (HPA) axis is activated, increasing the secretion of cortisol, epinephrine, glucagon, growth hormone, aldosterone, and antidiuretic hormone. Cytokines mediate the inflammatory response and further stimulates the HPA axis. As a result, metabolic changes occur, creating a catabolic state [2]:

- Hepatic glucose production increases along with diminished insulin sensitivity, leading to hyperglycemia and insulin resistance.
- Amino acids are mobilized from the breakdown of skeletal muscles and other tissues for gluconeogenesis and acute phase proteins.
- Fat in adipose tissue is broken down to provide substrates for gluconeogenesis, ketone bodies, or energy.

The degree to which these changes occur is dependent on the degree of surgical trauma. The more invasive the procedure, the more drastic and prolonged the metabolic derangements. Insulin resistance and elevated protein turnover can last for several weeks or up to several months after surgery [2].

Nutrition management can mitigate the negative effects of the above metabolic changes. Patients should be adequately nourished to maximize nutrient reserves prior to surgery. However, overnutrition resulting in obesity can increase the risk of poorer outcomes after surgery, so clinicians should encourage patients to maintain a healthy weight. Appropriate feeding immediately before and after surgery should occur to help blunt the catabolic state and promote optimal wound healing.

This chapter will detail the importance of nutrition for patients undergoing orthopedic surgery, with particular focus on specific nutrition interventions to maximize the potential for success and minimize the risk of complications that can be modified by nutrition status.

Preoperative Nutrition

The time leading up to surgery is a key time to optimize the patient's nutrition status. As suggested in the previous section, surgery can be a major insult to the body's homeostasis. Ensuring adequate nutrient reserves beforehand is essential to withstanding the metabolic changes.

The patient's nutrition status should be evaluated prior to scheduling surgery. Patients of all weight classes (underweight, overweight, and normal weight) should be assessed for possible malnutrition, as poorly nourished patients regardless of weight have been found to be at greater risk for adverse outcomes after surgery [3]. Indications for further evaluation include insufficient oral intake, unintentional weight loss, and low BMI < 18.5. Obese patients may have better postoperative outcomes following a weight loss program prior to surgery than without weight loss. Patients with diabetes mellitus (DM) but better glycemic control may have lower risk of complications than those with poor glycemic control.

Physicians who are concerned about their patient's nutritional status should refer the patient to a registered dietitian (RD) for nutrition counseling, ideally with enough time prior to surgery to achieve realistic nutritional goals and for stabilizing metabolic abnormalities. In some cases, delay of surgery may be necessary to ensure the best outcomes.

After assessment by the RD, appropriate interventions can be implemented for nutritional optimization. Patients who are malnourished or at high risk for malnutrition may additionally benefit from high-protein oral nutritional supplements (ONS) if they are not capable to consuming adequate nutrients through food alone. Severely malnourished patients may require enteral or parenteral nutrition support.

Traditional preoperative preparation included making the patient "nil per os" (NPO) after midnight prior to surgery, as a result of concerns for aspiration while under anesthesia. This effectively places the patient in a fasted state during the procedure. Glycogen stores are depleted and lean body mass is broken down during surgery to keep up with energy needs. However, research has prompted a change in guidelines to allow the patient to eat up to 6 hours prior to surgery and to drink clear liquids up to 2 hours before surgery [4]. Studies show no increased risk of pulmonary complications with this protocol [5].

Some patients may not be identified as high nutrition risk until after admission for surgery. The Joint Commission requires that all accredited institutions screen patients for malnutrition risk within 24 hours of admission. Many screening tools have been validated for various hospital populations, and screening criteria are often used to stratify patients to nutrition risk levels, dictating when a full nutrition assessment should be done by an RD. Assessments are performed to determine what, if any, nutritional interventions are needed for the postoperative period.

Enhanced Recovery after Surgery (ERAS)

Many institutions have adopted Enhanced Recovery After Surgery (ERAS) protocols for improving patient outcomes. ERAS protocols encompass multiple interventions involving various disciplines participating in surgical care. The aim of ERAS protocols is to maintain physiologic and metabolic processes as close to normal as possible, which can allow for shorter recovery time as compared to conventional care protocols. ERAS has been shown to decrease hospital length of stay, incidence of postoperative complications, improved return to normal function, and improved quality of life outcomes [6].

A key component of ERAS protocols is preoperative carbohydrate loading with an iso-osmolar carbohydrate beverage that the patient drinks up to 2 hours before the operation. This has been shown to improve insulin resistance, reduce hospital length of stay, and preserve lean muscle mass in the postoperative period [5]. Additionally, it improves the patient's comfort by reducing hunger, thirst, and anxiety.

Other elements of ERAS may include the following: improving physical fitness and patient education prior to surgery; administering preoperative antibiotic/antacid/prokinetic agents; selective use of nasogastric tubes for decompression, urinary catheterization, and abdominal drainage during surgery; maintaining normothermia during surgery; ensuring adequate hydration during surgery; minimizing operative time and invasiveness; pre-emptive analgesia and prophylaxis against postoperative nausea and vomiting; early removal of drains and tubes postoperatively if used; early ambulation; and early enteral feeding.

Early Feeding Postoperatively

Minimizing NPO Status

While many of the components of ERAS protocols are not directly related to nutrition, they help facilitate early enteral feeding. Traditional protocols maintained NPO status until the return of bowel sounds or passing of flatus or stools; however, this has been shown to be unnecessary and has insufficient scientific evidence for any benefits [4]. Prolonged gut starvation diminishes hepatic and peritoneal immune function. Prolonged NPO status can also physically compromise the gastrointestinal tract. Blunting of the intestinal villi and increased mucosal permeability results in decreased immune function and potential for bacterial translocation and bacteremia [5]. Additionally, healthy and intact gut-associated lymphoid tissue (GALT) is key to both innate and adaptive immunity, so minimizing starvation is important for overall immune function [5].

Earlier enteral feeding has been shown to reduce the incidence of postoperative ileus, improve postoperative insulin resistance, improve patient quality of life, decrease hospital length of stay, and reduce morbidity and mortality after surgery [6]. ERAS protocols can assist in promoting enteral feeding earlier with prophylaxis against postoperative nausea and vomiting, epidural analgesia, and minimizing use of tubes, drains, and catheters [6].

Diet Progression

In traditional postoperative protocols, patients would be fed only clear liquids or ice chips and gradually progressed as tolerated to full liquids, soft lower fiber foods, and finally a regular diet. This was due to concerns regarding poor tolerance while awaiting the return of bowel function. However, there is no evidence supporting the benefit of initiating postoperative feeding with clear liquids compared to a regular diet [7]. Further, starting patients on a regular diet postoperatively provides more nutrients and calories that are needed compared to clear liquids, which typically only provides carbohydrates and little to no protein and fat.

Providing early nutrition via the enteral route helps maintain structural integrity of the gut mucosa, promotes intestinal motility, prevents bacterial overgrowth, and maintains the immunological functions of the gut [2]. It also maintains insulin sensitivity and blunts insulin resistance [2], which will allow better nutrient uptake.

Adequate Postoperative Nutrition

Postoperative nausea and vomiting occurs in 25–30% of patients and results from a combination of surgical, anesthetic, pharmacologic (especially narcotic analgesia), and preexisting comorbid factors [7]. Nausea and vomiting can reduce appetite following surgery, therefore reducing oral intake. Such patients may benefit from alternative strategies that include working with inpatient dietitians to select nutrient-dense foods, adding snacks, or oral nutritional supplements. The goal for these patients is to increase calorie and protein intake beyond what they are able to get otherwise.

Protein and calorie needs after surgery are greater than those during the non-hospitalized period. Adequate protein and calorie intake postoperatively is essential for anabolism, reversing catabolism, and wound healing. However, calories without sufficient protein cannot achieve this outcome and results in loss of lean muscle mass. Conversely, adequate protein intake – regardless of adequate calorie intake – can maintain lean muscle mass in the short term [2].

Determining how much protein a surgical patient needs is not straightforward, however. Most studies recommend 1.2–2.0 grams of protein per kg body weight per day [2], but precise amount depends on various factors such as patient's age, weight status, comorbid conditions, and type of surgery undergone. (In comparison, protein needs of the non-hospitalized individual are 0.8–1 gram of protein per kg body weight per day.) Similarly, calorie needs vary from person to person and may depend on many factors including age, gender, body composition, severity of surgery, nutritional status preoperatively, medications, comorbid conditions, and degree of mobility following surgery. Calorie needs may be increased by a factor of 1.0–1.2 for minor surgery, 1.1–1.4 for major surgery, 1.2–1.4 for trauma, or up to 1.6–1.8 for extensive surgery/trauma or critical illness [8]. Working with a registered dietitian can be helpful in meal planning strategies (that may include high-calorie ad/or high-protein oral nutritional supplements) to achieve the necessary protein and calorie intake.

For the small subset of patients who have certain comorbidities or who develop complications that prevent adequate oral intake to meet postoperative estimated nutritional needs, nutrition support may be necessary.

Undernutrition and Malnutrition

Nutrition status before and after surgery plays an important role in how well a patient recovers. For a variety of reasons, patients may not be able to consume adequate nutrition, and they may become at risk for malnutrition. While there have been a variety of methods to identify malnutrition or poor nutrition status, undernutrition is strongly correlated to higher incidence of complications following total joint arthroplasty (TJA) and spine surgery. Such events include surgical site infection, prosthetic joint infection, persistent wound drainage, need for additional surgery, and development of deep infection [9].

Low body mass index (BMI) is often a consequence of undernutrition and malnutrition, but is not a criterion for diagnosing malnutrition. Many patients with low BMI may be adequately nourished and nutritionally stable. Regardless, many studies show that underweight status is correlated with increased risk of infections, readmissions, and other postsurgical complications. In a review by Valentijn and associates, underweight patients (BMI < 18.5) have the highest postoperative morbidity and mortality hazard (along with the morbidly obese with BMI 40 or greater) when compared to patients in other BMI classifications [10]. Of note, however, this review did not particularly focus on orthopedic populations. Manrique and colleagues showed that underweight patients undergoing total knee arthroplasty (TKA) were more likely to develop surgical site infections and to require blood transfusions [11]. Saucedo and associates found that BMI < 18.5 was an independent risk factor for readmission within 90 days after total hip arthroplasty (THA) [12]. And while Anoushiravani and colleagues did not find that underweight TKA patients were at an increased risk for postoperative infection, they did find that underweight patients undergoing THA were at higher risk for longer hospital length of stay and use of hospital resources, while underweight TKA patients were more likely to have greater use of hospital resources and discharge to a rehabilitation facility rather than home [13].

It is also important to note that overweight and obese individuals may have malnutrition. It should not be assumed that such patients have "adequate stores" to protect against malnutrition. Perhaps owing to the fact that obese patients tend to overconsume calorie-dense foods with low nutritional value, Huang and colleagues found that malnourished obese patients had a significantly higher incidence of complications compared to obese patients without malnutrition [14]. This suggests that it is crucial to evaluate obese patients for malnutrition and implement appropriate interventions to improve their nutritional status before scheduling surgery.

As poorly nourished patients are at greater risk for adverse outcomes postoperatively, it is in the best interest to have an undernourished patient work with a registered dietitian prior to surgery. Improvement in nutrition status may take time and ongoing nutritional intervention. This may necessitate delaying surgery until the patient's nutritional status is stabilized. Severely malnourished patients may require enteral or parenteral nutrition support if they are unable to consume adequate nutrients by mouth.

Identifying Malnutrition

Historically, a wide variety of methods have been used to screen for and identify patients with poor nutrition status and malnutrition. It is still widely accepted in most research studies and institutions to use serum markers such as albumin, prealbumin, and transferrin to assess for malnutrition, as these are objective and easily obtained measurements. Many studies have identified low levels of these serum markers are correlated with increased risk of infection and other postoperative complications. However, while many of these patients may indeed have been malnourished, these serum markers more accurately indicate the severity of illness rather than nutrition status [15].

Albumin is a negative acute-phase protein and levels can be affected by inflammatory conditions and medications that affect liver function [16]. Malignancy, acute infection, organ failure, and surgery are examples of conditions that trigger an inflammatory state that negatively affects serum albumin levels regardless of nutritional state. Additionally, hydrostatic and oncotic pressure changes can also falsely elevate or decrease serum albumin levels.

Prealbumin has a shorter half-life than albumin (2–3 days vs. 14–20 days, respectively) and has a smaller total body pool, which would in theory make it a better indicator to nutritional status changes. However, prealbumin is also a negative acute-phase protein produced in the liver, so it is subject to the same limitations as albumin [16]. Additionally, prealbumin is degraded by the kidneys, so its levels may be falsely elevated with kidney disease [16].

Furthermore, both albumin and prealbumin are not necessarily sensitive to non-inflammatory malnutrition states such as starvation. In a systematic review by Lee and colleagues, serum albumin and prealbumin levels did not decrease in starved patients until they had reached an extreme degree where starvation was already obvious [17]. This suggests that albumin and prealbumin are not reliable to detect malnutrition when the patient is not in an inflammatory state.

Transferrin is another protein that is predominantly produced in the liver and is a negative acute-phase protein. While transferrin levels have been shown to decrease in protein-energy malnutrition, it is also affected by inflammation and liver function like albumin and prealbumin regardless of nutritional status. In addition, due to its role in iron transport, transferrin levels increase in iron-deficiency states to increase iron absorption and are downregulated when there is iron overload.

Finally, total lymphocyte count (TLC) is another frequently used serum marker for malnutrition. However, studies have not been able to demonstrate that TLC is a reliable marker for malnutrition particularly in the elderly population [18].

Rather than identify malnutrition using unreliable serum markers, the Academy of Nutrition and Dietetics (AND) and the American Society for Parenteral and Enteral Nutrition (ASPEN) released a consensus statement in 2009 on methods for identifying adult malnutrition. In 2014, a similar consensus statement was released on identifying pediatric malnutrition. Both recognized a need for standardizing the process of assessing for malnutrition using evidence-based methods.

To meet the criteria for adult malnutrition, a patient must meet at least two of the following criteria [19]:

- Inadequate oral intake to meet estimated nutritional needs
- Significant weight loss
- Loss of muscle mass
- Loss of subcutaneous fat
- Localized or generalized fluid accumulation that may mask weight loss
- Diminished functional status as measured by hand-grip strength

The diagnosis of pediatric malnutrition is different from that of adults and relies on the determination of z scores for criteria [20]. Only one criterion is required for diagnosis of pediatric malnutrition.

- Weight-for-height z score
- BMI-for-age z score
- Length-for-height z score
- Mid-upper arm circumference z score
- Weight gain velocity (for <2 years of age)
- Weight loss (for 2–20 years of age)
- Deceleration in weight-for-length/height z score
- Inadequate nutrient (energy or protein) intake

Diagnosis of malnutrition may occur either prior to surgery or during the postoperative period. Upon identification, a nutrition care plan (NCP) should be developed with a nutrition professional. A thorough assessment, nutritional diagnosis, intervention, and protocol for monitoring and evaluation will ensure that the patient receives the appropriate nutrition care to correct malnutrition. This may include the addition of protein- and/or calorie-dense foods, oral nutritional supplements, micronutrient supplementation, enteral nutrition support, or parenteral nutrition support.

Even if a patient does not meet criteria for malnutrition but has exhibited signs of diminished nutritional status, they are at high risk for developing malnutrition and will equally benefit from nutritional intervention with a registered dietitian.

Obesity

On the opposite end being underweight, patients who are obese (particularly with BMI 40 or greater) also exhibit greater risks of complications following orthopedic surgery. It should be noted that the use of BMI as a measurement of overweight/obesity has its limitations as it does not differentiate weight from adipose tissues vs. lean body mass. However, it remains the most widely used classification system at this time.

Obesity is not just a matter of excess adipose tissue leading to increased weight. Adipose tissue has been found to be more than just passive storage cells for lipids as a result of excessive energy intake. Fat accumulation in adipocytes leads to the production and release of various peptides that influence appetite, energy expenditure, immunity, and inflammation [21]. The adipocytes in obese individuals produce cytokines and adipokines (peptides with cytokine-like

properties) that act locally and systemically. They promote a low-grade pro-inflammatory state, production of reactive oxygen species, and insulin resistance. Plasma levels of cytokines such as TNF-a, IL-6, and CRP in obese individuals are elevated, and those levels appear to increase and decrease in correlation with weight gain or weight loss, respectively [21]. This low-grade inflammatory state with increased likelihood of insulin resistance leads to greater challenges with obese surgical patients compared to the non-obese.

There currently is controversy in the literature regarding the efficacy and safety of orthopedic surgery in the obese population. It is difficult to separate the apparent higher rates of complications and decreased functional improvement as a result of obesity itself vs. the comorbid conditions that often accompany obesity. Regardless, greater body weight is associated with the development of osteoarthritis and an increased need for total joint arthroplasty [22, 23]. Interestingly, Ledford and colleagues found that increased body fat percentage was a better predictor for complications and postoperative function, while BMI and lower limb weight were not [24]. So, it may be more clinically relevant to assess percent body fat rather than BMI as risk for surgery.

Obesity due to excessive adipose tissue presents several unique challenges for surgery that are less common in the non-obese population. From a technical standpoint, airway management (especially with increased incidence of OSA and asthma), positioning on the operating table, and venous access are more challenging in patients who are obese [25]. Greater volume of tissue can result in larger incisions, higher volumes of blood loss, and longer operating time, which can increase the risk of infection [26]. Longer surgical time can also increase the risk of venous thromboembolism (VTE), which is already increased in the obese population vs. the non-obese [25].

The literature is inconsistent regarding outcomes following total joint arthroplasty (TJA) in the obese population; however, it is generally accepted that obesity increases the risk of postoperative complications and adverse events, and greater increase in risk appears correlate with increase in BMI. Irrespective of type of surgery, Valentijn and colleagues found that, like underweight patients, obese class III patients (BMI 40 or greater) have some of the highest risks for postoperative morbidity and mortality that even persist long term [10]. Pozzobon and coworkers performed a meta-analysis of cohort studies and determined that preoperative obesity (BMI 30 or greater) is associated with worse clinical outcomes of hip or knee arthroplasty with respect to pain, functional improvement, and complications compared to those who were non-obese (BMI < 30) [27].

Obese patients have increased risk of surgical site infections and wound dehiscence compared to non-obese patients. This is likely due to a greater degree of hypoperfusion/ischemia, dysregulated immune and inflammatory responses, and impaired vascular delivery of antibiotics in tissues [25]. Comorbid conditions such as diabetes, anxiety, and depression can further impair wound healing due to compromised circulation or immune response.

Obese patients tend to have similar functional improvement following TJA compared to non-obese patients, but with BMI over 40, functional improvement appears to diminish and/or is more gradual [28]. Arsoy and coworkers found that super obese (BMI 50 or greater) had an even higher (sixfold) risk of postoperative complications after THA and threefold higher risk of severe complications [29]. The increased risk of complications in patients with BMI over 40 may outweigh the functional benefits of TJA, especially if they have comorbid conditions [28]. Such patients may benefit from delaying surgery.

The effect of obesity appears to be similar in spine surgeries. Obesity (BMI 30 or greater) appears to be an independent risk factor for readmission within 30 days of discharge following elective spine surgery [30]. Additionally, Obese III (BMI 40 or greater) patients have increased complication rates for lumbar spine surgery, but this association is not consistently seen for anterior or posterior cervical fusion procedures [31].

Weight Loss Intervention

Obesity and many of its associated comorbid conditions are often modifiable. Many surgeons recommend weight loss for obese patients prior to performing surgery to decrease some of the surgical risks outlined above. However, the degree of benefit of preoperative weight loss has yet to be determined. In a systematic review by Lui and coworkers, weight loss of 5% or more in the year prior to TJA and maintained in the year after surgery was associated with greater risk of deep surgical site infection in THA patients and 90-day readmission in TKA patients, as compared to control groups whose weight remained the same during the study period [32]. They concluded that, at the time of writing, there was insufficient evidence to support the recommendation that patients who are obese should lose weight (5% or more) within the year prior to either total hip or total knee arthroplasty. However, this review did not identify the type of weight loss methods used by these patients or whether outcomes were better if weight loss occurred >1 year prior to TJA. Similarly, Inacio and coworkers did not find any difference in risk of surgical site infection and readmission between THA and TKA patients who gained or lost weight compared to those whose weight remained the same [33].

Gandler and coworkers found in a pilot study that obese individuals (BMI > 30) who lost weight with a dietitian-guided weight reduction program had significant better physical health scores 1 year after TJA than their control group

receiving "usual care," but had no difference in pain or functional scores between groups [34]. They did, however, identify that patients who gained weight after the start of the study had worse pain and functional scores after TJA than those who maintained weight. It seems, therefore, important to at least prevent further weight gain in patients undergoing TJA.

Bariatric surgery is another weight loss option that some surgeons are recommending for their morbidly obese patients needing orthopedic surgery, especially those who have been unable to lose weight with diet and exercise. In general, bariatric surgery is usually indicated for individuals with BMI > 40, or BMI > 35 with obesity-related complications. On average, bariatric surgery results in an average of 10–15-point decrease in BMI and improvement in obesity-related comorbidities like type 2 diabetes mellitus, hypertension, and cardiovascular disease [35]. Some studies have shown that bariatric surgery prior to joint arthroplasty [36, 37] or spine surgery [35] results in fewer complications and infections.

However, other studies have demonstrated bariatric surgery prior to orthopedic surgery confers no benefit or perhaps even worse outcomes than obese patients who do not undergo bariatric surgery [38–44]. McLawhorn and coworkers found that bariatric surgery decreased comorbidity burden and both in-hospital and 90-day postoperative complications for TKA, but only reduced in-hospital complications for THA [45]. Meanwhile, in this study, bariatric surgery did not reduce the risk for need for revision surgery for either TKA or THA, nor did it reduce risk of dislocation following THA. Most studies, however, do point out that adverse events and complications overall were still quite low. Fournier and associates propose that malabsorption and poor nutrition following bariatric surgery that are responsible for these negative outcomes [38].

The lack of supporting evidence for the role of weight loss (either via bariatric or conventional means) prior to orthopedic surgery may be due to the fact that weight loss via hypocaloric diets results in a catabolic state, setting the stage for greater risk of infection and poor wound healing. Drastic weight loss via bariatric surgery in particular may create a malnourished state that can persist for at least 2 years following the procedure [42]. Currently, there have not been enough longer-term studies evaluating orthopedic surgery outcomes when bariatric surgery is performed more remotely in a patient's history.

While weight loss in and of itself may not necessarily be strongly correlated to a decrease in risk of complications in orthopedic surgery, slow and gradual weight loss that results reduces the severity of any comorbid conditions which may be beneficial. For example, greater BMI is correlated with incidence of cardiovascular disease, type 2 diabetes mellitus, and metabolic syndrome, which are comorbid conditions that increase the risk of complications postoperatively independent from BMI. Reducing severity or eliminating these comorbidities with or without gradual weight loss may help reduce the risk of these complications.

Referral of these patients to a registered dietitian for long-term counseling well before surgery is scheduled can help patients achieve and adhere to health-related behavior changes.

Diabetes Mellitus

The incidence of type 2 diabetes mellitus has increased over the last few decades, strongly correlated with the increase in rates of obesity. Diabetes mellitus (DM) is also often accompanied by comorbid conditions such as cardiovascular disease, kidney disease, and hypertension. These comorbidities play a role in the higher incidence of postoperative complications (need for transfusion, pneumonia, delayed discharge, surgical site infections, and in-hospital mortality) in surgical patients with DM compared to those without DM [46]. Indeed, elevated HbA1c over 7% and postoperative hyperglycemia >200 mg/dl are associated with higher rates of surgical site infection, and both pre- and postoperative hyperglycemia (but not HbA1c) are associated with periprosthetic infection.

Glycemic control, regardless of previous diagnosis of diabetes, seems to play a role in risk of postoperative complications. Hyperglycemia (blood glucose >140 mg/dl), hypoglycemia (<54 mg/dl), and excessive glucose variability are associated with worse postoperative outcomes, even in patients that have not have a past diagnosis of diabetes mellitus. The exact mechanism for this relationship is not well understood, although it has been shown that hyperglycemia impairs innate immunity, increasing the likelihood of infection [47]. Preoperative screening for dysglycemia, preparation and appropriate perioperative management, and postoperative glycemic control are important in reducing risk of poor surgical outcomes.

It is not uncommon for patients without a previous diagnosis of diabetes mellitus to be found to have an elevated HbA1c or hyperglycemia prior to scheduled surgery. Preoperative screening for undiagnosed diabetes and assessment of glycemic control in patients both with and without diabetes will allow time to optimize patients prior to surgery. While there is an established association between elevated HbA1c and postoperative complications, there is no strong consensus supporting a specific cutoff for HbA1c to recommend for surgery [46, 48]. As HbA1c appears to be a continuous variable in its relationship to postoperative complications, it should be used in conjunction with other factors in the patient's clinical picture.

Patients with suboptimal glycemic control leading up to surgery may need to work with a multidisciplinary team that can include the primary care doctor, an endocrinologist, and

a registered dietitian. Together, they can determine the appropriate medications and dietary patterns needed to improve the patient's blood sugar control to prepare for surgery.

In the perioperative period, glycemic management should focus on avoiding hypoglycemia, severe hyperglycemia, electrolyte imbalances, hyperosmolar hyperglycemic state, and diabetic ketoacidosis. Glucose testing is essential for monitoring glycemic control in the perioperative period. Blood sugar should be tested every 4–6 hours in patients who are not eating and at least prior to each meal once eating by mouth has resumed. Corrective insulin therapy is the standard method of glycemic management in inpatients, though specific strategies vary by site. Sliding scale insulin protocols are common in many institutions; however they are associated with higher rates of hyperglycemia than other regimens and do not necessarily provide improved glycemic control. Weight-based basal insulin with mealtime and correctional dosing with short-acting insulin offers lower rates of hyperglycemia without increased rates of hypoglycemia, although there is little evidence to show shorter length of stay or improvement in other patient outcomes [49].

Tight glycemic control (blood sugar of 80–110 mg/dl) is no longer a recommended practice as patients frequently suffered from hypoglycemia and a corresponding increased risk of mortality. Rather, *safe glycemic control* is now the recommended focus. The American Diabetes Association recommends insulin therapy be initiated for patients with persistent hyperglycemia (180 mg/dl or higher) and to maintain a serum glucose range of 140–180 mg/dl once on insulin therapy. A more stringent goal of 110–140 mg/dl may be used for select patients without hypoglycemia [50]. Working with an inpatient diabetes specialist may be helpful for patients admitted on existing insulin regimens or when postoperative blood glucose is difficult to control.

Most outpatient oral hypoglycemic agent (OHA) medications are typically discontinued prior to admission due to various contraindications during surgery or postoperative care, with the greatest concern for hypoglycemia in patients that are made NPO for surgery and that may not be eating their usual intake of food after surgery. Glucophage (metformin) is generally not administered in the inpatient setting due to the risk of lactic acidosis particularly in impaired renal function and when imaging contrast may induce renal dysfunction. Other non-insulin medications for DM (e.g., sitagliptin and other incretin-based therapies) may offer assistance in achieving glycemic control during the inpatient stay [49].

Nutrition-Related Complications

Postoperative Ileus

Postoperative ileus is not an uncommon complication following orthopedic surgery. It is defined as a "temporary cessation of propulsive contractions of the gastrointestinal tract, with subsequent gut dilation and accumulation of secretions and gas within its lumen" [51]. It is often accompanied by abdominal distension, bloating, nausea, emesis, and constipation. In rare severe cases, it can lead to bowel perforation and death.

There appears to be multiple factors involved in the development of postoperative ileus. The combination of decreased parasympathetic nervous system activity and increased sympathetic nervous system activity as a result of pain is one possible cause [51]. Excess fluid administration during and after surgery can lead to edema, resulting in delayed gastric emptying [52]. Opioid pain medications are also implicated in decreasing gastrointestinal motility. Electrolyte imbalance (hyponatremia, hypokalemia, and hypocalcemia) have also been associated with ileus and may contribute to gastrointestinal dysfunction [51].

Patients are typically downgraded to a clear liquid diet or made nil per os (NPO) following diagnosis of postoperative ileus (usually by abdominal x-ray or CT scan), especially when nausea and vomiting are present. In some cases, a nasogastric tube is used for decompression when gastric and bowel secretions have accumulated in in the intestinal tract. A gradual return to a regular diet is usually allowed when nausea and vomiting have subsided and the patient is able to pass flatus and move their bowels.

In some cases, ileus may persist for many days without resolution. For these patients who are already in a catabolic state following surgery, this prolonged period of inadequate nutrition can impair wound healing and immune function and increase risk for malnutrition.

Implementing ERAS protocols can help reduce the risk of postoperative ileus. Judicious fluid administration during and after surgery, minimizing use of narcotic medications, early feeding postoperatively, and early ambulation are components of ERAS that minimize the conditions that promote development of postoperative ileus. Some studies have also shown that chewing gum may promote intestinal motility through cephalic-vagal stimulation, but the majority of these studies were in intra-abdominal surgical procedures, which may have limited application to orthopedic surgical populations [51].

Skin Integrity

Patients who are limited in their mobility and are limited to a wheelchair or bed for extended periods of time are at increased risk of compromised skin integrity. A patient's nutritional status also plays a large role in maintaining good skin integrity. Pressure ulcers and deep tissue injuries develop through a combination of weight on pressure points of the body and poor nutritional intake. Malnutrition and dehydration can make skin fragile and reduce the healing potential.

It is essential to assess a patient's skin status prior to surgery, optimize nutrition and hydration status if needed, and ensure adequate nutrient and fluid intake postoperatively.

Patients who have compromised skin have greater than baseline needs for calories, protein, fluid, and micronutrients. Energy needs may be increased to 30–40 calories/kg body weight/day, 1.2–2.0 g protein/kg body weight/day, and 30–40 ml fluid/kg body weight/day [53]. Patients who are unable to meet their nutritional needs through volitional intake may require oral nutritional supplements to do so.

Additional supplementation of zinc, arginine, and glutamine may be necessary to further promote healing of pressure wounds. However, zinc supplementation should be provided only when zinc deficiency is present, and the recommended practice is to provide 220 mg ZnSO4 twice a day for no longer than 2–3 weeks. Excessive zinc supplementation may interfere with copper absorption, which is also essential for maintaining skin integrity. Arginine is a nonessential amino acid that has been shown to increase collagen deposition in a wound. Glutamine is a conditionally essential amino acid that is used by inflammatory cells within the wound for energy and proliferation.

Enteral Nutrition Support

In some cases, patients may not be able to consume adequate nutrition by mouth to meet their needs. Patients who have difficulty swallowing either preexisting before surgery or that develops postoperatively, who are intubated for a prolonged period of time, who are severely malnourished, or who cannot consume adequate nutrition volitionally may need enteral nutrition support.

It is important to select the appropriate route (e.g., nasogastric tube, orogastric tube, gastrostomy [percutaneous endoscopic or surgical], nasojejunal tube, jejunostomy, etc.) to deliver the enteral formula. Considerations need to be made regarding risk of aspiration, functional anatomy, expected duration of enteral nutrition support, and expected tolerance. Similar considerations will also impact the type of formula selected for feeding, and the type of formula would also depend on any medical conditions present (e.g., diabetes mellitus, renal disease, pulmonary disease).

Parenteral Nutrition Support

A small subset of patients may require parenteral nutrition support when feeding through the gastrointestinal tract is not an option. While parenteral nutrition support can meet a patient's needs for calories, macronutrients, and micronutrients, it is recommended to use the gastrointestinal tract when it is available. Feeding through the gut maintains the integrity of the intestinal lumen and gut-associated immune function. Additionally, parenteral nutrition support carries its own risks owing to the need for central venous access when total parenteral nutrition is indicated, leading to potential for infection and sepsis. Hyperglycemia is common in parenteral nutrition and requires close monitoring and correction. Liver dysfunction is also not uncommon in patients receiving parenteral nutrition. Finally, typical parental nutrition formulations do not include important nutrients such as glutamine or omega-3 fatty acids [5]. Parenteral nutrition support is not indicated if the expected need for it is <4 days [52].

When parenteral nutrition support is required, *peripheral parenteral nutrition (PPN)* may be selected when it is expected to last 4–7 days and is generally hypocaloric, providing only carbohydrate and amino acids. This can be administered through a peripheral vein rather than a central vein. However, if expected to last more than 7–10 days, *total parenteral nutrition (TPN)*, also referred to as *complete parenteral nutrition (CPN)*, can fully meet the major nutritional needs with intravenous fat emulsion (IVFE) along with carbohydrate, amino acids, vitamins, and minerals. TPN/CPN can only be administered through a central vein using a dedicated central line due to its high osmolarity and volume, as well as longer duration of expected use.

Conclusion and Summary

Nutrition plays a key role in the management of the orthopedic surgical patient. A multidisciplinary approach in assessing, monitoring, and educating the patient is key to optimizing the patient's nutrition status in the preoperative, perioperative, and postoperative period. A well-nourished, nutritionally stable patient will have decreased risk of infection, lower risk of postoperative complications, improved wound healing, and increased physical function.

A patient's nutrition status should be assessed long before surgery is planned. If warranted, the clinician should refer the patient to nutritional counseling to optimize and stabilize the patient's nutrition status for the best potential outcomes. A nutrition care plan with appropriate interventions and realistic goals should be developed with the RD, patient, patient's caregiver(s) if warranted, and medical team. Finally, all disciplines involved in the patient's care before, during, and after surgery should implement evidence-based protocols that have been shown to improve recovery and minimize risk of complications.

Additional research is still needed in many areas regarding nutrition care of the orthopedic patient, and guidelines and recommendations are likely to evolve over time. However, it is clear that nutrition is an essential component to the medical care of all patients, but especially patients who are undergoing a catabolically inducing state such as surgery. Ensuring the best nutritional state of the patient will set the stage for the best outcomes.

Summary Bullet Points

- Multidisciplinary approach in assessing, monitoring, and educating the patient optimizes the patient's nutrition status in the preoperative, perioperative, and postoperative period.
- Patient's nutrition status should be assessed long before surgery is planned.
- A well-nourished, nutritionally stable patient will have decreased risk of infection, lower risk of postoperative complications, improved wound healing, and increased physical function.
- If warranted, the clinician should refer the patient to nutritional counseling to optimize and stabilize the patient's nutrition status for the best potential outcomes.
- ERAS protocols can minimize the postoperative catabolic state and promote recovery.
- Obesity, diabetes mellitus, and hypoglycemia put the patient at risk for postoperative complications.
- Early feeding after surgery, minimizing use of narcotic medications, and careful administration of intravenous fluids can help reduce the risk of postoperative ileus.
- Enteral nutrition and parenteral nutrition support are sometimes crucial to help patients meet nutritional needs when they are unable to do so on their own by mouth.
- Evidence-based protocols have been shown to improve recovery and minimize risk of complications.

Case Study

EF is a 76-year-old female admitted yesterday for severe back pain and recurrent nausea and vomiting, is s/p right total hip replacement 1 month ago. Pt denies trauma. Imaging reveals medial acetabulum fracture and L4 compression fracture. Past medical history includes osteoarthritis, Hodgkin's lymphoma treated with radiation, high cholesterol, hypertension, hypothyroidism, Sjogren's syndrome, and h/o bleeding ulcer. Pt reports unintentional 20–30 lb weight loss × 2–3 months. Poor appetite began 1–2 months prior to THR surgery due to pain, and poor appetite persisted after surgery, compounded with recurrent nausea and vomiting. Reports usual body weight of 170 lbs., dropped as low as 139 lbs, but has likely regained some weight (unable to quantify amount). States not being able to cook for herself as much recently due to pain and fatigue. Has tried Ensure supplements in the past, but dislikes due to them being too "thick and sweet." Pt currently NPO due to recurrent nausea and vomiting. Pt given Zofran, notes mild improvement in symptoms, eager to try drinking some liquids. Amenable to trial of Ensure Enlive supplement diluted with seltzer water.

Inpatient Registered Dietitian Initial Assessment Note

Assessment

A 76-year-old female admitted yesterday for severe back pain and recurrent nausea and vomiting, s/p right THR 1 month ago. Review of nutritional history reveals inadequate oral intake and unintentional weight loss of approximately 20 lbs × 3 months (12%, clinically significant) due to poor appetite and recurrent nausea and vomiting. Had tried Ensure for oral nutritional supplementation, but disliked its "thick and sweet" nature.

Height: 5′ 5.5″ (163.8 cm).

Current weight: 151 lb (68.9 kg) – estimated weight in chart.

BMI: 25.02 kg/m2.

Estimated daily nutritional needs: 1970 calories (based on Harris-Benedict for REE × 1.55 activity and stress factor, 28.5 calories/kg body weight), 90 g protein (1.3 g protein/kg body weight), 2205 ml fluid (32 ml fluid/kg body weight).

Current diet order: NPO (for n/v per PA note) – unable to meet estimated nutritional needs at this time. Pt willing to try consuming liquids, including Ensure Enlive diluted with seltzer water.

Current nutrition problems: Nausea/vomiting – mild improvement with Zofran administration.

Overall appearance: Pt appears normal weight, but Nutrition Focused Physical Exam reveals pt has mild to moderate orbital and rib cage subcutaneous fat loss, and mild temple, shoulder, and clavicle muscle mass loss.

Diagnosis

Malnutrition in the context of chronic illness related to pain/hospitalization/persistent nausea and vomiting as evidenced by >7.5% weight loss in 3 months, mild to moderate subcutaneous fat loss (orbital range and rib cage), and mild muscle mass loss (temples, shoulders, clavicles).

Intervention

- Advance diet as tolerated to regular diet.
- Oral nutritional supplement options: Ensure Enlive BID (each 8 fl oz serving provides 350 calories and 20 g protein).
  - Encouraged pt to try mixing Ensure Enlive with seltzer water to thin and dilute, to make it more palatable.
- Continue anti-emetic medications as indicated.

- Obtain actual weight as current weight is estimated and previous weight from 12/1/17 is stated.
- Encourage PO intake of at least 75% of all meals.
- Encourage small frequent meals/snacks with emphasis on protein-rich foods to promote increased calorie/protein consumption.
- Provided education to patient on consuming adequate calories and protein to support healing after surgery.
- Inpatient goals/discharge goals:
  - PO intake of meals and supplements to meet >75% of estimated nutrient needs.
  - Continue oral nutritional supplements if PO intake of meals and snacks is insufficient to meet estimated nutrient needs.
  - Pt to tolerate PO intake without s/s GI distress.
  - Preserve lean body mass, no further unintentional weight loss.

Monitoring and Evaluation

Monitor diet tolerance, PO intake and PO adequacy, GI status and symptoms, and weight. RD to reevaluate in 2 days.

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Infection and Perioperative Orthopedic Care

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Objectives

To outline primary considerations in

- Preoperative risk assessment for infection
- Perioperative surgical prophylaxis
- Fever in the immediate postoperative period
- Preoperative management of the infected patient

Key Points

- The preoperative medical assessment should include evaluation for the presence of active infections and for the presence of risk factors for surgical infection. The issues surrounding preoperative evaluation for *Staphylococcus aureus* colonization of the skin, routine testing for subclinical urinary infections, and dental clearance will be discussed.
- Perioperative skin preparation and antibiotic prophylaxis decrease surgical site infections, when used appropriately.
- Fever in the immediate postoperative period is rarely due to surgical infection; the need for a complete workup depends on specific medical and surgical concerns.
- Orthopedic surgery in the patient with known infection requires strategic thinking and careful analysis of risk and benefit.
- Avoidance of late hematogenous infections is an important concern in arthroplasty patients.

Introduction

Infection is among the most common and serious complications of orthopedic surgery. The importance of prevention, early recognition, and appropriate therapy of orthopedic surgical infections cannot be overstated. More than 500,000 arthroplasties, and more than six million ambulatory orthopedic procedures are performed annually in the United States [1, 2]. Large increases in arthroplasty rates are projected in the coming decades. Surgical infection rates and volumes differ by center and by procedure type, ranging from nil to above 5%.

Besides representing a substantial burden to patients and physicians [3], surgical infections are quantifiable units of quality of care and are of interest to financial (i.e., Medicare) and quality (i.e., CDC/SCIP, NHSN, and the Joint Commission) entities. Decreasing surgical infections is a major piece of the quality and safety initiatives spearheaded by the CDC and other agencies at the federal, state, and professional society level. While there may be a baseline, non-zero minimum rate of infection in orthopedic surgery, there is little to suggest that the nadir rate has been achieved in this era.

Some risk factors for infection in orthopedic surgery are modifiable, while others are not. *Modifiable* risk factors include the presence of active infection remote to or contiguous with the surgical site, smoking, hyperglycemia of diabetes, and colonization with *Staphylococcus aureus* (although risk modification by decolonization is controversial, as discussed below). In addition, active liver disease, chronic renal disease, intravenous drug use, and untreated dermatitis of peri-incisional skin are frequently encountered modifiable risks in the perioperative patient. *Non-modifiable* factors that increase infection risk include previous same-site surgery, the presence of foreign material (i.e., prosthesis, graft) at the operative site, a history of orthopedic trauma at the site of surgery, male gender, and age. Underlying medical illnesses (diabetes, autoimmune disorders and their related treatment-induced immunodeficiencies, vasculopathy, morbid obesity)

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often fall in a middle ground, where disease optimization mitigates a portion, but not all, of the increase in risk.

The preoperative medical assessment, which has traditionally focused on evaluation of cardiopulmonary risk, offers an opportunity to stratify patients' risk of infection and to address important modifiable risk factors.

Antimicrobial prophylaxis (AMP), when properly administered, is effective at decreasing surgical infections in almost every field of surgery. AMP is indicated "… for all operations or classes of operations in which its use has been shown to reduce surgical site infection (SSI) rates based on evidence from clinical trials or for those operations after which incisional or organ/SSI would represent catastrophe" [4]. Multiple publications have documented AMP's efficacy in decreasing orthopedic infections, particularly when prosthetic hardware is being placed into an uninfected joint. Considerations in the proper administration of AMP include the local ecology of nosocomial pathogens (particularly methicillin-resistant *S. aureus* [MRSA]); the class, timing, and dosing of the antibiotic; the proposed surgery; patient factors (body mass index [BMI] and allergy history); and the preoperative concern for the presence of infection.

Fever in the immediate postoperative period is rarely due to SSI, is usually self-limited, and can lead to unnecessary and expensive testing. Although careful assessment of the surgical wound, and careful consideration and management of treatable nosocomial infections (IV line sepsis, *C. difficile* colitis, hospital-acquired pneumonia), are always required, it is equally important to consider non-infectious causes (hematoma, ileus). Multiple studies have underlined the low yield and high cost of a "fever workup" early in the course of the postoperative patient without focal symptoms.

Orthopedic infections, whether iatrogenic or not, are diverse in presentation and management. Bacteria, in particular Gram-positive cocci, predominate, but there is tremendous microbiologic diversity of pathogens in orthopedic infections. Microbiologic diagnosis is a key to management. In the absence of sepsis, empiric systemic antibiotic therapy is often not indicated in suspected orthopedic infection, because it can interfere with the diagnostic workup and because it is frequently noncurative. Strategic thinking, and early involvement of experienced infectious disease consultative services, can be helpful for optimal management of perioperative care of infected patients.

Preoperative Risk Assessment and Risk Reduction

The preoperative medical assessment, which has traditionally focused on evaluation of cardiopulmonary risk, offers an opportunity to stratify patients' risk of infection by assessing for known risk factors for postoperative infectious complications. Some of these risks factors, such as colonization with *S. aureus* and diabetes mellitus, can be modified preoperatively, potentially decreasing the risk for infectious complication. They are not intrinsically fixed risk factors.

There are also a number of intrinsic risk factors specific to the patient that can also contribute to an increased risk for infections following orthopedic surgery. Although they cannot be changed, these non-modifiable risk factors should be taken into consideration both when determining if a patient is an appropriate candidate for surgery, discussing the risks and benefit of surgery with the patient and when monitoring the patient in the postoperative period. There are also a range of risk factors, including many chronic illnesses such as diabetes, cirrhosis, and end-stage kidney disease, where disease optimization may mitigate, but never eliminate the risk for postoperative infectious complications.

Non- modifiable Risk Factors

Many of the important non-modifiable risk factors pertain to the patient's prior history of surgery at the operative site. Infectious complications have been shown to be significantly higher in patients who have undergone prior surgery on the same joint, particularly patients with foreign material, such as fracture-fixations hardware, already present at the operative site, or who have undergone revision arthroplasty for non-infectious indications, including recurrent dislocations [5–8]. The presence of prior infection at the operative site, including treatment for prior prosthetic joint infections (PJI) or a history of previous SSI have also been reported as independent, non-modifiable risk factors [9].

Several factors pertaining to the indication for the primary arthroplasty have been found to be independent risk factors for infectious complications; this includes victims of trauma, either if arthroplasty is required acutely to repair a fracture [10] or later on to treat post-traumatic arthropathy. Patients undergoing arthroplasty for avascular necrosis also have higher rate of postoperative infection [11], as do patients who require megaprostheses as part of the treatment for osteosarcoma or other bone malignancies. Male gender [12, 13] and increased age [14] have both been reported to be non-modifiable risks factors, although these characteristics may in part serve as markers for other comorbidities.

Modifiable Risk Factors

Metabolic Disease

Metabolic disease risk factors include diabetes, obesity, and malnutrition. All three of these diseases have been shown on a molecular level to impair the immune system [15, 16] and

lead to increased perioperative infectious complications following a wide range of surgeries, including arthroplasty and other orthopedic surgeries [17, 18]. However, their precise impact as well as the impact of interventions to mitigate these risk factors has been less well established owing largely to the retrospective nature of much of the applicable literature, which is often confounded by multiple coexisting variables.

Diabetes/Hyperglycemia

The presence of diabetes has been reported to be risk factor for infectious complications following orthopedic surgery [17, 19, 20]. It is currently recommended that all patients undergoing elective orthopedic surgery should be screened for diabetes, especially as 23.8% of diabetic patients are currently undiagnosed [21]. The relationship between diabetes and postoperative infectious complications has been difficult to quantify. Some studies have found significant associations between hemoglobin A1c (HbA1c) levels [22–24] or perioperative glucose levels and SSIs and/or PJIs [22, 25, 26]. Other studies have failed to replicate these findings [27–29]. Although some authors have proposed specific thresholds of glycemic control as predictors of postoperative complications [30–33], the inconsistency in the literature makes it difficult to determine what the level of optimization is required or, at the very least, desired, in order to proceed safely with elective arthroplasty [19, 34, 35]. Some of the inconsistency is due to the fact that both chronic diabetes mellitus and acute perioperative hyperglycemia (even in people without diabetes) can predispose patients towards infectious complications, with differing pathogeneses. Chronic diabetes can lead to a wide range of end-organ disease, including neuropathy and vascular disease, which can impair wound healing and predispose to infection. Acute hyperglycemia can initiate multiple systemic effects that directly impair the immune system, including compromising leukocyte function, complement activation, and phagocytosis. In addition, acute hyperglycemia causes oxidative stress, leading to a pro-inflammatory and pro-thrombotic state [36]. Neither HbA1c nor blood glucose levels adequately reflect both the impact of chronic diabetes and the impact of acute hyperglycemia. Furthermore, the risk posed by diabetes and hyperglycemia can be confounded by other, closely related comorbidities which further complicates the interpretation of the literature. The practical implications of this issue remain uncertain: a recent technical review identified no studies that address the clinical impact of preoperative optimization of diabetes management on the outcome of arthroplasty [35].

Obesity

Obesity is associated with increased risk of infectious complications following orthopedic surgery via multiple mechanisms including concurrent medical comorbidities, impaired wound healing, longer operative times, and increased surgical duration [37–39]. Unfortunately, obesity is a risk factor for end-stage degenerative joint disease and the need for orthopedic surgery [40]. Obesity is most commonly based upon the body mass index of the patient. According to the World Health Organization definition, patients with a BMI > = 30 qualify as obese [41]. Establishing firm thresholds of BMI for above which elective orthopedic surgery should be deferred remains been elusive. Morbid obesity (BMI > = 40) has been reported as an independent risk factor for postoperative infectious complications in multiple studies [14, 42, 43]; some groups have reported BMIs of > = 30 [10, 44, 45] and > =35 [46, 47] to also be independent risks factors. A recent arthroplasty-focused literature-based review noted that all obese patients (BMI > = 30) are at increased risk and proposed a delay in elective arthroplasty in patients with a BMI >40, but acknowledged the weaknesses within the available literature, including small study size, the use of obesity as a dichotomous rather than continuous variables, and the lack of accounting for other associated variables that also impact upon outcome [48]. The effectiveness of preoperative weight loss to mitigate the obesity as a risk factor is also not well understood [35, 49, 50]. In a study comprising over 15,000 total joint arthroplasties, the risk of SSI and the 90-day readmission rate did not significantly vary among patients who lost or gained weight in the year prior to arthroplasty versus those whose weight remained stable [51, 52]. Likewise, preoperative bariatric surgery has not been found to lead to risk reduction, although the published experience is limited [53, 54].

Malnutrition

Malnutrition is a term used to capture a wide range of nutritional deficiencies, many of which have been shown to increase the risk for postoperative infections and wound healing complications following surgery, including arthroplasty [55, 56]. Numerous studies have found an association between hypoalbuminemia and increased rates of postoperative complications, including infection [57, 58]. Similarly, low transferrin levels and low total lymphocyte counts have been reported to lead to similar complications [31]. However, although a number of serologic markers, anthropometric measurements, and standardized nutritional scoring tools have been assessed, no single preoperative test has been found to be sensitive and specific for malnutrition [35].

Smoking

Tobacco use has multiple systemic effects that can negatively impact clinical outcomes following orthopedic surgery [59]. Decreased blood flow and oxygen delivery, increased platelet aggregation, reduced bone density, and direct impairment of the immune system can all increase the risk for postoperative infectious complications. Multiple studies have highlighted both the short-term and long-term risks for SSI and PJIs in patients who smoke tobacco [60–62]. In addition, there is

a dose-dependent effect of tobacco smoke on surgical outcomes; among smokers, consumption of more than one pack of cigarettes daily may confer a higher risk of hip arthroplasty surgical complications [63]. Preoperative tobacco cessation has been demonstrated to decrease postoperative complications, including infection, in both orthopedic and mixed-surgical populations [64–66]. However, former smokers may still remain at increased risk for wide range of postoperative complications, including infection [67, 68]. The ACS SSI guidelines recommend smoking cessation at least 4 weeks prior to surgery to lower the risk of SSI [69]; however, a recent survey of orthopedists' practice patterns found this recommendation was often not followed [70].

Inflammatory Arthritis

Infections, including perioperative infectious complications and PJIs, are found with increased frequency in patients with inflammatory arthritis, including rheumatoid arthritis, spondylarthritis, and psoriatic arthritis [71–74]. Both the presence of the inflammatory arthritis itself and the immunosuppressive therapies can increase the risk for perioperative infections, although it has been difficult to tease out which factors are the most important [75]. The risk for opportunistic infections posed by anti-tumor necrosis factor (TNF) agonist and other biologic agents has been a major focus of research since their introduction. The literature regarding perioperative management of these agents, however, is inconclusive and inconsistent [35, 76], with some studies finding no association between biologics and perioperative infections [77, 78] and others reporting a significant association [79, 80]. While they have been in use longer, studies examining the impact of methotrexate (MTX) and other conventional disease-modifying antirheumatic drugs (DMARDs), including leflunomide, sulfasalazine, and hydroxychloroquine, on the development of perioperative infectious complications have also produced conflicting results [56]. The only randomized controlled trial (RCT) designed to compare continued perioperative treatment MTX versus withholding treatment found no difference in outcomes [81]. Supporting this finding, a number of observational studies have found that the continuation of non-biologic DMARDS throughout the perioperative period is safe [35, 82].

While acknowledging a paucity of high-quality data, the most recent guidelines for the perioperative management of antirheumatic medications in patient undergoing elective hip or knee arthroplasty, published jointly by the American College of Rheumatology and the American Association of Hip and Knee Surgeons, recommend continuing conventional DMARDS and withholding anti-TNF agonist or other biologics one dosing cycle, with resumption of treatment once the wound shows evidence of healing, sutures/staples are removed, and no significant swelling, erythema, or drainage is present (usually not sooner than 14 days) [83]. These guidelines also review the use of lupus-specific medications, including mycophenolate mofetil, azathioprine, cyclosporine and tacrolimus, with recommendations for perioperative management based on the severity of disease at the time of surgery.

Solid-organ transplant (SOT) patients represent another expanding group of patient requiring chronic immunosuppression for years on end. Nonetheless, the number of SOT patients undergoing elective orthopedic surgery, including arthroplasty, is very small. An analysis of nearly 800,000 patients in a Medicare database of patients who had undergone total hip arthroplasty between 2005 and 2011, less than 0.5% had undergone prior SOT [84]. While very often the outcomes of these surgeries are successful, with one single-center study reporting implant survivorship of 98% at 2 years and 93% at 5 years [85], increased rates of perioperative infectious complications and late PJIs have been reported in multiple studies [86–88]. In addition, the risk may vary depending on the organ that has been transplanted [84]. Similarly, the number of hematopoietic stem cell transplants is steadily increasing. Successful arthroplasty in this cohort of patients has been reported, but the collective published experience is very limited. Analyses of single-center cohorts have reported a wide range of infectious complications, some with outcomes paralleling those of SOT patients [89], and others finding little impact [90].

Corticosteroids

Chronic use of glucocorticoids is a well-known cause of opportunistic infection and wound healing complications and, as expected, has been associated with perioperative infectious complications following orthopedic surgery [5, 91, 92]. For patients on high doses of steroids for active flares of disease, it is recommended to delay elective arthroplasty until the patient stabilizes and the steroid dose can be lower or stopped altogether [83]. Intra-articular steroids are a common treatment modality in both patients with rheumatic arthropathies and with osteoarthritis. The impact of this treatment on future infectious complications in joints that later undergo arthroplasty is not well defined in the literature. A recent systematic review of the literature found most studies assessing this issue to be underpowered [93]. However, there are several published analyses of large databases which have shown that injections prior to 3 months have no impact on the risk of PJI, while injections within 3 months increase the risk for PJI [94–96].

Human Immunodeficiency Virus (HIV)

As expected, patients suffering from poorly controlled HIV/AIDS have poor outcomes following arthroplasty [97]. CD4 cell counts under 200 and comorbidities such as hemophilia or hepatitis C virus infection have been reported to be associated with increased rates of postoperative infections [98–100].

With the dramatic improvements in treatment developed over the past several decades, the majority of patients with HIV indicated for arthroplasty are being treated with highly active antiretroviral medications (HAART). Analyses of Nationwide Inpatient Sample data from the post-ART era have found patients with HIV have small but significantly increased rates of postop wound infections within 30 days of surgery [101–103]. The longer-term outcomes of HIV+ patients are less well studied, but in non-hemophilia patients with well controlled HIV, limited data available suggest outcomes similar to HIV-negative patients [104–107]. Overall, joint arthroplasty has been shown to be a safe and successful procedure in patients with undetectable viral loads and CD4 cell counts greater than 200.

Chronic Illness

In addition to diabetes, rheumatologic diseases and other disorders discussed above, there are a number of other chronic illnesses that have also been identified as independent contributors to the development of postoperative infectious complication. This includes cirrhosis, congestive heart failure, chronic renal disease, and the presence of malignancy [5, 7, 34]. However, given their broad-ranging impact, it can be difficult to quantify attributable risk of various illnesses, some of which may not be true risk factors, but markers for other conditions conferring risk. Using validated measurement assessing the overall health of patients and the impact of comorbid illnesses, both higher American Society of Anesthesiologists (ASA) Score and higher score on the modified Charlson comorbidity index have been reported as an independent risk factor for postoperative infections [7, 108, 109]. The complexity of these patients and the retrospective nature of much of the literature exploring these issues make it difficult to know what impact optimization of these chronic medical illnesses may have, if any, on decreasing the incidence of perioperative infectious complications following orthopedic surgery. Regardless, evaluation and optimization of all comorbidities prior to elective orthopedic surgery is recommended, not only to reduce the risk of SSIs but also to minimize the risk for all postoperative infectious complications, including pneumonia and urinary tract infections.

Preoperative Screening

Dental

The relationship between the presence of periodontal disease and the development of orthopedic infections, specifically PJIs, has been a subject of debate for many decades [110, 111]. This concern has been driven by the known occurrence of transient bacteremia following dental procedures coupled with the recovery of pathogens from infected prosthetic joints that are generally regarded as part of the usual oral flora. A direct association between periodontal disease and postoperative infectious complications, including late PJIs, has never been conclusively demonstrated in the literature [112, 113]; in fact, the incidence of bacteremia following single tooth extraction equals that of tooth brushing, suggesting that prosthetic joints and other orthopedic hardware are constantly subjected to transient bacteraemias of oral pathogens but rarely cause infection [114]. Regardless, the potential for such a relationship has led to the practice at some centers of preoperative dental evaluations prior to elective orthopedic surgery. As one may suspect, there are very few published data to support this practice [115–117]. It is a common-sense approach to address active dentogingival infection prior to major orthopedic surgery.

S. aureus Colonization

At any given time, 15–30% of the general population is colonized with methicillin-susceptible *S. aureus*, and 1–3% are colonized with MRSA [118]. There is an increasingly robust body of evidence suggesting that colonization with *S. aureus* at the time of orthopedic surgery is associated with postoperative surgical site infections (SSI) [119–121]. Guidelines regarding the prevention of SSI emphasize the potential benefits of identifying patients colonized with *S. aureus* preoperatively and also note that the optimal protocols for screening and for decolonization are not known. Areas of uncertainty include the ideal number of sites to screen and the cost-effectiveness of assorted screening and treatment protocols.

There is no standard or recommended approach to decolonization. Both targeted decolonization [122] and universal decolonization protocols [123] have been reported to be successful in reducing the occurrence of postoperative infections. Most often a combination of intra-nasal mupirocin and topical chlorhexidine gluconate (CHG) is used, although success with povidone has been reported. Studies have also revealed that failure of these decolonization protocols is not uncommon [124]. Whether or not this cohort of patients represents a particularly high-risk group or if patients require "proof-of-decolonization" prior to orthopedic surgery is not well studied, although current recommendations counsel against this practice.

UTI/Bacteriuria

Asymptomatic bacteriuria (ASB) is a common finding in older patients, particularly in women. Arthroplasty patients with ASB noted on preoperative urinary testing have a small but significantly increased likelihood of PJI [125], but there is no evidence that preoperative testing or treatment improves outcomes [126]. Bacteriuria is more likely

a nonspecific general marker of susceptibility to infection, and not a major etiologic agent. Even in patients with bacteriuria who go on to develop PJIs, the organism cultured from the urine is only very rarely the organism that causes the PJI [125, 127] strongly suggests the association between preoperative bacteriuria and the postoperative infections is not direct. As a result, routine preoperative urine screening is not recommended [31]. However, active symptomatic UTI should be identified and treated prior to surgery. If this is not feasible (e.g., in emergent cases), adequate perioperative treatment of the urinary infection is indicated.

Infections at Other Sites

A significant number of PJIs, especially late PJIs, develop as a result of hematogenous spread [7]. Although there is a lack of literature bearing out this association in the perioperative period, delaying elective arthroplasty until active infections at other sites of the body have been appropriately treated is recommended [31, 56].

Infection at the Operative Site

It became clear early on that joint replacement of infected or recently infected joints were at high risk for subsequent infectious complications [128, 129]. As techniques and strategies have improved, staged arthroplasty has been shown to successfully treat uncontrolled septic arthritis or severe post-infectious arthropathy shortly after resolution of the infection [130, 131].

Dermatologic Disease

There is little literature regarding the risk for perioperative infectious complications in patients undergoing elective orthopedic surgery in patients with active ulceration, dermatitis, lymphedema, or otherwise impaired integument at or near the incision site. However, it is intuitive that surgical incisions created at sites with impaired integument will heal poorly and predispose the patient to postoperative infectious complications [132], and this practice is recommended against [133]. Like active infection, active dermatologic disease should be evaluated and treated prior to arthroplasty. Conditions that cannot be readily cured, such as chronic venous stasis or lymphedema, should at least be optimized, with the understanding on both the patient and the surgeons part that the risk of postoperative infectious complications will be increased; the decision to proceed with surgery in patients with chronic dermatologic disease needs to be made on a case-by-case basis [5].

Perioperative Management of Infection Risk

Skin Preparation

The condition of peri-incisional skin and its local microbial flora is an important concern, and a variety of techniques have evolved to prepare surgical sites for surgery. CHG or povidone-iodine preparations applied the night before surgery may be beneficial in arthroplasty [134, 135] although this is not borne out in wider analyses of surgical patients where no difference over ordinary soap is noted [136]. Preoperative CHG wipes administered the night before surgery did not have significant effectiveness in two smaller observational prospective studies [134, 137] although this is a common practice. Shaving peri-incisional hair at home or in the holding area prior to surgery is abrasive and may increase infection risk and should be avoided; hair clipping or depilatories immediately prior to surgery are advisable, when necessary [138]. It is important to mention that bacteria reside within skin structures (hair follicles, sebaceous cysts, and epidermis) so that true skin antisepsis is never achieved with topical agents [139–141].

Preparation of the skin at the site of surgical incision at the time of surgery is a critical factor in the prevention of surgical site infection. Selection of an ideal agent remains controversial, although the preponderance of randomized trial evidence favors alcohol-based agents (over those not containing alcohol); superiority of CHG or iodine-based antiseptics has not been fully demonstrated. A large RCT demonstrated superiority of a CHG-alcohol preparation over povidone-iodine in prevention of SSI [142], but it is unclear whether this demonstrated the benefit of alcohol, CHG, or combination antisepsis; the trial is therefore of uncertain value in making clinical decisions regarding antiseptic selection. Cost of the newer preparations, dermatologic hypersensitivity to CHG [143], drying time of selected agents, and the unusual but morbid spectre of operating room fires from pooled ethanol [144] are important considerations in the selection of skin preparatory agents.

Antibiotic Prophylaxis

Perioperative antibiotics administered near the time of initial incision have been known for decades to decrease microbial persistence and growth from operative beds and to decrease the incidence of SSI [145]. Direct and indirect data, in animal and human clinical studies, demonstrate that effect is highly timing dependent [146]. The need for more than a single dose of antibiotics in orthopedic surgery has not been demonstrated, despite common practice in many orthopedic centers of providing 24 hours prophylaxis. Evidence for the benefit of prophylactic perioperative antibiotics in orthopedic surgery is

strongest for spine [147] and arthroplasty [148] procedures, but may exist for a range of other orthopedic procedures even in the absence of hardware placement [149]. Prophylaxis for low-risk patients undergoing arthroscopy is not clearly of benefit [150, 151] but commonly administered nonetheless.

The effect of antibiotic dose on the protective effect of peri-incisional prophylaxis has been well demonstrated [152, 153]. The choice of a prophylactic antibiotic depends on local microbial ecology, particularly as it pertains to the prevalence of cephalosporin-resistant Gram-positive organisms. First-generation cephalosporins (especially cefazolin) are typical routine choices because of their low risk of immediate-type hypersensitivity reactions, potency against most Gram-positive skin flora (as well as against some Gram-negative and anaerobic organisms), low cost, ready availability, and familiarity. While first-generation cephalosporins are adequate for the majority of non-allergic orthopedic patients, vancomycin is a reasonable alternative if there are contraindications (such as a history of anaphylaxis) to the use of beta-lactam antibiotics. Because vancomycin is less effective [152, 154], much slower to infuse, and more nephrotoxic than cefazolin, its use as a prophylactic agent should be limited to special circumstances such as beta-lactam allergy or high concern for MRSA. In patients with known or suspected colonization with MRSA, addition of vancomycin to cefazolin may be beneficial. Beyond cefazolin and vancomycin, other agents such as cefuroxime and clindamycin are listed as alternatives in official guidelines but much less commonly used except in cases of allergy or drug shortage. Dosing of antibiotics should ideally be completed before incision and application of surgical tourniquets.

Appropriate dosage of antibiotics requires consideration of body mass and renal function [120, 138]. Additional doses should be given when (a) there is significant intraoperative blood loss or (b) the procedure time exceeds twice the half-life of the antibiotic (e.g., after 4 hours and 10 hours, for cefazolin and vancomycin, respectively) [155].

A detailed discussion of antibiotic prophylaxis in orthopedic surgery following open fractures and other traumatic injuries with damage to the overlying skin and soft tissue envelope is outside the scope of this chapter, but guidelines typically suggest 3–5 days of prophylaxis, with duration based on the severity of injury and antibiotic selection guided by local resistance patterns of likely pathogens [156].

We believe that the benefit of obtaining deep operative cultures prior to administration of peri-incisional antibiotics outweighs the risk of delayed administration in cases of suspected orthopedic infection, where intraoperative cultures are of high value. Making a firm microbiological diagnosis is key in orthopedic infections, and in the absence of new orthopedic hardware placement, the benefit of antibiotics is limited.

Postoperative Management

Postoperative Fever

Body temperature in the surgical patient can be altered via multiple pathways. Fever is an important component of the presentation of sepsis, which requires emergent evaluation and management, but an isolated fever is generally a separate entity. Evaluation of the isolated postoperative fever in the first 3 days after surgery is costly and rarely results in a diagnosed infection. Postoperative fevers caused by orthopedic surgical site infection are rare in the initial 72 postoperative hours; the need for a complete workup depends on specific medical and surgical concerns.

A representative study evaluated fever (temperature greater than 38.5 °C) in 1100 arthroplasty patients at a single institution over a two-year period [157]. In this study, chest x-ray and blood cultures were positive in 2% and 6% of cases of fever in the first 72 hours. Fever after postoperative day 3 (Odds Ratio [OR] 23; $p < 0.001$) and multiple days of fever (OR 8.6; $p < 0.05$) independently predicted the likelihood of a positive workup. Temperature >39.0 °C was associated with diagnostic findings 25% of the time, whereas patients with fevers less than 39.0 °C were less than 7% likely to have a positive fever workup. These findings have been validated in other data [158, 159].

In our hospital, fever in the first 72 postoperative hours is generally evaluated by interview and physical examination. A brief interview and physical examination is a low-cost way to occasionally detect critical focal issues (e.g., peripheral intravenous line infections or wound cellulitis) and to provide reassurance to the patient and treatment team that the postoperative febrile state is within expected limits.

Postoperative Wound Issues

Early Postoperative Period

Evidence does not favor any specific arthroplasty wound closure technique over others despite multiple studies. Draining surgical wounds are evidence of a process other than cellulitis and should not generally be treated with empiric antibiotics. The use of antibiotics for the treatment of draining wounds can easily interfere with the ability to establish microbiologic etiology of any subsequently diagnosed SSI. Moreover, antibiotics given in the face of a draining wound alter the wound's microbial ecology, potentially predisposing towards colonization and infection with resistant flora.

Surgical Site Infections

Monitoring of the wound for evidence of infection is an important component of the postoperative care of orthopedic patients. In general, orthopedic SSI are categorized as

to their presence in the supra- or subfascial spaces (or, not uncommonly, both). Suprafascial infections do not communicate with bony tissue or orthopedic instrumentation and present with evidence of wound infection: local swelling and induration, redness, and wound complications such as dehiscence and drainage. While cellulitis in the absence of wound drainage can be treated with antibiotics alone (generally targeting Gram-positive pathogens such as staphylococci and beta-hemolytic streptococci), drainage generally suggests a different issue – a potential collection (hematoma, seroma) potentially indicating surgical debridement – and we generally recommend holding off on initiation of empiric antibiotics if the patient is stable. In this way, the surgical site can be assessed, and microbiologic diagnosis might be made via radiologic or surgical approaches.

Deep (subfascial) infections following orthopedic surgery often involve muscle, joint, bone, metal instrumentation, or allograft. Deep infections may present acutely and shortly after surgery, or with a lengthy latency before symptoms develop. The variety of microbes, modes of presentation, and management strategies causing deep orthopedic SSI are wide. In general, treatment is multimodal (surgery, systemic antibiotics, local antibiotics, advanced wound coverage techniques, medical optimization, etc.). Removal of hardware may be necessary to maximize likelihood of microbiologic cure but can be morbid and delay or prevent orthopedic recovery. These cases require multispecialty management with orthopedics, medicine, infectious disease, and often mental health and social work input for optimal management.

Orthopedic Surgery in the Patient with Known Orthopedic Infection

Perioperative management of the patient with known or suspected orthopedic infection requires thought and expertise.

The decision to operate on a patient with infection requires consideration of multiple factors including acuity, risks of morbidity and mortality with and without the surgical procedure, the likelihood of obtaining a meaningful diagnosis, the likelihood of controlling or curing the infection, the possibility of other foci of the same infection, and the underlying medical and social factors that often play major roles in the decision making process.

Elective orthopedic surgery is typically not recommended in patients with any active bacterial infection. Considering the possibility of infection is always necessary in cases of revision surgery for painful or loose prostheses, for non-unions of fractures and arthodeses, and for spontaneous loosening of internal hardware. Indolent infection can present without gross visual cues, and frequently without histopathological correlates, making microbiologic diagnosis a key.

Isolating the pathogens in orthopedic infection is critical to proper management. Molecular methods may someday become routine, but today, microbiologic culture remains the mainstay of pathogen detection. Obtaining specimens of optimal quality is the clinicians' job. Cultures taken from an infected patient while the patient is on effective antibiotics are frequently negative. A sufficient antibiotic-free interval (2–6 weeks) increases the yield of cultures and minimizes the potential of false-negative misdiagnosis [160]. Sonication of infected prostheses may be more sensitive than traditional culture when the patient has taken antibiotics in the prior 14 days [160].

Orthopedic infections present in varied ways. The microbiologically astute clinician must consider the specific advantages and disadvantages of every culture taken. The site and type of culture are critical, as outlined below.

Surface Cultures

The surface of human skin, including the exterior of surgical wounds, is colonized by a diverse group of culturable bacteria which are also frequently implicated in orthopedic infection. For this reason, surface cultures are rarely a useful part of the workup of most deep orthopedic infections. Cultures from sinus tracts draining sites of chronic osteomyelitis can occasionally be helpful (but never definitive), in some studies: they are more likely to be correct when they detect *S. aureus* than when they detect other pathogens, and they can detect bacteria (not necessarily the pathogen) that are important in terms of hospital infection control (i.e., vancomycin-resistant *Enterococci* and MRSA) [155, 161, 162]. However, limited correlation is seen between cultures of the superficial wound/fistula and deeper surgical cultures. Surface cultures cannot be relied upon for diagnosis of deep orthopedic infection.

Synovial Fluid

Cultures of synovial fluid are critical specimens in the evaluation of the potentially infected joint. Cultures must be interpreted in the context of arthrography, cell count and differential, cytopathology (for crystal arthropathy), and gross appearance. As always, there is a distinct decrease in sensitivity when the patient is on antibiotics. In our view, there is no need to divide a single sample of synovial fluid into aliquots for serial culture (unless there is concern for a loculated process). The constant possibility of inadvertent contamination of cultures, and the rare but serious risk of inoculating pathogens into an uninfected space, must be considered before deciding to aspirate any fluid collection in settings where the pre-test likelihood of infection is low. Inoculation of synovial fluid into aerobic and anaerobic blood culture bottles appears to improve pathogen detection in PJI [163].

Other Collections

Cultures of other fluid collections (for instance, in the postoperative spine patient with a potentially infected seroma/hematoma) are frequently performed although operator characteristics for such evaluations are poorly described. At our institution, the use of radiographic imaging and guided drainage of fluid collections (Roentgenographic abscessogram/fistulogram, computed tomography, ultrasound, and magnetic resonance imaging) are commonly utilized.

Wound Cultures

Intraoperative wound cultures should be performed without the use of culturette swabs, which have suboptimal sensitivity. Ideally, multiple specimens (tissue, fluid) from multiple sites within the operative field, obtained with single-use sterile instruments, should be obtained. We routinely culture for aerobic (5 days) and anaerobic (10–21 days) bacteria; fungal and mycobacterial cultures are sent when clinically indicated. The importance of obtaining multiple specimens cannot be overestimated, although excessive cultures increase cost and labor and increase the likelihood of contaminated cultures. We use 5–6 cultures as a standard optimum target based on institutional experience and published literature [164].

Blood Cultures

Blood cultures have a limited but important role in orthopedic infectious diseases; bacteremia is commonly implicated, but only sometimes detected, in PJI which occur more than 6 months beyond the surgical date. Positive blood cultures are specific but insensitive as a method of pathogen detection in orthopedic infections. Prosthetic and native joint infections and vertebral osteomyelitis are occasional but important initial presentations of bacterial endocarditis. Astonishingly, one out of three patients with an arthroplasty and documented *S. aureus* bacteremia seeds the prosthetic joints [165]. All patients with fevers after the initial 72 hours post-surgery or who appear septic should have blood cultures drawn, even if on antibiotics, preferably before such antibiotics are started.

Late Considerations in Arthroplasty Patients

Implants, in particular large joint replacements, can present with infection at any time, whether hematogenously, by contiguity, or chronically in a late low-grade infection (for instance, *Cutibacterium* [*Propionibacterium*] *acnes* associated with shoulder or spine implants). Chronic and acute skin integrity threats (i.e., eczema, paronychia, animal bites) need maintenance and prompt care. Periodic dental care and dental cleaning reduce the magnitude of dentogingival bacteremias. Genitourinary, gastrointestinal, and respiratory infections need to be treated promptly to reduce the risk of bacteremia.

Use of prophylactic antibiotics in anticipation of bacteremic events (e.g., dental surgery, cystoscopy, surgical procedures on infected or contaminated tissues) has been suggested on the same basis on which endocarditis prophylaxis has been recommended. This approach to prevention is controversial, and no data are available with which to determine the adequacy or the cost-effectiveness of such measures. The American Dental Association and the American Academy of Orthopedic Surgeons advise that a single dose of prophylactic antibiotic be given for certain patients undergoing dental procedures associated with gingival manipulation or invasion and significant bleeding, including periodontal scaling [166]. Selected patient populations for dental antibiotic prophylaxis include those with inflammatory arthropathies, immunosuppression, diabetes, malnutrition, hemophilia, or previous PJI, as well as all patients undergoing these procedures within 2 years following joint replacement, although controversy continues [166]. Guidelines advise that prophylactic antibiotics be considered for similar selected patient populations undergoing urologic procedures associated with higher bacteremic risk [167]. Clinical decisions regarding prophylactic antibiotics in patients with prosthetic joints undergoing other procedures should be made on an individual basis but generally are not recommended.

Summary

Infections are part of orthopedic surgical and perioperative practice. Prevention, prompt diagnosis, and appropriate therapy are critical. Patients and families, medical professionals, payers, and government agencies share a strong interest in minimizing the impact of these potentially devastating complications.

Risk factors for infections can be identified, and often decreased, preoperatively. Dental, skin, and genitourinary disease, tobacco use, uncontrolled hyperglycemia, unstable cardiovascular disease, and immunosuppressive diseases and medications are examples of conditions that raise the infection risk and can often be decreased in the preoperative period. *S. aureus* colonization, as discussed above, may be a modifiable risk factor. Non-modifiable risk factors, such as age, number of prior same-site surgeries, and presence of indwelling hardware, still are important factors in the risk-benefit analysis of proposed surgeries.

Antimicrobial prophylaxis is of known benefit in spine and arthroplasty procedures and is commonplace in arthros-

copy. Its benefit is dependent on peri-incisional timing and intelligent thinking. Attention to local ecology of pathogens, body size and renal function, allergy history, and operative time is important.

Fever immediately following orthopedic surgery is rarely from an infection and even more rarely from a surgical site infection. Data suggest that, within the first 72 hours, most patients without septic appearance do not benefit from the traditional fever workup of blood studies, urine and blood cultures, and a chest x-ray. However, focal complaints or exam findings, high or persistent fever, and other clinical considerations must be taken into account when dealing with this entity. Nosocomial infections can and do occur in the post-surgical patient, and clinical vigilance is always appropriate.

Management of the infected patient is rarely routine; patients present with varied acuity and symptoms, and standard protocols for orthopedic infections need to be kept flexible. There is microbiologic diversity of pathogens in orthopedic infections. Empiric antibiotics in the absence of deep cultures frequently prevent microbiologic diagnosis, rarely cure the infection at hand, and are rarely indicated (unless there are life-threatening reasons to employ them). Strategic thinking and early involvement of experienced personnel can optimize care of these unfortunate patients.

Summary Bullet Points

- Risk factors for infection can be modifiable or not, and surgery can be elective or not. Optimizing patients' modifiable risk factors for infection prior to surgery is an important part of the preoperative evaluation.
- Postoperative fever is rarely infectious within the first 72 hours, and routine cultures and chest x-ray are unlikely to be helpful.
- Perioperative patients with known or suspected orthopedic infection require careful evaluation and thought, with strategic use of the array of diagnostic tests.
- Making a microbiologic diagnosis of infection – identifying the offending microorganism – is primary in the patient presenting with possible orthopedic infection.

Case Study

A 54-year-old woman with a history of asthma, diabetes mellitus on oral agents, obesity, eczema, and ongoing tobacco use is scheduled for elective, multilevel, revision instrumented thoracolumbar spine surgery because of severe multilevel lumbar disk disease despite previous microdiscectomy 3 years ago. The surgery is expected to last 7 hours. She is not on immunosuppressive medications. She has no known drug allergies. Exam reveals a healthy-appearing woman weighing 100 kg with a BMI of 34. Eczematous skin is noted on the hands, legs, and near the proposed surgical incision. Preoperative labs reveal no evidence of active infection.

The patient has risk factors for surgical site infection. Obesity and smoking are modifiable risk factors, but frequently cannot (or will not) be modified in the perioperative setting. Surgeon- and culture-specific norms dictate the progression of patients with such risk factors to surgery. However, in our view, patients should be plainly told that these are established risk factors for infection, that infection can be a devastating complication, and that the risk can be decreased. In a limited number of patients, tobacco cessation and diet modification are part of preoperative preparations.

The patient's eczema may be an important modifiable risk factor as well. Patients with eczema usually harbor *S. aureus* on their skin [168] and therefore are likely to be at increased risk of surgical site infection. The patient should have her dermatitis evaluated and treated aggressively prior to surgery. Making an incision through skin with an active dermatitis is relatively contraindicated in elective orthopedic surgery. In addition, strong consideration should be given to screening the nares, eczematous skin, and perhaps other sites as well to detect the presence of MRSA or to perform empiric *S. aureus* decolonization with topical mupirocin/bactroban. MRSA carriage may guide the choice of perioperative antibiotics and infection control procedures in the inpatient setting.

Prior same-site surgery is a non-modifiable risk factor.

In the hour prior to incision, the patient should receive 2 grams of intravenous cefazolin (or, in case MRSA is detected, 1 gram of vancomycin). In the absence of compelling data in either direction, some suggest giving both vancomycin *and* cefazolin prior to incision (given cefazolin's antimicrobial spectrum and its added potency against beta-lactam sensitive organisms). The expected surgical time for this complex spine case exceeds 4 hours (two half-lives of cefazolin), and therefore a second dose of 2 grams of cefazolin would be recommended at that time.

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Risks and Benefits of Bilateral Total Knee Replacement Surgery

28

Elina Huerfano, Kate Shanaghan, Ettore Vulcano, Stavros G. Memtsoudis, and Alejandro González Della Valle

Objectives

- To describe the different options for the surgical treatment of patients presenting with bilateral knee osteoarthritis.
- To describe the advantages of undergoing bilateral total knee arthroplasty under the same anesthesia (single-stage).
- To describe the drawbacks and complications of single-stage bilateral total knee replacement surgery.
- To provide guidelines for the selection of candidates for single-stage bilateral total knee replacement surgery based on risk stratification.

Key Points

- Bilateral total knee replacements can be performed under the same anesthetic or the so-called single-stage (simultaneously or sequentially) or under different anesthetics or the so-called staged (during the same or different hospitalizations).
- The main advantages of single-stage bilateral total knee replacement surgery include good clinical results, the need for a single anesthetic, less use of pain medication used, shorter surgical and rehabilitation time, high patient satisfaction, and possibly lower total cost.
- The drawbacks of single-stage bilateral total knee replacement surgery include increased risk of perioperative complications.
- Published guidelines for the selection of patients being considered for single-stage bilateral knee arthroplasty contemplate the exclusion of patients of extreme age—patients with significant end organ dysfunction (i.e., ASA physical status of 3 or greater).

Introduction

Knee osteoarthritis affects approximately 80% of the population above the age of 65 [1] and the number of total knee arthroplasties (TKA) performed in the USA has been steadily increasing over the last decades [2, 3].

Approximately 20% of patients undergoing primary unilateral TKA complain of severe pain in the contralateral knee [4], and about 10% of patients who have a primary TKA will undergo contralateral TKA surgery within 1 year [5].

Patients with debilitating bilateral joint disease represent a unique challenge. While proponents of performing single-stage bilateral total knee arthroplasties (BTKA) point

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out its low complication rates, high patient satisfaction, and cost-effectiveness [6–13], concerns persist that BTKA performed during the same anesthetic session is associated with increased morbidity and mortality [12–18]. Despite extensive research into risks and benefits of single-stage BTKA, some questions related to the safety of the procedure remain unanswered [19–24].

In order to clarify terms to describe the chronologic relationship of the first and second joint arthroplasty in this chapter, the following definitions have been chosen:

1. *Single-stage BTKA*: Both TKAs are performed during the same anesthetic session. Single-stage BTKA can be performed (a) *simultaneously*, when both TKAs are performed at the same time by different surgical teams, or (b) *sequentially*, when TKAs are performed consecutively by the same surgical team.
2. *Staged BTKA*: Each TKA is performed in a separate anesthetic sessions. Staged procedures can be done *during the same hospitalization* (generally a few days apart) or *during different hospitalizations* separated by weeks to months.

The objective of single-stage BTKA surgery is to reduce the risk of repeated anesthetic procedures, total hospitalization and recovery time, and cost. The goal is to perform single-stage BTKA while maintaining patient safety, and the clinical and functional outcomes observed in patients undergoing unilateral TKA or staged BTKA [8, 9, 24–36]. In view of the divided opinions on the use of single-stage BTKA surgery, careful patient selection appears to be the safest clinical approach, as proponents point to good outcomes in selected patients at their institution [6, 14, 37–41]. In an attempt to reconcile competing factors in the decision making process to perform single-stage BTKA procedures, many institutions, including ours, have developed guidelines for the selection of patients considered to be at a low perioperative risk.

In this chapter we will discuss the published evidence in regard to multiple aspects surrounding BTKA procedures, including the epidemiology and trends, benefits and risks, and the approach taken at our institution as an example of how consensus can be reached to reconcile the benefits with concerns for patient safety.

Epidemiology and Trends

The performance of unilateral and BTKA has increased dramatically over time [3, 21]. The proportion of BTKA to unilateral TKA in the USA was approximately 4% between 1990 and 1994. The proportion rose to 6.5% in the period between 1998 and 2006, indicating an increased popularity for this approach [42]. The absolute number and use of BTKAs also increased in the last two decades [21, 43]. Of an estimated total of 258,524 BTKAs performed between 1999 and 2008 in the USA. The number of annual procedures increased by 75% (from 19,288 to 33,679) (Fig. 28.1).

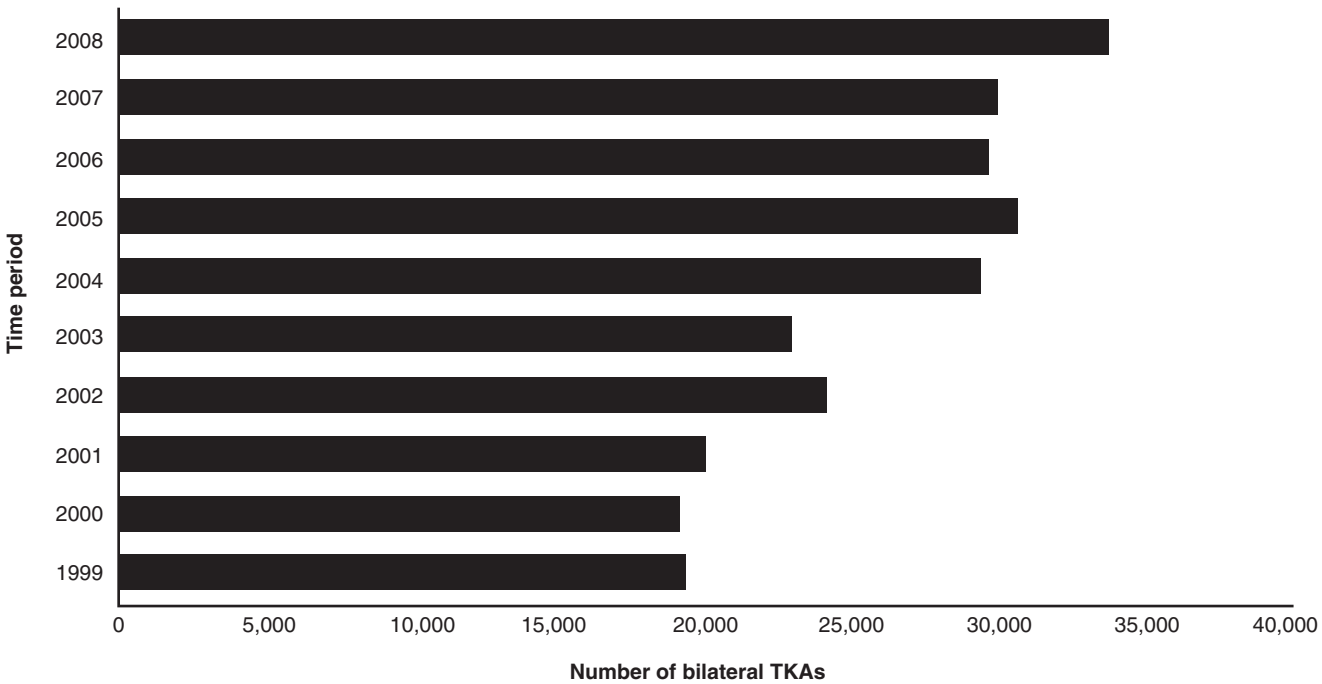

Fig. 28.1 A graph shows the total number of bilateral TKAs with time in 1-year periods. The data were obtained from the Nationwide Inpatient Sample data files for 1999 to 2008. There was a 75% overall increase in the number of procedures performed per period from 1999 to 2008. (Used with permission of Wolters Kluwer from Memtsoudis et al. [43])

Patients undergoing BTKA are on average younger and healthier compared with their counterparts undergoing unilateral TKA [22, 42, 43]. Trends toward decreasing average age have paralleled those of unilateral TKA recipients [21]. However, while a shift toward increasing comorbidity burden was seen over time in the latter group, decreased rates of cardiac and pulmonary disease and utilization among the elderly (i.e., >85 years) have been noted in the BTKA group starting in the mild 1990s (Fig. 28.2). These trends may be explained by the desire of clinicians to perform BTKA, especially single-stage, in a healthier and younger group of patients, presumably in order to decrease the risk of perioperative complications.

Similarly, to unilateral TKA, more women underwent bilateral TKAs compared with men [21, 22, 43]. These trends may be driven by the expansion of indications for TKA to younger, more active patients, the epidemic of obesity and its consequences in the progression of osteoarthritis [44], all factors resulting in a higher demand for the procedure. Advances in anesthesia, surgery and perioperative care may further contribute to the increase in utilization of BTKA [21], as physician and patient confidence increase.

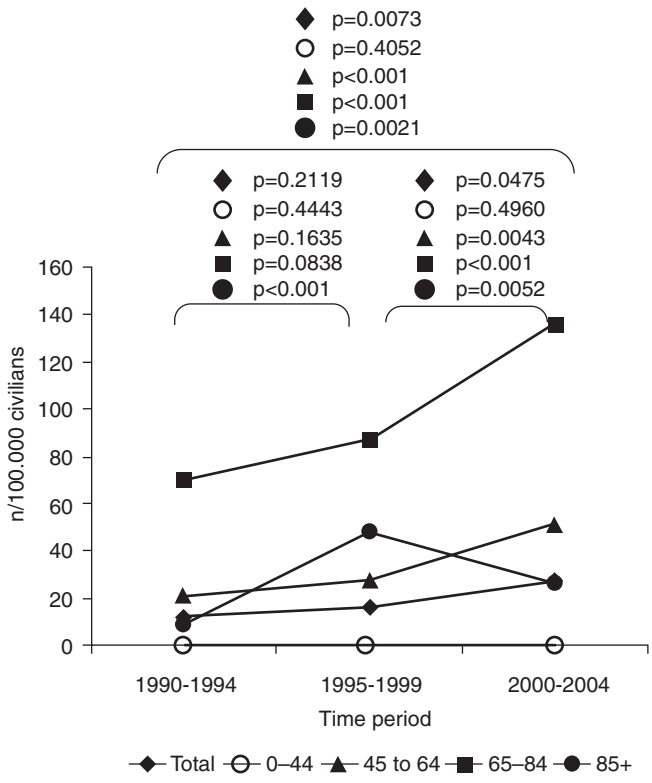

Fig. 28.2 Changes in age group-adjusted and unadjusted use of BTKAs by time. All age groups experienced an increase in use of BTKAs throughout the study period, except the group 85 years and older. Between the second and third periods of study, a decline of nearly 50% was seen. The values are expressed as number per 100,000 US civilians per time. (Used with permission of Wolters Kluwer from Memtsoudis et al. [21])

Benefits of Single-Stage Bilateral Total Knee Arthroplasty

The use of single-stage BTKA has advantages that include good clinical results, the exposure to only one anesthetic, lower total amount of pain medication used, shorter overall surgical and rehabilitation time, high patient satisfaction, and possibly lower cost.

Clinical Results of Bilateral Total Knee Arthroplasty

More than ten studies [8, 10, 12, 15, 26, 36, 45–49] reporting on the clinical results of a combined number of 4307 BTKA patients support that single-stage BTKA is a very successful operation, with results that are comparable to those of unilateral TKA. BTKA patients demonstrated similar or better results in terms of range of motion [15, 47, 50], Oxford Knee Score [15, 48], WOMAC [36, 51], SF-36 [36], SF-12 [46], Knee Society Score (KSS) [26, 46, 47, 51], Modified Hospital for Special Surgery Knee Scoring System [10, 45, 49], and survivorship at 7 years [12] and 10 years [10].

Number of Anesthetic Sessions

Although major anesthesia-related complications are rare, the risks associated with potential procedures, such as endotracheal intubation in the case of general anesthetic, neuraxial complications with a regional technique and those associated with the administration of drugs and insertions of invasive lines cannot be discounted completely. Thus, it is obvious that strictly from an anesthetic procedural aspect the avoidance of a second exposure may be of benefit.

Surgical Time

Predictably, surgical time varies with the type of BTKA performed. In 1998, Liu and colleagues compared operative time between 64 patients undergoing sequential BTKA, and 24 patients undergoing staged BTKA 7 days apart [52]. The mean operative and tourniquet time for patients undergoing sequential procedures was 19 min and 26 min shorter than for those undergoing staged BTKA, respectively. This is reflected not only in lower operating room costs but also in the reduction of potential risks associated with tourniquet application, such as nerve palsy, vascular injury, muscle damage, and postoperative swelling and stiffness [53]. Other less frequent complications have also been reported with tourniquet use, such as intraoperative cardiac arrest at the

time of deflation, reactive hyperemia, early infection, and wound healing disorders due to perioperative hypoxia and reduced postoperative tissue perfusion [54].

Use of Pain Medication

The general belief is that patients undergoing single-stage BTKA will experience worse pain and will have a higher requirement for narcotics than those undergoing unilateral TKA.

Powell and colleagues [55] observed that narcotic requirements were slightly greater but not significantly different for the simultaneous BTKA group compared with a unilateral TKA group during the first 72 hours after surgery. Other authors have reported the opposite findings [15, 50, 55]. Similarly, Shetty and colleagues [50] prospectively studied 50 patients undergoing sequential BTKA and 50 undergoing unilateral TKA. The mean difference in postoperative VAS scores was significant only on the first postoperative day, becoming non-significant during the remainder of the hospitalization and at discharge. Tsukada and colleagues [56] recommend use of periarticular injection in patients undergoing single-stage BTKA, in a randomized controlled trial comparing the use of periarticular injections and epidural analgesia; they found that the use of periarticular injections was associated with better pain relief during the first 24 hours following single-stage BTKA and decreased opioid-related side effects compared with patients receiving only epidural analgesia.

Kim and colleagues and Sun and colleagues [57, 58] reported that patients undergoing staged BTKA experience more postoperative pain in the knee that was operated on last. Kim and coauthors [57] attributed this finding to hyperalgesia, in which central sensitization may be involved. A different therapeutic approach to enhance the analgesic strategy in the second operation may be considered.

Patient Satisfaction

Along with functional outcome, health status and perception of well-being are becoming increasingly important markers when evaluating TKA results [59]. In terms of functional results and implant survivorship, there is strong evidence suggesting that single-stage BTKA patients do as well as unilateral TKA recipients [8, 10–12, 16, 26, 28, 45, 60]. Furthermore, a large survival analysis conducted by Ritter and coauthors [8] on 2050 simultaneous BTKA patients, 152 staged BTKA patients (performed within 1 year), and 1796 unilateral TKA patients at 5, 10, and 15 years postoperatively concluded that patients who had undergone unilateral TKA had significantly lower (KSS) compared with patients with simultaneous BTKA.

Patient satisfaction and health perception are also advantages of single-stage BTKA. It has been reported that the majority (94.7%) of patients who had experienced BTKA would opt for the same procedure again [12]. Similar results were presented by other authors, reporting that patients undergoing simultaneous BTKA have improved physical and social function, less pain, and better general and mental health than patients undergoing unilateral TKA [36].

Cost

If the combined cost of two unilateral TKAs exceeds the total cost of a single-stage BTKA, then the latter can be considered to be more economical. Cost analysis performed by numerous authors [7, 25, 28, 32, 36, 61] showed that single-stage BTKA results in overall savings in the range of 18–58% compared with the cost of staged procedures. The cost advantage of single-stage BTKA surgery is driven by numerous factors that include a reduced hospital stay [27, 62], lower charges for laboratory tests, medical consultations, operating room fees, anesthesia and surgical fees, recovery room time, medications, and physical therapy [5, 12]. The cost in surgical fees for the insurance company are also lower as in the USA most insurers including Medicare reimburse the second joint replacement performed during the same anesthetic at 50%.

When calculating the overall cost of care, both transfer to a rehabilitation center and re-admission should be taken into consideration. One study [63] compared actual hospital costs of 225 simultaneous BTKA and 337 staged BTKA patients. The proportion of patients being discharged to a rehabilitation center was higher in the simultaneous BTKA group (81%) than in the staged BTKA group (72%), and the mean hospital length of stay was significantly shorter for the staged procedures than the simultaneous procedures (p <0.001). When the overall cost of care was considered, including that of inpatient rehabilitation, there was no significant difference between the cost of staged and single-stage BTKA.

Drawbacks of Single-Stage Bilateral Total Knee Arthroplasty

Numerous studies have compared outcomes and complications associated with single-stage BTKA vs unilateral TKA [1, 8–11, 13–17, 26, 27, 34, 36, 39, 40, 42, 45, 46, 49, 55, 64–72]. Although numerous reports have noted significantly higher systemic complications [1, 8, 13, 14, 16, 27, 36, 40, 42, 45, 64, 66, 67, 70, 72] and mortality [17, 42, 69] in patients undergoing simultaneous BTKA, other reports identified a higher number of local complications following unilateral TKA [8, 27, 72], whereas others have not found any

significant differences within these procedures [9–11, 15, 26, 34, 39, 46, 49, 55, 65, 68, 71] (Fig. 28.3).

In order to determine whether complications and mortality are increased in simultaneous BTK, other studies have compared outcomes associated with single-stage BTKA vs staged BTKA [9, 29, 34, 38, 42, 46, 51, 52, 61–63, 69–76]. Data from several studies have consistently shown significantly higher systemic complications [62, 63, 70, 72, 76] and mortality [69, 72, 73, 76] in patients undergoing simultaneous BTKA and a significantly higher incidence of local complications in staged BTKA population [42, 51, 61, 72, 76] (Fig. 28.4).

Outcomes that have been measured encompass systemic complications that include cardiac, neurologic, gastrointestinal, and pulmonary complications including thromboembolism and local complications like wound-related complications and surgical site infection. Also, the use of allogenic blood transfusions and discharge to tertiary rehabilitation centers have been evaluated. The pathophysiology of bilateral procedures may be in part explained by the increased surgical insult, blood loss, and embolic load affecting the various organ systems.

Mortality

Whether simultaneous BTKA is associated with an increased risk of mortality remains controversial. Only few studies in the literature have sufficient power to detect potential differences in mortality [42, 69, 72, 76]. Three meta-analyses reported a significant higher mortality at 30 days postoperatively in the population who had undergone simultaneous BTKA compared with those who had undergone staged BTKA [77–79].

In our analysis of the National Hospital Discharge Survey from the years 1990 to 2004 [22], we found that the in-hospital mortality rate of BTKA patients (0.5%) was higher

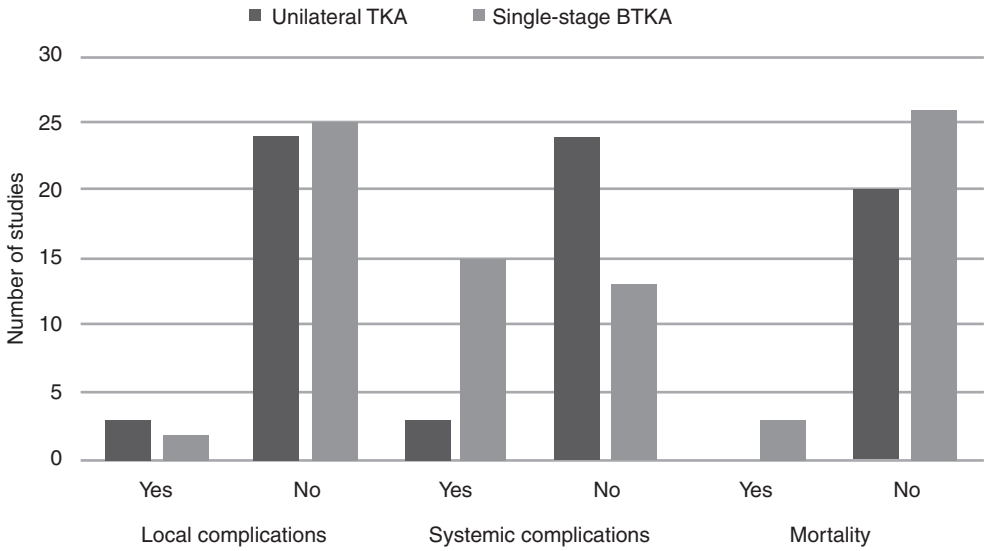

Fig. 28.3 Studies reporting significantly differences in mortality, local and systemic complications comparing unilateral TKA and single-stage BTKA surgery

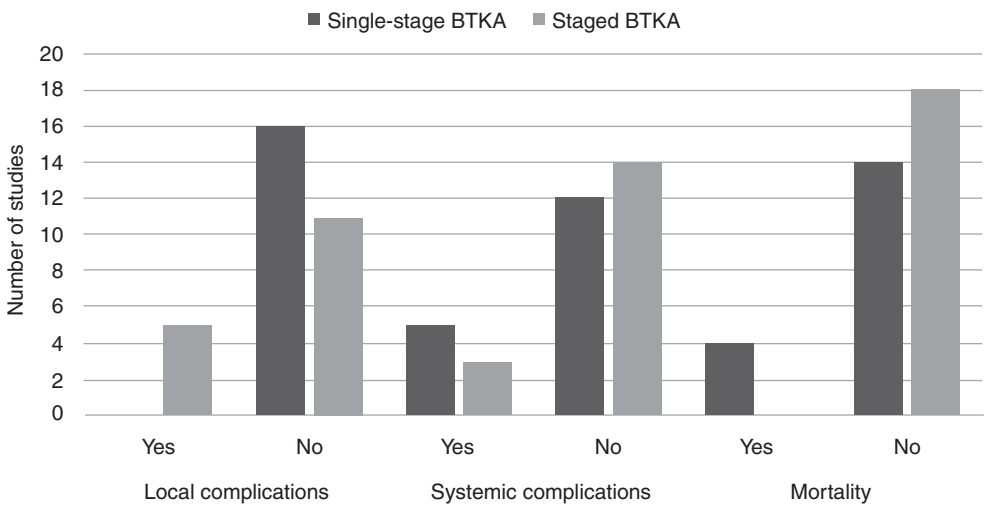

Fig. 28.4 Studies reporting significantly differences in mortality, local and systemic complications comparing single-stage BTKA and staged BTKA surgery

than that of patients undergoing unilateral TKA (0.3%). Our multivariate analysis revealed that the risk-adjusted mortality among patients undergoing BTKA was three times higher compared with those receiving unilateral TKA (Fig. 28.5). The discrepancy in mortality between BTKA and unilateral TKA was confirmed in analysis of nationally representative data collected for the Nationwide Inpatient Sample [42]. In both studies in-hospital mortality among BTKA patients was higher despite the fact that this population was younger and overall healthier than unilateral TKA recipients. Recently, we analyzed institutional data at a high-volume institution where a selective preoperative screening process has been adopted that tends to drive practice away from single-stage BTKAs in patients with more severe medical complications. We compared 3960 single-stage, 172 staged 0–3, and 1533 staged 3–12 BTKAs performed between 1998 and 2011. We did not find a significant difference in mortality among the three groups. A mortality of 30 days was 0.03% for the single-stage group, 0% for the staged 0–3 group, and 0.07% for the staged 3–12 group (p = 0.75) [61]. Additionally, we did not find differences when we compared 30-day mortality between same-admission staged and staged-within 1-year BTKA (0% versus 0.06%; p = 0.754) [80]. These findings suggest that for patients who are not appropriate candidates for single-stage BTKA based on a selective preoperative screening process, it is preferable to undergo the procedure as a staged intervention over 1 year and avoid same-admission staged BTKA.

Cardiac Complications

Several authors have expressed concern about a higher risk of cardiac complications in patients undergoing single-stage BTKA. The most frequently encountered cardiac complications include myocardial infarction (MI), arrhythmias, angina, and congestive heart failure [8, 9, 33, 40, 43, 45, 64]. A meta-analysis by Restrepo and colleagues [77] indicated that simultaneous BTKA may be associated with an increased the risk of cardiac complications (odds ratio = 2.49). We also identified congestive heart failure (CHF) as an independent risk factor for major morbidity or mortality in patients that are undergoing single-stage BTKA [61, 81]. These findings are probably explained by the stress imposed by longer operative times, larger fluid shifts, a more significant hyperadrenergic state, risk for anemia, and overall higher invasiveness of BTKA compared to unilateral TKA. Patients with reduced end-organ reserve and thus decreased ability to compensate for these insults may be at especially high risk [22]. Therefore, the physicians have been cautioned against worsening of cardiopulmonary function, especially in the setting of single-stage BTKAs. Two more recently meta-analyses did not find a significant difference in cardiac complications within patients that have undergone simultaneous BTKA compared with those who had undergone staged BTKA, a tendency that is also reflected in the last

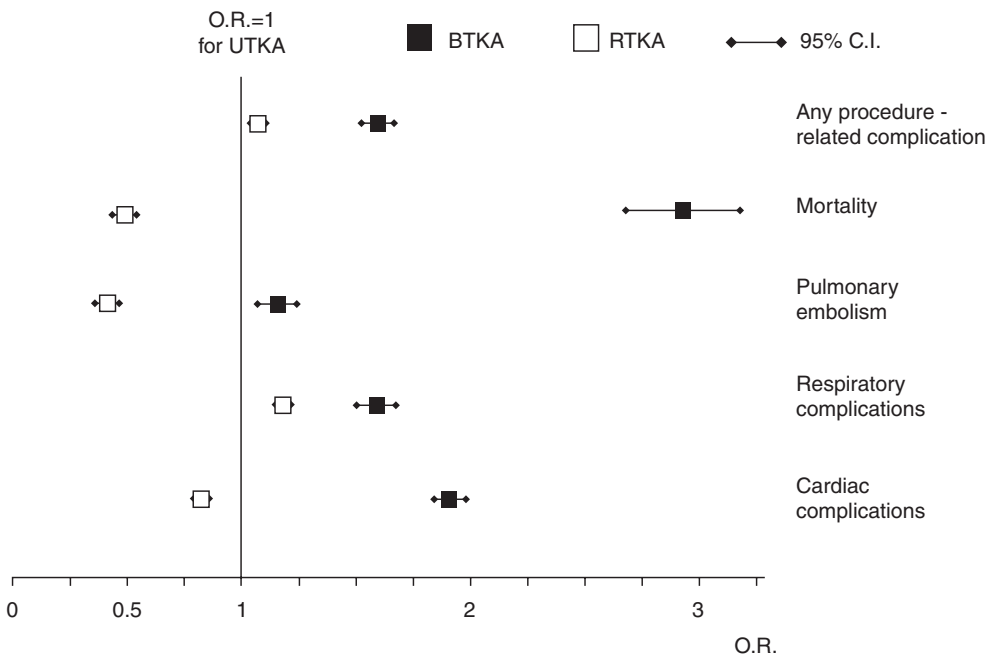

Fig. 28.5 Odds ratios (ORs) and 95% confidence intervals (95% CIs) for in-hospital mortality and selected medical complications in patients undergoing BTKA and RTKA (Referent is UTKA; OR, 1.) All ORs are different from UTKA = 1. BTKA bilateral TKA, RTKA revision TKA, UTKA unilateral TKA. (Used with permission of Wolters Kluwer from Memtsoudis et al. [22])

published studies [51, 74]. This finding might be the result of selecting younger and healthier patients for BTKA during the last years.

Complications Including Thromboembolism

Fat and pulmonary emboli are more frequent in patients undergoing single-stage BTKA than in those undergoing unilateral TKA [18, 40]. Some authors suggested using a fluted intramedullary rod, slow rod insertion technique, and over-drilling the entry point for the guide rod [30, 82] to reduce the risk of forcing medullary contents into the venous system. However, Lane and coauthors [16] concluded that even when no intramedullary rods are used during surgery, fat embolism is still a concrete threat.

Pulmonary embolism seems to be associated with increased operating time of single-stage BTKA, the cementing of the components, the surgical intervention at both lower extremities, and a prolonged duration of relative immobility. All of which contribute to trigger the Virchow triad of venous stasis and turbulence, endothelial injury, and hypercoagulability [83]. The majority of studies alert about a higher risk of pulmonary embolism in patients undergoing single-stage BTKA [22, 42, 43, 84, 85]. Restrepo and coauthors [77] reported that the probability of pulmonary embolism in patients who had undergone single-stage BTKA was higher than that in patients who had undergone a unilateral TKA (odds ratio of 1.8).

This concern has led to select young and healthy individuals to undergo BTKA in an attempt to diminish the incidence of complications. Two subsequent meta-analyses [78, 79] that compared single-stage BTKA with staged BTKA did not find a significant difference in the prevalence of pulmonary embolism. We analyzed our institutional data from 3960 single-stage and 172 staged 0–3 and 1533 staged 3–12 BTKA between 1998 and 2011 [61]. Although complication rates were also similar among groups and thrombotic events were comparable among groups, we identified pulmonary hypertension as significant risk factor for major morbidity or mortality in the single-stage BTKA cohort. Therefore, it seems prudent to screen patients who are suspected of having increased pulmonary pressure or right heart dysfunction, including patients with sleep apnea, and those with a history of pulmonary embolism, and consider them at high risk. This is because these conditions may be associated with higher impedance to venous return due to increases in right heart pressures, especially after additional increases in pulmonary vascular resistance brought upon by embolizing debris after bilateral procedures [81, 86]. In addition, we advocate routine thromboprophylaxis with Coumadin in patients undergoing single-stage BTKA surgery.

Postoperative Confusion

There seems to be agreement on the higher rate of postoperative confusion after single-stage BTKA compared to unilateral TKA [16, 22, 49, 87]. Hu and associates [78] reported that neurological complications were significantly higher in the population who had undergone single-stage BTKA compared with those who had undergone staged BTKA (odds ratio of 2.906). The neurological complications reported in this meta-analysis refer to changes in mental status that include confusion and cerebrovascular accidents. The cause for this complication seems to lie within higher degree of systemic inflammation and higher rates of fat and debris embolization [16, 88]. Some researchers have conducted intraoperative hemodynamic monitoring, electroencephalography, and direct ultrasound imaging of the carotid artery in patients undergoing bilateral lower limb replacements, observing debris embolization into the arterial circulation especially upon tourniquet deflation immediately after the second of two sequential arthroplasty procedures [88].

Potential Increase in Wound Infection Rate

The literature reports contrasting opinions regarding wound infection rates following single-stage BTKA and unilateral TKA [1, 27, 62]. Those who have observed a higher infection rate in single-stage BTKA surgery [1, 27] blame the longer operating times, increased number of medical personnel in the operating room, and no re-scrubbing, no re-draping, and no instrument change for the second knee arthroplasty.

We studied the deep and superficial wound infection rates 1 year after single-stage bilateral total hip arthroplasties performed with 1 or 2 sets of sterile instruments [89]. The rate of infection in 271 patients who had a new sterile setting for the second hip was similar to that of 294 patients who had both hips done using the same instruments ($p \sim 1.0$).

Some authors suggested that single-stage BTKA surgery has a lower risk of perioperative infection in comparison to staged BTKA and unilateral TKA [8, 22, 90].

We studied in-hospital complications of over four million TKAs in the USA which showed that despite the higher rate of obesity in patients undergoing BTKA (8.3% vs. 6.3% in unilateral TKA patients), those undergoing unilateral TKA had higher rates of procedure-related in-hospital infection (0.1% vs. 0.2% in the unilateral TKA group) [22]. In addition, in a large retrospective cohort study on almost 17,959 patients [90], we observed a significantly lower overall infection rate following single-stage BTKA (0.57%) compared to staged BTKA (1.39%, $p = 0.029$) and unilateral TKA (1.1%, $p = 0.025$). This may be explained by the fact that the latter group had an increased prevalence of other comorbidities, and some are linked to an increased risk of infection, i.e., diabetes [91].

Use of Allogenic Blood Transfusions

Predictably, the incidence of post-hemorrhagic anemia is greater after single-stage BTKA than unilateral TKA. Utilizing nationally representative data, we found the incidence of postoperative anemia to be around 28.6% in BTKA and 15.3% in unilateral TKA patients [22]. Besides twice the blood loss related to the second procedure, Bould and coauthors [92] showed a prolongation in the prothrombin time, activated partial thromboplastin time, and thrombin time after release of the first tourniquet, hypothetically due to tissue trauma, tourniquet application with decrease in clotting factors, and perioperative hypothermia.

The increased risk of allogenic blood transfusions after single-stage BTKA has been reported to be as high as 17-fold [13, 16, 37, 72, 93]. In order to limit the need for allogenic blood transfusion, over the last years, some studies have demonstrated that the use of tranexamic acid (TXA) in single-stage BTKA is effective and safe for reducing perioperative blood loss and the need for transfusion as a well as in unilateral TKA [94–96]. Bagsby and associates [95] showed that intravenous TXA is an effective tool in reducing the transfusion rates by almost 70% drop in single-stage BTKA, whereas Chen and associates [96] also found a significant decrease in blood loss, drainage volumes, and hemoglobin drop using TXA.

Use of Tertiary Rehabilitation Centers

There is an increased proportion of patients undergoing single-stage BTKA surgery that are discharged to an acute/subacute rehabilitation facility, than following unilateral TKA surgery [7, 15, 16, 22, 43, 45, 55, 66, 72]. In our study reporting on the trends of TKA surgery in the USA between 1990 and 2004, we observed that 37.2% of 153,259 BTKA patients in comparison to 19.6% of 3,672,247 unilateral TKA patients were discharged to short- or long-term facilities [22]. The reason for this seems to lie not solely in the slower postoperative mobilization of patients undergoing BTKA but also in surgeon, physical therapist, and social worker expectation that dedicated rehabilitation after the hospital stay would be more frequently necessary in BTKA compared to unilateral TKA patients. The decision to transfer a patient to a rehabilitation facility is strongly affected by the patient ability to ambulate at the time of discharge. This difference can be accounted for by the fact that patients undergoing unilateral TKA most commonly have only unilateral OA and thus may be less affected in the ability to ambulate. This is in contrast to BTKA patients who have bilateral disease.

Timing of Surgery for BTKA

The appropriate timing of surgery between stages for staged BTKAs has not been well defined. However, some evidence suggests that BTKA surgery performed during the same hospitalization should be performed under a single anesthetic (single-stage). We analyzed nationally representative data comparing outcomes in patients undergoing same versus different day BTKA during one hospitalization and showed no difference in mortality but an increase in complication risk in the latter group [42].

Several small retrospective studies have proposed different timing between procedures. Forster and coauthors and Courtney and coauthors [38, 71] suggested that 1-week interval is a safe alternative, whereas Sliva and associates [75] proposed a staging interval of 4–7 days, and Wu and associates [97] did not find difference in major and minor complications within 2 or 7 days of staging interval. Ritter and associates [76] compare outcomes within patients undergoing simultaneous, 6 weeks, 3 months, 6 months, and 1 year staged BTKA among Medicare beneficiaries. They observed that none of the bilateral groups performed categorically better than the others, although 3-month staged BTKR was associated with the most favorable profile. In 2013, the consensus Conference on BTKA group recommended that if a patient is not deemed a candidate for same-day BTKAs, a second TKA should be scheduled for 3 months or later [41].

Recently, Liu and associates [98] studied the feasibility of staging BTKA during the same hospitalization. A total of 41,664 BTKA patients from Nationwide Inpatient Sample (NIS) between 1998 and 2010 were included in the study and were categorized into three groups, same day, staging 1–3 days, and staging 4–7 days BTKA. The incidence of peri-operative mortality was low among all three groups (0.23%, 0.09%, and 0.07% respectively; $p = 0.476$). Both staging 1–3 BTKA and staging 4–7 days BTKA groups had higher overall postoperative complications than same-day BTKA patients ($p < 0.001$), and staging 1–3 days apart

between two TKAs increased the likelihood of major complications compared to same-day bilateral TKA (13.21% vs 9.17%, p <0.001).

Therefore, in agreement with this study we recommend a single-anesthetic (single-stage) BTKA over staging BTKA during the same hospitalization. The previously mentioned data and suggestions are particularly important in light of findings by other authors, who reported that patients with equally severe bilateral knee osteoarthritis have a 75% probability of having both knees replaced within 1 year of each other [99].

Recommendations for Patient Selection

In view of the presented facts and figures and in order to diminish the rate of perioperative life-threatening complications of surgery and mortality for this elective procedure, it seems reasonable and prudent to carefully select patients that are candidates for BTKA surgery. We conducted a study aiming at identifying risk factors for morbidity and mortality following BTKA surgery using data from the Nationwide Inpatient Sample [81]. Of the 42,003 entries identified, representing an estimated 206,573 elective BTKA procedures performed in the USA between 1998 and 2007, 9.5% developed major complications or mortality during their hospitalization. Increasing age was an independent risk factor for major morbidity and mortality. Patients younger than 45 years were half as likely to have a major complication or mortality with respect to patients in the age group between 45 and 64 years (odds ratio: 0.49 – confidence interval 0.30; 0.81). Comparatively, the risk for patients aged 65–74 and greater than 75 years rose significantly (odds ratio: 1.81, confidence interval 1.67–2.30 and odds ratio: 2.52, confidence interval 2.30–2.77, respectively). Advanced age as a risk factor has been further supported by findings published by other authors [17, 100]. This is likely associated with the fact that older patients have a physiologic decline in end organ reserve putting them in a more vulnerable position. Age as a risk factor and its consideration when contemplating BTKA becomes especially a problem when considering that a large number of joint arthroplasty recipients falls into this category. Male gender was associated with increased odds for adverse outcome (odds ratio: 1.5, confidence interval 1.44–1.66); however, reasons for this finding have to remain speculative. A number of comorbidities were identified as independent risk factors for major complications and mortality: pulmonary hypertension, congestive heart failure, fluid and electrolyte abnormalities, cardiac valve disease, renal failure, neurologic disease, coagulopathies, and chronic lung disease. Specifically, pulmonary hypertension and congestive heart failure were the most significant comorbidities associated with increased odds (odds ratio: 4.10 and 5.55, respectively) for adverse outcome.

Our experience, body of research, and review of the literature have led to the creation of guidelines for the selection of appropriate candidates for single-stage BTKA, in a desire to reconcile benefits and concerns for safety (Table 28.1).

Although conclusive evidence is limited, the literature suggests that the following points should be considered when contemplating single-stage BTKA:

1. *Exclusion based on age*: The findings of several authors [8, 17, 22, 23, 41, 45, 64, 100, 101] support that single-stage BTKA surgery in patients of extreme age should be avoided.
2. *Exclusion based on American Society of Anesthesiologists (ASA) classification*: The findings of several authors [23, 37, 40, 41, 62, 81, 102] support the exclusion of patients with significant end organ dysfunction, i.e., an ASA physical status of 3 or greater.
3. *Exclusion based on specific comorbidities*: Patients at risk for occult derangements of pulmonary hemodynamics and right heart dysfunction (i.e., the morbidly obese and those with sleep apnea, chronic obstructive pulmonary disease, and previous pulmonary embolism) should undergo cardiopulmonary evaluation with echocardiography to rule out significant preexisting increases in pulmonary artery pressures, which may predispose patients to increased morbidity and mortality. Besides pulmonary hypertension, congestive heart failure, and chronic lung disease, other comorbidities should be used as exclusion criteria, including coronary artery disease, renal failure, neurological disease, hepatic dysfunction, and coagulopathies.

Table 28.1 Contraindications to single-stage BTKA

–	Absolute contraindication	Relative contraindication	Suggested further evaluation
Extreme age (>80)	X	–	–
ASA class: 3 or greater	X	–	–
Obesity	–	X	Echocardiography
Sleep apnea	–	X	Echocardiography
COPD	–	X	Echocardiography
History of thromboembolism	–	X	Echocardiography

ASA American Society of Anesthesiologist, *COPD* chronic obstructive pulmonary disease

Furthermore, recognizing the need for guidance on the subject, a national group of experts participated in an elaborate consensus project to produce guidelines on the perioperative management of patients requiring single-stage BTKA [41]. These represent a consensus of specialized institutions.

Summary

In our experience and with the awareness of the previously mentioned recommendations, single-stage BTKA represents a valid option for the treatment of severe pain produced by bilateral knee osteoarthritis in the carefully selected patient. The advantages include good clinical results, the use of a single anesthetic, a shorter overall surgical time, and similar or less pain with respect to unilateral TKA (especially after postoperative day 1), reflected in a lower use of narcotics. Additionally, total recovery time compared with staged BTKA is faster, predictably accelerating return to everyday life and work. Patient satisfaction is qualitatively and quantitatively at least equivalent to that of unilateral TKA, with the overwhelming majority of patients who have experienced single-stage BTKA declaring they would opt for the same procedure again. Finally, cost-effectiveness of single-stage BTKA represents a major advantage of the procedure, with overall savings between 18% and 58% compared with the cost of staged procedures.

On the other hand, the disadvantages of single-stage BTKA must be considered when evaluating a potential candidate. The higher mortality rate in single-stage BTKA compared with unilateral TKA patients represents the most feared outcome. Although most studies in the literature do not reach significant power to actually detect potential differences in mortality, the latter seems to be significantly increased in single-stage compared to unilateral procedures. Cardiac complications, in particular myocardial infarctions, arrhythmias, angina, and congestive heart failure, are more prevalent in single-stage BTKA patients. These findings are possibly related to stress imposed by longer operative times, larger fluid shifts, a more significant hyperadrenergic state, risk for anemia, and overall higher invasiveness of BTKA compared with unilateral TKA. Pulmonary complications including thromboembolism and postoperative confusion are also a concern when selecting patients for single-stage BTKA. Greater wound infection rates seem to be controversial. Further drawbacks of single-stage BTKA include the increased use of allogenic blood transfusions. Finally, the greater use of tertiary rehabilitation centers might be regarded as a disadvantage of BTKA. While an increased proportion of patients undergoing single-stage BTKA surgery are discharged to an acute/subacute rehabilitation facility compared to unilateral TKA recipients, patients belonging to the latter group appear to be more likely readmitted for postoperative knee stiffness.

In light of the presented data and according to our experience at the Hospital for Special Surgery, single-stage BTKA represents a valuable option to restore knee function and well-being in patients with bilateral knee osteoarthritis. However, despite the low prevalence of life-threatening complications, thorough patient selection is advised, with the ideal candidate for single-stage BTKA being motivated, young, and healthy. The need for prospective randomized studies remains crucial to further support of clinical recommendations for patient selection.

Summary Bullet Points

- Bilateral total knee arthroplasties can be performed during a single surgical session, sequential or simultaneous, or staged during different surgeries.
- Single-stage bilateral knee arthroplasty may be associated with reduced hospital costs and the advantage of a single hospitalization.
- Single-stage surgery may be associated with increased risk for perioperative complications in the unselected patient population.
- In order to reconcile higher risk with the benefits of single-stage bilateral knee arthroplasty, institutions and clinicians may want to consider the utilization of strict screening criteria to guide patient selection.

Case Study

A 56-year-old male, motivated, physically active, chemical engineer presented at our outpatient clinic complaining of a 5-year history of bilateral knee pain with severe varus deformity and osteoarthritis. With a body mass index of 28, his medical history was unremarkable except for hypertension treated with an ACE inhibitor. He had no medical history of pulmonary, renal, liver, vascular, hematologic, or thromboembolic disease. The patient had been trying to manage the symptoms of osteoarthritis conservatively using anti-inflammatory medication and doing physical therapy. He received a cortisone injection in each knee which provided him with relief for only 3 months. After discussing benefits and drawbacks of staged and single-stage bilateral knee replacement surgery, he elected to proceed with a single-stage procedure. Preoperative medical clearance included a stress test, which was within normal limits. The patient predonated 2 units of blood. He was admitted on the same day of surgery. Anesthesia consisted of combined spinal and

epidural. Bilateral femoral nerve blocks were placed to supplement postoperative epidural analgesia for the first postoperative day. An arterial line was placed for close blood pressure monitoring and in anticipation of frequent perioperative blood draws. The more painful knee was operated first. During the wound closure, the patient was found to be hemodynamically stable and a decision was made to proceed with TKA in the contralateral knee. Surgeries were performed by the same team, using the same surgical instruments for both procedures. Both surgeries were performed under tourniquet inflation which was released after curing of the cement for meticulous hemostasis. Vacuum drains were used. The total surgical time was 135 min. Upon completion of the second surgery, the patient was transferred to the post-anesthesia care unit for overnight monitoring. One unit of the predonated blood was transfused. Multimodal thromboprophylaxis included the use of intermittent pneumatic compression devices, immediate active ankle flexion and extension exercises, and early ambulation beginning on postoperative day 1. Coumadin was started on the same day of surgery with a target INR from 1.8 to 2 for 6 weeks, along with knee-high elastic stockings to be worn during the day following discharge. On postoperative day 3, the patient was transferred to a tertiary acute rehabilitation center. No medical or local complications were observed during the recovery period. At 6-week follow-up, thromboprophylaxis was discontinued, and the patient continued with outpatient physical therapy for an additional 6 weeks. The patient returned to his office work 1 month after surgery and to low-impact sports at 3 months.

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Compartment Syndrome and Orthopedic Surgery: Diagnosis and Management

29

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Objectives

- To define compartment syndrome and understand its etiology and incidence
- To explain how to identify and diagnose compartment syndrome
- To elucidate the spectrum of compartment syndromes
- To discuss treatment options and timing to surgical intervention
- To describe the most common post-treatment complications and patient outcomes
- To describe differences between adult and pediatric patients in terms of diagnosis, timing of fasciotomy, and outcomes in acute compartment syndrome

Key Points

- Compartment syndrome is defined as an elevation of intracompartmental pressure to a level that impairs arterial flow to muscles, nerves, and other local tissues.
- Compartment syndrome of the upper and lower extremities can have multiple etiologies, including traumatic, exertional, and iatrogenic in the perioperative setting.
- Early identification and diagnosis enabling prompt intervention is essential to providing patients the best possible outcomes.
- In cases of acute compartment syndrome, emergent fasciotomy is generally indicated. Delayed fasciotomies more than 12–24 h after onset of symptoms are not recommended as they increase morbidity and mortality; however, it is often difficult to establish a time zero for onset or irreversibility.
- Even with timely treatment, multiple surgeries are often necessary to ensure adequate wound debridement, appropriate soft tissue coverage and satisfactory wound closure. Long-term sequelae range from cosmetic concerns secondary to wound complications, the use of skin grafts, limb deformity, amputation, or systemic complications associated with rhabdomyolysis.
- Compartment syndrome may be more difficult to diagnosis in the pediatric patient, but fortunately, outcomes are generally better than in the adult population, even following delayed fasciotomy.

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Introduction

Compartment syndrome is defined as an increase in intracompartmental pressure sufficient to impair the micro and/or macrovascular circulation to a level that can cause ischemia and necrosis of local tissue, especially muscle [1]. A group of muscles bound by fascia are considered a compartment in the extremities, although paraspinal compartment syndrome has been described [2–6]. Quantitatively, relative ischemia of

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muscle begins when tissue pressures rise to within 30 mmHg of the patient's diastolic pressure. Experimental studies have shown significant muscle necrosis at sustained absolute pressures of 30 mmHg [7–12]. Diagnostic values vary based on institutional preference and surgeon experience, but our threshold for the diagnosis of acute compartment syndrome is a ΔP (diastolic blood pressure – intracompartmental pressure) of less than 30 mmHg in one or more compartment.

Compartment syndrome exists on a spectrum and ranges from acute to chronic. Despite a variety of causes, including burns, vascular injuries, and those that occur after surgical procedures, the vast majority of acute compartment syndromes seen by orthopedic surgeons are diagnosed in the setting of blunt trauma. Based on a study of 164 patients from the UK, tibial shaft fractures account for 36% of compartment syndromes associated with acute injuries [13]. Fractures in the upper extremity, hand, and foot account for the majority of other clinical scenarios where compartment syndrome is an important concern (Table 29.1). The same study reports the average annual incidence in men to be 7.3 per 100,000 and 0.7 per 100,000 in women, a tenfold increased risk of acute traumatic compartment syndrome for males. Nonetheless, for individuals presenting with acute tibial shaft fractures, a recent study out of Canada has found that the patient's sex does not predict the likelihood of acute compartment syndrome and open and closed tibial shaft fractures confer a statistically equivalent risk of acute compartment syndrome. Meanwhile, certain patient factors are in fact implicated in acute compartment syndrome, as the same study found that young adults with tibial shaft fractures are at higher risk of developing acute compartment syndrome when compared to older adults with similar injuries [14]. However, for those who care for orthopedic patients on a regular basis, it is imperative to keep in mind that treatment modalities such as surgical fixation of fractures and casting can also result in compartment syndrome. For this reason, vigilance in the post-injury as well as postoperative period is essential.

Table 29.1 Blunt trauma conditions in which compartment syndrome is diagnosed

Underlying condition	% of cases
Tibial shaft fracture	36
Soft tissue injury	23.2
Distal radius fracture	9.8
Crush syndrome	7.9
Diaphyseal forearm fracture	7.9
Femoral diaphyseal fracture	3.0
Tibial plateau fracture	3.0
Hand fracture(s)	2.5
Tibial pilon fractures	2.5
Foot fracture(s)	1.8
Ankle fracture	0.6
Elbow fracture dislocation	0.6
Pelvic fracture	0.6
Humeral diaphyseal fracture	0.6

Data from: McQueen et al. [13]

It is well documented that the primary cause of poor outcomes and failed treatment in compartment syndrome is delayed diagnosis [15–18]. A missed compartment syndrome may lead to additional surgical procedures, medical expenses, and patient morbidity, which often results in legal ramifications for those involved. Bhattacharyya and Varhas retrospectively reviewed 19 closed malpractice claims and found the following factors to be associated with "poor legal outcome": documentation of abnormal neurologic examination but no action, poor physician communication (i.e., disregarding telephone calls), and delay in fasciotomy after initial presentation. Furthermore, the number of cardinal signs of compartment syndrome (pain out of proportion, pallor, paresthesias, paralysis, and pulselessness) was linearly associated with the dollar amount of payment ($p < 0.001$, $R = 0.74$) and an increased number was associated with an increased chance of indemnity payment ($p < 0.02$) [19]. Within this cohort, 11 patients required an average of 3.5 additional procedures. Sixteen cases were settled without trial over an average of 5.5 years. The decision ratio was 9:7 (patient/surgeon) with an average indemnity payment of $426,000. Three cases went to trial with all three verdicts favoring the treating surgeon. The average defense cost of these cases was $29,500. Overall, the most common sequelae alleged by the patients were need for additional procedures, loss of motion, foot drop, chronic pain, and difficulty walking.

To limit the patient morbidity and legal sequelae associated with compartment syndrome, early and accurate diagnosis is essential. Despite modern diagnostic tools, history and clinical examination remain the primary means of diagnosing compartment syndrome. All providers caring for the orthopedic patient, including nursing assistants, registered nurses, nurse practitioners, physician assistants, residents, and attending surgeons, should be aware of the diagnostic criteria and have a thorough understanding of injuries and surgical procedures that put patients at risk for compartment syndrome.

Primary and follow-up assessment of all traumatic injuries should include specific attention to the cardinal signs or the "Ps" of compartment syndrome (Table 29.2). Although pain out of proportion to examination (or increasing analgesic

Table 29.2 Cardinal signs or the five "Ps" of compartment syndrome

"P"	Description
Pain	Pain associated with injury or necrosis; typically seen early
Palor	Loss of normal skin tone and/or capillary refill
Poikothermia	Loss of body heat in area of injury
Paresthesias	Numbness or tingling sensation; typically seen late
Pulselessness	Loss of pulses distal to site of injury

requirements in younger patients) is considered to be the first indication of an impending compartment syndrome, patients may present with any combination of signs or symptoms.

Work by Bae and coauthors has shown that the traditional five "Ps" of compartment syndrome are unreliable in the pediatric population, with the exception of pain as inferred from an increasing analgesia requirement. All patients in their study with access to patient-controlled analgesia (PCA) demonstrated increasing analgesia requirements. Agitation/restlessness and anxiety were also noted in their study population. Their findings have led the adoption of a separate mnemonic for pediatric compartment syndrome known as the three "As" for agitation, anxiety, and analgesia (shorthand for increasing analgesia requirement) [20].

Perioperative Considerations

Acute Assessment

As stated previously, despite advances in quantitative diagnostic devices, history and physical examination are essential to diagnosing acute compartment syndrome.

In our institution, serial physical exams are performed every 2–4 h on all patients deemed to be at high risk. Such patients include tibial shaft and plateau fractures, crush injuries, and any patient with a concerning physical exam at presentation (i.e., significant swelling, pain out of proportion to exam, etc.). It is also very important to recognize that specific operations such as intramedullary nailing and osteotomies may lead to postoperative compartment syndrome, and thus these procedures mandate serial exams for a minimum of 24 h postoperatively. Lastly, to avoid iatrogenic compartment syndrome, all postoperative immobilization is performed with splints or bivalved casts to allow for tissue expansion and easy, rapid removal if necessary.

The use of catheter insertion to measure compartment pressure has become more common since the initial use of needle manometry in 1975 [7], but those using such devices should be aware that tissue pressures will vary based on distance from the site of injury with peak pressures being encountered within a few centimeters of fractures [21]. Often, such quantitative measures are used in the operating room to confirm a clinical diagnosis rather than to make a diagnosis.

Recent studies have focused on new diagnostic modalities for the detection of acute compartment syndrome. Cathcart and colleagues showed that near-infrared spectroscopy detects changes in oxygenation in muscle tissue in response to compartment syndrome induced in a porcine model, including a return of oxygenation to the muscle following fasciotomy [22]. Tissue ultrafiltration catheters have been explored for both their diagnostic potential to measure compartment pressures and biomarkers associated with compartment syndrome such as lactate dehydrogenase and creatine kinase as well as their therapeutic capacity to remove fluid and thus decrease intracompartmental pressures [23]. Lastly, implantable microchip pressure sensors and transmitters have been proposed as minimally invasive, portable continuous compartment pressure monitors [24]. Nevertheless, these new technologies still need to be validated in the clinical setting, and clinical examination remains the mainstay of diagnosis.

Anesthetic Considerations

Advances in regional anesthetic techniques over the past several decades have allowed for excellent perioperative pain control while limiting excessive narcotic use. A combination of spinal anesthesia for lower extremity procedures and short- and long-acting peripheral nerve blocks in both the upper and lower extremities is increasingly common. However, patients with suspected impending compartment syndrome or those undergoing high-risk surgical procedures should not be administered long-acting peripheral blocks under any circumstances. Such anesthetic techniques can mask pain associated with increased compartment pressures and severely limit a practitioner's assessment [25]. Any spinal or peripheral anesthetic used should be either short acting or easily titrated down to zero so that a formal assessment of pain and neurologic status can be obtained rapidly and accurately.

Sign-Out/Documentation

Orthopedic practice has seen a rapid increase in patient volume. Simultaneously, new regulations, such as residency work hour restrictions, have led to an increase in the number of care providers involved with a patient's care. The number of "sign-outs" is only increasing, with patients often changing hands several times each day. The potential for error, due to a failure of communication is great [26].

Given that compartment syndrome is one of the few, true orthopedic emergencies, any patient at risk for developing this condition should receive special attention during sign-out sessions. The outgoing team must personally relay the information to the person who will be assuming care of the patient. E-mail, a common form of communication in the healthcare field today and one that is frequently used as a sign-out tool at many institutions, is neither appropriate nor adequate when transferring care of a patient, especially one at risk for developing a compartment syndrome. Further, in such situations where a patient will be receiving compartment checks from more than one practitioner over a given

time period, every attempt should be made for both individuals to see the patient together at the time care is transferred to establish an accurate baseline examination by the practitioner who is assuming care.

Given the medical-legal implications of delayed diagnosis and/or missed diagnosis of a compartment syndrome, timed documentation has become a point of emphasis for patients being monitored for a possible compartment syndrome. Each "compartment check" should be carefully documented and attention paid to both the patient's subjective complaints and objective findings. The patient should be asked specifically about their pain, subjective tightness, as well as any emerging neurologic symptoms such as decreased sensation and dysesthesias. Objective findings and subjective complaints should be compared with prior exams.

The physical exam of a patient with possible compartment syndrome is fourfold. First, careful palpation of each compartment should be conducted, although findings are entirely subjective and have been shown unreliable. Shuler and colleagues showed that in a cadaveric model, palpation of compartments had a sensitivity of only 54% for detection of elevated compartment pressures [27]. Next, the muscle groups of each compartment should be stretched passively. If compartment pressures are significantly elevated, muscle stretching within that compartment should elicit significant pain. Passive stretch is perhaps the earliest objective finding and arguably the most important component of examination. Third, a careful neurologic examination including both motor and sensation should be conducted. It is essential to include all potential nerve distributions, especially in the splinted patient where particular distributions may be more difficult to access. Lastly, vascular status should be assessed with palpation of pulses, skin temperature, and capillary refill. Patients who are sedated, intubated, or otherwise unresponsive (including the pediatric patient) and cannot express their symptoms may require manometric monitoring and a lower threshold for intervention.

As with any physical examination, that of a patient with compartment syndrome can vary widely with each subsequent exam. Cascio and colleagues retrospectively reviewed 30 consecutive patients undergoing fasciotomy for acute compartment syndrome over a 10-year period and found 90% to be lacking in documentation of a complete physical exam (Table 29.3). Of the 30 patients, ten had permanent sequelae [28]. As stated previously, documentation of an abnormal neurologic examination and failure to act upon those findings is associated with indemnity payments during malpractice cases [19]. For these reasons, accurate documentation of a physical examination at the time it is performed, along with any actions taken at that time is crucial.

The rise of electronic medical records highlights certain medical-legal pitfalls in documenting "compartment checks." Some practitioners choose to document all compartment examinations in one note at the end of their shift to increase efficiency. The authors strongly discourage against this practice and recommend immediate documentation of each compartment check individually. Similarly, back-dating of notes undermines the practitioner's legal credibility. If a practitioner wishes to clarify or correct an existing note in the chart, the authors recommend documenting this information in a timed addendum rather than attempting to edit the existing text of a note, as alterations to the original note are tracked in the electronic medical record and may appear suspect.

Table 29.3 Of 30 consecutive patients undergoing fasciotomy for acute compartment syndrome over a 10-year period, 90% are found to be lacking in documentation of a complete physical exam

Core H&P findings	Patients with inadequate documentation (n = 30)
Tenseness	3 (10%)
Pain	5 (17%)
Compartment pressures	6 (20%)
Pulses	7 (23%)
Motor examination	8 (27%)
Sensory examination	9 (30%)
Pain on passive stretch	10 (33%)
Paresthesias	11 (37%)
Diastolic blood pressure	16 (53%)
Pallor	28 (93%)
Overall (excluding pallor)	21 (70%)

Data from: Cascio [28]

Informed Consent/Patient Expectations

Perhaps one of the most overlooked issues surrounding the diagnosis and is treatment of compartment syndrome centers around the topic of informed consent. For any patient suspected of having an acute compartment syndrome, an impending compartment syndrome, or a surgical procedure associated with a high risk of compartment syndrome, it is the responsibility of the treating surgeon and team to discuss with the patient the risks associated with the diagnosis, the treatment options, and the possible long-term sequelae associated with both the diagnosis itself and the treatment (i.e., fasciotomy). Proper expectations must be set. Consent should be obtained for possible fasciotomy in such patients. If proper consent is obtained and the patient has a thorough understanding of possible outcomes, sequelae can be looked at as expectations rather than a complication.

The importance of early fasciotomy as treatment for acute, traumatic compartment syndrome is well-documented dating back as early as 1914 [29]. Any compartment in question should undergo early fasciotomy, and in many cases prophylactic fasciotomies are performed on neighboring compart-

ments – for example being the tibial shaft fracture with elevated intracompartmental pressures in the anterior compartment that is treated with a four compartment fasciotomy. All nonviable tissue is debrided at the time of fasciotomy. Surgeons often use the mnemonic of the four Cs – color, contractility, consistency, and capacity to bleed – as indices of muscle viability. However, the four Cs may not be reliable markers of muscle viability based on a recent study correlating intra-operative appearance and histology [30].

After fasciotomy and debridement, treating surgeons are frequently left with two issues, the first being fracture fixation, as the majority of compartment syndromes occur in the setting of osseous injury [31], and the second being wound closure. In order to decompress the compartments and allow for soft tissue swelling to subside, fasciotomy wounds are left open, frequently with negative pressure dressings (VAC). Delayed primary wound closure is typically attempted after 48 h, assuming there is viable muscle coverage of the underlying osseous structures and a tension-free closure can be achieved. Split thickness skin grafting or gradual closure techniques are indicated if the wound is under tension. For more severe cases, patients may require rotational or free muscle flap coverage and experience donor site morbidity, or they may require fitting of a prosthetic if amputation was required. The patient should be aware prior to fasciotomy that repeat procedures and possible plastic surgery intervention may be required, and, in some cases, amputation may be necessary.

Systemic complications of acute compartment syndrome should also be discussed with the patient and include sepsis stemming from infection of necrotic tissue and rhabdomyolysis with resulting renal failure. It is important to monitor serum CPK levels and renal function in patients suspected of compartment syndrome. Patients should also be counseled regarding cosmesis following wound closure, and muscle weakness secondary to necrosis and debridement. Recent murine studies demonstrate that much of the damage caused by acute compartment syndrome is mediated by inflammatory processes, and these pre-clinical studies also suggest that anti-inflammatory medications such as indomethacin may be protective if administered prior to or even after the onset of acute compartment syndrome [24].

It has been our experience that compartment syndromes of the foot is unique in that fasciotomy often results in poor functional outcomes. For these reason, we believe that select patients may be observed clinically, provided both the surgeon and patient are prepared to address the sequelae, which are often treatable with minor surgery and more tolerable than those associated with fasciotomy. Toe-clawing and contracture, fibrosis, stiffness and aching, atrophy of intrinsic muscles, and sensory disturbances [32] should all be discussed with the patient at length and the conversation documented before the decision is made to observe a diagnosed compartment syndrome.

The Spectrum of Compartment Syndrome

As we have discussed, the criteria for diagnosis of compartment syndrome are predominately clinical. In the cases of acute compartment syndrome in a patient with a high-risk injury and rapid diagnosis, intervention is clear and well defined. The actual onset of compartment syndrome is often unknown, however. As is the case with many conditions in medicine and orthopedics, compartment syndrome frequently exists in a spectrum ranging from the classic acute presentation to delayed timing to diagnosis to the late or "missed" case.

The delayed or late compartment syndrome is a particularly important consideration in the orthopedic patient, especially in patients unable to convey their pain or symptoms (pediatric or ICU patient) or the patient transferred from an outside hospital facility hours or days following injury. Rorabeck and Clarke demonstrated that muscle function irreversibly deteriorated when fasciotomies were performed greater than twelve hours after the onset of acute compartment syndrome in a dog model, suggesting some degree of myonecrosis by this point [33]. While some studies indicate no increased risk with late fasciotomies [18], others suggested that fasciotomy-related morbidity, particularly with regard to infection, increases with delay in diagnosis as necrotic muscle exposed to the outside environment at the time of surgery is highly susceptible to bacterial pathogens [34, 35]. In fact some authors have reported increased morbidity and mortality in patients treated with fasciotomies more than 24 h after diagnosis [36]. Sheridan and Matsen noted that early fasciotomy patients had a complication rate of only 4.5%, while those treated with late fasciotomies were exposed to a 54% morbidity rate – half of which ultimately proceeded to amputation [35]. Finkelstein and colleagues reported a case series of five patients with closed lower extremity injuries who underwent late fasciotomies, more than 35 h after injury (average 56 h) [37]: one patient died from sepsis while the other four ultimately required amputations (3 secondary to infection and 1 secondary to lack of function). Prior to the era of renal dialysis, death from crush/compartment syndrome occurred most commonly from renal failure. The authors contend, however, that with modern means of dialysis, death from these injuries is predominately due to infection. They conclude that late fasciotomies convert a closed fracture into an open injury and put the patient at risk of overwhelming infection and related morbidity and mortality. Further to this end, Ritenour and colleagues more recently reported a two-fold increase in amputation and threefold increase in mortality in trauma patients treated with delayed fasciotomies [38].

Recent data, however, suggest that delayed treatment of compartment syndrome in the pediatric population may allow for acceptable results with a low risk of infection. Flynn and colleagues retrospectively reviewed 43 cases of acute traumatic compartment syndrome of the lower leg treated at two

institutions with fasciotomy [39]. Of the 43 cases, nine had fasciotomies beyond 24 h post-injury (up to 118 h). 7/9 had excellent outcomes, 2/9 had fair outcomes with fasciotomies at 82.5 and 86 h (weakness with dorsiflexion) and there were no cases of infection. Pediatric upper extremity acute compartment syndrome similarly had favorable outcomes following fasciotomy in a study conducted by Wadji and coauthors, with an average time from injury to fasciotomy of 32.8 h and no effect of time to fasciotomy on final outcomes [40].

Compartment syndrome following hip and knee arthroplasty is relatively rare. Lasanios and colleagues reviewed the literature for cases in which compartment syndrome complicated total joint arthroplasty and identified 41 such cases, with nearly a 50/50 split between hip and knee arthroplasty [41]. The most common site of compartment syndrome following total hip arthroplasty was gluteal, accounting for nearly 73%. Not surprisingly, the most common site of compartment syndrome following total knee arthroplasty was the calf (61%), but gluteal compartment syndrome occurred with relative frequency (17%). The mean time to diagnosis was 26 h and the mean time to surgical intervention was 53 h. Gluteal compartment syndrome was almost exclusively attributed to body habitus and prolonged positioning either intraoperatively or postoperatively.

Gluteal compartment syndrome most commonly is atraumatic in etiology. This is of particular importance when considering the obese orthopedic patient who undergoes a prolonged procedure. Henson and coauthors performed a systematic review of seven publications including 28 patients diagnosed with gluteal compartment syndrome [42]. They noted that the most common cause of gluteal compartment syndrome was prolonged immobilization in men with an average age of 45 years. The patient's body weight was connected with the condition in 50% of the cases studied. Of the cases, 21% occurred in the contralateral (down side) of postoperative total joint arthroplasty patients. Trauma was identified as the causative source in less than one quarter of patients. Less than half of the patients were diagnosed with quantitative pressure assessments with the remainder diagnosed based on history and physical examination. Only 71% of diagnosed gluteal compartment syndromes were treated with surgical decompression. Of those treated without surgical intervention, the majority of cases included delayed presentation or diagnosis. Patient outcomes are variable based upon the compartments involved, extent of damage, and chronicity of diagnosis.

Special Consideration in the Perioperative Patient

While the most common etiology of compartment syndrome is trauma, it is crucial to recognize other potential causes in the perioperative orthopedic patient. Iatrogenic compartment syndromes may be prevented with attention to patient positioning, selection, appropriate tourniquet use, and careful application of immobilization devices.

It was initially thought that intramedullary nailing increased compartment pressures and thus increased the risk of postoperative compartment syndrome. Two studies, however, refute this notion. Tornetta and French prospectively evaluated 56 tibial shaft fractures without compartment syndrome preoperatively, each case being treated within 72 h of incident injury [43]. They performed continuous pressure monitoring of the anterior compartment and found transient increase in intracompartmental pressures highest during manual reduction (34 mmHg) and undreamed nail passage (26 mmHg), but noted immediate return to baseline pressures following nail passage. Nassif and colleagues reported on 49 tibial shaft fractures treated with intramedullary nailing within 72 h of injury [44]. They measured anterior and deep posterior compartment pressures and compared reamed and unreamed techniques. Their pressure measurements were similar to those found by Tornetta and French, noting rapid return to baseline. Further, they found no significant difference in reamed versus unreamed nailing on anterior compartment pressures, but statistically significant lower pressure in the deep posterior compartment for reamed nails. In each case, there were no cases of postoperative compartment syndrome.

The use of modern pneumatic tourniquets during orthopedic surgery is commonplace and allows improved visualization in a relatively bloodless operative field and reduced surgical blood loss. Temporary stoppage of blood flow to a limb results in tissue hypoxia and acidosis [45]. Inappropriate use, both pressure and duration, however, can lead to postsurgical complications including compartment syndrome. More than 2 h of sustained extremity ischemia may lead to post-tourniquet syndrome including pallor, swelling, and stiffness without neurologic symptoms due to myocyte injury [46, 47]. Post-tourniquet syndrome typically resolves within 1 week [46]. In extreme cases, however, extended tourniquet duration or excessive pressure can lead to frank compartment syndrome. Current guidelines for tourniquet use include duration less than 2 h [48]. In prolonged surgical cases, requiring greater than the recommended 2 h tourniquet time, Townsend and coauthors recommends a 30-min interval off tourniquet prior to reinflation [49]. The magnitude of tourniquet inflation should be 50–75 mmHg above preoperative systolic pressure for upper extremity surgery and 100–150 mmHg for lower extremity surgery [48]. Even with proper tourniquet use, however, compartment syndrome can occur. Hypervigilance and an open differential diagnosis are critical to recognition.

Compartment syndrome has also been reported in the well leg of patients undergoing orthopedic procedures on the trac-

tion table [50–53]. Development of this pathology is thought to be associated with direct compression of the lateral calf on the supportive post and the relative hypoperfusion of the limb in the elevated position if lithotomy position is used. The well leg may be dropped down into a scissor position to theoretically decrease the risk of hypoperfusion relative to positioning the well leg in lithotomy. Hypoperfusion of the limb may also be exacerbated in the patient undergoing regional anesthesia.

Application of pre- and postoperative splints and bandages must be undertaken with care and caution as over constriction of a limb may lead to the development of iatrogenic compartment syndrome [54]. Hinderland and coauthors reported a case of iatrogenic isolated lateral lower leg compartment syndrome in a 44-year-old man caused by ill-fitting compression stockings placed for DVT prophylaxis [55]. Others have reported cases of IV infiltration leading to compartment syndromes of the forearm and foot [56].

Compartment syndrome of the calf is most common, accounting for 36% of cases. This pathology can occur in any fascial bound muscle group including the foot, hand, and gluteal region. Regardless of the location, diagnosis and management occurs in a similar fashion. With regard to the less common regions, however, the most important diagnostic factor is a high clinical suspicion and inclusion of compartment syndrome on the differential diagnosis of pain. Roberts and coauthors looked at several of the less common compartment syndromes and noted that compartment pressures were performed in 64% of patients with compartment syndrome of the foot and less than 50% in the other less common areas such as the forearm, gluteal compartment, and the thigh [57].

Ojike and coauthors reviewed compartment syndrome of the foot in a systematic review and note the most common etiologies to be crush injuries, falls from height, and motor vehicle accidents in 28%, 26%, and 34% of cases, respectively [58]. Calcaneal fractures and Lisfranc fracture dislocations accounted for nearly half of the cases studied. While we have not found reports of foot compartment syndrome following elective corrective osteotomies, these are certainly to be considered a potential source of foot compartment syndrome. There exists significant debate as to the necessity of surgical decompression for treatment of foot compartment syndrome. Advocates argue that fasciotomies decrease the incidence of sequelae such as claw toes, impaired mobility, stiffness, and sensory deficits. Others argue, however, that the morbidity associated with surgical intervention may outweigh the morbidity of observation and later corrective procedures.

Sequelae of treated and untreated compartments syndrome have significant functional and aesthetic ramifications. Nerve deficits and stiffness are the most common sequelae following compartment syndrome regardless of the location. Ultimately, a timely and accurate diagnosis provides patients with the most optimal circumstances for recovery.

Summary

Compartment syndrome has devastating implications for surgeons and patients alike. The sequelae include patient morbidities, both functional and cosmetic. Failure to identify and document findings can have profound ramifications. The most effective treatment is early diagnosis.

Diagnosis of compartment syndrome is overwhelmingly clinical. Members of the medical or surgical care team must pay particular attention to the earliest findings – pain out of proportion, increasing analgesic requirements, and pain with passive stretch of muscles in a suspect fascial compartment. Other findings such as palpation for fullness are subjective and have been linked with poor interobserver reliability. Further the other traditional findings (pallor, paresthesias, paralysis, and pulselessness) are late findings. The most reliable findings in the pediatric population are increasing analgesia requirement (such as in cases with PCA), agitation, and anxiety. Newer technologies are being assessed for their ability to diagnose and potentially even treat compartment syndrome, but these technologies are still in early phases.

Compartment syndrome exists on a spectrum ranging from acute to delayed to late recognition. An acute compartment syndrome should undergo immediate fasciotomies. Some more recent literature points to observation in cases of late compartment syndrome, as exposing necrotic muscle dramatically increases the risk of infection. Unfortunately, there is often an unclear distinction between these phases of compartment syndrome. As such, the authors urge fasciotomy in any case where there is a question as to the timing to onset of the condition. Furthermore, while delayed fasciotomies in the pediatric population tend to produce more acceptable outcomes than the severe morbidity seen in the adult population, immediate fasciotomy is best in all cases of acute compartment syndrome.

While compartment syndrome is traditionally thought of as occurring in the setting of trauma (fracture or crush), there are a number of other etiologies including iatrogenic ones. As a medical community, we have the opportunity to limit these risks by paying particular attention to details such as positioning, placement of stockings, and splints. Further, we have an obligation to identify those at particular risk, perform appropriate examination, communicate with colleagues, and take immediate action as a patient's condition changes.

Summary Bullet Points

- Compartment syndrome is typically seen in the setting of acute trauma and osseous injury; however, patients undergoing specific operative interventions are at risk in the perioperative period, along with those treated with restrictive dressings (i.e., casts).
- A timely diagnosis of acute compartment syndrome can be difficult with patients experiencing a wide range of signs and symptoms but is essential to allowing for the best clinical outcomes. Compartment pressure measurements may be helpful, but serial clinical examinations are still the most important diagnostic tool.
- In most cases, urgent fasciotomy with adequate release of elevated compartment pressures will allow for the best possible clinical outcomes; however, all patients should be made aware that they may require multiple procedures and of the complications associated with both compartment syndrome and its treatment.

Case Studies

Case 1

A 43-year-old male underwent a right-sided wide excision of a supra-acetabular chondrosarcoma with subsequent reconstruction using an allograft-prosthetic composite total hip replacement. The patient was noted to have diminished dorsalis pedis and posterior tibial pulses on the right side on immediate postoperative assessment. Overnight the patient developed increasing pain in the right lower extremity. Compartments remained soft, but the patient's pulses were no longer palpable or dopplerable on examination the next morning.

The vascular surgery service was consulted, and angiography was recommended. The patient was taken to the operating room by the vascular surgery service for angiography which demonstrated a thrombus in the right common femoral artery, and the patient underwent open thrombectomy and common femoral artery reconstruction on postoperative day 1. Dorsalis pedis and posterior tibial pulses were again palpable. In the recovery room, the patient complained of increasing pain and swelling in the right leg despite elevation and ice applied to the affected region. On examination, the patient had clinically worsening of swelling and tense compartments circumferentially in the right leg. Passive extension of the ankle and great toe elicited severe pain. Over the next several hours, the patient began experiencing sensory changes in the foot, ankle, and leg.

The patient was taken back to the operating room later in the day for four-compartment fasciotomies of the right leg. The patient was noted to have bulging but red, robust, contractile muscle with a capacity to bleed in all four compartments. Following the fasciotomies, a negative pressure dressing was applied to the fasciotomy wounds and primary closure deferred.

Over the next several days, the patient continued to complain of right lower extremity pain and progressive loss of sensation in the right lower extremity, eventually resulting in frank numbness below the mid-shin and calf level. The patient's right leg continued to feel clinically tense, and the patient still demonstrated considerable pain with passive extension of the ankle and toes. The patient's urine became a dark cola color, and the patient's laboratory values indicated that the patient was experiencing acute kidney injury from rhabdomyolysis. Ultimately, the patient required hemodialysis.

The patient was again taken back to the operating room for revision fasciotomies by the vascular surgery service and was noted to have bulging muscle with a much less robust appearance that at prior surgery, particularly in the anterior and lateral compartments. The fasciotomies were nevertheless extended, and brownish-gray necrotic muscle was debrided. The wounds were thoroughly irritated, and again a negative pressure dressing was applied.

The patient remained in the hospital for several weeks. He underwent subsequent revision irrigation and debridement procedures of his fasciotomy sites due to recurrent bleeding in the setting of venous thromboembolism prophylaxis and for concern of infection as the patient remained intermittently febrile for over a week. Once the patient had overcome his recurrent fevers and the wound bed appeared healthy enough to accept a graft, the patient's fasciotomy wounds were covered using splitness skin graft from the anterolateral thigh. The patient's kidney function eventually recovered such that he no longer required dialysis. Despite best efforts with bracing and physical therapy to maintain a supple foot and ankle, the patient's right ankle developed an equinus contracture, and claw toes developed. Even several months after the index procedure, the patient had not regained sensation in the right lower extremity below the mid-leg.

This case underscores the importance of a high index of suspicion for compartment syndrome in the setting of revascularization. The patient was taken back to the operating room for fasciotomy, but it was unclear to what degree and exactly how long the patient's right leg had been ischemic. Compartment syndrome must be addressed surgically as soon as possible to afford the best outcomes. Additionally, this patient may have suffered additional sequelae of compartment syndrome due to an incomplete initial release of the anterior and lateral compartments, further delaying effective intervention. A complete release of all affected compartments is essential. A surgeon who is uncomfortable with the anatomy

of the leg may perform an incomplete release due to fear of injuring the superficial peroneal nerve. Regardless of whether vascular or orthopedic surgery performs the fasciotomies, the surgeon must be comfortable with the relevant anatomy to thoroughly decompress all the affected compartments.

Case 2

An 87-year-old female with mild dementia was admitted for a revision of a primary total knee arthroplasty due to pain and prosthetic loosening. Preoperatively, the patient had full motor strength and intact sensation in all nerve distributions. A revision left total knee arthroplasty was performed under combined spinal/epidural anesthesia and with use of a tourniquet. The tourniquet was let down after 2 hours, but the overall case lasted approximately three-and-a-half hours and ended late in the evening. Two hours postoperatively, the patient had no motor function or sensation below the knee of the left leg when the on-call orthopedic provider made rounds. The left lower extremity was edematous below the compressive postoperative dressing, and distal pulses were faintly palpable on the operative side. Compartments were firm, but the patient was comfortable with passive ankle dorsiflexion. The patient denied issues with pain control. When questioned, the nurse in the recovery room reported that the patient was maxing out her epidural PCA pump. The patient's son was at bedside and admitted to pushing the PCA button for his mother several times because he "didn't want her to suffer and didn't think she understood how to use the pain pump."

The orthopedic provider, following institutional policy, requested that the epidural PCA pump be discontinued, and the on-call anesthesiologist agreed. The resident also loosened the postoperative dressing, flexed the patient's knee, and made a note to check back in an hour. One hour later, the patient's neurological exam had not improved at all, and the provider grew increasingly concerned. He did not want to disturb the attending surgeon overnight, but per hospital policy, the resident immediately escalated his findings to the attending surgeon.

The attending surgeon advised the resident to make the patient NPO in anticipation of possible revision surgery and requested immediate evaluation by the neurology and vascular surgery services. The neurology service recommended a lumbar MRI which was unrevealing and showed no evidence of epidural hematoma. Vascular surgery was also consulted, and at this point the patient had lost palpable distal pulses. An MRI/MRA of the affected leg was performed, revealing a popliteal thrombus and poor perfusion. A thrombectomy, four compartment fasciotomy, and deep dorsalis pedis artery bypass were performed at that time. The anterior and lateral compartments were found to be bulging at the time of fasciotomy, and all visible necrotic muscle was debrided.

The patient underwent one more incisional irrigation and debridement procedure to remove a small amount of additional necrotic muscle. At the next procedure, the medial fasciotomy wound was closed primarily, and a split-thickness skin graft was performed laterally over a clean, viable muscle bed. Neurology continued to follow the patient through her recovery, and the patient spent several months in physical therapy. Ultimately, the patient required an ankle-foot orthosis for ambulation.

Again, this case highlights the risk of compartment syndrome associated with specific surgical procedures, including those with extended tourniquet times. Further, the use of spinal and/or epidural anesthesia can inhibit a postoperative examination, and there should be a low threshold for removing pain catheters if there is any question of a compartment syndrome. Great care must be exercised when running an epidural or peripheral pain catheter, especially in patients whose understanding or ability to comply with a history and exam – such as this patient with mild dementia – may be compromised.

Furthermore, this case illustrates the power of thoughtfully designed institutional policy to influence and often improve postoperative care. This provider followed institutional policy and called the attending surgeon after hours, setting off a chain of events that led to a more timely surgical intervention than would have otherwise resulted. Our institution has implemented an algorithm for all arthroplasty patients affected by neurologic deficits in the early postoperative phase. Nurses, physical therapists, physician assistants, nurse practitioners, residents, fellows, and attending surgeons at our institution have undergone training in this algorithm to better detect and manage postoperative foot drop, as described by Derman and coauthors [59]. Promising early results of this initiative have shown that more orthopedic providers in our hospital are consulting with anesthesia regarding the use of pain management strategies such as epidural PCAs that might mask a potentially serious complication, delaying timely intervention. Algorithms designed to rapidly detect such serious complications and promote early communication and appropriate escalation may become increasingly important as the population ages, orthopedic surgical demand increases, and hospitals face financial pressures to decrease postoperative length of stay.

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Bone Health and Orthopedic Surgery

30

Linda A. Russell

Objectives

- To introduce the concept of bone health
- To appreciate the magnitude of bone disease and its implications to orthopedic surgery
- To appreciate the evolving role for bone-active therapies in the orthopedic setting

Key Points

- Vitamin D levels at the time of an orthopedic procedure may affect outcome.
- Bisphosphonates may be beneficial after total joint arthroplasty.
- Medications used to treat osteoporosis may affect fracture repair.
- Teriparatide may improve the rate of bony fusion and outcome after spine fusion.
- Maximizing bone health preoperatively should be the goal for all orthopedic procedures.

Introduction

Traditionally, orthopedists have not evaluated the quality of bone prior to orthopedic procedures. Nonetheless, in recent years an assortment of pharmacological agents targeting bone quality has been developed; the agents are in common use, mainly in the treatment of osteoporosis. Growing evidence suggests that the maximization of bone quality and health perioperatively will result in better surgical outcomes. This chapter reviews current knowledge concerning this clinical experience, examining specifically vitamin D, its putative role in orthopedic surgery; the use of various medications in the setting of total joint arthroplasty, in spinal fusion, and in the fracture repair is presented.

Background

Osteoporosis is a common condition. One half of US women and ¼ of men over 50 years suffer an osteoporotic fracture during their lifetime, with more anticipated as the population ages. Many will require orthopedic procedures, including total joint arthroplasty, spinal fusion, and procedures to address fracture, most significantly of the hip. To best care for these patients and to promote successful outcomes, efforts directed at the optimization of bone, both its strength and quality, have become important perioperative imperatives. Nonetheless observations of contemporary orthopedic practice have shown how infrequently bone health is even evaluated. In perhaps the most important domain, the fracture setting, few patients currently receive bone-directed therapy; indeed 60% of patients in one study were instructed to take calcium alone as a treatment for their osteoporosis [1–3]. A survey of orthopedic surgeons performing total hip arthroplasty demonstrated that only 4% reviewed the result of a bone mineral density (BMD) preoperatively, but 66% of orthopedic surgeons noted that low bone mineral density would influence their surgical plan [4].

An osteoporotic fracture is defined as a fracture that results from a standing height or from a low-energy activity (i.e., raking leaves). Although many patients feel that they fell so firmly that "anyone would have broken their wrist," patients must be educated about this fallacy as all will benefit from therapy for osteoporosis. Supporting the recommendation for treatment are observations that the strongest predictor of

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osteoporotic fracture is prior fracture and that treatment does work. Indeed medications for osteoporosis have been shown to reduce the risk of subsequent fracture within 6 months of their administration [5]. Thus, based on these observations, practices ensuring that a patient's bone health is addressed after osteoporotic fracture have been advocated [6].

The other important clinical domain also largely ignored in orthopedic practice and in the perioperative medicine literature is the preoperative evaluation of bone health in patients undergoing orthopedic surgery. There are many ways in which poor bone health could affect surgical outcome. For instance, in patients with low bone formation rates, fracture repair and bone fusion may be impaired. One of the more common and treatable causes of impaired bone formation is tobacco use. Tobacco is directly toxic to the osteoblast; therefore counseling patients on the importance of smoking cessation when undergoing orthopedic procedures is critical [7]. However, if the patient requires a smoking cessation aide, it should not be a nicotine product, as nicotine also impairs bone formation.

Patients should have an up-to-date bone density prior to undergoing an orthopedic procedure. The US Preventative Task Force recommends a bone density on all women 65 years of age (earlier if there are risk factors); no recommendations for assessment of bone density in men have been developed by this organization. Alternatively, the National Osteoporosis Foundation (NOF) recommends that all women have a baseline bone density at menopause and men at 70 years of age, earlier if there are risk factors. The current literature does not fully address the benefit of vitamin D and parathyroid hormone determinations preoperatively. Nonetheless it seems intuitive that for overall bone health, it would be advisable to insure normal vitamin D levels and an absence of hyperparathyroidism, prior to an orthopedic procedure.

Another modifiable risk factor includes the evaluation of balance in every patient, and in those with deficits, balance training should be prescribed. The home environment should be inspected for falls risk, a procedure usually performed by a visiting nurse in conjunction with a physical therapist.

In patients with a history of an osteoporotic fracture or those who plan to undergo an orthopedic procedure, the medical history should be reviewed to assess both medical conditions and medications that predispose to poor bone health. Conditions known to be associated with poor bone health include hyperparathyroidism, diabetes, hypogonadism, hyperthyroidism, depression, fragility/inactivity, celiac disease, and multiple myeloma. Medications associated with poor bone health and osteoporosis include glucocorticoids, aromatase inhibitors, lupron/androgen inhibitors, lithium, and thyroid replacement resulting in oversuppression, common in patients with a history of thyroid cancer, thiazolidinediones, probably proton pump inhibitors, serotonin reuptake inhibitors, and many anti-seizure medications. Whenever possible, these problems should be addressed by employing such measures as using the lowest possible steroid dosage or through the aggressive treatment of poorly controlled diabetes. Recognizing such risk factors will, at a minimum, sensitize physicians that bone quality may be worse than expected. Indeed in patients with a *Z*-score more than one standard deviation below age-matched controls, a metabolic bone evaluation should be considered (Table 30.1).

Table 30.1 Bone biomarkers

Markers of bone formation	Markers of bone resorption
Osteocalcin	Urine N-telopeptide
Bone alkaline phosphatase	Serum C-telopeptide
P1NP	Urine C-telopeptide

Although there are many as yet unanswered questions in the area of perioperative bone health, certain areas are emerging as topics for further study. Does the preoperative vitamin D level influence orthopedic outcomes? Does vitamin D repletion diminish the rate of falls? Does it improve timed walking distance? What influence does bisphosphonate therapy have on total joint arthroplasty? What are the potential effects of osteoporosis medications on fracture repair? What are the beneficial and detrimental effects of antiresorptive and anabolic therapy on spine fusion? These and other questions are addressed in this chapter.

Vitamin D and Orthopedic Procedures

Vitamin D is essential for bone development, skeletal remodeling, and fracture repair. An Institute of Medicine (IOM) report has recently recommended adult levels of 20 ng/ml or greater. In patients with osteoporosis, most experts argue that even higher levels are beneficial and that calcium and vitamin D intake should be sufficient to prevent secondary hyperparathyroidism (that leads to further bone loss).

A serum 25-vitamin D level is the best indicator of adequate vitamin D intake in any given patient yet many questions exist concerning the optimal vitamin D level in the setting of orthopedic procedures. Does an adequate vitamin D level promote successful fracture repair and enhance fusion in spine surgery? What about the effects of vitamin D in total joint arthroplasty? Do adequate perioperative vitamin D levels facilitate postoperative rehabilitation and prevent postoperative falls?

A retrospective review of 723 patients undergoing surgery at an orthopedic hospital revealed that 40% of patients were vitamin D deficient by IOM standards with 25-OH vitamin D levels $\leq$20 ng/ml [8]. A smaller study in patients undergoing total hip and knee arthroplasty examined the association between bone mineral density (BMD), vitamin D, and

osteoarthritis; 84.7% of patients had a level of vitamin D ≤30 ng/ml with *T*-scores below −2.5, indicative of osteoporosis, demonstrated in 20% of men and 23.2% of women [9]. In a large prospective study the association between baseline vitamin D status, BMD, and the development of radiographic osteoarthritis of the knee, those with the lowest levels of vitamin D at baseline had the most rapid progression of knee osteoarthritis [10]. In a study evaluating vitamin D level and attainment of in-hospital functional milestones after total hip arthroplasty, low vitamin D levels (≤32 ng/ml) did not compromise short-term functional outcomes [11]; therefore the authors concluded that surgery did not have to be postponed if a low preoperative vitamin D level was detected but vitamin D should be corrected postoperatively. Adequate calcium and vitamin D from diet and supplementation is recommended for elderly hip fracture patients. A recent study demonstrated that 12 months after hip fracture repair, 28.4% of patients took calcium inconsistently and 35.7% took calcium consistently. For vitamin D, 26.2% took vitamin D inconsistently and 39.1% took it consistently (Sprague). Education of clinicians is clearly needed. Another study revealed that in patients with a hip fracture, a low 25 vitamin D level was independently associated with postoperative medical complications [12].

There is a considerable literature concerning the effect of vitamin D on muscle function. In general adequate vitamin D levels appear to promote muscle strength and balance, although all studies have not demonstrated a benefit. One study comparing a 3-month daily course of 5000 IU was more effective at raising vitamin D levels when compared to 2000 IUs; however, both doses showed trends in improvements in muscle strength [13]. Another study showed that 25-OH vitamin D levels of ≥20 ng/ml were needed for better muscle function and strength [14]. Also a recent review of vitamin D supplementation on muscle strength, gait, and balance in older adults demonstrated that supplemental vitamin D with daily doses of as low as 800–1000 IU showed consistent beneficial effects on these parameters [15]. One other study of postmenopausal woman examined the effects of a 3-monthly oral 150,000 IU supplementation of cholecalciferol (versus placebo) on falls, mobility, and muscle strength, and it failed to demonstrate benefit [16].

Total Joint Arthroplasty

As many people who require a total joint arthroplasty (TJA) are older and therefore more likely to have low bone mass, the bone health of patients undergoing TJA has also come under scrutiny. In 1 observational study, DEXAs were performed on 199 patients, aged 65–80 years, awaiting total knee and hip replacement. The overall rate of osteoporosis (any site) was 23%, while an additional 43% had osteopenia [17]. Another, smaller (n = 53) study, examined the prevalence of osteoporosis in women scheduled for cementless total hip arthroplasty (THA); 28% were osteoporotic, and 45% had osteopenia [18]. Thus the prevalence of low bone mass appears high (>2/3) in this patient population.

The clinical significance of this overall bone deficiency is compounded by observations concerning decreased bone density at the bone prosthetic (cement) interface. These conditions, acting in concert, raise concern that such poor bone stock may increase the subsequent risk of periprosthetic fracture. Though not frequently encountered, this postoperative complication is associated with significant morbidity. In order to address this issue, a group of investigators compared the periprosthetic BMD in patients undergoing cemented TKA to patients undergoing uncemented TKA. In both groups (n = 30 per group), bone density determinations at a median of 4 years after surgery were reduced at various periprosthetic sites, regardless of method of TKA [19]. The important point of this study is that, after TKA, there is a decrease in periprosthetic BMD perhaps due to disuse. Taking these observations another step, a population-based study examined the risk of periprosthetic fracture for 5 years after THA and TKA. The rate of fracture was as follows: 0.9% after primary THR, 4.2% after revision THR, 0.6% after primary TKR, and 1.7% after revision TKR. Fractures were more likely in females over the age of 70 years [20]. More recently it has been appreciated that during computer-navigated TKA, a procedure in which pinholes are drilled in the femur and tibia for the placement of navigation trackers, fractures associated with these pinholes have been reported. One study postulates that the presence of osteoporosis serves to intensify stresses around the pinholes and may thereby increase the risk of fracture [21]. Further another study found that osteoporosis affected tibial component position in computer-assisted navigation TKA [22].

As arthritis progresses in a hip or knee, patients tend to weight bear less on the painful limb, and the concept of disuse osteoporosis arises. One group evaluated 450 patients with knee osteoarthritis and found the T score was lower in the patients with worse knee OA grade [23]. There are now many studies that demonstrate that if bisphosphonates are used perioperatively for both THA [24, 25] and TKA [26], there is less loss of periprosthetic bone. This has also been demonstrated with denosumab [27] and with teriparatide [28, 29]. Results were similar when teriparatide was compared to alendronate [30]. There is also evidence that the use of a bisphosphonate in a patient who has undergone TKA is associated with a lower revision rate, even in patients with a normal BMD [31, 32]. One group looked at changes in total hip and spine BMD 1 year after TKA. BMD did decrease significantly over the 1-year period [33]. This is another reason to focus on the bone health of a patient perioperatively.

Also relevant to this discussion is the debate in the literature concerning the use of cement in THA. The current

view is that in patients with normal bone quality, cementless THA is preferred as the patient's bone would readily integrate into a porous implant. In contrast, if a patient with poor bone quality received a cementless implant, the risk of component migration prior to fixation has been felt to be significant. Further if revision THR is required, it tends to be easier to remove the implant if cement has not been used. Traditionally cement has been used in patients 50 years and older; currently, there is a trend to use cementless implants perhaps only in patients felt to have good bone quality intraoperatively, regardless of age. A recent study evaluated the quality of intertrochanteric cancellous bone as a predictor of femoral stem migration in THA. Intraoperative biopsy from the site of stem implantation was performed and subjected to structural analysis with μCT. Unexpectedly, the major differences observed in the quality of trochanteric cancellous bone had only a minor relationship to the migration of the femoral stems [34]. This is an area that requires much more orthopedic research because if there is early migration of the femoral component, the patient will often need a revision procedure.

Resurfacing THA has gained in popularity for young patients who require THA, though most will ultimately require revision arthroplasty later. While there is better bone preservation in hip resurfacing as compared to THA, a major argument for this procedure, this advantage should be juxtaposed against the greater risk of femoral neck fracture after hip resurfacing. Thus patient selection for resurfacing arthroplasty should include the evaluation of a patient's bone health prior to surgery. Precise criteria are not yet well understood, and the development of guidelines remains an important area of research. One group of investigators has shed light on this problem. This work involves 20 postmenopausal (53–60 years) women with either osteoporosis or osteopenia by hip BMD. Surgery was delayed for 12 months in order to treat patients with a bisphosphonate, calcium, and vitamin D. Among the 12 patients who showed an improvement in BMD, resurfacing THA was performed. None subsequently suffered an intraoperative fracture [35]. The major importance of these observations is the need for a better understanding of the impact of bone health and specifically how it may affect outcome after TJA.

Fracture

Bisphosphonate Therapy

Fracture repair involves both bone resorption and bone formation, and since bisphosphonates slow bone resorption, there is concern that they may negatively affect fracture repair. Several animal models of fracture healing have demonstrated that for fracture healing by enchondral ossification, bisphosphonates increase callus volume, trabecular bone volume, and bone mineral content, though delaying the maturation and remodeling of the callus [36, 37]. Thus the initiation of callus formation appears unaffected by bisphosphonate therapy; however, once a calcified cartilage is formed, both its remodeling to woven bone and the subsequent remodeling to mature lamellar bone are delayed. This remodeling delay has not been considered to be clinically significant but clinical evidence is sparse [38]. From a prospective study, zoledronic acid given after hip fracture has been shown to reduce the risk of subsequent (hip) fracture, improve overall mortality, as well as improve quality of life [39]. This benefit was observed if the bisphosphonate was given within 2 weeks of hip fracture; however, why this is so is not clear. The observation has nonetheless prompted a recommendation to delay intravenous bisphosphonate therapy for up to 6 weeks after hip fracture repair, a caution that may not be true for oral bisphosphonates as they are given in divided doses rather than as a single yearly dose [40].

The effect of bisphosphonate therapy on stress fracture repair has not been well studied. Nonetheless, stress fractures mend through direct bone remodeling, a healing process unaffected by bisphosphonates [40]. Apropos of this observation it is therefore relevant that bisphosphonates do not prevent the deterioration of mechanical properties of rat bone subjected to repeated cyclic loading and, further, did not prevent healing of stress fractures in military recruits during basic training [41, 42].

Denosumab

Denosumab is a new antiresorptive agent approved for the treatment of osteoporosis; its mechanism of action is the slowing of osteoclast differentiation. In animal models of fracture healing, denosumab did not show significant effects on rate of fracture healing. Similar to the effect seen with bisphosphonate treatment, denosumab use was associated with increased callus volume and delayed remodeling. Mechanical properties were not compromised [43]. Denosumab treatment in postmenopausal women with osteoporosis did not interfere with fracture healing in the FREEDOM trial [44].

Teriparatide

Teriparatide is a human derivative of parathyroid hormone. FDA approved for the treatment of postmenopausal osteoporosis, steroid-induced osteoporosis, and male hypogonadal osteoporosis, it is administered by daily, self-administered subcutaneous injection. As the first approved anabolic agent for the treatment of osteoporosis, it induces true bone formation on all bone surfaces including trabeculae, endosteal, and periosteal bone [45]. In animal models, supraphysiologic doses of PTH demonstrate increased fracture site strength

and callus quality in treated animals [46]. One clinical trial assessing the potential role of parathyroid hormone in fracture repair has been conducted [47]. This study, in postmenopausal women, compared a 20 versus 40 mcg daily dosage in the setting of fracture of the distal radius. The 20 mcg daily dose, not the 40 mcg dose, demonstrated accelerated healing. Huang and colleagues looked at 169 patients with intertrochanteric hip fractures, and the group treated with teriparatide had better outcomes and less complications and mortality [48]. Teriparatide also may help healing of bisphosphonate-associated femur fractures [49]. Multiple case reports suggest accelerated fracture (acute and nonunion) healing in patients treated with teriparatide. Such clinical observation suggests differential benefit, more in trabecular bone than in cortical bone. Teriparatide may hasten pelvic fracture healing; a randomized study is under way.

Spinal Fusion

Despite the large number of orthopedic spine surgeries performed worldwide, the effect of osteoporosis on the outcome of various spine procedures has not been well studied. In addition, the most widely used test to evaluate bone density, DEXA, often gives a falsely elevated bone density in an arthritic spine. While this is the case for many with degenerative spine disease, others have shown that patients with degenerative spine disease can have lower BMD than controls without degenerative spine disease [50]; this was attributed to less weight-bearing activity. This study also demonstrated that patients with degenerative spine disease had higher levels of bone resorption; this has been correlated with a higher fracture rate. Schmidt did show that in 144 patients scheduled to have spine surgery, osteoporosis was present in 27.1% and osteopenia in 43.8%. Only 11.1% of patients had received an anti-osteoporotic therapy and 37.5% had an indication for therapy. Vitamin D was inadequate in 73.6%, and secondary hyperparathyroidism was present in 34.7%, indicating inadequate calcium intake [51].

There is concern that successful use of hardware in spine stabilization procedures will be compromised in patients with low bone mass. Bennett measured cadaveric vertebral bone densities using computed tomographic scans and correlated these findings to the measured bone densities [52]. While average BMD varied widely among the specimens, the average bone densities of the pedicle and of the vertebral body for individual specimens were well correlated. He demonstrated that the unstable spine can be stabilized using fixation, but the immediate stability provided by pedicle screws is greater in the lumbar vertebrae with the higher bone density.

So what is known about bone augmentative medications and spine surgery? Many animal studies suggest that bisphosphonate therapy may hinder spine fusion. Huang studied posterolateral lumbar fusion in rats in the setting of alendronate therapy demonstrating lower rates in the alendronate groups as compared to controls [53]. Despite the lower fusion rates, increased fusion mass area and optical density were noted with the alendronate groups. In addition, Sama and colleagues have looked at the effect of alendronate on osteoclast and osteoblast function in a pseudoarthrosis model in rats [54]; no notable differences between groups were reported. However, in animals receiving alendronate at supratherapeutic doses, qualitatively limited histological remodeling and poor osteoclastic and osteoblastic function was noted. The percent of osteoblasts per surface area were also lower in the high-dose alendronate group, suggesting a possible negative effect on spine fusion. Another study demonstrated a decrease in fusion mass remodeling but not a decrease in fusion rate in a porcine model of posterior lateral spine fusion [55]. Babat looked at spine fusion in a rat model. Pamidronate, but not calcitonin, leads to a less mechanically robust fusion [56].

Other studies have demonstrated improved spine fusion, in patients receiving bisphosphonate therapy around the time of spine fusion. In a rabbit model, a single dose of zoledronic acid, in combination with iliac crest bone graft, increased fusion-mass size and bone mineral content. There was also an increased fusion rate compared to animals that had iliac crest bone grafting alone [57]. Two publications by Xue demonstrated that alendronate treatment in a porcine model increased the bone purchase of stainless screws and did not inhibit bone formation within biphasic calcium phosphate ceramics [58, 59]. Nagahama looked prospectively at lumbar fusion in 40 patients with osteoporosis; bridging bone formation was more frequently observed in the alendronate group at all assessment periods. Specifically, at 1-year follow-up, a solid fusion was achieved in 95% of the patients in the alendronate group as compared to 65% in the controls [60]. Nakao has also demonstrated that in an animal model, alendronate was effective for radiologic, biochemical, and histologic success of spine fusion [61]. Another study looked at the effect of zoledronic acid and hyperbaric oxygen on posterior fusion in a rat model. Treatment improved radiographic, biomechanical, and histologic outcomes.

O'Loughlin studied the use of parathyroid hormone on a posterolateral rabbit spinal fusion model [62]. Animals treated with PTH had a significantly greater rate of fusion than controls (81% vs. 30%). Bone mass and histologic determinants were also improved in the PTH group. Another study suggests teriparatide enhances histologic spinal fusion in rats compared to controls and compared to calcitonin [63]. In postmenopausal women with osteoporosis, teriparatide enhanced lumbar posterolateral fusion [64]. When teriparatide and bisphosphonate therapy were studied in the use of pedicle screws, the incidence of pedicle screw loosening was less in the teriparatide group; the extent of pedicle screw loosening was similar in the risedronate group compared to controls

[65]. Weekly teriparatide promoted bone formation at the surgical fusion site and decreased bone resorption in female patients ≥50 [66]. Thus as teriparatide is FDA approved for the treatment of osteoporosis, it may also be appropriate for a select patient population undergoing spinal fusion.

More recent studies have begun to tackle some clinical questions. In a rat model of spinal fusion, teriparatide was associated with greater fusion mass and an increased fusion rate, when the rats were exposed to continuous glucocorticoid [67]. Ohtori demonstrated that teriparatide was more effective than bisphosphonates for lumbar fusion and that the use of teriparatide for more than 6 months was more effective than a shorter duration of treatment [68]. When teriparatide was compared to alendronate in 47 osteoporotic women undergoing lumbar fusion, there was no significant difference in the rate of fusion, but the teriparatide group showed faster bony union [69]. Another study demonstrated that, when comparing teriparatide to a bisphosphonate group of osteoporotic women having spine fusion, the patients who received teriparatide had less adjacent vertebral fractures, fusion failure, and pain [70]. Ohtori demonstrated that in 19 osteoporotic women undergoing spine fusion, if teriparatide was started 2 months preoperatively and this medication was continued for an average of 11.5 months and then patients were transitioned to weekly risedronate, fusion mass volume was maintained for up to 3 years after surgery [71]. A recent meta-analysis examining the use of bisphosphonate and teriparatide use in thoracolumbar fusion noted that bisphosphonates do not appear to impair spine fusion compared to controls, but teriparatide was associated with higher fusion rates. Additionally, bisphosphonate use was associated with decreased odds of cage subsidence and vertebral fractures compared to controls [72].

Taken collectively, it appears that teriparatide does promote spine fusion more than bisphosphonates. Bisphosphonates may not impede spine fusion, and in osteoporotic patients, bisphosphonates preoperatively may improve bone quality and decrease the risk of vertebral fractures and hardware pullout. More study is needed as intellectually, bisphosphonates slow bone resorption and spine fusion requires bone remodeling (i.e., both resorption and formation). Parathyroid hormone, an anabolic agent, may enhance spinal fusion and appears to have positive effects on spine surgery outcome.

The Clinical Assessment of Bone Health

Although our current biomarkers of bone turnover have limitations, the use of biomarkers in treatment decision-making can be helpful. Markers of bone formation include osteocalcin, bone alkaline phosphatase, and P1NP (Table 30.1). For example, a patient may have a low rate of bone formation if on an antiresorptive for a prolonged period especially with ongoing tobacco use and in old age. A low rate of bone formation may lead the clinician to consider an anabolic agent, such as teriparatide. In this situation, teriparatide may foster spinal fusion and help in fracture repair; it may also help bone ingrowth into porous joint implants. Markers of bone resorption include urine *n*-telopeptide, serum C-telopeptide, and urine C-telopeptide. If a patient was found to have a high rate of bone resorption, the clinician may opt to treat a patient with an antiresorptive agent, such as a bisphosphonate or denosumab. This would suffice after joint arthroplasty. Although still an active area of research presently, it seems prudent to avoid antiresorptive agents until fractures have healed and spinal fusion completed, as antiresorptives may delay and prevent proper healing.

Treatment of low bone density should be strongly considered in all patients with osteoporosis and in patients with osteopenia who have an elevated FRAX®. FRAX®, an assessment tool developed by the World Health Organization, allows the clinician to import patient-specific information and calculate the overall risk of (any) fracture and the risk of hip fracture, over the next 10 years, if the patient is not treated for low bone mass. If the overall risk of fracture over the next 10 years is ≥20% or risk of hip fracture is ≥3%, treatment is indicated (Box 30.1). As BMD may be falsely elevated in the lumbar spine, in patients with degenerative lumbar disease, for patients undergoing spine surgery, a QCT or trabecular bone score (TBS) may be more accurate. The TBS can be obtained at the time the BMD is performed.

Box 30.1 Fracture Risk Assessment Tool FRAX® (WHO)

- Tool developed by WHO to evaluate fracture risk of patients
- Gives 10-year probability of hip fracture and major osteoporotic fracture (clinical spine, forearm, hip, or shoulder fracture)

Variables

  - Ethnicity
  - Age
  - Weight
  - Height
  - Previous fracture
  - History of parental hip fracture
  - Current tobacco use
  - Use of glucocorticoids
  - Rheumatoid arthritis
  - Secondary osteoporosis
  - Alcohol ≥3 units/day
  - Femoral neck BMD

- Treatment with an FDA-approved medication for osteoporosis is recommended if the risk of overall fracture is ≥20% or the risk of hip fracture is ≥3%

Thus, the evaluation and treatment of bone health perioperatively should result in better outcomes. Recognizing that an important opportunity to address bone health is frequently missed, a consensus conference concerning this issue has been held. Entitled *Treatment of Osteoporosis for Orthopedic Surgeons*, the conference was an attempt to educate the orthopedic community concerning treatment options in osteoporosis [73]. Similarly the American Academy of Orthopedic Surgeons has adopted the "Own the Bone Program" the intent of which is similar [74]. Other approaches include a Fracture Liaison Service, dedicated to the evaluation and treatment of patients with fragility fractures [75]. Standing discharge orders have also been offered as a solution [76].

Summary

Until recently bone health and its optimization was a concept associated mainly with the prevention and treatment of osteoporosis. Spurred on by an advancing science and pharmacology, the importance of this nascent field to orthopedics cannot be overstated. As discussed in this chapter, current interest is focused on problems arising in specific clinical settings, that of fracture repair, total joint arthroplasty, and spinal fusion. Other applications are doubtless on the horizon. As essentially medical therapies, this area presents opportunities for an enhanced collaboration between orthopedics and internal medicine. Further it is likely to become an important content domain in the field of perioperative medicine where these considerations are, at present, underappreciated.

Summary Bullet Points

- The prevalence of vitamin D deficiency and diminished bone density is high in orthopedic populations and despite widely available therapy is largely ignored.
- The preoperative evaluation of bone strength and quality may improve outcomes after orthopedic procedures.
- Relevant clinical problems include fracture repair, total joint arthroplasty, and spinal fusion.
- Bone health as a concept is an emerging area with relevance to orthopedic surgeons and others involved in perioperative care.

Case Studies

Case 1

A 65-year-old Caucasian female with lumbar spondylosis and chronic low back pain presented for spine surgery. Treated unsuccessfully with various medications, physical therapy, and several epidural injections, she remained in severe pain, and consequently a spinal fusion was advised.

Her past history was notable for menopause at 44 years of age, a wrist fracture at 52 years of age when she slipped shoveling snow, and diabetes mellitus for which she was taking pioglitazone and metformin. A former smoker, she did not drink alcohol. A bone density test several years ago was said to be "okay." Her mother fractured her hip at the age of 72, when she fell down over the steps in her home. The patient has never been treated for osteoporosis and did not know what her vitamin D level was.

Given her clinical profile, with several important bone-related risk factors (early menopause, previous fracture, cigarette exposure, diabetes, and family history), the patient's bone health was addressed. Beginning with a bone density determination, T-scores for the lumbar spine and hip (femoral neck) were obtained and revealed −2.6 and −2.5, respectfully, which was in the osteoporotic range. FRAX analysis in this patient equated these bone densities with a 10-year overall fracture risk of 21% (5.4% in the hip), if untreated. Her 25 vitamin D levels were also low (20 ng/mL), and her intact parathyroid hormone (PTH) was mildly elevated at 85 pg/mL (serum Ca^{++}9.0 mg/dL).

As a conservative target, the 25-oH vitamin D requires supplementation to maintain a level of 32 ng/mL with some experts recommending levels as high as 50 ng/mL. In addition, the secondary hyperparathyroidism, demonstrated by the elevated PHT level, should be corrected with dietary calcium or calcium supplements and vitamin D.

Further the patient should be started on treatment for osteoporosis. Evidence suggests that teriparatide promotes spine fusion more than bisphosphonates. Beginning teriparatide 2 months preoperatively and continuing this medication for at least 6 months postoperatively with transition to a bisphosphonate is advised.

Case 2

A 76-year-old Caucasian male was admitted with a hip fracture after having slipped on wet leaves walking to his car. He was treated only for hypertension, Barrett's esophagitis, and CKD Stage 3 with a GFR of 34 ml/min. He was a 1 pack per day smoker since 18 years of age and admitted to alcohol consumption of 2–3 cocktails nightly. Currently 5′11″ in height, he reported his high school height to have been 6′2″. He weighed 165 lbs. He underwent open reduction and internal fixation and did well postoperatively.

His internist ordered a bone density scan and related laboratory work postoperatively. Bone densitometry revealed T-scores of −2.8 (lumbar spine) and −3.0 in the nonoperative femoral neck. Additional fracture assessment revealed an old L4 fracture. His 25 vitamin D level was 19 ng/mL,

serum calcium 8.9 mg/dL, and intact parathyroid hormone level elevated at 92 pg/mL, consistent with secondary hyperparathyroidism.

This patient had several risk factors for osteoporosis including his race (Caucasian), tobacco use including during his peak bone-forming years, and regular alcohol use (intake of 3 or more units per day is a risk factor for osteoporosis). He also took a proton pump inhibitor, which may decrease the absorption of calcium carbonate and may contribute to the development of osteoporosis. In addition, a loss of more than 2 inches in height is considered a predictor of a prior vertebral fracture.

Thus, in order to address this patient's bone health, he should be counseled to discontinue tobacco and limit his alcohol use. Given his history of Barrett's esophagitis, the continued use of a proton pump is warranted, despite the negative effect on bone health. Further, he should begin vitamin D3 in conjunction with an increase in calcium intake. Lab work should be repeated in 8–12 weeks to ensure improvement in his vitamin D level and correction of the secondary hyperparathyroidism. Bisphosphonates should not be given if the creatinine clearance is <35 ml/min, as there is concern about contributing to a low bone turnover state. Denosumab 60 mg sq every 6 months would be a reasonable option.

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Perioperative Care of the Complex Spine and Scoliosis Surgery Patient

31

Darren R. Lebl and Michael K. Urban

Objectives

- To explore the complex nature of modern spine surgery and to understand the need for a multidisciplinary team approach to the care of the spine surgery patient
- To review the risk factors for complications associated with spine and scoliosis surgery with special considerations to the increased risk of complications involving the cardiopulmonary system
- To review the usefulness of intraoperative neurologic monitoring and the special anesthetic considerations imposed by this monitoring
- To review strategies for blood management in complex spine and scoliosis surgery
- To explore the approaches to postoperative pain management and rehabilitation

Key Points

- Modern spinal surgery can range from relatively simple ambulatory micro-discectomy to complex anterior, lateral, and/or posterior approaches to deformity correction and spinal fusion. Patients are best served by a multidisciplinary team including surgeons, perioperative medical specialists, intensivists, subspecialty-trained anesthesiologists, nurses, and physical therapists.
- Complications are an unfortunately intrinsic reality of complex modern spine surgery in a subset of patients. Complications are observed more commonly as the complexity of the surgery is increased as well as in patients with preoperative medical comorbidities. Cardiopulmonary complications are the most common necessitating careful preoperative evaluation and optimization.
- Intraoperative neurologic monitoring has become the standard of care and has benefitted from recent technological advances such as the ability to monitor motor evoked potentials (MEPs). Specialized anesthetic techniques including total intravenous anesthesia may improve the accuracy and effectiveness of the monitoring.
- Postoperative vision loss occurs infrequently following complex and prolonged spinal procedures. The most common cause is ischemic optic neuropathy. The etiology of postoperative ION at present is unknown and unpredictable. However, several possible pathogenic factors have been suggested including duration in the prone position, blood loss, anemia, hypotension, abnormal optic nerve blood supply, low cup-to-disc ratio, use of vasopressors, excessive crystalloid infusion, and patient comorbidities, particularly smoking, diabetes, and vascular disease. The ASA practice advisory on POVL recommends the use of both colloids and crystalloids to maintain intravascular volume in spine surgery patients who have substantial blood loss. Since ION occurs in the absence of vascular injury to other critical organs and in cases where neither hypotension or anemia are reported, optic nerve blood supply may be uniquely vulnerable to hemodynamic perturbances in the prone position.

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- Blood management should include preoperative autologous donation. Antifibrinolytic agents have been demonstrated to be a useful adjunct in reducing perioperative blood loss.
- Pain management can be a challenging problem for the complex spine patient. Patient-controlled intravenous analgesia is associated with higher patient satisfaction. Specialized pain management teams will often provide for better resource and pain management utilization.

Introduction

The modern practice of spinal surgery and therefore the associated perioperative considerations may encompass a wide spectrum of procedures ranging from outpatient micro-discectomies for acute disk herniations to complex reconstructive surgery for spinal deformities requiring postoperative critical care. These procedures may involve anterior approaches to the cervical spine, posterior decompression, and instrumentation at the base of the skull, thoracotomy, transabdominal/retroperitoneal exposures, or extensive dissection of the posterior spinal musculature with corrective osteotomy to name a few. In addition, spinal fusions may be performed under minimally invasive techniques with the goals of a reduced hospital stay and an earlier return to function. Although the effectiveness of minimally invasive techniques has recently been questioned, the concepts of early recovery developed for these procedures (ERAS) should be valuable for all complex spinal procedures [1, 2]. As such, the optimal surgical treatment of spinal disorders requires not only a detailed understanding of the anatomy of the axial skeleton from all perspectives but may also require interdisciplinary collaboration between surgical, anesthesia, medical, nursing, ENT, and physical therapy teams.

Complications after spine surgery are associated with surgical complexity, age of the patient, increased BMI, and preexisting comorbidities [3–6]. In a large database of mandatory surgeon morbidity and mortality reporting by its member surgeons, the Scoliosis Research Society identified a series of complications in 108,419 spinal operations. Patients with higher American Society of Anesthesiology (ASA) grades were found to have significantly higher morbidity [7]. New neurologic deficits were identified to occur more commonly in revision cases (1.25%) than primary cases (0.89%) and more often in pediatric procedures (1.32%) and then adult (0.83%) [8]. In the adult scoliosis patient, an overall complication rate of 13.4% was found, most commonly a dural tear (2.9%), and higher complication rates have been found in patients requiring osteotomies, revision surgery, and/or combined anterior–posterior surgery [9]. Of the 23,918 pediatric cases reported in the database, the most common medical complications were respiratory (0.9%), and these were also the most likely cause of mortality.

Complications are unfortunately an intrinsic reality of spine surgery for a small subset of patients. Both patient and clinician demand for improved clinical outcomes have created driving forces toward less invasive, faster, cheaper, and now biologically augmented spinal surgery. Patient age, cardiac disease, preoperative neurologic abnormality, prior wound infection, corticosteroid use, history of sepsis, and prolonged operative times have been found to be independent risk factors for complications [10]. The avoidance of complications and successful surgical treatment of patients with spinal disorders begins with a thorough preoperative evaluation and planning [11, 12].

Preoperative Evaluation

The extent of preoperative evaluation is a function of the individual patient age, presentation, diagnosis, and comorbidities. For instance, the polytrauma patient with spinal fracture or dislocation has a high associated rate of intra-abdominal injury, pulmonary contusion, and long-bone fracture. Patient care in this setting requires effective communication between the various consultant services and is usually coordinated by the trauma surgical team. Oncology patients pose a unique set of considerations and risk profile as well. The most frequent spinal tumor in the spine is metastatic spread from a distant primary tumor which may be accompanied by impairment in visceral organ function or immunosuppression from chemotherapeutic treatment. Prior to consideration of spinal surgical intervention, an organ system-based approach may help minimize the patient's perioperative risk.

Cardiac Risk

A major risk factor for perioperative mortality after orthopedic surgery (including spine surgery) is advanced age, and the most common organ system involved in perioperative complications is cardiac [3, 13, 14]. The reported incidence of a postoperative myocardial infarction (PMI—elevated troponin I) after nonambulatory orthopedic surgery is relatively low at 0.6%. However, in the patient population with preoperative cardiac risk factors, the incidence increases to 6.5% [14]. The patient population with the highest risk for PMI is the one undergoing posterior spinal fusion. Long posterior spinal fusion constructs may be associated with relatively high blood loss and perioperative fluid shifts, not to mention catecholamine surge from postoperative pain [15]. These factors may be additive in the perioperative stress response

leading to tachycardia, hypertension, increased oxygen demand, and ultimately myocardial ischemia.

The preoperative assessment of patient cardiac functional status is often limited due to musculoskeletal limitations in patient mobility. Limited data are available that preoperative risk stratification and/or coronary revascularization may have an effect on postoperative outcome. A recent report by Salerno and colleagues [13] suggested that preoperative abnormal noninvasive cardiac testing rarely changed medical management prior to orthopedic surgery. The Decrease-II study questioned the value of preoperative cardiac testing in patients of intermediate risk before noncardiac surgery [16]. The measurement of brain natriuretic protein (BNP) before surgery may enhance perioperative cardiac risk stratification [17]. In the CASS registry, Eagle reported that CABG surgery offered no advantage before orthopedic surgery in reducing cardiac mortality [18]. Similar results have been obtained using percutaneous coronary intervention (PCI). According to previous reports, PMI and death have not been reduced for noncardiac surgery in patients at cardiac risk when preceded by PCI [19, 20]. Furthermore, in patients in whom PCI includes stenting, there are the added risks of restenosis and thrombosis if antiplatelet therapy is discontinued before surgery and perioperative bleeding if they are not discontinued [21]. Patients who have been revascularized with drug-eluting stents (DES) may require treatment with dual antiplatelet medication for at least 6 months, which may make it necessary to delay elective spinal surgery [22]. For non-DES the required period for dual antiplatelet therapy is shortened to about 2 months. In all cases, low-dose aspirin should be continued perioperatively. The risk of postoperative coronary artery thrombosis must be balanced against the risk of reinitiating anticoagulation or dual antiplatelet therapy soon after spinal surgery.

Preoperative cardiac testing and revascularization have not been conclusively shown to lower postoperative cardiac morbidity; however, hemodynamic stress reduction may minimize the risk of cardiac event perioperatively. Numerous studies have indicated that the use of perioperative β-blockers can reduce myocardial ischemia and PMIs [16, 23, 24]. Recent reports have questioned the efficacy of β-blockers in preventing postoperative cardiac complications, particularly in patients at intermediate risk [25, 26]. In patients on chronic β-blockers therapy, continuation of β-blockers may have benefit, and in patients at high cardiac risk, β-blockers may be initiated with a target heart rate of less than 80 beats per min [24, 27].

Pulmonary Optimization

Pulmonary complications are also relatively common following major spine surgical procedures. Prolonged intubation, prone positioning, long operating times, and advanced age may predispose patients to postoperative pulmonary issues. With each decade of life, a progressive decrease in arterial oxygen tension, an increase in closing volumes, and a decrease of approximately 10% in FEV1 occurs. These time-dependent changes may be influenced by alterations of chest wall mechanics, which can be exacerbated in the elderly patient with osteoarthritic spinal pathology. Patients with preexisting pulmonary disease, such as chronic obstructive pulmonary disease (COPD), are at elevated risk of postoperative pulmonary complications [28]. Preoperative spirometry in this population may have limited value with the exception of patients with severe COPD in which the surgical procedure is extensive or involves thoracotomy [29]. Patients with reactive airway disease such as asthma or a bronchospastic component to their COPD may benefit from bronchodilator therapy. Cigarette smoking not only increases the risk of postoperative pulmonary complications but also has a clear negative impact on the success of spinal fusions and wound healing [30]. In one study patients were encouraged to stop smoking at least 8 weeks prior to surgery in order to reduce the risk of pulmonary complications to that of nonsmokers [31]; however, a recent report suggests that smoking cessation for 4 weeks prior to surgery may be sufficient to reduce the complication risk to that of nonsmokers [32].

Patients with spinal deformities, large main thoracic idiopathic scoliosis, may have a reduced chest cavity volume with decreased chest wall compliance and restrictive lung disease. These patients are at an increased risk for pulmonary complications [33]. Preoperative exercise tolerance provides a functional assessment of pulmonary function; however, formal pulmonary function tests (PFTs) provide objective quantification of the extent of disease. PFTs may guide the surgical and anesthesia teams regarding the extent of surgery, considerations for staged procedures, and the potential requirement for postoperative ventilatory support. A vital capacity of less than 40% of normal is predictive of the necessity for postoperative ventilation. In this setting, arterial blood gases may reveal hypoxemia secondary to ventilation–perfusion inequalities caused by alveolar hypoventilation, elevated pulmonary vascular resistance, and may ultimately result in cor pulmonale. An echocardiogram to evaluate for pulmonary hypertension and right ventricular hypertrophy (RVH) in spinal deformity patients may reveal moderate to severe pulmonary hypertension which may require the surgeon consider curtailing the invasiveness of the planned procedure or staged procedure options [34].

Perioperative Glycemic Management

Patients with diabetes are not only at increased risk for perioperative complications from associated comorbidities (myocardial ischemia, vascular disease) but also have a higher incidence of postoperative infection and death from

sepsis [35, 36]. Although tight perioperative glucose control has been advocated to reduce these complications, more recent reports suggest that non-fluctuating glucose levels below 200 mg/dl may be safer [36–38]. Our institutional policy is that HgbA1C >8 is a hard stop for elective spinal surgery, and recent data suggest that even lower levels may further minimize the risk of perioperative infection [39].

Intubation and Airway Considerations

Cervical spine instability, severe cervical stenosis, thoracic hyperkyphosis with compensatory cervical hyperextension, and advanced cervical spine spondylosis are a few examples of spinal pathologies that may make routine tracheal intubation challenging. Awake, sedated fiberoptic intubation of many of these patients is the safest approach to general anesthesia. These patients are intubated first with a flexible fiberoptic bronchoscope under light sedation and then positioned prone for surgery, and then spinal cord integrity is assessed with voluntary movements of both upper and lower extremities before the induction of general anesthesia. Baseline neuromonitoring potentials both before and after prone positioning can be utilized to assess any potential cervical injury during the positioning process itself.

Patients with rheumatoid arthritis (RA) and achondroplasia have a high incidence of occipitocervical instability and deserve focused preoperative consideration (Fig. 31.1a–f). Patients with ankylosing spondylitis (AS) have a high rate of occult fracture and altered biomechanics resulting in highly unstable fracture patterns. Anterior subluxation of C1 on C2 (atlantoaxial subluxation) may occur in up to 40% of patients with RA, with symptoms of progressive neck pain, headache, and myelopathy. Basilar invagination/vertical migration of

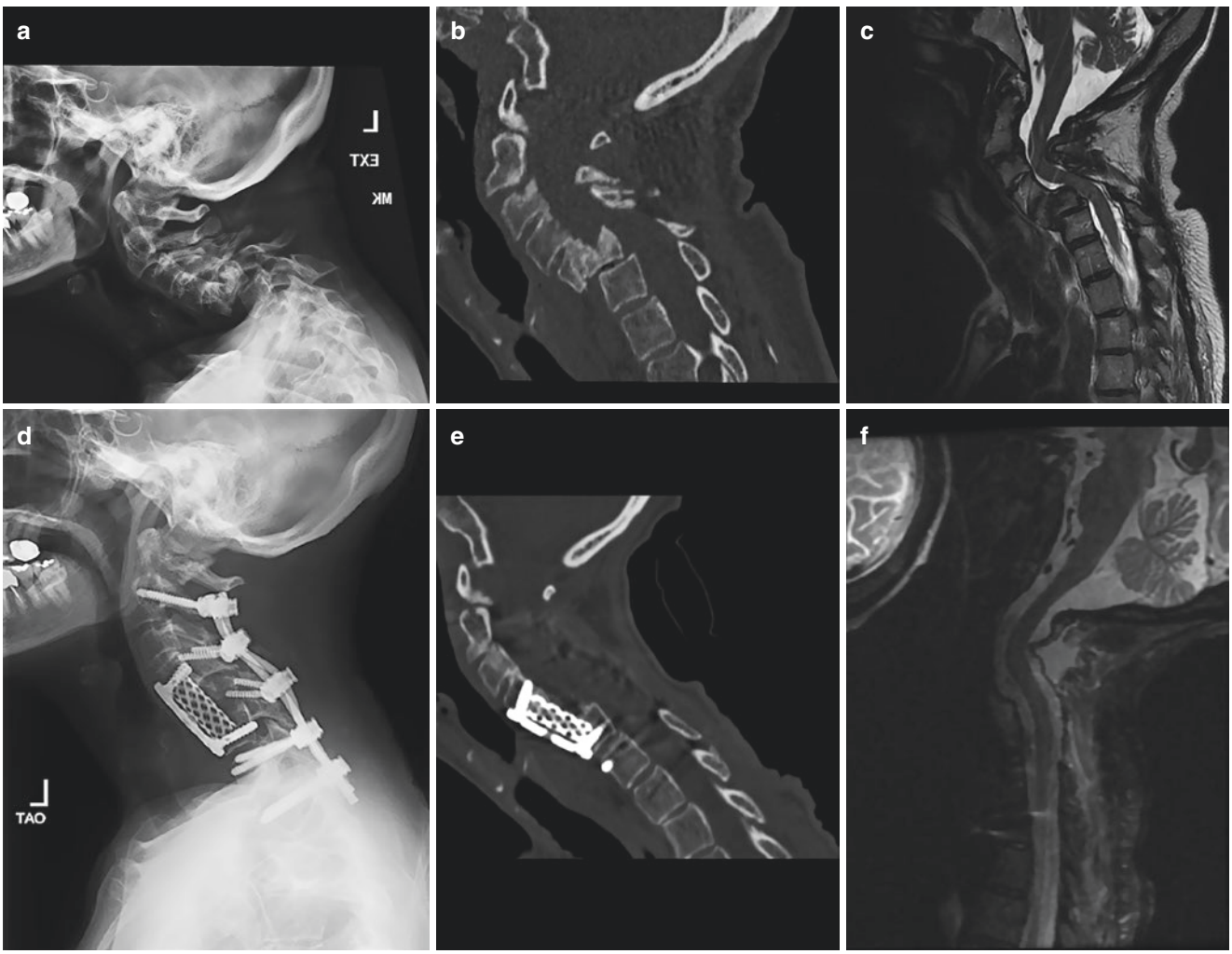

Fig. 31.1 (**a**–**f**) A 70-year-old rheumatic female with spontaneous subaxial cervical spine dislocation requiring preoperative Gardner-Wells tong traction, anterior cervical corpectomy, and cage reconstruction with posterior decompression and fusion. Preoperative lateral cervical spine X-ray (**a**), CT scan (**b**), MRI scan (**c**), and postoperative images (**d**–**f**)

the odontoid process inside of the foramen magnum may also be associated with RA, degenerative processes, or infection. Gross movement of the head in the presence of occipitocervical instability may result in the displacement of the odontoid process into the cervical spine and medulla, compression of the vertebral arteries, and catastrophic sequelae such as quadriparesis, spinal shock, and death.

When possible, preoperative cervical spine flexion–extension radiographs may provide preoperative information about the stability of the occipitocervical complex. Awake fiberoptic tracheal intubation may be performed with the cervical spine protected in a hard cervical collar during the procedure. Additionally, systemic inflammatory conditions such as AS may present additional challenges to intubation due to the reduced movement of both the cervical spine and temporomandibular joint. Increased rigidity of the thoracic spine in cases of AS may present additional challenges and may require intraoperative controlled mechanical ventilation. The syndromic spine patient or congenital spine patient such as certain Klippel–Feil subtypes or achondroplastic dwarfs also deserves special consideration prior to intubation. Conventional laryngoscopy and tracheal intubation may be both difficult and dangerous in this patient population. Awake fiberoptic tracheal intubation is the safest approach to securing the airway in these patients. Once the airway is secured, dwarfs can still represent an anesthetic challenge secondary to restrictive lung disease and pulmonary hypertension.

Preoperative Assessment of Bone Health

Osteoarthritis is a disease of the aging, affecting 70% of adults over 55 years old in the western world. Hence older patients with multiple comorbidities are more likely to have spinal conditions requiring surgery for degenerative spondylotic processes. It is the author's preferred practice to order DEXA bone density studies on all female patients over age 55 and all male patients over age 65 prior to consideration for any instrumented spinal procedures. Rigid implant fixation systems may be problematic in the setting of low bone density with high potential for implant subsidence, screw pullout, and peri-implant fracture. Preoperative assessments of Vitamin D, Calcium, NTX and possible medical management with Teriparatide (TPTD) 1,34 PTH prior to surgery should be considered. TPTD has been shown to stimulate new bone formation and shift the bone homeostasis pathways toward a positive bone balance with increased bone mass [40–42]. Delay of spinal fusion procedures may be required for up to a year or more while the substrate bone mineral density is optimized such that rigid fixation and stabilization may be safely obtained.

Anterior Thoracic Spine Surgery

Surgical spinal corrections involving high anterior thoracic levels or video-assisted thoracoscopic surgery (VATS) may require the isolation of one lung (OLV). OLV has been traditionally achieved with a double-lumen endotracheal tube (ETT). In single-staged anterior and then posterior spinal fusions, before the postoperative procedure, the double-lumen ETT should be replaced with a single-lumen ETT. Transthoracic interbody cages have been placed in recent years with newer less invasive techniques and may require this anesthetic technique [43]. A single-lumen ETT with an enclosed bronchial blocker can also provide OLV, but has the advantage of being left in place as a single-lumen ETT with the blocker deflated at the end of the anterior procedure [44]. In patients with restrictive lung disease, adequate oxygenation may be difficult during OLV and may require CPAP to the non-ventilated lung and PEEP to the ventilated lung.

Positioning

The careful positioning of patients for spinal surgery is an important shared responsibility of the anesthesiologist and surgeon. As stated previously, patients at risk for spinal cord compression may be best positioned under light sedation and then observed for upper and lower extremity movement prior to inducing general anesthesia. Prone positioning on a Hall–Relton frame allows the abdominal contents to hang freely to reduce venous pressure with four-poster pads on either iliac crest and the anterior chest wall (with care to leave the axillae free from compression).

Complex spinal deformity procedures will often require both anterior and posterior approaches to the spine. For a low lumbosacral anterior lumbar interbody fusion (ALIF) approaches, the patient is supine with their legs spread widely apart. Since pelvic retraction during this procedure may compromise blood flow to the legs, a pulse oximeter may be placed on a toe. Anterior thoracolumbar procedures are usually positioned in the lateral decubitus position with an axillary support, and attention must be focused on the dependent arm and leg and the position of the neck.

Lateral access/retroperitoneal minimally invasive procedures for lumbar interbody fusion are being performed on an increasingly widespread basis. A report of 600 transpsoas cases recently identified perioperative complications in 6.2% of patients including surgery-related events in 1.5%. These unique complications of this approach will need to be weighed with the purported benefits of decreased blood loss, shorter hospital lengths of stay and operative times, and improved interbody bone support on the outer apophyseal ring. Vertebral body fracture [45], approach-related hip

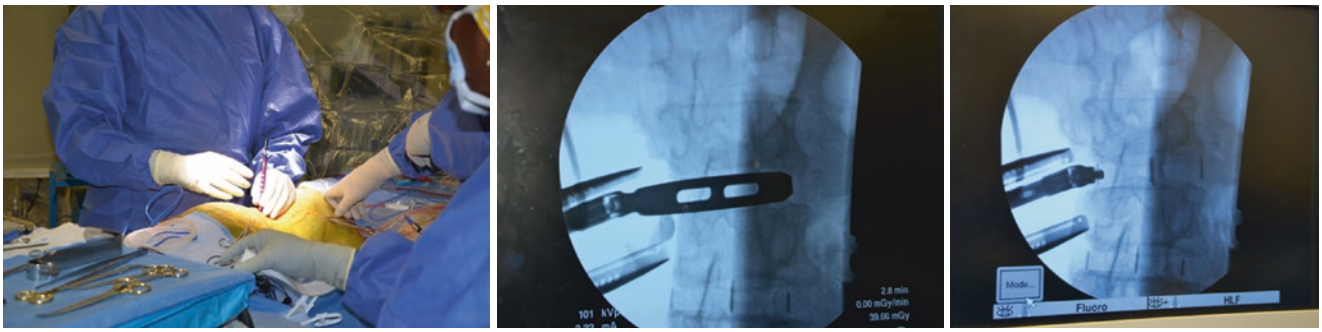

Fig. 31.2 Placement of percutaneous dilators through minimally invasive retroperitoneal approach (left), trialing of intervertebral disk space after complete diskectomy (middle), and placement of interbody cage (right)

flexor trauma, and ipsilateral [46] and contralateral neurologic deficits [47] have been reported to occur and require careful preoperative consideration of both bone quality and neuroanatomy. Positioning with the hip and knee slightly flexed will reduce the tension on the psoas and lumbosacral plexus to help minimize the risk of iatrogenic neurological deficit during placement of percutaneous dilators on the lateral lumbar disk spaces (Fig. 31.2).

Intraoperative Neurological Evaluation

Stagnara [48] introduced the concept of a "wake-up text" during spinal surgery to determine spinal cord function intraoperatively. The Stagnara wake-up test is limited to gross motor movements of the lower extremities and can be influenced by anesthetics and the cognitive responsiveness of the patient. In addition, the potential for inadvertent extubation during movement in the prone position or air embolism during a deep inspiration exists.

Multimodal intraoperative neurophysiological monitoring (IONM) has become the standard of care for complex reconstructive spinal surgery in recent years [49–52], since it provides for the real-time detection and verification of intraoperative neurological events. The IONM includes somatosensory (SSEP), MEP, and EMG monitoring. EMGs may be used to monitor nerve root impulses during pedicle screw insertion, spinal deformity corrective maneuvers, and neurological decompressions. The posterior, sensory, portion of the spinal cord is evaluated using SSEP monitoring. MEPs assess the integrity of the motor portions of the anterior cord (e.g., corticospinal tracts). There are several potential adverse effects of MEP monitoring, including cognitive deficits, seizures, bite injuries, intraoperative awareness, scalp burns, and cardiac arrhythmias. A soft bite block may be employed during MEP monitoring to prevent tongue biting and dental injury. MEP monitoring avoidance is recommended in patients with active seizures, vascular clips in the brain, and cochlear implants. SSEPs involve sending an electrical impulse from a peripheral nerve that is subsequently measured centrally as a cortical response. Conversely, MEPs involve an impulse that is triggered in the brain and monitored as movement of a specific muscle group in the trunk or extremities. SSEPs and MEPs are evaluated with regard to amplitude and strength of the electrical signal and latency and duration of time it takes the signal to travel through the nerve and spinal cord. These data are then compared to the patient's perioperative, nonsurgical baseline values to make conclusions about any untoward intraoperative event.

A number of physiological factors may attenuate SSEP and MEP monitoring, including hypotension, hypothermia, hypocarbia, hypoxemia, anemia, and anesthetics. The potent inhalational agents reduce the amplitude and increase the latency of spinal cord monitoring. In addition potent inhalational agents reduce systemic vascular resistance and act as negative inotropes, which can contribute to hypotension and reduced tissue perfusion. If an inhalational agent is used for the anesthetic, the concentration should be kept at about half MAC (minimum alveolar concentration) and at a constant blood concentration throughout the procedure. Nitrous oxide has been a preferred inhalational anesthetic since it provides amnesia and can be eliminated rapidly; however, it produces a decrease in the amplitude of the signal during MEP monitoring. Furthermore, nitrous oxide is poorly tolerated in patients with preexisting pulmonary hypertension and restrictive lung disease. Total intravenous anesthesia (TIVA) has been used successfully for both MEP and SSEP monitoring. MEPs are the least affected by narcotics, midazolam, and ketamine, but are depressed by propofol. However, the depressant effect of propofol can be diminished with ketamine. Ketamine, an NMDA antagonist (*N*-methyl-D-aspartate), will also reduce narcotic requirements and may prevent postoperative hyperanalgesia. The best TIVA anesthetic for complex spinal procedures then would include an infusion of a synthetic narcotic (fentanyl, remifentanil), ketamine at subanesthetic doses to potentiate the effects of the narcotic and reduce the MEP-negative effects of the intravenous anesthetic and propofol [53, 54]. Recently, dexmedetomidine and lidocaine have

been included in the TIVA anesthetic. Dexmedetomidine a selective α2 agonist does not significantly affect SSEP or MEP monitoring and may improve the quality of recovery by reducing the systemic inflammatory response [52]. The infusion of intravenous lidocaine at 1–2 mg/kg/hr during spine operations has been shown to reduce postoperative opioid requirements and the incidence of nausea and vomiting, as well as the faster return of bowel function [55]. In addition, methadone, administered at the beginning of the procedure, has the advantage of long duration of action and has both opioid and NMDA properties. Intraoperative administration of methadone has been shown to reduce postoperative opioid consumption and pain scores [56].

Muscle relaxants are usually not administered during MEP monitoring, but a low concentration infusion may be employed to reduce the background "muscle noise" degrading the SSEP signal. This TIVA anesthetic should provide hemodynamic stability and not contribute to the attenuation or loss of spinal cord monitoring during the procedure. Then if a problem occurs with spinal cord monitoring, other causes can be investigated, including hypotension, hypothermia, hypocarbia, anemia, and surgical correction. At this point the TIVA can be rapidly eliminated and the "wake-up" test performed. In most spinal corrective surgery, a stable intravenous anesthetic should provide the environment for reliable spinal cord monitoring and eliminate the need for a "wake-up" test.

Intraoperative Hemodynamic Management

Complex spine surgery, particularly corrective deformity surgery, may be associated with high blood loss and large-volume shifts perioperatively. Multiple factors have been suggested to influence the magnitude of this blood loss, including surgical technique, operative time, number of vertebral levels fused, anesthetics, mean arterial blood pressure, platelet abnormalities, dilutional coagulopathy, and primary fibrinolysis [57]. Several techniques have been employed to reduce this blood loss and limit the need for homologous blood transfusions: proper positioning of the patient to reduce intra-abdominal pressure, surgical hemostasis, deliberate controlled hypotensive anesthesia, reinfusion of salvaged blood, intraoperative normovolemic hemodilution, the use of pharmacological agents which promote clot formation, and the preoperative donation of autologous blood. Although widely practiced in the United States, the predonation of autologous blood for these procedures suffers from several disadvantages: patients often are anemic on the day of surgery; the pre-donation and storage of autologous blood is expensive; it does not eliminate the risk of a patient receiving the "wrong" unit of blood; blood is stored as packed RBCs, which eliminates coagulation factors; and if the surgery is rescheduled, the stored unit may expire. Predonation of blood in combination with erythropoietin injections to restore a normal hemoglobin has been shown to be effective in some studies [58]. In patients with normal preoperative hematocrits, whole blood can be removed in the operating room prior to surgery and replaced with colloid or crystalloid such that the patient remains normovolemic [59]. This technique permits a reduction in red cell mass intraoperatively, and the blood which has been removed contains platelets and coagulation factors not present in stored packed red blood cells. In patients undergoing posterior lumbar fusions, this technique has been shown to reduce the need for additional blood transfusions [57].

Several studies have demonstrated the efficacy of systemic antifibrinolytics (ε-aminocaproic acid, EACA and tranexamic acid, TXA) in reducing blood loss and the transfusion of homologous blood products [60–62]. The most efficacious dosing has yet to be determined, as loading doses from 10 mg/kg to 50 mg/kg of TXA have been reported in the literature. Recently, the administration of topical TXA has also been evaluated for the reduction of blood loss during spine surgery [63]. Although there are no reports in the literature linking these agents with prothrombotic complications, their administration to patients with preexisting thrombophilias or pretreated with anticoagulates for coronary artery stents or prosthetic valves remains controversial.

Controlled hypotensive anesthesia has become the standard of care in limiting blood loss during idiopathic scoliosis corrections in adolescents, but must be used with caution in older patients [64] (Fig. 31.3a, b). In a young healthy patient, an MAP of 50–60 mmHg is well tolerated, but higher pressures may be required in the adult population with cardiovascular disease. In addition, perfusion of the spinal cord during deformity-correcting surgery may be exquisitely sensitive to low perfusion pressures. Furthermore, the adequacy of end organ perfusion may be difficult to predict. Hypotension is usually best achieved with short-acting agents, which achieve both a reduction in blood pressure and heart rate. The calcium channel blocker clevidipine reduces blood pressure by decreasing systemic vascular resistance without affecting myocardial contractility and is rapidly metabolized by plasma esterases.

The role of the anesthesiologists during complex spine surgery is to maintain end organ perfusion despite large blood losses in an attempt to prevent complications such as spinal cord ischemia, renal failure, myocardial ischemia, stroke, and ischemic optic neuropathy (ION). The consequence of replacing assumed perioperative deficits with large volumes of crystalloid solution, however, can also result in severe complications [65]. How, then, is end organ perfusion best achieved during complex spine surgery? Theoretically the adequacy of end organ perfusion can be estimated with invasive monitoring and urine output and periodic arterial

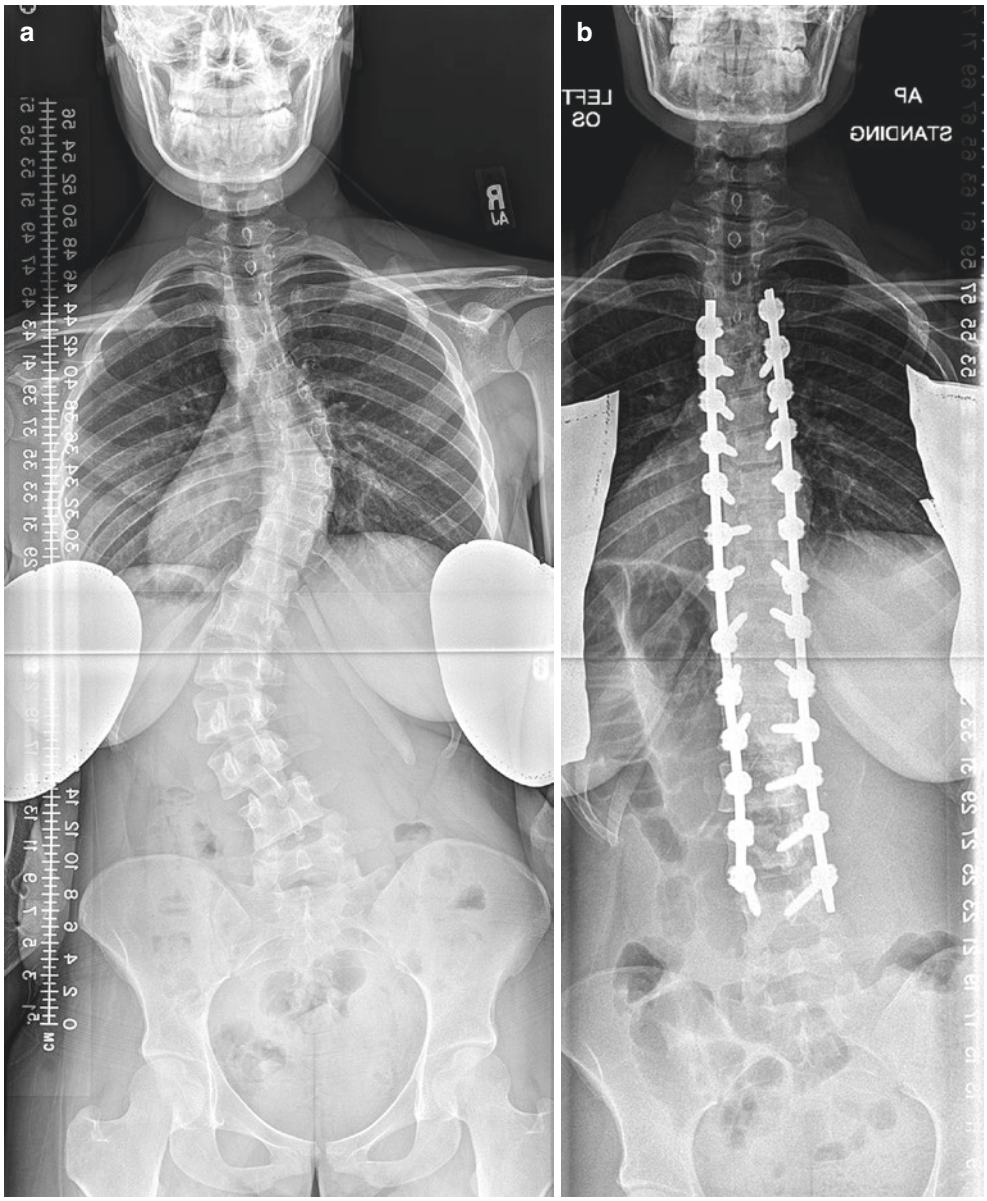

Fig. 31.3 (**a**, **b**) A 19-year-old female with double major idiopathic scoliosis preoperatively (**a**) and after posterior spinal fusion (**b**)

blood gas (ABG) analysis looking for evidence of metabolic acidosis. Despite the ubiquitous use of central venous pressure (CVP) monitoring during large blood loss procedures, the majority of the published literature suggests a poor correlation between CVP and blood volume and the inability of changes in CVP to predict the hemodynamic response to a fluid challenge [66]. Volume resuscitation with a pulmonary artery catheter (PAC) has been shown to be beneficial during adult reconstructive spinal surgery [67]. However, multiple published reports have questioned the value of PAC monitoring [68]. Oliguria during corrective spinal surgery may be a consequence of excess antidiuretic hormone release rather than hypovolemia [69]. Therefore, attempts to increase urine output intraoperatively may result in excessive fluid administration. ABG and central venous blood gas analysis provide information regarding tissue oxygenation requirements and perfusion [70].

Recently, clinicians have been investigating newer methods to determine tissue perfusion and fluid responsiveness (physiological assessment of intravascular fluid requirements; goal-directed fluid therapy). Devices which measure arterial pulse pressure variation and provide noninvasive cardiac output measurements have demonstrated utility in tracking fluid responsiveness during large blood loss procedures [71]. In hypovolemic patients, large changes in arterial pulse pressure variation will occur because of a decline in right ventricular preload, a relative increase in right ventricular afterload, and a decrease in systemic vascular resistance [72]. Thoracic bioreactance has also been utilized to noninvasively access stroke volume and fluid responsiveness.

These monitors may permit early intervention and volume resuscitation, before the onset of hemodynamic shock and the initiation of a systemic inflammatory response syndrome (acidosis, membrane permeability, coagulopathy, tissue hypoxemia). A meta-analysis of RCTs demonstrated that goal-directed fluid therapy decreased postoperative morbidity, infections, and length of ICU stay [73].

Postoperative Visual Loss

In addition to postoperative neurological deficits, postoperative visual loss (POVL) is another devastating complication of spinal surgery. POVL has been reported to be as high as 0.2% and as low as 0.028% in a large surgical population from a single hospital [74, 75] after spinal surgery. In the US Nationwide Inpatient Sample from 1996 to 2005, the prevalence rate of POVL after spinal fusions was 0.0309% [76].

The primary causes of POVL are ischemic optic neuropathy (ION), retinal artery (CRAO) or vein occlusion, and cortical brain ischemia. CRAO decreases blood supply to the entire retina, while branch retinal artery occlusion (BRAO) affects a portion of the retina. In an attempt to delineate the etiology of POVL, the ASA Committee on Professional Liability established the POVL Registry to collect detailed information on these cases [77]. Many patients with CRAO had evidence of unilateral ocular trauma, suggesting that improper positioning may have played a role. Funduscopic findings associated with CRAO included macular/retinal edema and a characteristic cherry red spot. Patients with CRAO often had unilateral vision loss, no light perception, periorbital edema, eyelid edema, chemosis, proptosis, ptosis, and paresthesias of the supraorbital region [78]. In the ASA registry, none of the patients with CRAO were positioned with Mayfield tongs, while two were positioned on horseshoe headrest [77]. The use of head positioning devices, which include foam cutouts for the eyes and a mirror to view the eyes, should reduce the incidence of this complication. Retinal microemboli are another potential cause of CRAO and more frequently in BRAO. ION was the most common cause of POVL after spinal surgery. ION can be divided into anterior (AION) or posterior (PION) ischemic optic neuropathy depending on the visual field cut and whether edema to the optic disk presents early (AION) or later (PION). Both are the result of reduced blood flow or oxygen delivery from endarteriole branches of the ophthalmic artery. Most cases occurring after spine surgery are PION and are often bilateral, while AION is more frequently reported after cardiac surgery.

The etiology of postoperative ION at present is unknown and unpredictable. However, in the ASA registry, the patients who developed ION after spine surgery were healthy, had a blood loss of greater than 1 liter, and were positioned in the prone position greater than 6 h. The ASA registry reported that prolonged procedures (>6 h) combined with substantial blood loss (44% of EBL) increased the risk of ION after spine surgery. Intraocular pressure (IOP) increases during anesthesia in the prone position, which could result in a decrease in ocular perfusion pressure despite the maintenance of normotension [79]. Hence, hypotension could be a causative factor in cases of abnormal optic nerve vascular autoregulation and/or decreased compensatory perfusion after hours in the prone position. However, in a retrospective case–control study of spine surgery, in patients with or without ION, anemia and hypotension were not associated factors [80]. In the ASA registry in 1/3 of the patients with ION, the lowest systolic pressures were greater than 90 mmHg. Although blood loss appears to be a risk for ION, several studies have been unable to determine how low or how long the hemoglobin level must decrease to lead to ION [78, 81]. When the patients in the ASA registry (80) with ION were matched with spine patients who did not develop ION (controls, 315), the risk factors associated with ION were male sex, obesity, the use of the Wilson frame (head positioned below the heart), duration in the prone position, blood loss, and increased infusion of crystalloid as compared to colloid [82]. The 2012 revised ASA practice advisory on POVL recommends the optimization of hemodynamics, Hb >8 gm/dl, avoiding direct pressure on the orbits, neutral or head-up positioning of the head, use of both colloids and crystalloids to maintain intravascular volume in patients who have substantial blood loss, the staging of potentially long operative procedures and early ophthalmologic consultation when ION is suspected [83]. Since ION occurs in the absence of vascular injury to other critical organs and in cases where neither hypotension or anemia are reported, optic nerve blood supply may be uniquely vulnerable to hemodynamic perturbances in the prone position.

Postoperative Ventilation

Many patients will require postoperative ventilation after complex reconstructive surgery. Those patients with preexisting pulmonary disease (restrictive lung disease, FEV <50% of predicted), intraoperative blood loss greater than one body blood volume, intraoperative evidence of decreased perfusion (metabolic acidosis), changing ventilatory parameters (increasing peak inspiratory pressures), and evidence of impending ALI (paO_2/FIO_2 <300) are candidates for postoperative ventilation. The goals for sedation for these patients include hemodynamic stability, analgesia, and tolerant of the ventilator but awake enough for regular neurological evaluations. Dexmedetomidine alone or in combination with propofol and narcotics has been shown to provide stable hemodynamics for sedation with the ability to assess neurological function when required [84].

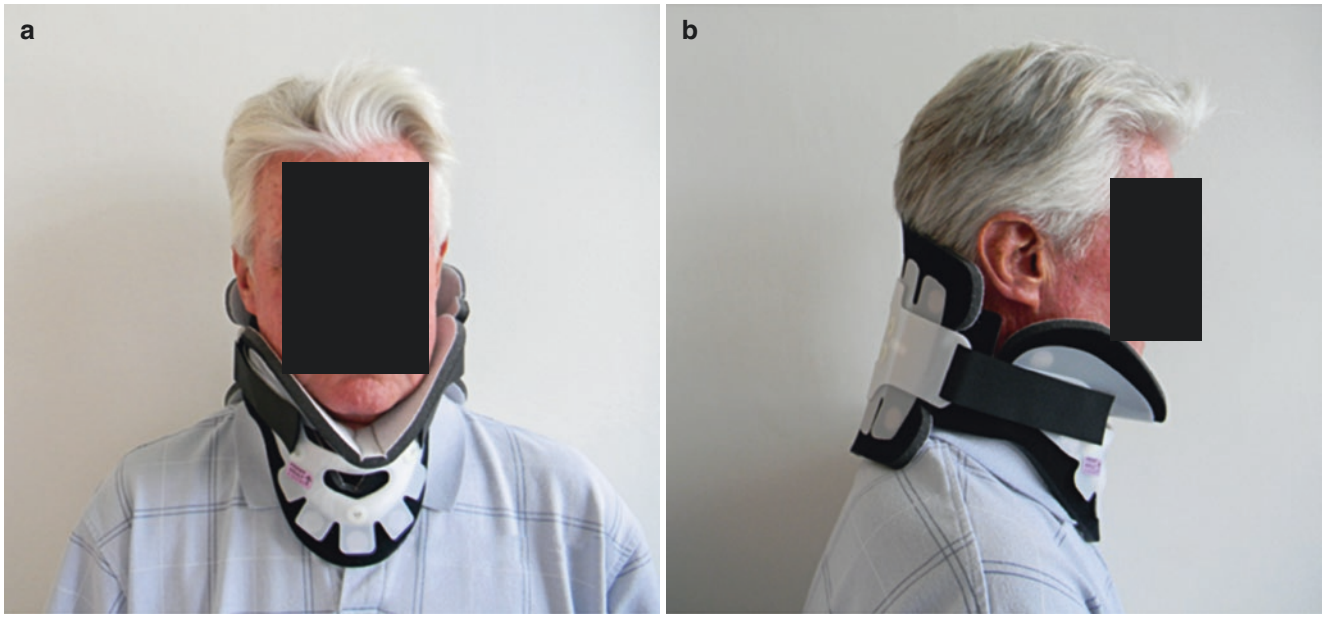

Fig. 31.4 Cervical orthoses

Postoperative Orthoses and Mobilization

The utilization of an orthosis after spine surgery procedures varies greatly according to individual surgeon preferences. In the cervical spine, hard cervical collars are often prescribed for spine stabilization following surgery for traumatic or degenerative conditions. Despite the routine use of hard cervical collars for postoperative bracing after surgery for degenerative conditions in many centers, there is a lack of consensus on the indication, type of collar, and duration of immobilization [85]; further there are data to suggest that for an unstable cervical spine, an orthosis is insufficient for reduction of motion [86]. The reported adverse effects of hard cervical collars include pain, tissue ischemia, breathing restriction, increased risk of aspiration, and high cost [87]. A prospective, randomized controlled pilot trial of 34 patients compared various patient-reported outcomes in patients both with and without postoperative hard cervical collar usage after ACDF. These data suggested that hard cervical collar usage may improve neck pain and disability 6 weeks postoperatively [88].

Theoretical arguments for the utilization of hard cervical collars postoperatively are the reduction of pain, increase in fusion rates, and a subjective increase in the individual patient's sense of security. For this reason, cervical orthoses such as the Miami J® hard cervical collar (Ossur, Foothill Ranch, CA, USA) are commonly implemented in clinical practice. Identifying an optimal time period for hard cervical collar wear while achieving positive outcomes in ACDF patients would be beneficial in minimizing unnecessary patient discomfort are areas of ongoing research. The common practice at our institution is implementation of a hard cervical collar for a 2-week duration after a multilevel ACDF (Fig. 31.4).

Lumbosacral orthoses may provide additional support for the patient's core musculature after spinal decompression or fusion procedures of the lumbosacral spine (Fig. 31.5). Immobilization of the lower lumbar spine and lumbosacral (L5-S1) motion segment in particular is poor with a lumbosacral model orthosis and would require a cumbersome hip extension for effective stabilization [89]. Many patients report an improved sense of stability and security with a lumbosacral orthosis after lumbar or lumbosacral spinal procedures, although, with modern rigid pedicle screw fixation, a contribution to fusion rates is unlikely.

Postoperative Pain Management

Patients often experience considerable pain after complex spine surgery. This pain usually has several components, including nociceptive (surgical), inflammatory, and neuropathic pain. In addition many of these patients suffer from chronic pain and will have been treated with opioids prior to surgery. Hence a multimodal approach to postoperative pain will most likely provide the most efficacious pain control with the least deleterious side effects [12, 90]. The majority of these patients will initially require treatment with intravenous opioids; however, the addition of intravenous acetaminophen, NSAIDs, local anesthetics (both as wound infiltration and intravenous), ketamine, and gabapentins will provide superior analgesia while reducing the deleterious opioid

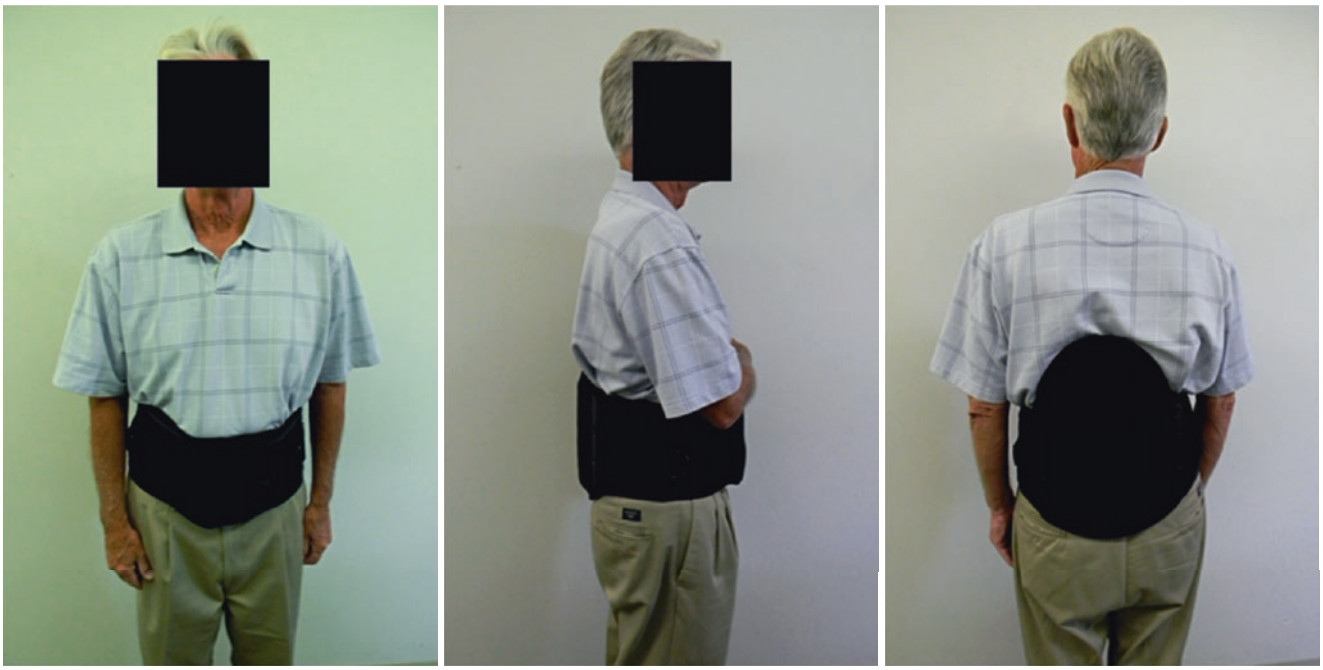

Fig. 31.5 Lumbosacral orthoses

side effects. For procedures involving more extensive spinal levels, intrathecal morphine administered during surgery has been shown to provide reliable postoperative pain control [91]. For narcotic-tolerant patients, subanesthetic doses (0.2 mg bolus, then 2 μg/kg/h) of ketamine reduced postoperative pain after posterior spine fusions [92]. Preemptive and postoperative administration of gabapentin and pregabalin has demonstrated mixed efficacy in the management of pain with few side effects [93, 94]. Although NSAIDs have been reported to have a negative effect on the success rate of spinal fusions, their short-term use immediately after surgery appears to provide excellent analgesia without inhibiting the fusion process [95]. Furthermore, every attempt should be made to reduce the daily opioid consumption of chronic pain patients and eliminate mixed agonists (buprenorphine) prior to surgery.

There is little doubt that multimodal analgesia after spinal fusions provides superior analgesia with the least side effects; however, there is still a deficiency in evidence-based studies to suggest which combination of agents will provide the best results.

Summary

Perioperative anesthetic management of the complex adult spine patient challenges the full scope of the clinician. These patients often have multiple medical comorbidities, the operative procedures are long with the potential for considerable blood loss, the anesthetic must match the requirement for continuous spinal cord monitoring yet provide enough depth to prevent intraoperative awareness and maintain hemodynamic stability, and the operative plan must extend into the postoperative period sometimes with postoperative ventilation and always with a consideration for analgesia.

Summary Bullet Points

- A multidisciplinary team including surgeons, perioperative medical specialists, intensivists, subspecialty-trained anesthesiologists, nurses, and physical therapists best serves complex spinal and scoliosis surgery patient.
- Careful preoperative evaluation and optimization of comorbidities are essential, especially in order to avoid cardiac complications.
- Specialized anesthetic techniques including total intravenous anesthesia may improve the accuracy and effectiveness of the monitoring. This is especially essential as complications are an unfortunately intrinsic reality of complex modern spine surgery in a subset of patients.
- Intraoperative hemodynamic management and intraoperative neurological assessments can positively influence outcomes.
- The ASA practice advisory on POVL recommends the use of both colloids and crystalloids to maintain intravascular volume in spine surgery patients who have substantial blood loss. Since ION occurs in the

absence of vascular injury to other critical organs and in cases where neither hypotension or anemia are reported, optic nerve blood supply may be uniquely vulnerable to hemodynamic perturbances in the prone position.

- Blood management should include preoperative autologous donation, and antifibrinolytic agents have been demonstrated to be a useful adjunct in reducing perioperative blood loss.
- Many patients will require postoperative ventilation after complex reconstructive surgery. The goals for sedation for these patients include hemodynamic stability, analgesia, and tolerant of the ventilator but awake enough for regular neurological evaluations.
- Patient-controlled intravenous analgesia is associated with higher patient satisfaction. Specialized pain management teams will often provide for better resource utilization.

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Management of Blood Products in Orthopedic Surgery

32

Jad Bou Monsef and Friedrich Boettner

Objectives

- To review typical blood loss from orthopedic procedures and common treatments including allogeneic blood transfusions for the resulting acute blood loss anemia
- To review the efforts toward bloodless surgery including the various modalities that have been devised to target different aspects of blood loss, which range from correcting preoperative anemia, reducing blood loss, and maximizing the use of autologous blood
- To review strategies that aim at optimizing patient preoperative status and red blood cell stock
- To explore operative approaches and surgical techniques as well as pharmacologic and other modalities that can minimize perioperative blood loss as opposed to simply replacing it
- To discuss the threshold for transfusion and the choice of blood-saving measure vary among patients. While there is no consensus on the appropriateness and benefit of each method, the blood management approach to orthopedic surgery holds the potential to minimize risks associated with transfusion.

Key Points

- This chapter illustrates current transfusion practices and highlights the risk-to-benefit ratio of allogeneic blood in elective orthopedic surgery.
- Exploring the various alternatives at our disposal is paramount to achieve adequate management of blood products.
- Striving for a "bloodless" surgical practice and enhanced safety depends on the integration of such modalities into algorithms tailored to specific patient needs.

Introduction

Most orthopedic surgeries require extensive bone and soft tissue dissection. Coupled with the inability to cauterize bleeding bony surfaces, orthopedic procedures harbor the potential for substantial blood loss. Significant bleeding occurs in pelvic and long bone fractures as well as primary and revision joint replacements and spinal procedures. Anemia is common in patients undergoing elective orthopedic surgery and could be found in up to a 50% of patients preoperatively [1–8]. Preoperative anemia has long been recognized as an independent risk factor for postoperative complications [9–11]. It has been associated with increased risk of adverse outcomes, infections, renal and pulmonary complications, longer hospital stay, increased 90-day readmission rates, and higher morbidity and mortality with almost any surgical procedure [12–26]. Even mild anemia was shown to increase relative risk of transfusion and adverse events by 30–40% [14, 27, 28]. It is also the major predictor of the need for transfusion of allogeneic blood [29]. Preoperative Hgb has been independently associated with transfusion risk despite routine TXA use [30, 31]. Other factors such age, gender, and body mass index contribute to perioperative risk of transfusion [16, 32, 33]. As joint arthroplasties are performed in an older individuals, almost 50% of octogenarians require a blood transfusion during their hospital course regardless of the estimated intraoperative blood loss [34].

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Defining Anemia

The 1968 WHO definition of anemia (preoperative Hgb <13 g/dL for men and <12 g/dL for women) may underestimate patients at risk of transfusion [30, 35]. Lower starting hemoglobin Hb constitutes an independent risk factor for requiring a perioperative blood transfusion and for the volume of transfusion. Different thresholds have been suggested for suboptimal hemoglobin levels that would warrant treatment and optimization and reduce transfusion risk. A preoperative cutoff value of 12.5 g/dL for females and 13.5 g/dl for males has been found to be optimal across all participants, as adjusted by sex and TXA use [30]. It has been suggested that postoperative full blood counts need not routinely be ordered in total joint patients with Hb >13 g/dL [36].

Postoperative anemia is more common due to surgical blood loss as well as the ensuing systemic inflammatory response that inhibits erythropoiesis and creates a state of functional iron deficiency despite normal iron stores [37, 38]. The ubiquitous treatment for symptomatic anemia (tachycardia, shortness of breath, change in mental status, cardiac ischemia) remains transfusion of packed red blood cells. Risks of allogeneic transfusion are rare but can be life threatening. Inherent risks of allogeneic transfusions persist in the form of an increased susceptibility and transmission of infections, transfusion reactions, altered immune response, circulatory overload, and transfusion-related acute lung injury [39, 40]. Therefore, blood transfusions are independently associated with infections, poorer function and recovery, and overall increased mortality, hospital stay and costs, as well as surgical complications including periprosthetic infections and venous thromboembolic events [13, 28, 41–45].

A growing awareness of the risks of perioperative anemia and blood transfusion has highlighted the need for comprehensive blood management in surgical patients. Blood management is a multimodal approach that relies on three pillars: optimizing erythropoiesis, minimizing perioperative blood loss, and optimizing the patient-specific physiological reserve of anemia [46]. The World Health Organization (WHO) has recognized the importance of perioperative blood management (World Health Alliance resolution A 63.12) and has urged all member countries to adopt it as standard of care [47]. This primarily advocates going beyond the concept of appropriate use of blood and addressing modifiable risk factors that increase the risk for transfusion before the need arises for one [48]. The move to adopt patient blood management is driven not only by the lack of efficacy and safety of current transfusion practices but also by their direct and indirect costs and the burden on healthcare resources [49, 50]. Blood management relies on sustainable and cost-efficient interventions individualized to each patient and risk level. It has been identified as one of the ten overlooked opportunities for significant performance improvement and cost savings for hospitals and health systems [51]. Blood management options encompass the preoperative workup and optimization, the surgery itself, and the postoperative period.

The standard treatment for preoperative anemia remains transfusion of allogeneic blood. In light of the exponential increase in number of procedures, orthopedic surgery accounts for a considerable portion of the average 13 million yearly blood transfusions in the United States [52]. Inherent risks of such transfusions persist despite improvement in safety and management of allogeneic blood. Ranging from the relatively common nonhemolytic febrile transfusion reactions, febrile allergic reactions, and alloimmunization reactions to the less common but more serious transfusion-related acute lung injury (TRALI) and transfusion-related immunomodulation (TRIM), such adverse events undermine the safety of allogeneic transfusions. TRALI is thought to be induced by a capillary leak syndrome instigated by neutrophil-mediated endothelial cell cytotoxicity [39]. Characterized by acute onset of noncardiogenic pulmonary edema within 6 hours of blood transfusion, it has been implicated as the leading cause of all transfusion-related fatalities [41]. TRIM is yet another immunosuppression-mediated syndrome caused by foreign blood. It is stipulated to increase the incidence of postoperative infections by up to 10%, delay postoperative wound healing, and prolong hospitalization [42–44]. Contamination and transmission of infection remain the most feared complications. The potential risks coupled to worldwide shortage and increasing cost of blood units have triggered the search for alternatives to allogeneic blood [52]. This in turn has led to major changes in transfusion practice and perioperative blood management.

It is clear that blood management in surgery involves much more than transfusing blood to increase preoperative hemoglobin. This traditional rule for transfusion dates back to 1942, when based on clinical observations, Adams and Lundy recommended preoperative transfusion for patients who have a hemoglobin level of less than 10 grams per deciliter before the operation [53]. The World Health Organization (WHO) Global Database on Anemia compiled data from 1993 to 2005 estimates a 24.8% worldwide prevalence of anemia, with varying thresholds for the different population groups [54]. While the overall prevalence in the United Stated ranges from 2% to 5% [54], this number rises rapidly after the age of 50, affecting 11% of men and 10.2% for women over 65 and 20% of people 85 years and older. Preoperative anemia is prevalent in surgical patients as iron-deficiency anemia, anemia of chronic disease, or both, as well as B12 or folate deficiency in the elderly. Identifying patients at higher risk for transfusions is key to reducing the routine use of allogeneic blood in elective procedures. Preoperative hemoglobin levels are the most consistent predictor for an increased risk of allogeneic blood transfusion [29, 25, 55, 56]. Other factors such age, gender, and body mass index contribute to transfusion risk when two or more of these parameters are present [32]. A hemoglobin of less than 10 g/dL before total

joint arthroplasty implies a nearly 90% chance of requiring transfusion, decreasing progressively to 40–60% between 10 and 13.5 g/dL and 15–25% beyond 13.5 g/dL, reflecting the inverse relationship between preoperative hemoglobin and allogeneic transfusion risk [57].

An estimated 24% of the patients scheduled for a hip or knee replacement are moderately anemic and at higher risk for transfusion, compared to 44% of the patients undergoing surgical treatment for a hip fracture. The prevalence of anemia further increases after surgery, reaching up to 90% on discharge [6]. Compounding the blood loss from the surgery, the ensuing systemic inflammatory response inhibits erythropoiesis through humoral mediators such as interleukin-1, interferon-γ, and tumor necrosis factor-α. This is achieved directly by suppressing erythroid colony growth and indirectly by suppressing erythropoietin production [37]. What follows is a state of functional iron deficiency in which iron is not available for erythropoiesis despite normal stores in the marrow macrophages [38].

Limiting the need for transfusion requires defining a transfusion threshold and optimizing the preoperative erythrocyte stock, surgical technique, and proper blood management to reduce exposure to allogeneic blood, transfusion-related complications, and cost. The efficacy of such interventions is measured by the reduction in blood loss or transfusion rates. However, the variations in parameters and study designs produce inconclusive results and have caused a lack of consensus between guidelines and practices. Taking into account that every blood conservation technique carries its own benefits as well as limitations and risks influenced by institutional and patient factors, no single method can be expected to represent the way to bloodless surgery. The best choice depends on the time available before surgery, the expected blood loss for the procedure, the patient's threshold for transfusion, and the efficacy of technique in the given setting [17]. Preoperative interventions focus on physiologic optimization and encompass iron supplementation, erythropoietin, and autologous blood donation. Intraoperatively, anesthetic practices such as controlled hypotension, epidural blockade, and acute normovolemic hemodilution complement surgical technique and pharmacologic agents to minimize blood loss. Postoperative interventions mainly consist of transfusion triggers and autologous transfusion.

Preoperative Interventions

Preoperative Optimization

Effective preoperative evaluation of the patient undergoing elective orthopedic surgery is crucial for perioperative blood management. The process of detection, evaluation, and treatment of anemia begins with obtaining hemoglobin and hematocrit levels 30 days prior to the surgery, leaving room for further investigations if needed. The workup of anemia is guided by the mean corpuscular volume, warranting serum B12 and folate levels if greater than 100 fl or ferritin and transferrin saturation levels if below 80 fl. A microcytic anemia with ferritin saturation below than 12 ng/mL or transferrin saturation less than 15% indicates iron deficiency and the need for supplementation (and possible GI evaluation). Normocytic anemia could be the result of possible blood dyscrasia, hemolysis, blood loss, or chronic kidney disease, in which case the reticulocyte count and serum creatinine level should be screened. Anemia of chronic disease is a diagnosis of exclusion, where inadequate reticulocytosis is found despite sufficient iron stores and normal MCV.

Identification and optimal management of medical conditions or drugs that may interfere in coagulation and bleeding is paramount before surgery. Vitamin K antagonists, antiplatelet agents, or anticoagulants such as heparin or any thrombin inhibitor should be stopped preoperatively when possible. The bleeding risk with aspirin is increased by 2.5–20%, reaching 30–50% when aspirin and clopidogrel are combined [58]. The risk is similar for low- molecular-weight heparins (LMWH), vitamin K antagonists, and aspirin. Unfractionated heparin carries the highest risk of bleeding [59]. Aspirin irreversibly inhibits platelet aggregation and requires discontinuation 7 days prior to the procedure. Optimal timing for elective procedures is beyond the first year in patients with coronary stents, to minimize the risk of acute stent thrombosis [60]. High cardiovascular risk patients should not stop aspirin therapy in the perioperative period [61].

Reconsidering the historic transfusion triggers of 30/10 has established that hemoglobin levels of 8 g/dl and even to 7 g/dl can be safely tolerated in a patient with no major comorbidities. Nevertheless, anemia is an important risk factor for perioperative mortality. This is documented in patients who declined the use of blood products. A hemoglobin level less than 6 g/dL was found to increase the mortality risk within 1 month of surgery by a factor of 26 as compared to patients with a hemoglobin level of 12 g/dL [12].

Rotational thromboelastometry provides a method of intraoperatively and rapidly testing for deficiency in coagulation pathways, platelet function, and fibrinolysis. It allows identifying high-risk patients and tailoring the treatment whenever possible. It has shown effective and cost-efficient with or without tranexamic acid in spine surgery [62].

Preoperative Autologous Blood Donation

Preoperative donation of autologous blood emerged in the 1980s fueled by concerns over transmission of diseases, namely, HIV, through allogeneic transfusions [63]. Albeit more and more unlikely, the devastating repercussions of such adverse events in addition to the persistent possibility

of human error underscored the premise that the safest blood would be the patient's own [64]. Utilizing the patient's own blood can be achieved through preoperative autologous blood donation (PABD), perioperative hemodilution, intraoperative salvage and reuse of blood from the operative field, or postoperative reinfusion of drained blood [65]. Owing to the elective nature of nontraumatic orthopedic procedures with increased blood loss, PABD gained significant momentum and established itself as the standard alternative to allogeneic transfusions in orthopedic surgery [66]. A blood unit is drawn every 5–7 days, with the last one at least 3 days prior to the surgery [39]. In children, the volume of each donation must be lower than 13% of their circulating blood volume, unless simultaneous volume replacement is performed [67]. The optimal range for donation is 4–6 weeks prior to surgery with iron supplementation to ensure adequate compensatory erythropoietic response. 325 mg ferrous sulfate or ferrous fumarate 3 times daily are the most common iron supplements. The blood is then stored at the hospital's blood bank for later intraoperative or postoperative transfusions. According to the National Heart, Lung, and Blood Expert Institute Panel on the Use of Autologous Blood, autologous blood donation is possible in most patients who are healthy enough to undergo elective surgery and constitutes a safer alternative than allogeneic blood. The panel defines appropriate patients as those (1) undergoing elective surgery that can be scheduled at least 7 weeks in advance, (2) undergoing a surgical procedure for which blood is usually crossmatched, (3) having a hemoglobin >11 g/dL (hematocrit, 0.33), and (4) having no contraindications to autologous blood donation [64]. The absolute contraindication due to concerns of reinfection during transfusion is bacteremia or conditions predisposing to bacteremia such as urinary or cutaneous catheters. Other contraindications include pregnancy, severe pulmonary disease, unstable angina, myocardial infarction within the previous 3 months, congestive heart failure, and significant aortic valve stenosis with an A-a gradient >70 mmHg [68].

The appeal of PABD as a blood-saving modality stem from three major benefits:

1. Safety from viral infection, graft-versus-host disease, alloimmunization, and Rh sensitization
2. "Preemptive" early stimulation of the reticulocytosis preoperatively, thus overriding the intraoperative blood loss as a trigger for the erythropoietic response [69]
3. The reduction of effective RBC mass by diluting the blood, resulting in a lower RBC loss during surgery [70].

With the established safety of autologous blood donation, its efficacy in reducing or even preventing exposure to allogeneic blood comes into question. Extensive studies conducted in the last two decades concluded that PABD effectively decreases the risk of allogeneic transfusion but increases overall transfusion rates. A Cochrane review studying preoperative donation in surgery including orthopedic estimated a 68% reduction in exposure to allogeneic blood in the PABD group, at the expense of a 24% higher risk of receiving any transfusion (allogeneic and/or autologous). The latter risk of exposure to any transfusion was attributed donation-induced anemia, as well as a tendency to more liberal transfusion of autologous blood [71].

Although some data suggest that PABD effectively can reduce exposure to allogeneic blood in spine surgery [72, 73], other studies have questioned its efficacy in adult spinal deformity patients in whom no protective effect of donation against allogeneic blood exposure was observed [74, 75]. In total joint arthroplasty, PABD significantly reduced allogeneic blood transfusion rates in a meta-analysis of 950 patients in 3 randomized trials (RR 0.16, 95% CI), as well as 18 observational controlled studies covering 19,239 patients (RR 0.29; 95%Cl) [76]. Similar results were reported by the Orthopedic Surgery Transfusion Hemoglobin European Overview (OSTHEO) study of 3996 patients [1], as well as a multicenter center study of 9482 patients from 330 TJA surgeons in the United States. However, these studies also shed light on the inefficiency of the collection and use of autologous blood [5].

Critical evaluation of this intervention has raised a number of concerns with PABD, including high cost, increased transfusion rates, and high incidence of wasted blood. Preoperative autologous blood donation is not associated with an increase in either the morbidity or mortality rates or the length of hospital stay [67]. However, the high percentage of wasted blood units (up to 50%) [5] and the potential risks of transfusion reactions, vasovagal episodes, circulatory volume overload, bacterial contamination, and clerical errors undermine the universal acceptance of autologous predonation. The logistically difficult procedure requires a setup in place to adequately handle the blood units. It is also time-consuming and costly for the patients. The endogenous erythropoietin response in patients with mild anemia might be insufficient, exacerbating the preoperative anemia and increasing the likelihood of a transfusion [57].

In addition to that, PABD seems to have less impact when integrated in a transfusion protocol. Its combination with rHuEPO proved more effective in reducing ABT rate than any of them alone [77]. The administration of rHuEPO to adults, children, and adolescents has been found to enhance the effectiveness of PABD [78].

Preoperative hemoglobin level plays an important role in balancing risk and benefit. Patients with hemoglobin above 13 g/dL have a five times lower transfusion risk than those in the 11–13 g/dL range. Preoperative hemoglobin levels of >13 g/dL are associated with the highest percentage of

wasted autologous blood, up to 90% reported in shoulder arthroplasty [79]. Predonation of autologous blood may not be indicated when Hgb levels are greater than 15 g/dl or between 13 and 15 g/dl in those who are less than 65 years old undergoing primary TJA. In THA, for instance, PABD failed to show benefit for nonanemic (Hb > 12.5 g/dL) patients [80].

A rationale approach to determining transfusion risk would be stratifying of patients based on preoperative hemoglobin levels and estimated blood loss of each procedure (unilateral vs. bilateral, primary vs. revision) [57]. One of the main disadvantages of preoperative donation remains its cost. Cost-effectiveness is compromised when at least one unit of allogeneic blood must be transfused or when more than 15% of the donated blood must be discarded [68]. Insurance coverage of autologous donation is questionable, sometimes reflecting a direct cost on the patient as well as the hospital. The high cost associated with PABD coupled to the global adoption of tranexamic acid has limited the efficacy and use of autologous blood [81–83].

Iron

Baseline hemoglobin at or exceeding 13 g/dL has been deemed essential for reducing exposure to blood products, improving postsurgical recovery, reducing complications, and optimizing patient status at discharge [5]. In light of the role of starting RBC stock in dictating transfusion needs, pharmacological enhancement of erythropoiesis can be achieved by supplementing iron and folic acid, with or without recombinant erythropoietin. Preoperative iron has been advocated as a potential adjunct in both anemic and nonanemic patients [84, 85]. As the release of iron from its ferritin stores is a slow process, iron supplementation is advised even with normal ferritin levels [86]. Iron can be administered orally and parenterally, but intravenous administration is five times more effective in inducing the erythropoietic response after significant blood loss and is cost-effective [87, 88].

Coupled to a restrictive transfusion protocol, oral iron was shown to reduce transfusion requirements in total knee arthroplasty patients [89]. Similarly, perioperative administration of intravenous (IV) iron, with or without single doses of erythropoietin, in knee replacement or hip fracture showed a reduced number and volume of transfusions [90, 91].

Chronic anemia from inflammation, infections, and malignancies is often mild to moderate but is probably one of the most common forms of anemia after iron deficiency [92]. These patients are important to distinguish from the patients with iron-deficiency anemia, because iron supplementary has no therapeutic benefits. As opposed to iron deficiency, anemia of chronic inflammation is associated with high serum hepcidin levels. Hepcidin impairs the absorption of orally administrated iron and increases the sequestration of iron in macrophages by inducing the internalization of ferroportin in enteric cells and macrophages [93]. In such patients intravenous iron is able to overcome this effect [86], and they may require higher doses of erythropoietin to trigger sustained erythropoiesis [94].

Cobalamin (vitamin B12) and folate deficiency are responsible for 5–10% of anemias in the elderly population and must be supplemented in cases of macrocytic anemia [95].

Oral iron supplementation protocol increased preoperative Hb and ferritin levels before THA or TKA and reduced the number of patients with a preoperative Hb level <13 g/dL as well as the number of patients requiring either EPO or IV iron supplementation [96]. The physiological response to oral iron supplementation has been correlated with serum ferritin, Hb, and mean red cell volume [97]. The recommended treatment for iron-deficiency anemia, which is the most common etiology for anemia, includes 3 months of oral iron supplementation [19]. A recent meta-analysis reported a modest increase in Hb of 0.35 g/dL after 4–6 weeks of oral iron supplementation in the elderly [98]. A meta-analysis of RCTs using preoperative IV iron administration showed significantly higher Hb levels, lower transfusion risk, and better patient outcomes [99]. IV iron can effectively and rapidly replenish iron stores and is highly effective as part of blood management protocols when combined with tranexamic acid and/or erythropoietin [100–103].

Safety

Although iron therapy has been found to be generally safe and effective, especially high-molecular-weight iron, dextran has the disadvantage of potentially life-threatening dextran-associated anaphylactic reactions [104]. While no clinically relevant adverse reaction to iron administration was observed in studies, the administration of IV iron should be avoided in patients with pretreatment ferritin values >500 ng/ml or with ongoing bacteremia [84]. Oral iron is available in four preparations: ferrous sulfate, ferrous gluconate, ferrous fumarate, and iron polysaccharide. Gastrointestinal side effects may limit these preparations' tolerability. Iron supplements with a high elemental value will require fewer pills and fewer doses, reducing the risk and frequency of side effects. Intravenous (IV) iron preparations including iron sucrose and iron gluconate exhibit greater safety than past formulations infamous for anaphylactic reactions. The effect on hemoglobin levels usually occurs starting at 1 week, with the maximum effect achieved at 2 weeks [105]. Hypotension, arthralgia, abdominal discomfort, and back pain are potential side effects of IV iron. Intravenous iron presents a safer alternative to blood transfusion and is associated with a lower risk of death (0.4 per million vs. 4 per million, respectively) as well as life-

threatening adverse events (4 per million vs. 10 per million, respectively) according to the Network for Advancement of Transfusion Alternatives [84].

Erythropoietin

The process of erythropoiesis is greatly dependent on erythropoietin (EPO), a glycoprotein hormone synthesized in the kidney and secreted by renal cortical interstitial cells. Released in response to tissue hypoxia, EPO acts on erythrocyte colony-forming units in the bone marrow and stimulates RBC production. In the United States, recombinant human erythropoietin has been approved for use in the treatment of anemia in patients with chronic renal failure, human immunodeficiency virus, and people receiving chemotherapy [106]. Through subcutaneous or intravenous administration, erythropoiesis-stimulating agents such as epoetin alfa and darbepoetin boost hemoglobin level and decrease or eliminate transfusion needs in chronic renal patients [105]. This effect was explored in patients undergoing elective procedures such as cardiovascular and orthopedic surgeries. Extensive studies established the effectiveness of perioperative EPO in stimulating erythropoiesis (Table 32.1) [106–108, 111–145]. It was found to increase preoperative hemoglobin concentration, hematocrit, reticulocyte count, and autologous blood units donated. In addition, such agents significantly reduce the rate of allogeneic transfusion (AOR 0.63; 95% CI) [107–109]. A meta-analysis of 15 RCTs involving 2155 patients found a 60% reduction in the need for allogeneic transfusion [110].

The erythropoietic response depends on the dose of EPO and the availability of iron [146]. It is physiologically triggered by acute blood loss in surgery, showing evidence of erythroid hyperplasia after 3–6 days and maximal response in 7–10 days [147]. However, the erythropoietic response is often impaired in older patients with medical comorbidities [148]. This contributes to a delayed postoperative recovery of hemoglobin levels even after allogeneic blood transfusion. The anticipated benefit of erythropoietin is creating a period of magnified erythropoietic response. Reticulocyte levels have been shown to normalize 2 weeks after discontinuation of erythropoietin [149]. In patients with preoperative hemoglobin levels of 10–13 g/dL, erythropoietin significantly reduces transfusion risk to 16% from 45%. The results directly reflected on readiness to resume daily activities and muscle strength measured as postoperative vigor and functional ability. This reduces the length of hospital stays and facilitates postoperative rehabilitation [57]. In light of the diminished postoperative intestinal absorption of iron, administration of IV iron with erythropoietin reduces the delay to recover baseline hemoglobin levels [90]. IV Iron and EPO are suggested for cases in which allogeneic blood is not available or accepted.

Safety

Despite FDA approval for elective surgery, the risk of erythropoietin came under scrutiny in 2007, fueled by concerns over perioperative thromboembolic events. The Food and Drug Administration alerted to the preliminary results of a 681 patient randomized study of recombinant erythropoietin (4 × 40,000 IU) in patients undergoing elective spine surgery. While all patients did not receive anticoagulation, those treated with erythropoietin experienced twice the frequency of deep venous thrombosis relative to the control group (4.7% vs. 2.1%) (FDA alert 16 November 2006, updated 16 February 2007 and 9 March 2007).

Other studies have shown erythropoietin to be safe and effective in treating anemia and decreasing patient exposure to allogeneic blood transfusion. However, it is important to note that the available agents are prothrombotic especially in the absence of pharmacologic DVT prophylaxis. As hemoglobin levels may exceed normal levels, a higher risk of thromboembolic events are the results of an increased blood viscosity and platelet concentration. EPO is contraindicated for patients with comorbidities that may predispose to adverse side effects, such as uncontrolled arterial hypertension, previous acute myocardial infarction or stroke, unstable angina, and severe carotid stenosis. The FDA subsequently required a warning to be added to the package inserts to specify the increased risk of DVT in surgical patients not receiving prophylactic anticoagulation. The warning urges to consider the use of DVT prophylaxis in surgical patients receiving erythropoietin [105]. Monitoring hemoglobin and hematocrit levels in all patients treated with EPO is indicated. The more common side effects, though still rare, include local skin irritation at the injection site, increased blood pressure, and headaches [63].

The reversibility of erythropoietin's effect on the bone marrow has come into question, possibly as a form of withdrawal or antibody-mediated mechanism. However, pure red cell aplasia occurring after EPO administration has not been reported in orthopedic surgery patients. Therefore, this does not seem to be an issue with short-term use of EPO [65, 67].

The high cost of this intervention has led to different regimens in an attempt to achieve optimal cost-efficiency. The initially suggested regimen involved daily administration of 300 IU/kg body weight for 15 days, starting 10 days before surgery. Alternatively, 600 IU/kg of subcutaneous EPO weekly on preoperative days 21, 14, and 7 and on the day of surgery is now recommended. In adults with a mean weight of around 65 kg, 40,000 IU once weekly is authorized as a preoperative treatment dosage. In conjunction with a PABD protocol, the recommended dose is 600 IU/kg (or a 40,000 IU vial), twice a week throughout the period of blood donation. In both cases, the use of EPO is discontinued if hemoglobin levels reach 15 g/dl [106, 145, 150–154]. Blood levels of ferritin, folic acid, and vitamin B12 should be checked and corrected before initiating therapy. Iron supplementation is necessary with both protocols [132].

Table 32.1 Efficacy of epoetin alfa in major orthopedic procedures

Study (year)	No. of patients	Procedure	Treatment, dose	Key findings with epoetin alfa
Biboulet et al. (2018) [111]	100	Total joint arthroplasty	40,000 EPO subcutaneously × 3 preop doses with oral or IV iron	EPO with IV iron higher Hb and less GI side effects than PO
Bernabeu-Wittel et al. (2016) [112]	200	Hip fracture	40,000 IU of subcutaneous EPO + 1 g of IV ferric carboxymaltose	Quicker recovery from anemia 60 days postop with EPO, same transfusion risk
So-Osman et al. (2014) [113]	683	Total joint arthroplasty	EPO 40,000 IU SC weekly ×3 weeks vs. EPO + PABD	50% reduced transfusion risk with EPO, unacceptably high cost
Buljan et al. (2012) [114]	93	Hip arthroplasty	15,000 IU IV 2×/week or 30,000 IU once a week (total 90,000 IU) + oral iron PABD 12% of total blood volume	IV EPO once a week optimal for PABD
Na et al. (2011) [115]	108	Bilateral knee arthroplasty	3000 IU of EPO subcutaneously during the operation + 200 mg of iron sucrose IV over 1 hour	Higher postop Hb, significantly lower transfusion rate and mean number of units
Moonen et al. (2008) [116]	100	Total joint arthroplasty	Epoetin alfa, 40,000 IU ×4/week for 3 weeks preop subcutaneously + iron PO (orally) vs. postoperative retransfusion of shed blood	Lower allogeneic transfusion rate in epoetin group vs. retransfusion group (4% vs. 28%)
Vitale et al. (2007) [117]	61	Scoliosis surgery	Epoetin alfa, 10,000 IU or 300 IU/kg 21, 14, and 7 days preop and on the day of surgery subcutaneously + iron PO	Higher mean preoperative and discharge hematocrit level
Keating et al. (2007) [118]	251	Total joint arthroplasty	600 IU/kg EPO weekly for 3 weeks and within 24 hours postoperatively + PABD: 1 U for TKA, 2 U for THA	EPO better than PABD for vigor, but not for handgrip strength. EPO had higher hemoglobin levels and required fewer transfusions
Deutsch et al. (2006) [119]	50	Total joint arthroplasty	EPO 40,000 IU SC 14 days and 7 days preop + PABD 2 U if Hb between11 and 13 g/dL	EPO higher Hb than PABD, same allogeneic transfusion rates
Weber et al. European Epoetin Alfa Surgery Trial (EEST) (2005) [108]	695	Orthopedic	Epoetin alfa, 40,000 IU/week or placebo subcutaneously ×3 weeks preop and on the day of surgery + iron PO	Higher Hb values from the day of surgery until discharge and lower transfusion rates (12% vs. 46%)
Rosencher et al. (2005) [120]	93	Orthopedic	Epoetin alfa, 40,000 IU/week subcutaneously preop until they reached a maximal Hct of 40% vs. PABD-only group	Increased RBC production, higher hematocrit on days 1 and 3 postop and at discharge; better energy score; two EPO injections were sufficient to reach a Ht of 40% in the majority of patients
Franchini et al. (2004) [121]	51	Scoliosis surgery	Epoetin alfa, 10,000 IU ×2/week subcutaneously for 3 weeks preop + iron PO	Increased predonation of blood units and hemoglobin levels; all of the patients completed the PABD program; decreased allogeneic blood requirements
Feagan et al. (2000)	201	Hip arthroplasty	Epoetin alfa 20,000 or 40,000 IU per week ×4 weeks	Lower allogeneic transfusion rates, less complications
Colomina et al. (2004) [122]	250	Spine surgery	Epoetin alfa 40,000 IU ×2/week subcutaneously + PABD starting approximately 2 months preop vs. PABD only + iron PO	Higher hemoglobin and hematocrit values at time of surgery; more predonated units retrieved per patient; reduced allogeneic transfusion requirements
Lee et al. (2003) [123]	53	Two-stage reimplantation hip arthroplasty	Epoetin alfa, 40,000 IU subcutaneously at intervals of 21, 14, and 7 days before reimplantation + iron PO vs. controls	Increased preop hemoglobin levels and decreased rate of allogeneic transfusion
Wurnig et al. (2001) [124]	194	Orthopedic or cardiovascular	Epoetin beta, 125 or 250 IU/kg/week subcutaneously or no therapy for 3–4 weeks before surgery + iron PO	Increased preop hemoglobin levels and decreased rate of allogeneic transfusion
Tamir et al. (2000) [125]	56	Total joint arthroplasty	Epoetin alfa, 100 IU/kg/day for those with hemoglobin (Hb) >13 g/dl, 300 IU/kg/day for Hb <13 during the 10 days prior to surgery and the 4 days following the operation + iron PO	Decreased allogeneic transfusion rates vs. controls
Stowell et al. (1999) [126]	490	Total joint arthroplasty	Epoetin alfa, 600 IU/kg/week ×4 weekly doses subcutaneously or PABD	Higher hemoglobin pre- and postoperatively and at discharge versus PABD patients; lower transfusion rate than PABD group

(continued)

Table 32.1 (continued)

Study (year)	No. of patients	Procedure	Treatment, dose	Key findings with epoetin alfa
Mercuriali et al. (1998) [127]	40	Hip arthroplasty	Epoetin alfa, 300, 150, or 75 IU/kg, or placebo, ×2/week + iron intravenously	Dose-dependent increases in PAD (4.3 units, 300 IU/kg; 3.4 units, 150 IU/kg; 3.0 units, 75 IU/kg; 2.1 units, placebo)
Vitale et al. (1998) [128]	178	Scoliosis surgery	Epoetin alfa, 10,000 IU/week for 3 weeks or 300 IU/kg/week for 3 weeks subcutaneously + iron PO	Higher hematocrit levels overall, decreased hospital stay and lower transfusion rates in idiopathic scoliosis group
Cazenave et al. (1997) [129]	80	Orthopedic or cardiovascular	Epoetin alfa, 600 or 300 IU/kg or placebo ×3/week for 1 week starting 18–21 days preop intravenously + iron PO	Increased predonation of >4 units of blood; dose-related increase in red blood cell volume
Tryba et al. (1996) [130]	125	Orthopedic	Epoetin alfa, 150,100, or 50 IU/kg of body weight or placebo ×2/week for 3 weeks beginning 18–21 days preop intravenously + iron intravenously	Increased reticulocyte count; increased predonation blood; reduced risk of exposure to allogeneic blood
de Andrade et al. (1996) [131]	290	Hip and knee arthroplasty	Epoetin alfa, 300 or 100 IU/kg or placebo daily for 15 days beginning 10 days preop subcutaneously + iron PO	Dose-related increase in reticulocyte count and hematocrit; reduced risk of exposure to allogeneic blood
Faris et al. (1996) [106]	185	Hip and knee arthroplasty	Epoetin alfa, 300 or 100 IU/kg or placebo daily for 15 days beginning 10 days preop subcutaneously + iron PO	Dose-related increase in reticulocyte count, hemoglobin, and hematocrit; reduced risk of exposure to allogeneic blood
Goldberg et al. (1996) [132]	140	Hip and knee arthroplasty	Epoetin alfa, 600 IU/kg subcutaneously for four doses beginning 21 days preop or 300 IU/kg intravenously daily for 15 days beginning 10 days preop + iron PO	Increased hemoglobin concentration; weekly subcutaneous regimen equivalent to daily intravenous regimen
Goodnough et al. (1994) [133]	116	Orthopedic	Epoetin alfa, 600, 300, or 150 IU/kg or placebo ×2/week for 3 weeks intravenously + iron PO	Increased reticulocyte count and red blood cell volume
Schlaeppi et al. (1994) [134]	62	Orthopedic	Epoetin alfa, 100 or 200 IU/kg/week or placebo ×4 weeks subcutaneously + iron PO	No allogeneic transfusions in epoetin group
Mercuriali et al. (1994) [135]	23	Hip arthroplasty	Epoetin alfa, 300 IU/kg or placebo intravenously ×2/week for 3 weeks + iron intravenously	Increased predonation of >2 units of blood; reduced risk of exposure to allogeneic blood
Beris et al. (1993) [136]	101	Orthopedic	Epoetin alfa, 150–180 IU/kg ×6 in 3 weeks or placebo subcutaneously + iron PO	Increased reticulocyte count; reduced drop in hemoglobin
Canadian Orthopedic Perioperative Erythropoietin Study Group (1993) [137]	198	Hip arthroplasty	Epoetin alfa, 300 IU/kg daily for 14 days beginning 10 days preop; placebo for 5 days, beginning 10 days preop, and then epoetin alfa, 300 IU/kg of body weight, for the next 9 days; or placebo	Dose-related increase in reticulocyte count and hemoglobin concentration; reduced risk of exposure to allogeneic blood
Biesma et al. (1993) [138]	40	Hip arthroplasty	Epoetin alfa, 500 IU/kg or placebo ×2/week for 3 weeks preop subcutaneously + iron PO	Sixfold increase in reticulocyte count, recovery of baseline hemoglobin after PABD
Mercuriali et al. (1993) [139]	50	Hip arthroplasty	Epoetin alfa, 600 or 300 IU/kg or placebo ×2/week for 3 weeks intravenously + iron PO and intravenously	Increased predonation of blood; reduced risk of exposure to allogeneic blood
Goodnough et al. (1992) [140]	44	Orthopedic	Epoetin alfa, 600 IU/kg or placebo ×2/week for 3 weeks intravenously + iron PO	Increased predonation of blood; increased red blood cell production
Hochreiter et al. (1992) [141]	82	Hip arthroplasty	Epoetin alfa, 200 or 100 IU/kg or placebo, ×2/week for 3 weeks intravenously + iron PO	Increased predonation of blood by mildly anemic patients
Tasaki et al. (1992) [142]	25	Orthopedic	Epoetin alfa, 9000, 6000, or 3000 IU, ×2/week for 3 weeks intravenously + iron PO and intravenously	Dose-related increase in red blood cell volume
von Bormann et al. (1991) [143]	10	Hip arthroplasty	Epoetin alfa, 200 IU/kg or placebo × 7 doses subcutaneously + iron PO	Increase in reticulocytes, maintenance of hemoglobin levels during PABD
Graf et al. (1990) [144]	10	Hip arthroplasty	Epoetin alfa, 150–200 IU/kg ×3/week for 2–6 weeks (6–18 doses) intravenously + iron PO	Predonation of a mean of 4.4 units of blood; no allogeneic transfusions
Goodnough et al. (1989) [145]	47	Orthopedic	Epoetin alfa, 600 IU/kg or placebo ×2/week for 3 weeks intravenously + iron PO	Minimized drop in hematocrit; increased red blood cell volume

Intraoperative Interventions

Pharmacologic Antifibrinolytics

Secondary hemostasis depends on cleavage of fibrinogen to fibrin by thrombin. This process is regulated by different mechanisms, namely, the degradation of fibrin by plasmin. Synthesized in the liver, circulating plasminogen is proteolytically cleaved in lysine-rich areas by endothelium-produced tissue plasminogen activator. The resulting plasmin promotes degradation of fibrin. Antifibrinolytics such as tranexamic acid (TXA), aprotinin, and ε-aminocaproic acid (EACA) have been shown to prevent dissolution of blood clots and stop bleeding [39]. They have come into use in dental extraction, tonsillectomy, prostate surgery, heavy menstrual bleeding, and cardiac surgery and in patients with hemophilia. These products allow pharmacologic manipulation of the coagulation cascade through different mechanisms that inhibit fibrinolysis or promote coagulation. An extensive review of their application in over 25,000 surgical patients including orthopedics highlighted significant reductions in blood loss and allogeneic red cell transfusion [155]. Even though slightly less effective than aprotinin, the lysine analogues effectively reduce blood loss during and after surgery with a superior safety profile and cost-efficiency [155].

Lysine Analogues: Tranexamic Acid and Epsilon-Aminocaproic Acid

Lysine analogues are synthetic amino acids that block the lysine-binding sites on plasminogen molecules. They effectively displace plasminogen and plasmin from fibrinogen, inhibiting fibrinolysis. This category encompasses epsilon-aminocaproic acid and tranexamic acid, the latter exhibiting stronger binding and thus around ten times more potency than the former [156–158]. The benefits of both EACA and TXA have been evaluated in various clinical scenarios including cardiac surgery, prostrate surgery, liver transplantation, and subarachnoid hemorrhage. The fibrinolytic system is activated transiently after any surgery, especially in tissues with high tissue plasminogen activator content [159]. In orthopedic surgery, this is particularly applicable to total knee arthroplasty. Employing a pneumatic tourniquet to create a bloodless field results in increased fibrinolytic activity, contributing to early postoperative blood loss [160]. Tranexamic acid displays a six- to tenfold higher affinity to plasminogen compared to EACA and is less costly (Fig. 32.1).

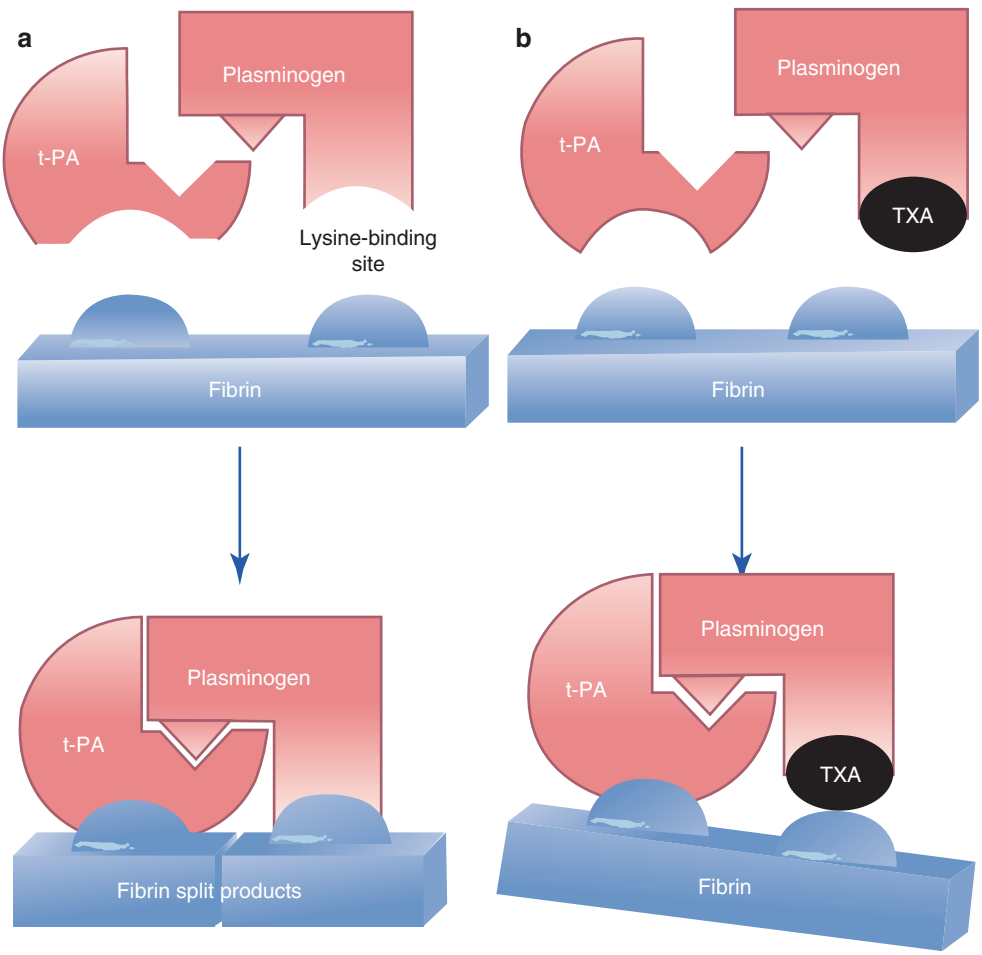

Fig. 32.1 Inhibition of fibrinolysis by tranexamic acid. (**a**) Activation of fibrinolysis. (**b**) Tranexamic acid (TXA)-mediated inhibition of fibrinolysis by competitive binding to lysine-binding site on fibrinogen. T-PA tissue plasminogen activator

Tranexamic Acid

Many recent prospective randomized clinical trials and meta-analyses have reported TXA to be effective and safe in reducing allogenic blood transfusion and blood loss, without increasing thromboembolic complications, and recommend routine use in anatomic and reverse total shoulder arthroplasty, primary and revision total knee and total hip arthroplasty, trauma, as well as spine surgery [161–171]. TXA is a synthetic drug that limits blood loss through inhibition of fibrinolysis and clot degradation. Oral, topical, and intravenous administration of TXA, in a variety of dosing regimens or combinations, have proven effective and safe [172–185]. A Cochrane review including 21 trials of tranexamic acid compared with controls in total hip and knee arthroplasty, including 993 patients, demonstrated that tranexamic acid significantly reduces allogeneic blood transfusions by 56% and total amount of blood lost during perioperative period by an average of 440 mL [186]. TXA was not found to increase thrombosis in free tissue transfer and safely reduced hematoma formation and blood loss in microsurgery [187]. 3 g of topical tranexamic acid has shown equivalent results to preoperative autologous blood donation in anemic patients and reduces transfusion rates and increases Hb levels in non-anemic patients, at much lower cost [81]. TXA is one of the most efficient of all interventions in terms of cost-efficacy [188]. Topical dosage of 2 g or more is more efficient than lower doses [163]. Oral dosage ranges from a single dose of 25 mg/kg to a maximum of 2 g delivered 2 hours preoperatively or 1 g of preoperatively continued for three additional doses Q6 hours postoperatively [189]. IV dosage is typically 10–20 mg/kg preoperatively, with possible additional postoperative dosing [163]. Higher doses (20 mg/kg) have been suggested for spine surgery [164]. Plasma concentration of TXA peaks within 5–15 minutes of intravenous (IV) injection, 30 minutes of intramuscular (IM) injection, and 2 hours of oral administration [190]. Tranexamic acid is rapidly excreted by the kidneys, and topical absorption approximates 30% of the same intravenous dose [191].

With more evidence showing the safety and cost-efficacy of tranexamic acid in high-risk patients, it is increasingly incorporated into routine practice [192, 193]. Transfusion A recent meta-analysis showed IV TXA was effective in reducing allogenic blood transfusion by 50% and limiting blood loss intraoperatively and through drains in patients undergoing primary THA [194]. It is beneficial for patients undergoing total joint arthroplasty regardless of preoperative Hgb, with more pronounced effects in anemic patients [192, 195–197]. Reduction of transfusion rates by almost 70% has been reported in patients undergoing bilateral TKA with one dose (10 mg/kg) of IV TXA [161]. Moreover, TXA use in TKA was associated with 20% more ambulation in postoperative physical therapy [198], as well as greater ROM and functional Knee Society Score at 6 weeks postoperatively [199–201].

Safety

Tranexamic acid is generally well-tolerated. Uncommonly reported dose-dependent side gastrointestinal side effects have been reported, as well as headache, orthostatic reactions, blurred vision, and vertigo. Despite the theoretical concern for hypercoagulability, no data have shown a significant association of thromboembolic events and TXA [202–205].

Aprotinin

Aprotinin is considered an antifibrinolytic agent with a different mechanism of action than EACA and TA, as it is not a lysine analogue. This nonspecific serine protease inhibitor occurs naturally and was first isolated from bovine lungs [206]. Much of the current knowledge about aprotinin and its inherent antifibrinolytic properties stems from the experience with cardiac surgery, specifically cardiopulmonary bypass surgeries (CPB). It has been rationalized that the negatively charged surface of the bypass circuit activates factor XII, converting prekallikrein to kallikrein. Kallikrein, a peptidase enzyme, acts in a positive feedback loop, activating factor XII and converting plasminogen into plasmin [207]. While the exact mechanism of action remains unclear, it is thought that aprotinin functions to inhibit several serine proteases, including trypsin, plasmin, and plasma and tissue kallikrein. This indirectly inhibits the contact phase of coagulation and decreases thrombin production. By protecting membrane-bound GPIb platelet receptors, aprotinin has been theorized to prevent postoperative platelet hyporeactivity [39, 207, 208]. In a large meta-analysis of 45 trials involving 5805 patients, aprotinin clearly demonstrated reduction in blood loss and allogeneic transfusion rates [209, 210].

Aprotinin was associated with a higher risk of myocardial infarction, renal dysfunction, and anaphylactic reactions as reported by some trials involving cardiac surgery [210, 211]. Even though a Cochrane review of aprotinin use with more than 6000 patients reported no increased risk of myocardial infarction [155], concerns regarding its safety were raised by the Canadian Blood Conservation Using Antifibrinolytics in a Randomized Trial (BART). While comparing the antifibrinolytic agents in cardiovascular surgery, the study reported a 30-day mortality rate of 6% in the aprotinin arm, as compared with 4% in the tranexamic acid and aminocaproic acid groups. This amounts to a 1.53 relative risk of death associated with aprotinin. The study was subsequently terminated and aprotinin was withdrawn from the market in 2007 [212].

In addition to that, an IgG reaction to aprotinin is possible in patients upon repeated exposure, resulting in anaphylactic reactions and even shock in 6–9% of cases [213]. The incidence drops to 1% 6 months after exposure, compared to less than 0.1% with no history of prior exposure [214]. Neither EACA nor TXA have been linked to anaphylactic reactions [206]. Decreased glomerular filtration rate and electrolyte excretion has also been attributed to aprotinin. Such an effect

might be secondary to its affinity for renal tissue and rapid accumulation in proximal tubular epithelial cells or to inhibition of kallikrein and decreased prostaglandin synthesis [39].

DDAVP

Desamino-8-D-arginine vasopressin (desmopressin or DDAVP) is a synthetic vasopressin analogue with V2 vasopressin receptor agonism and little or no activity at the V1 vasopressin receptor. DDAVP has been used for treatment of diabetes insipidus and nocturnal enuresis. Its hemostatic potential is observed in patients with coagulation disorders such as von Willebrand disease, factor VIII deficiency (hemophilia A), thrombocytopenia, and platelet dysfunction secondary to uremia [215]. Stimulating the V1A vasopressin receptor is believed to trigger the release of vWF from endothelial storage sites complexed to factor VIII, thus activating factor X and the coagulation cascade.

Varying reports compare the benefit of desmopressin in cardiac surgery, but its role in orthopedic procedures has yet to be established. DDAVP reduces blood loss by 32.5% and transfusion rate by 25.6% in patients undergoing posterior spinal fusion and is also effective in scoliosis surgery [216]. However, its benefit has been challenged in hematologically normal patients undergoing spine surgery [217] as well as elective joint arthroplasty [218]. Several studies including a Cochrane review established the lack of evidence supporting desmopressin as a successful intervention to reduce allogeneic blood transfusion in orthopedic surgery patients who do not have congenital bleeding disorders [219, 220].

Safety

Rapid administration of DDAVP could cause systemic vasodilation, possibly due to endothelial cell release of prostacyclin. While the selectivity for V2 receptor spares smooth muscle, antidiuretic hormone activity might result in decreased free water clearance and hyponatremia with excessive preoperative administration of free water [221, 222]. Despite scattered reports of arterial thrombosis, this has not been confirmed in prospective studies comparing CABG patients who received DDAVP and control groups [223, 224].

Recombinant Factor 7

Local hemostasis is triggered by the interaction of tissue factor (TF) exposed at the site of vascular injury with activated factor VII (FVIIa) circulating in the blood. The resulting complex initiates the extrinsic pathway by activating factor X on the TF-bearing cell, in turn generating thrombin (FIIa) from prothrombin (FII). Consequently, thrombin activates factors VIII, V, and XI, fibrin-stabilizing factor XIII, and platelets and promotes the conversion of fibrinogen to fibrin [225]. The sustainability and stability of the fibrin plug and its resistance to fibrinolysis is a function of the rate and amount of thrombin generated. Activated factor VII serves as a general hemostatic agent, developed to control bleeding episodes and surgical blood loss in hemophilia patients with inhibitors or autoantibodies against FVIII or FIX (acquired hemophilia) [226]. It was first used in 1988 in a knee surgery patient who suffered from hemophilia with antibodies to factor VIII. Factor VII promotes hemostasis by enhancing thrombin formation on activated platelets [39]. This led to question its potential use to control acute bleeding in nonhemophiliac patients with coagulopathies of various etiologies, as well as qualitative or quantitative platelet abnormalities. Furthermore, rFVIIa has been used to control life-threatening hemorrhage when other modalities such as FFPs have failed and has proven beneficial in controlling massive surgical or traumatic bleeding in hemophilic patients [39, 227].

The off-label use of factor VII was explored in different surgical specialties, including trauma, urology, and neurosurgery. Its perceived benefit in the nonhemophiliac surgical patient is based on the premise that a preoperative bolus would provide a high thrombin burst to cover the operative as well as the postoperative period [52]. The prophylactic administration of rFVII reduced perioperative blood loss but not transfusion requirements in patients undergoing major pelvic fracture surgery [228] as well as spinal fusions [229, 230]. However, the efficacy of factor VII in orthopedic surgery remains unclear in light of the lack of randomized controlled trials [67]. The current recommended dose is about 70–90 mg/kg and could be repeated after 4–6 hours. With the cost of a single dose of 90 mg/kg reaching over $5000 [72] and high rates of thromboembolic events that increase with age [231], the use of rFVIIa is currently not supported in orthopedic procedures. It may, however, be considered in cases of persistent bleeding when the coagulopathy does not respond to FFP or when practical, timing, or religious concerns preclude the use of blood products [39].

Fibrin Sealants

A variety of topical agents have been developed to promote platelet aggregation (primary hemostasis) or the coagulation cascade (secondary hemostasis). These interventions can be stratified as either passive or active. Passive agents act through providing a physical structure for contact activation and promotion of platelet aggregation [232]. Examples include collagen-based products such as gelatin sponges, gelatin matrices, and microfibrillar collagen or plant-based compounds containing cellulose, both of which activate the intrinsic pathway of coagulation. Active agents possess intrinsic biological activity and rely on the interplay of fibrinogen with thrombin in the presence of calcium to bypass much of the coagulation cascade and generate a fibrin clot. Their hemostatic action is less susceptible to coagulopathies caused by clotting-factor deficiencies or platelet dysfunction [72].

First-generation sealants contained animal-derived products and have fallen out of favor fueled by concerns about their potential for disease transmission and alloimmunization. Second-generation sealants are derived from humans and have improved the safety profile. Autologous platelet-rich plasma (PRP) sprays and fibrin sealants derived from the patient's own blood are currently available [218].

Fibrinogen and thrombin are the active components of all fibrin sealants [218]. When sprayed onto the wound, the activation of fibrinogen by thrombin leads to the formation of a semirigid clot. In the context of orthopedic surgery, the efficacy of fibrin sealant treatment in reducing postoperative blood loss has been substantiated in a Cochrane meta-analysis as well as in multiple trials. Fibrin sealants reduced the risk of exposure to allogeneic RBC transfusion by 32% and postoperative bleeding by half [233] in patients undergoing total joint arthroplasty [234, 235]. However, more recent studies have failed to show significant benefit in blood-saving potential [236, 237]. Coupled to their much higher costs compared to readily available TXA, fibrin sealants remain useful in select cases, namely, spine surgery. When the sealant is applied on a gelatin matrix, it acts as a base that allows the clot to form.

The fact that fibrin sealants are derivative from human blood products remains a theoretic concern although there has never been a reported case of infection transmission. While bovine-derived preparations entail a risk of transmission of CJD or inducing immunogenicity, commercial preparations are theoretically free of that risk. However, there is no guarantee of a "zero" risk even with the use of autologous preparations, as operators and equipment are always potential sources of contamination [238]. So far, fibrin sealants have not shown to increase the risk of transmitted infections, wound infections, duration of hospital stay, or mortality [239].

Non-pharmacologic

Electrocautery

High-frequency coagulation, or electrocautery, is a common hemostatic instrument in the orthopedic surgical field. It does so by heating the tissue to the point of denaturation and coagulation of blood vessels. However, as temperatures exceed 300 °C, standard electrocautery leads to circumscriptive damage of the tissue and deep conical eschars [240]. Postoperative breakage or detachment of such clots would result in postoperative blood loss. Bipolar sealing devices such as the Aquamantys System (Salient Surgical Technologies, Portsmouth, NH) have been suggested as blood-saving alternatives to standard cautery. The system is designed to seal blood vessels in soft tissue and bone through a bipolar generator that delivers radiofrequency energy coupled to a saline pump. The saline functions as coolant as well as a conductive medium to promote even distribution of energy into the tissue. By keeping the surface temperature under 100 °C, this method limits tissue damage while effectively denaturing and shrinking collagen in arterial walls [241].

Meta-analyses exploring the efficacy of such systems in total joint arthroplasty and spine surgery have shown reduction in blood loss by up to 40%, as well as in transfusion requirements and operating time [242–245]. A meta-analysis of 9 clinical trials involving 871 total joint patients showed reduced total measured blood loss, intraoperative blood loss, and operative time, especially in revision cases and primary total knee arthroplasty without tourniquet use. However, no significant differences were reported in hemoglobin decrease, transfusion requirements, length of stay, and complications [246]. On the other hand, some studies report no significant benefits of bipolar sealing devices in total hip and even revision knee arthroplasty, especially with the use of tranexamic acid [247–250].

Hypotensive Anesthesia

The concept of controlled hypotension was first described in 1989 [251]. It entails dropping a patient's systolic blood pressure to 80 or 90 mmHg and mean arterial pressure (MAP) to 50–65 mmHg. In pediatrics, the procedure aims for a 30% reduction of baseline MAP. The technique was first achieved with phlebotomy and evolved with the advent of ganglionic blockade [39]. A lower arterial blood pressure during surgery is believed to decrease blood extravasation and local wound blood flow, thus limiting blood loss and improving surgical field visibility. Its application during joint arthroplasty as well as spine surgery reported up to 50% reduction in intraoperative blood loss [252–254] and 40% lower transfusion rates [255, 256]. An overview of controlled trials in the last two decades covering 636 patients revealed that deliberate hypotension to the MAP range of 48–78 mmHg reduces blood loss most effectively for total hip arthroplasty (503 mL reduction), followed by spine fusion (318 mL reduction) [257]. It has been reported to substitute for tourniquet use in TKA [258]. The blood-saving effect of hypotensive anesthesia is potentiated with the use of tranexamic acid [259]. In parallel, hypotensive epidural anesthesia was associated with decreased volumes of blood lost and number of transfusions, with no increase in serious complications in pediatric, spine, as well pelvic and sacral tumor surgery [260, 261].

The main concern with this technique is the risk of tissue hypoxia by reducing end-organ perfusion. The autoregulatory function of the arteriolar bed in end-organ tissues is responsible to maintain perfusion and blood flow over the autoregulatory limits of the tissue during the drop in MAP [262]. It has been established that the relative reduction in pressure and not cardiac output is the primary determinant of intraoperative blood loss [263]. The controversy remains as to which of the many available agents is optimal for inducing the drop in

blood pressure hypotension. The effect can be achieved with spinal or epidural anesthesia, inhalational anesthetic agents, nitrovasodilators, and others such as calcium channel blockers or adrenergic antagonists. The degree of hypotension with the best risk-benefit ratio has come into question as well. A comparison between MAP levels of 60 and 50 mmHg failed to demonstrate any reduction in transfusion requirements, postoperative hematocrit, or the duration of surgery, even though lower pressures were associated with less intraoperative blood loss. Lower mean arterial pressures may be useful in cemented arthroplasty, as less blood improves the interdigitation at the cement-bone interface [264].

Safety

Hypotensive anesthesia has been associated with a morbidity rate of 2.5% and mortality between 0.02% and 0.60%. The most common complications are delayed wakening, blurred vision, and delayed bleeding [265]. Given the risk of organ hypoperfusion, it is advised to use this method with caution in patients with known cardiac, cerebral, peripheral vascular disease or severe anemia. It should not be used in combination with other hypotension-inducing approaches such as hemodilution.

Hemodilution

Acute normovolemic hemodilution (ANH) involves the extraction and anticoagulation of a predicted blood volume from the patient and its simultaneous exchange for a cell-free crystalloid or colloid solution to maintain normovolemia. If colloid is used for the replacement fluid, 1 mL of colloid solution is infused for each mL of blood drawn; if crystalloids are used, 2–3 mL of crystalloid solution are infused for each mL of blood drawn [266, 267]. The amount of blood that can be extracted is estimated by the formula [267]:

$$V = \mathrm{EBV} \times \left(\mathrm{H\,i} - \mathrm{H\,f}\right) / \mathrm{H\,av}$$

where V is the volume of blood to be removed, EBV is the estimated blood volume (body weight in kg × 70 mL/kg for an adult), H i is the patient's initial hematocrit level prior to the onset of hemodilution, H f is the patient's desired hematocrit level at the end of hemodilution, and H av is the patient's average hematocrit level during hemodilution (average of H i + H f). Infusion of crystalloid solution without phlebotomy, or hypervolemic hemodilution, bears similar theoretical advantages and limitations [268].

The proposed advantage of such a procedure lies in diluting the blood lost during surgery and preserving higher concentrated autologous blood for reinfusion. The activity of coagulation factors and platelets is maintained in the blood as it is only stored for a short period of time [39]. Furthermore, with virtually no risk of bacterial contamination or administrative error, this procedure does not require testing or screening. It is therefore less costly and more practical than PABD [269]. The induced state of anemia is countered by increased venous return, peripheral vasodilation, increased cardiac output, and rightward shift of the hemoglobin dissociation curve. These compensatory physiological mechanisms preserve oxygen delivery and optimize oxygen extraction at the tissue level [39]. As long as normovolemia is preserved during the process, stroke volume and cardiac output increase with no change in heart rate [270].

While some studies support the finding that ANH is equivalent to PABD in both total hip [271] and total knee [272] arthroplasty as well as spinal fusion and instrumentation [273], others including two meta-analyses revealed a modest efficacy in reducing allogeneic transfusions [76, 274, 275] or none at all [276–278]. The meta-analyses failed to support the widespread adoption of this intervention [275] due to lack of properly randomized controlled trials and reduced efficacy of hemodilution when integrated in a transfusion protocol [76]. As the cost of ANH runs at approximately 50–75% less than PAD [272, 271], it may be of value to procedures with more than 1000 ml of blood loss, especially in combination with other blood-sparing measures [279] such as intraoperative blood salvage or preoperative erythropoietin administration, known as "augmented ANH" [39].

Safety

ANH has not been reported to increase rate of morbidity, infection, hospital stay, or mortality [76]. It is contraindicated in patients with coronary, renal, pulmonary, or severe hepatic disease [280, 281].

Tourniquet

The widespread use of pneumatic tourniquets in elective surgery stems from the belief that they serve to decrease intraoperative blood and create a bloodless surgical field. They are inflated above systemic pressure to optimizing exposure and cementing in total knee arthroplasty [282, 283] and in foot and ankle surgery [284]. While it may in fact facilitate the procedure and reduce operating time, the efficacy of tourniquets as a blood-saving measure is not widely accepted [285].

In a meta-analysis of 1040 TKRs in 991 patients, employing a tourniquet decreased intraoperative blood loss, but failed to affect postoperative drain output, or overall transfusion rates [286, 287]. This suggests that patients with a tourniquet have more hidden blood loss after the operation [288]. The inefficiency of this intervention is attributed to reactive hyperemia which peaks within 5 minutes after the tourniquet is released [289]. In addition to that, a certain degree of reperfusion injury and edema ensues after tourniquet. Reports of increased risk of nerve palsy, vascular injury, muscle damage, postoperative swelling, and stiffness are abundant in the literature [290–293]. Perioperative hypoxia and reduced postoperative tissue perfusion might undermine

immune function and wound healing, risking early postoperative infection [294, 295]. Applying a tourniquet during TKA could cause fibrinolysis, platelet dysfunction, venous stasis, and blood vessel wall damage [296]. The combination of these factors might increase the rate of deep vein thrombosis (DVT) and pulmonary thromboembolism (PE) in total knee arthroplasty [297–299]. Some data show no significant advantage in terms of blood loss but raise concerns over detrimental effects on muscle function and postoperative rehabilitation with tourniquet in TKA [299–301].

The general recommendation is less than 250 mmHg in the upper extremity and less than 300 mmHg in the lower extremity [302]. The impact of timing on tourniquet release is equally controversial. While deflation of the cuff before closure of the wound has been advocated to optimize hemostasis, it has been found to increase blood loss [303]. On the other hand, tourniquet release after wound closure can increase the risk of postoperative hematoma [304, 305]. A meta-analysis of 16 trials involving 1010 total knee patients demonstrated no significant differences in blood loss, drop in hemoglobin, transfusion rates or volume, or major complications including deep vein thrombosis. More total blood and longer operative time were reported when the tourniquet was released prior to wound closure [306].

Huang and colleagues conducted a prospective, randomized controlled trial that divided 150 patients undergoing primary TKA into 3 equal groups, comparing TXA, tourniquet, and combined use of both. TXA was administered intravenously for five doses, with a dose of topical TXA administered after component implantation. The study reported similar operative time and blood loss but less pain and higher satisfaction with TXA alone [307].

No clear consensus has been reached on this topic and tourniquet use is guided by personal preference.

Intraoperative/Postoperative Blood Reinfusion

Intraoperative blood salvage involves the collection of drainage or suction blood and its reinfusion [308]. This technique offers recovery of up to 60% of the blood loss using filtered or unfiltered cell savers [69, 309].

As with other interventions targeting autologous blood, the efficacy of perioperative cell salvage depends on the overall blood loss. Cell savers are indicated if the estimated blood loss exceeds 20% of total estimated blood volume, as approximately 750 ml of drainage blood are required to recover the equivalent of 1 unit of packed red blood cells [76]. They are commonly utilized in spine surgery and if allogeneic blood is not available or accepted [310]. The use of washed and unwashed cell salvage in orthopedic surgery showed very similar results in reduction of the relative risk of exposure to red cell transfusion (52% vs. 53%) [311–313]. A recent meta-analysis of involving 1534 patients comparing autologous blood drainage retranfusion to closed suction drainage in total knee replacement found lower blood transfusion rate and fewer units transfused per patient with no adverse effects [314].

However, the safety of perioperative reinfusion remains controversial [152] as it has been associated with adverse events such as febrile reactions possibly due to increased cytokine concentrations in the transfused drainage blood [315]. Complications of unwashed reinfusion included hypertension, hyperthermia, upper airway edema, coagulopathy, febrile reaction, and even death [316, 317].

Safety

No association with increased mortality or morbidity was reported in two meta-analyses of randomized trials and observational studies of either intraoperative or postoperative cell salvage [76, 318]. Transfusion is reportedly safe within the first postoperative 6 hours to minimize infection risk [319, 320]. Contraindications to the use of blood recovery include the potential for aspiration of malignant cells, the presence of infection, and contaminants [321].

Postoperative Interventions

Drains

Postoperative wound drains aim at avoiding postoperative hematoma formation. By increasing tension and decreasing perfusion, a hematoma impairs wound healing and provides a medium for bacterial growth [322]. Inefficient drainage might cause pain and stiffness resulting in delayed rehabilitation and extended hospital stay [323]. Conversely, drains may provide a conduit for the entry of bacteria and compromise resistance to infection [324, 325]. Ninety percent of the blood is collected within the first 24 hours after which the risk of retrograde infection surpasses any proposed benefit, and the drain should be discontinued [326].

A Cochrane meta-analysis failed to note any significant difference in the incidence of wound infection, hematoma, dehiscence, or reoperations between drained and undrained wounds in orthopedic patients [327]. Whereas more blood transfusions were associated with the use of drains, increased bruising and more frequent dressing reinforcement were reported in the control group. The review concluded that there was insufficient evidence to support the routine use of closed suction drainage in orthopedic surgery, even decreasing the incidence of hematoma after spinal procedures [57, 322, 323, 327–332].

Transfusion Trigger

According to current guidelines from the American Society of Anesthesiologists, RBC transfusions are recommended if the hemoglobin concentration drops below 6–10 g/dl.

While transfusions in patients with a hemoglobin over 10 g/dl are rarely indicated, there is little debate that patients with a hemoglobin below 6 g/dl should be transfused [333]. Hemoglobin levels below 6.4 g/dl have been associated with impaired cognitive function and below 4.8 g/dl with a mortality of 50% [334].

Lower transfusion triggers have also been shown to be safe and effective for patients undergoing cardiac surgery [335] and critically ill patients [336]. Thus, transfusion trigger might be lowered for younger patients (Hb ≤ 70 g/dl) and should be raised (Hb ≤ 80 g/dl) for older patients and those with comorbidities [67]. A recent meta-analysis evaluated 10 trials involving 3968 participants who underwent hip or knee surgery and compared restrictive (hemoglobin level of 8.0 g/dL or symptomatic anemia) and liberal (hemoglobin level of 10.0 g/dL) thresholds. Restrictive transfusion was associated with increased risk of cardiovascular events (8 trials; 3618 patients; relative risk [RR], 1.51; 95% $p = 0.003$) that was significant in hip fracture patients but not elective arthroplasty (RR, 1.51; $p = 0.02$), but did not reach significance in those undergoing elective arthroplasty (RR, 1.53; $p = 0.07$). No significant differences were detected in rates of all infections, 30-day mortality, thromboembolic events, wound infection, stroke, or pneumonia [337]. Teng et al. reported a 35% reduction in infection risk associated with restrictive RBC transfusion strategy (Hb < 8 g/dL) [338].

In 1988, the Health Consensus Development Conference advocated a hemoglobin level of 8 g/dL as the indication for transfusion, and recommended that decisions regarding transfusion should include an assessment of clinical needs and symptoms rather than depend on laboratory values. Setting a transfusion trigger is ultimately the function of:

1. The underlying health of the patient
2. The change in the level of hemoglobin
3. The absolute level of hemoglobin
4. The development of cardiovascular symptoms

Combination of Techniques/Algorithm

Many of the techniques and concepts discussed in this chapter can be combined. The Conference of Experts on the Rational Use of Drugs, convened by the World Health Organization, states that "the rational use of medicines requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community" [67]. Such individualized approaches to blood management lead the way to bloodless orthopedic surgery. "The determination of whether intermediate hemoglobin concentrations justify or require red blood cell transfusion should be based on any ongoing indication of organ ischemia, potential or actual ongoing bleeding (rate and magnitude), the patient's intravascular volume status, and risk factors for complications of inadequate oxygenation" [333]. The growing push for outpatient surgery and cost-efficacy in orthopedic procedures makes multimodal blood loss management programs essential to any orthopedic practice.

Summary

Elective orthopedic procedures such as total joint arthroplasty involve significant blood loss. Despite the evolution of safer transfusion practices, transmission of infection remains a potentially devastating complication to any patient. Blood management interventions help to reduce allogeneic transfusions in various surgical disciplines. Individual preoperative assessment of transfusion risk is crucial to identify the best-suited modalities to minimize blood requirements. Intravenous and topical tranexamic acid has revolutionized modern blood management. Bloodless procedures are best achieved through patient-tailored protocols that employ the best-suited modalities for each case, maximizing efficacy while reducing cost and adverse effects.

Summary Bullet Points

- Major orthopedic procedures entail significant blood loss in patient groups with high prevalence of anemia.
- The vital role of allogeneic blood is widely established in managing life-threatening blood loss. However, the safety profile of such transfusions is still far from perfect.
- Various perioperative modalities have proven capable of minimizing or even eliminating transfusion requirements in elective orthopedic procedures.
- Perioperative blood management is a multimodal planned approach to patient care. It should be regarded as the standard of care in elective orthopedic procedures.

Case Study

A 47-year-old female with sickle-cell disease scheduled for unilateral total hip replacement after presenting with debilitating pain due to osteonecrosis and secondary osteoarthritis. Baseline hemoglobin levels averaged 8.7 g/dL, with a BMI of 21 kg/m^2. The patient took ferrous fumarate, vitamin B12, and folic acid supplementation 6 weeks prior to surgery. In the operating room, spinal-epidural anesthesia was administered. 3 g of topical tranexamic acid was used. Estimated perioperative blood loss amounted to 500 cc. The postoperative hemoglobin dropped to 7.8 on day 1, 7.6 on day 2, and 7.4 on day 3, the lowest point. No symptoms of anemia manifested and she did not receive any allogeneic blood.

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Part V

Role of Allied Services

Professional Nursing Practice in the Orthopedic Care Setting

33

Stephanie Goldberg and Patricia Quinlan

Objectives

- To describe the Magnet Model for Nursing Excellence as paradigm for profession nursing practice in the context of orthopedic surgery
- To detail three key care delivery processes, namely, nursing assessment, coordination care, and patient education across setting transitions
- To describe nursing practice in three commonly encountered orthopedic surgical complication scenarios: compartment syndrome, thromboembolism, and surgical site infection

Key Points

The Magnet Model for Nursing Excellence® provides a conceptual framework to guide orthopedic nursing practice:

- Assessment is the cornerstone of patient care delivery.
- Communication is a key factor of effective care coordination.
- The nurse coaches and supports patients and families through multiple care transitions.
- Nurses with advanced degrees provide individual and specialized care to the complex orthopedic patient.
- Patient and family education build self-care knowledge and competency.

Introduction

The American Nurses Credentialing Center's Magnet Model for Nursing Excellence provides a framework for nurses to practice in the acute care setting. The Magnet paradigm supports nursing excellence with an emphasis on patient safety and satisfaction [1]. The aim of this chapter is to describe how, through application of the Magnet Model, nurses provide care to patients in the setting of orthopedic surgery. The chapter begins with a brief description of the ANCC Magnet Program. Three key care delivery processes within the exemplary practice construct of the Magnet Model, nursing assessment, care coordination, and patient teaching, are detailed. These elements of practice are further described in the context of three orthopedic surgical complications, specifically compartment syndrome, thromboembolism, and surgical site infection.

Magnet Recognition Program

Through its prestigious Magnet Recognition Program®, the American Nurses Credentialing Center (ANCC), a subsidiary of the American Nurses Association, recognizes and endorses health-care organizations that demonstrate nursing excellence. The Magnet Model is an organizational paradigm to facilitate best practice. The model has four essential constructs: (a) transformational leadership, (b) structural empowerment, (c) exemplary professional practice, and (d) new knowledge, innovation, and improvement. These components are interdependent within a global health-care backdrop to generate positive empirical outcomes [1].

According to the Magnet Model, care delivery is an essential element of exemplary practice demonstrated through continuous, accountable clinical assessment, care coordination, and patient teaching. Nurses are stewards of these processes. They support patient healing and recovery toward primary goals of independent mobility and the absence or reduction

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of pain. Nurses regularly assess patients before, during, and after surgery. They make clinical judgments about readiness for surgery, pain control, mobility, and wound healing. Nurses monitor and report signs and symptoms of postoperative complications. They coordinate the interdisciplinary treatment plan and serve as patient advocates and teachers to support transitions along the care trajectory. The next section of this chapter describes patient assessment in more detail.

Patient Assessment

Assessment is the cornerstone of nursing practice. Nurses need proficiency in this competency in order to identify physical and psychosocial issues that may influence care before and after surgery. Before surgery, nurses conduct a comprehensive assessment that begins with an extensive review of the patient's health history. Nurses physically examine the patient, documenting important data to inform medical and surgical treatment plans. Identified concerns are communicated to the operating room team to anticipate care delivery adjustments that meet individual needs or preferences. For example, nurses activate special care protocols for preexisting clinical conditions such as sleep apnea to assure adequate respiratory support during surgical recovery. Head-to-toe examination may also identify a skin lesion unrelated to the planned surgery that requires further evaluation and preoperative treatment so as not to introduce the risk of postoperative infection.

Nurses in the operating room work with the surgical team to assess patient response to surgery and to conduct multiple safety checks that minimize the risk of medical errors. Nurses activate safety protocols such as time-out procedures and assess the operative site before surgical incision to avert wrong-side surgery. They implement safety checklists that include prosthesis verification as well as instrument and sponge count procedures. Nurses carefully position and assess patients at regular intervals to minimize risk for peripheral nerve and skin injury.

Patient assessment continues once the patient leaves the operating room. Nurses evaluate the patient's response to the operative procedure and monitor anesthesia recovery. They review the perioperative sequence of events and initiate physician orders and/or appropriate protocols. Comprehensive nursing assessment includes evaluation of central and peripheral neurological presentation as well as the patient's cardiorespiratory status. Nurses read and interpret cardiac monitoring to identify arrhythmias. They monitor pulse and blood pressure and report significant deviations that might indicate inadequate hemodynamic functioning. Nurses assess the condition of surgical dressings, casts, and traction to ensure proper functionality and body alignment. Skin integrity is examined over bony pressure points and patients are repositioned to prevent injury. Nurses assess fluid balance through careful tracking of intravenous and oral intake as well as urinary output. The presence and function of wound drains are frequently checked to evaluate fluid status and blood loss. Devices used to prevent venous thrombosis are inspected to be sure that they are correctly placed on the patient and are in continuous working order. Nurses determine readiness for oral intake and advance diet based on nutritional need and gastrointestinal status.

Nurses use assessment skills to evaluate patient response to standardized, surgery-specific protocols. They work with patients to determine response to standardized pain control treatment using the Pain Numeric Rating Scale [2]. These data combined with information gleaned from direct observation of signs such as facial expressions are used to determine pain status. Progression with mobility is another important clinical assessment. Nurses assess the patient's response to the rehabilitation treatment plan and work with rehabilitation therapists to progress patients through therapeutic milestones toward independent mobility.

Nurses evaluate patient's cognitive function and rational decision-making at each step along the orthopedic surgical care trajectory. Baseline assessment data drive the nurse's approach to patient education, an integral element of care provision aimed toward building self-care competencies and participation in the treatment plan. Nurses assess learning barriers such as low health literacy, to construct teaching plans that will help patients understand their treatment and assure they are able to carry out self-care instructions [3]. Accessibility and commitment of family caregivers or significant others must also be determined to augment patient support as well as to reinforce accurate and consistent self-care information.

Care Coordination

Data collected by nurses while caring for patients are shared with appropriate members of the multidisciplinary care team to estimate clinical progress along standard, procedure-specific, pathways. Patient progress is discussed at interdisciplinary rounds that include all members of the care delivery team. Nurses provide information at these rounds specific to patient activity and response to treatment during the previous 24 hours. The interdisciplinary team comprised of nurses, prescribers, rehabilitation therapists, case managers, and registered dieticians analyze patient data and adjust the plan of care accordingly. Smaller groups of nurses and prescribers convene patient care huddles during evenings and nights hours to discuss the condition of complex patients to anticipate problems and the need for care plan alterations.

Failures of patients to progress as expected generate plan modifications, delivered by nurses who closely monitor the responses to these changes. Nurses communicate complications or concerns that require immediate attention directly to prescribers as they occur.

Communication is a central factor in effective coordination of care. Nurses channel information to all members of the health-care team and during multiple patient care transitions. Several best practices used by nurses to facilitate communication include face-to-face "patient hand-offs." Nurses from the inpatient units personally go to the postanesthesia care unit (PACU) to meet patients to be transferred to their care. The PACU nurse provides a face-to-face report with the inpatient nurse who then transports the patient to the inpatient unit. These in-person exchanges allow for the validation of patient data and application of treatment plan elements such as intravenous fluid, assistive device settings, as well as socialization to the change in care setting. Nurses orient patients to their new surroundings to familiarize them about unit routines, introduce personnel, and instruct how to access help when needed.

Nurses work with patients to communicate and adapt to ongoing changes in their treatment. A best practice to improve this communication is the use of individualized "White Boards." Erasable boards mounted near patients' beds provide standard information specific to patient care, for example, the name of the nurse caring for the patient and the last time that patient received pain medication.

Nurses conduct multiple patient interventions based upon the interdisciplinary treatment plan and continual reassessment. Rest and activity are balanced. Nurses check on their patients hourly to assess pain. Adjuvant measures such as repositioning and ice therapy augment carefully administered pain medication. Consistent hourly checks also serve as a means for influencing patient safety. Such rounds can preempt patient misjudgment about going to the bathroom unassisted and thereby reduce risk for falling. Moreover, patients regularly visited by their nurse report greater satisfaction with care provided [4].

Patient Education

Nurses play a key role during transitions in care. Nurses are responsible to help patients and their caregivers build the knowledge necessary to participate in the treatment plan and competently apply self-care instruction. Self-care competency is important during all care transitions but particularly after discharge. Education is initiated before, during, and after admission. Before surgery, preoperative patient education classes are a resource for patients and their caregivers to work with nurses toward mutual health-care goals.

Preoperative Education

The preoperative classroom setting affords an opportunity to develop a quality nurse-patient relationship that will continue to grow throughout the hospital experience. Nurse-driven classroom education sessions are multimodal in content, combining written materials, multimedia presentations, and hands-on demonstration. Nurses emphasize patient and family expectations with particular focus on participation in care management. Major educational topics addressed during the preoperative class include pain management, mobility, discharge planning, and prevention of surgical complications (i.e., wound infection and venous thrombosis). Expectations are outlined in a sequential format beginning with the admission and ending with the discharge process. Patients and families are encouraged to ask questions throughout the session. Nurses provide contact information when patients need further clarification about class content or ask additional questions once they return home.

Nurses also use technology to provide easy access and as an alternate means for patient education. Electronic access to information has improved dramatically with rapidly advancing technology. Working with media specialists, nurses supply Web-based instruction via physician practice portals or live webinar classes through the Internet. This alternative to traditional classroom learning is especially useful for patients who are to undergo less invasive surgery. An important advantage of this approach is the elimination of the need to travel long distances to attend preoperative classes. Disadvantages include the inability to assess visually, indications that patients may be having difficulty understanding the material. The format is generally reserved for patients who can navigate electronic media and is used to processing information that is Web-based.

Postoperative Education

Once admitted to the hospital, the patient receives one-on-one education on a daily basis. As previously stated, nurses continuously educate patients to the treatment they receive and progressively introduce information that patients need once they leave the hospital. One-on-one teaching is essential for patients to learn how to use equipment such as mechanical devices that provide cold therapy or compression boots to prevent deep vein thrombosis. Devices that assist with ambulation such as crutches require meticulous systematic instruction and return demonstration. Similarly, medications such as inhalers or injections need hands-on demonstration with return presentation to assure self-care competency. Each time patients receive medication, these medications are reviewed with the patient as to purpose and function. As

the patient progresses toward discharge, the nurse reinforces medication information and expands on previous instruction to include side effects, the importance of taking the medication according to the prescribed dosage and frequency, as well as when to call the provider with questions.

The "teach-back" method is a way to confirm that the patient [5] understands information explained to the patient. Nurses ask open-ended questions and require the patient to draw from his/her memory to repeat the instruction and apply information learned. A sample question is, "What are you going to do when you get home?" Another example could be, "I want to be sure that I explained your medication correctly. Can you tell me how you are going to take this medicine?" If patients cannot remember the information or accurately repeat instructions, the material is clarified, and patients are asked to teach content back again. Nurses repeat the process until the patient can correctly describe what they need to do or understand in their own words. Understanding is validated when patients and/or caregivers explain information back to the clinician. The teach-back technique can also help familiarize clinicians with individual, patient learning preferences.

Follow-Up After Discharge

Telephone contact by a nurse after discharge is a best practice for exchanging information with patients about their progress, providing additional health education, and verifying adherence to treatment [6]. Firsthand experience at our organization has demonstrated that patients appreciate post discharge phone calls from nurses. Surveyed patients who receive postoperative telephone calls report greater overall satisfaction than patients who do not receive calls [4]. Telephone calls to patients complete the care delivery cycle and should be made by nurses familiar with the patient's hospital experience and plan of care. The telephone exchange offers yet another opportunity for a teach-back exchange to elicit continued understanding of treatment. It is also a chance to ask the patients about healing, mobility, signs of infection, medication management, and physician follow-up.

Complex Care and Nurse Specialization

Multiple health-care practitioners provide patient care across numerous settings during an orthopedic surgical experience. Although transitions in care can be challenging for all patients, they are particularly onerous for older patients and patients with chronic conditions [7, 8]. Patients transferring between settings may experience fragmented care and as a result incur negative outcomes such as falls, medication errors, and delirium and nosocomial infections [9].

Orthopedic surgery patients transition through numerous phases of care. Once the patient decides to have surgery, preparation is a multilayered process that requires evaluation by medical practitioners, laboratory and diagnostic testing, education classes, and rehabilitation review services. On the day of admission, multiple professionals interview the patient and ask questions, largely focused on the operation soon to take place. Patients relay medical history information such as medication use and allergies. All of this information is entered into the electronic record at different time intervals, by different clinicians for future reference by all involved practitioners. This is an intense but systematic experience for most patients and generally proceeds without a problem. However, for the aged patient with comorbid conditions, getting ready for surgery, each step of the preparation process can uncover interdependent clinical issues that could complicate surgery and influence recovery.

For patients that present with complex care needs, transitions are particularly tedious and fraught with potential gaps in service. Surgical complexity can also put patients at risk, as demands on their physical reserve are more extensive and treatment plans are transitionally intricate. In the orthopedic surgical setting, nurses with advanced education serve to guide transitions for complex patients. Nurse engage these patients and their families prior to admission, based on clinical criteria. These include preexisting medical conditions or surgical complexity that put patients' risk for perioperative complications. Nurse check for overlooked steps in care processes such as the timely communication of laboratory values that influence recovery. The nurse guides patients and families through important activities such as intensive medication management, glucose control, and self-care education. These activities are particularly important during the preoperative phase of care and throughout the patient care trajectory. Education techniques such as teach back and motivational interviewing ensure patient understand their role in the treatment plan as well as establish the behavioral commitment to continue self-care post discharge.

In the perioperative orthopedic setting, nurse practitioners work with medical staff and surgeons to optimize patient's chronic health status going into surgery and throughout recovery. For example, advanced practice nurses that specialize in diabetes serve as consultants for the interdisciplinary team, to control blood glucose and related complications such as delayed wound healing. Moreover, these specialized nurses provide focused attention to assist patients with anticoagulation management, wound care assessment, and follow-up post discharge.

Though research is available describing the positive impact nurse practitioners working collaboratively with physicians to care for patients, orthopedic specific studies are few [10]. In 2016, researchers evaluated the effect of care delivered by nurse practitioners in an orthopedic practice [11].

Patients coached by these nurses began calcium and vitamin D supplements more often than patients that did not receive intervention. Haan and colleagues [12] evaluated the inclusion of nurse practitioners to the trauma team at an academic acute care center. Nurse practitioners coordinated interdisciplinary rounds for the service. Data compared 3 years before and 3 years after the practice change noted a significant decrease in readmissions. Researchers attributed the success to nurse practitioner communication across multiple surgical services including orthopedics, anesthesia, and houses staff. In a second trauma service study, investigators evaluated the effect of a nurse practitioner on length of stay and cost in a Level I orthopedic trauma center [13]. Comparison of data collected 1 year before and 1 year after hiring a nurse practitioner noted a significantly shorter length of stay ($p = 0.001$) and less patients discharged on antibiotics and wound VAC therapy ($p = 0.017$). More research is needed to augment current knowledge regarding the benefits of adding advanced practice nurses in the orthopedic care delivery context.

Identification and Management of Postoperative Orthopedic Complications

The next section of this chapter will focus on care delivery specific to the identification and management of orthopedic complications. Standard nursing management of three orthopedic complications is described: (1) compartment syndrome; (2) thromboembolism, that is, deep vein thrombosis and pulmonary embolism; and (3) surgical wound infection. Though these are only three of a longer list of potential postoperative complications, they provide an opportunity to describe nursing care delivery in the orthopedic surgical setting.

Compartment Syndrome

Compartment syndrome is a complication caused by increased pressure within a confined myofascial space resulting in circulatory compromise, ischemia, and, if not treated, tissue necrosis [14]. Subsequent tissue damage may result in permanent neurologic injury and necrosis of muscle. Increased internal pressure within a compartment may be caused by swelling, bleeding, or increased capillary permeability, while external compartment pressure is caused by peripheral compression such as tight casts or dressings.

Nurses detect compartment syndrome by frequent and reliable assessment. Pain beyond what is expected, and which is not responsive to narcotics and intensified by passive stretching and elevation, may be indicative of compartment syndrome. Inspection of the skin may note shininess related to increased internal pressure. Skin color may progress from bright pink during the initial inflammatory phase to a pale and dusky color with increased arterial compression. The skin becomes cold to touch and capillary refill is usually less than 3 seconds. Paresthesia related to nerve compression implies decreased neurovascular function, and pain is likely to decrease with progressive injury. Serious injury is imminent when pulses are not palpable or if the patient shows signs of limb paralysis [15].

Communication of compartment pressures and patient symptoms to the surgeon and medical team is paramount. Ongoing pain management is also crucial, and medication may be needed to treat anxiety, which may compound the vasoconstriction. Surgical treatment consists of relieving pressure, achieved through fasciotomy for internal compression or, in the case of excessive external pressure, a bivalve cast. Nurses carry out prescribed wound care, monitor and report red and white blood counts, as well as administer antibiotics to avert or mitigate infection. Nurses also provide teaching to explain to patients and caregivers why vigilant monitoring is necessary. Emotional support may also offset some of the anxiety and discomfort.

Thromboembolism

Thromboembolism is a widely acknowledged complication of orthopedic surgery and includes both deep vein thrombosis and pulmonary embolism. Three factors that contribute to thromboembolism are venous stasis, blood coagulability, and vessel wall damage. Arthroplasty and spinal surgery patients are among those at high risk for thromboembolism. Other factors commonly seen in the orthopedic patient population include (a) obesity, (b) lack of mobility, (c) smoking, (d) chronic heart disease, and (e) hormone replacement [16].

Nursing care for these patients consists of an assessment of signs and symptoms as well as administering and monitoring prophylaxis regimes. For venous thromboembolism, signs and symptoms are dependent on the size of the clot. Symptoms include erythema, pain, and tenderness in the clot location as well as thigh and/or calf swelling [16]. Signs and symptoms of pulmonary embolus include dyspnea or tachypnea, lower arterial pressure, cough with hemoptysis, anxiety and restlessness, chest pain, and tachycardia [17].

Nurses administer prescribed chemical and mechanical prophylaxis and continually evaluate and report the effects thereof. Management of anticoagulants requires careful dosing, contingent on findings of physical assessment and laboratory analysis. Nurses report deviations in clinical results to prescribers for ongoing anticoagulation adjustment. They teach patients and their caregivers about these drugs, which they will need to manage once discharged. Nurses review the purpose, dose, frequency, side effects of the medications, and in what circumstances their provider should be contacted.

Therapeutic devices such as intermittent pneumatic compression stockings and venous foot pumps are useful to prevent venous stasis [18]. Nurses assure application as well as

evaluate proper fit and function of these assistive devices. Patients are encouraged to dorsiflex and plantar flex ankles and toes. Nurses support early mobilization to promote lower extremity venous return. Mobility is encouraged throughout hospitalization through discharge transition. Nurses contact patients after discharge to assess self-management and effects of chemical and mechanical anticoagulation.

Nosocomial Surgical Site Infection

Postoperative wound infection is a particularly serious complication as it poses the threat of joint prostheses compromise notwithstanding the consequences associated with prolonged hospitalizations, treatments, and propensity for readmission. The Center for Disease Control and Prevention, guideline for prevention of surgical site infection, describes conditions that place patients at risk for postoperative infection [18]. Risk factors include: (a) age, (b) obesity, (c) uncontrolled diabetes, (d) smoking, (e) obesity, (f) colonization of microorganisms, (g) preexisting infection, (h) compromised immune system, (i) preoperative anemia, and (j) increased hospital stay.

Nurses work with multidisciplinary colleagues before the surgical event to identify comorbid vulnerabilities and adjust the treatment plan to prevent and/or minimize the possibility of surgical site infection. The role of the nurse in the prevention of surgical site infections consists of preoperative assessment followed by communication of risk, timely administration of antibiotic prophylaxis, careful surgical skin preparation, and competent aseptic technique in the operating room as well as meticulous and frequent evaluation of the wound postoperatively [18].

As mentioned earlier in the chapter, nurses assess patients as they ready them for surgery. They communicate unexpected findings that impose infection risk such as a shingles or an upper respiratory infection to the surgical team, which may result in postponement of the operation. A history of methicillin-resistant *Staphylococcus aureus* (MRSA) likewise prompts a nurse to activate special protocols that minimize risk to the individual and other patients who enter the operating room. While readying the patient for surgery, hair removal is done by clipping, and the nurse uses products such as chlorhexidine antiseptic to prepare the skin for incision. In the operating room, nurses reduce infection risk through meticulous surgical scrub and personal hygiene of their hands. Hand hygiene continues to be of paramount importance during the postoperative period where nurses evaluate surgical dressings and wounds for healing. Signs and symptoms of infection such as pain, redness, swelling drainage, odor, and fever are promptly communicated to the prescriber for further analysis and treatment.

During the postoperative period, the nurse teaches the patient and caregiver about how to protect the wound and inspect it for healing, signs and symptoms of infection, how to do a dressing change if necessary, and how to contact their provider with concerns. Evaluation of patient understanding determines if home care referral may be necessary to supervise self-management particularly if wound care is complex. Nurses contact patients after discharge to determine competency and evaluate adherence to the treatment plan.

Summary

Professional nursing practice adapted to orthopedic surgery is critical to the modern care of the orthopedic patient. Nurses deliver continuous and accountable patient care that is unique to a specialized body of knowledge. Patient assessment, care coordination, and teaching are important facets of care delivered by nurses. Through these processes, nurses support patient healing and recovery toward primary goals of independent mobility as well as the absence or reduction of pain. Nurses monitor and report signs and symptoms of postoperative complications. They coordinate the interdisciplinary treatment plan and serve as patient advocates and teachers to support transitions along the episode of care. Nurses provide specialized attention to the needs of complex orthopedic patients. Overall, nurses across all levels provide meaning to conceptual models of nursing excellence by delivering the very best care to the patients they serve.

Summary Bullet Points

- The Magnet Model for Nursing Excellence provides a paradigm for a work environment that supports optimum nursing practice demonstrated through continuous accountable assessment, care coordination, and patient teaching.
- Patient assessment is a key aspect of nursing practice. In the context of orthopedic care, nurses continuously evaluate the patient to align the plan of care to individual needs and establish effectiveness of the treatment plan.
- Nurse involvement is vital to care coordination to ensure a holistic approach to care transitions. Accurate and complete communication of patient information across transitions is essential for safe, patient-centered care.
- Nurses help patients and their caregivers develop self-care competency through education and coaching. Education is provided during all phases of the

surgical episode of care to achieve independence with health-care goals.

- Advanced practice nurses and nurse navigators serve to guide patients with complex surgery or comorbidities across the perioperative care trajectory.
- Complications of orthopedic surgery can be devastating. Signs and symptoms of circulation impairment and infection are continuously monitored and findings reported to the prescriber to facilitate prompt and appropriate treatment. Nurses support patients both clinically and emotionally through discomfort and treatment.
- Transitional care models conceptualize gaps in care and strategies to guide patients through their numerous transfers [10]. These models focus on processes vulnerable to lapses in care. The paradigms emphasize early recognition and attention to changes in response to treatment, the importance of patient and family involvement in care management, and supported follow-up to symptoms and instructions. Most models include post discharge attention to coach patients to maintain their plan of care and to discuss any issues that may hinder participation or clinical progress.

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The Approach to Physical Therapy Following Orthopedic Reconstructive Surgery

34

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Objectives

- Illustrate the benefits of comprehensive preoperative education programs including the use of 1:1 preoperative screening and microsites.
- Discuss the benefits of a multimodal approach to achieve effective pain management and day of surgery mobilization to optimize early rehabilitation progression for patients undergoing total joint and spine surgeries.
- Review the importance of collecting and utilizing discrete data to inform optimal changes in the clinical pathway.
- Explain key therapeutic principles in the acute care phase of rehabilitation.

Key Points

- Rehabilitation is an integral component before and after orthopedic surgery to facilitate a safe discharge. At HSS, our Rehabilitation Therapists consistently re-evaluate specific postoperative guidelines they created concomitantly with changes in anesthesia and surgical techniques to allow for early mobilization.
- Day of Surgery mobilization with Rehabilitation Therapists results in earlier achievement of functional independence following joint replacement and spine surgeries.
- The interdisciplinary care team at HSS integrates rehabilitation guidelines into hourly clinical pathways for joint replacement and spine procedures to ensure critical steps are implemented in order for patients to achieve specific outcomes.
- A well-designed comprehensive preoperative education program that includes classes, pamphlets, microsites, and one-to-one preoperative visits is essential to enhance the patient experience, decrease anxiety, and align patients' expectations in the postoperative phase.

Introduction

HSS, an elective orthopedic specialty hospital, performed over 30,000 orthopedic procedures in 2016 keeping 32 operating rooms at consistent occupancy [1]. This unique hospital setting and sheer volume of joint replacement and spine procedures position their health care team to be laser-focused on ensuring both the institution and the patient, are optimally prepared for every surgery with an individualized plan of care. Being an elective surgery hospital allows the health care team to preplan for all patients' episodes of care and communicate through the use of an electronic medical record. From a rehabilitation perspective, the team can identify individuals who may encounter barriers to clinical pathway adherence for a variety of reasons and better prepare for more complex discharge needs for those individuals. HSS created a comprehensive interdisciplinary preoperative education program for our patients undergoing joint replacements to prepare and educate them for their hospitalization.

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This includes both a class-based session and an individual session which allows the information to be spaced and redundant. During the one-on-one preoperative consult, the physical therapist reviews therapeutic exercises, functional mobility, practice with an assistive device, and activity expectations and/or modifications. This interaction between therapist and patient assists with alleviating patient anxiety which may hinder rehabilitation progress through fostering trust between the clinician and patient. Through this early preoperative patient education, the team can help the patient establish realistic expectations.

At HSS, our interdisciplinary team recognizes the impact of optimally managing postoperative pain to maximize functional independence. An effective pain management program is of utmost importance to reduce pain while maximizing mobility throughout the episode of care. HSS's clinical pathways are based on evidence, as well as our experience in reducing postoperative pain which contributes to a reduction in length of stay (LOS) and progression of patients to a higher level of function.

Initiating mobilization on the day of surgery has fostered earlier achievement of patient's functional mobility. It is imperative that the Acute Pain Service (APS) and the rehabilitation team discuss important considerations that are required for safe postoperative mobility. To prepare for early mobilization on the day of surgery, pain is not the only factor to be considered. Minimizing the effects of orthostatic hypotension, nausea, and pain with the full return of motor and sensory function can be a challenging balance. Our institution optimized the anesthetic management which contributes to day of surgery mobilization and improved functional outcomes. Syncope due to fluid shifts is also a factor to be considered. For example, patients are now allowed to drink up to 3 hours prior to surgery and are encouraged to consume increased fluids within 12 hours of surgery as long as they do not have any medical reason to restrict fluids. With an increase in fluid intake, syncope is less likely to occur in the immediate post-op phase.

Lastly, tracking data is essential to benchmark functional outcomes, identify variances to pathway adherence, and assess opportunities for improvement in the clinical pathway. The HSS functional milestone database is the largest rehabilitation acute care arthroplasty database in the United States since its inception in 1992 [2]. This database has allowed HSS to track joint replacement functional progress for more than 25 years and to evaluate the impact of anesthesia and surgical techniques on functional mobility. With the implementation of the Electronic Medical Record (EMR) in 2016, our department continues to collect and evaluate HSS functional outcomes so the clinical pathways can be adjusted to meet the patient's accelerated progress.

Preoperative Education

Patient education is a key component to a successful orthopedic surgery [3]. As length of stay continues to decrease, preoperative education is critical. The preoperative program at HSS continues to evolve. Traditionally, patients undergoing total knee arthroplasty (TKA) and total hip arthroplasty (THA) attend an interdisciplinary education class to prepare for surgery. The preoperative joint replacement program now includes an individual physical therapy assessment with education and the addition of microsites or web-based activity and exercise instruction modules. At HSS, patients who received a one-on-one education program with a physical therapist and access to a web-based microsite prior to joint replacement achieved independence with functional milestones earlier than those patients who only attended a group class preoperative program [4]. One-on-one physical therapy assessments allow each program to be customized as needed to each individual patient. The HSS microsites were developed to provide a way for patients to view exercises, precautions, and mobility instructions that were presented to the patient either in the class setting or at a one-to-one physical therapy session (https://www.hss.edu/rehab-guides.asp). The HSS microsites are lateralized so each video is specific to the side of surgery which mimimizes confusion by patients when viewing. In addition, preoperative planning allows our team to identify high-risk patients or those with special needs. These requests may include an interpreter, bed extender, c-pap machine, specific rehabilitation equipment, or an alternative discharge plan to home. Early identification of potential issues allows for adequate preplanning prior to the patient's hospitalization. A social worker contacts all joint replacement patients at least 2 weeks prior to surgery to review their individual physical and social situation and discuss their discharge plan.

It is estimated that utilizing preoperatively physical therapy prior to joint replacement surgery is associated with a 29% decrease in the need for postoperative services [5]. Outpatient physical therapy prior to surgery allows the therapist to evaluate and fully implement a program to enhance a patient's mobility after surgery. Objective measures such as range of motion (ROM), manual muscle testing, gait deviations, and functional deficits can be evaluated, in addition to identifying the patient's potential postoperatively. Subjective questionnaires, objective scales, and functional tests such as the Timed Up and Go (TUG), Functional Reach, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), modified Knee injury and Osteoarthritis Outcome Score (KOOS), the hip disability and osteoarthritis outcome score (HOOS), or single leg balance can be completed which will allow a comparison for preoperative and postoperative function.

For patients undergoing spine surgery, the surgeon's office provides written materials including exercises, mobility, and precautions prior to surgery. These materials are made available on our website as well. Patients undergoing same-day spine surgeries are provided with a pre-op PT session to educate in spinal precautions, don/doff any prescribed brace and gait or stair negotiation with or without an assistive device.

Functional Milestones

The HSS's rehabilitation team has developed a valid and reliable tool to track the functional progression of total joint arthroplasty (TJA) patients in the acute care phase (Fig. 34.1). The Functional Milestone Form was the catalyst to the development of the hospital clinical pathways. Tracking the data enabled us to predict when a patient would be able to reach independence. Prior to the EMR, information was tracked quarterly to identify trends on patient's functional mobility, anesthesia type, preoperative level of function, attendance of preoperative class, and component type along with the medical comorbidities. Information from this database is an integral part of our research projects and has allowed our team to modify clinical pathways based on the accelerated progress of patient's recovery and function. At HSS, we have more than 25 surgeons performing joint replacements; therefore, it is essential we are tracking outcome measures with similar variables. Patient databases are essential in monitoring patient progress, as well as providing a baseline of statistics which can be evaluated and addressed based on current trends and advances in the field of orthopedics, anesthesia, and technology.

Postoperative Rehabilitation Following Orthopedic Surgery

A common goal following joint replacement and spine surgeries is independent function while minimizing patient impairments in the acute phase. Our functional goals for patients that have a discharge disposition to home, regardless of the surgery, are independent transfers in and out of bed, independent ambulation with the appropriate assistive device, independence with therapeutic exercises/range of motion (if indicated), and independence with any prescribed postoperative precautions. For patients who are weight-bearing as tolerated (WBAT), our goal is to progress the patient to the assistive device which normalizes their gait pattern and minimizes gait deviations. Each case is individualized, rather than protocol based, which provides the patient the ability to progress to the highest level of function for home management. Increased activity immediately after surgery and keeping the operated limb in a dependent position for prolonged periods of time may increase swelling and pain. The patient's progression may have to be modified based on their response to activity and subjective complaints. In most cases, patients at HSS use a rolling walker to initiate ambulation after surgery. This device assists with normalizing a patient's gait pattern. Our clinical pathways have been revised in 2017 from a one-size-fits-all into three levels based on patient complexity. These pathways have allowed for a more individualized approach and plan of care which is attainable for the majority of the patients. Our clinical pathways for each of the following surgeries provide a guideline for surgery and post-op care for total knee arthroplasty, total hip arthroplasty, and spine procedures. The following information is broken down to highlight critical components of each of these surgeries.

Postoperative Rehabilitation Following Total Knee Arthroplasty

Physical therapy following total knee arthroplasty (TKA) can be a challenging balance maintaining effective pain management and mobility. Physical therapy is initiated as early as two hours after a TKA or as soon as it is medically appropriate. At our institution, patients s/p TKA may utilize a variety of postoperative pain management techniques based on surgeon preference and the patients' past experience with anesthesia. These may include epidural patient-controlled analgesia (PCA) pump, with or without a concomitant saphenous nerve block (SNB), periarticular injection, interspace between the popliteal artery and the capsule of the posterior knee (IPAK), or an oral analgesic course. The posterior knee capsule is rich in sensory innervation and that the IPAC block is very effective in the relief of pain s/p surgery which allows for more comfortable mobility and earlier achievement of functional milestones. Quadriceps inhibition is typical after TKA arthroplasty. Quadriceps strength is closely and consistently evaluated by the team, including the physical therapist, to determine the effects of the anesthesia to ensure safe mobilization. Active knee extension may be used in sitting to quickly assess quadriceps strength or possible impairments from the block, in addition to a straight leg raise. Walking is initiated with a rolling walker and progressed as tolerated to a cane or crutch for discharge home. A patient is instructed to progressively weight bear and the appropriate device is determined when gait impairments are minimized. A heel toe gait pattern is emphasized to restore a normal gait as early as possible.

Knee functional ROM is critical to achieve within 6–8 weeks after surgery. Preoperative ROM is the primary indicator of postoperative ROM [6]. Ideal extension after surgery is 0° and minimum target flexion ROM by 6 weeks

HSS TOTAL KNEE ARTHROPLASTY – FUNCTIONAL MILESTONES FORM

REHABLITATION DEPARTMENT
PT Initials: _____
Diagnosis:_____ **Age**:_____
Left / Right / Bilateral Initial / Revision / Reimplant
Unicondylar Staged Rapid Recovery
WBAT PWB TTWB NWB
Height_____(in) **Weight**_____(lbs)

Day of Surgery: Su M T W Th F Sa

Anesthesia: EPI GEN
PCA: EPI IV
Femoral Nerve Block: YES NO
Sciatic Nerve Block: YES NO
Other:_____

Pre-op Class: YES NO
Pre-op Amb: w/c bound <1 1-5 6-10 >10 Blocks
Pre-op Assistive Device: Cane / Crutches / Walker / None
Need to negotiate stairs: YES NO
Pre-op Lives Alone: YES NO

BID																
Discharge																
Stairs Unassisted																
Stairs Assisted																
Cane Unassisted																
Cane Assisted																
Walker Unassisted																
Walker Assisted																
Stand Only																
Transfer Unassisted																
Transfer Assisted																
Dangle Unsupported																
Dangle Supported																
CPM																
Active Ext R																
Active Flex R																
Active Ext L																
Active Flex L																
Pain Level																
Date of Surgery _____																
P.O.D	RR	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15

Discharge To: Home Rehab SNF
If D/C Home: Home PT Outpatient PT No PT
If D/c home, with: Friends/Family/Other Alone
Complications/PT Held: _____

Fig. 34.1 A version of the Total Knee Replacement Functional Milestone form used to collect data from 1992 to 2016. Milestones were tracked on POD achieved. Currently PT milestones are tracked in hours. (Copyrighted © Hospital for Special Surgery Rehabilitation Department. Used with permission)

is 120° to allow patients to participate in functional activities. Activities such as tying shoes require 106° of knee flexion, while squatting and lifting an object off the floor requires 117° of knee flexion [7]. Our main goal in the immediate postoperative phase is to emphasize full knee extension. When supine, patients are encouraged to lie in passive extension. The principles of low load prolonged stretch are implemented and the patient is supine with a towel roll under the ankle. The principles of low load prolong stretch have been studied and found to be the most effective technique to successfully achieve

elongation of tissue and restoration of ROM [8, 9]. It is critical to maintain neutral hip rotation during passive extension as patients have a tendency to externally rotate at the hip and flex at the knee for comfort. In addition, it is important to maintain flexibility at the gastrocnemius and hamstrings if deficits are present. "Aggressive Flexion ROM" can adversely affect gains in ROM. Aggressive ROM often leads to muscle guarding, increased edema, and increased pain which may hinder the patient's progress. Consistent ROM sessions are encouraged in a position that is optimal for the patient. Moderate discomfort may be experienced during ROM sessions and should not be severe. Prone quadricep stretching is not recommended in the early phases as a tight rectus femoris may limit knee joint ROM.

In 2016, the HSS clinical pathway for TKA patient population was revised from a 4-day LOS into three levels of hourly clinical pathways to allow patients to be managed based on level of complexity, ranging from 30 to 90 hours. On average, patients undergo approximately three to six physical therapy sessions during their hospitalization with an additional walking session during every nursing shift. Ideally, patients participate in at least one physical therapy session on the day of surgery and two physical therapy sessions with the physical therapist on subsequent days until their functional goals are achieved. Physical therapy during the hospitalization includes basic home exercise program:

- Including ankle pumps
- Quadriceps sets
- Active range of motion knee flexion
- Active assistive knee flexion
- Gluteal sets
- Stair stretch (if tolerable)
- Passive extension
- Straight leg raise (if tolerable)

The continuous passive motion machine (CPM) continues to be a controversial device after TKA [10]. The CPM machine is not part of our clinical pathway and must be ordered specifically by the surgeon if desired. In the HSS experience, the CPM had no clinical impact on patient's ROM at 6 weeks or 12 weeks [10]. It was noted that patients who did not use the CPM machine were discharged earlier from the hospital and experienced a cost savings of $235.50 per patient [11]. Simplistically, the CPM machine keeps the knee joint in motion, alleviates patient anxiety, and may play a role in pain control.

Cryotherapy is extremely important particularly after TKA. Cryotherapy is effective in reducing swelling and as an adjunct to pain management. There are many options for cryotherapy devices including commercial devices or simplistic options such as a gel pack or crushed ice. Frequent icing for at least 15–30 minutes with minimal compression is easily reproducible for patients at home and as effective as compared to commercial devices [12]. Preoperative discussions can educate patients on cryotherapy options.

Within 2–3 days after surgery, most patients have achieved independence with bed mobility, transfers, and ambulation with an appropriate device on level surfaces and stairs, which will allow the patient to be safely discharged home with home care services, if needed.

When functionally appropriate, outpatient physical therapy services may be initiated to facilitate the patient to return to a higher level of function. During the outpatient phase, the goal is to continue to emphasize end ROM and flexibility and to minimize gait impairments. In addition, lower extremity strength and balance deficits are addressed to allow a patient to negotiate stairs reciprocally and perform functional activities, such as getting out of a chair without compensatory movements. Subjective questionnaires are a means to assess patient's reported progress, in addition to, objective measures and functional scales to measure functional progress.

Postoperative Rehabilitation Following Total Hip Arthroplasty

Total hip arthroplasty (THA) is known to have a very high success rate to reduce pain and increase function. As reported in HSS Arthroplasty Registry, 99.4% of patients reported pain relief and 98.8% of patients reported improvement in functional mobility after THA [13]. THA rehabilitation and precautions may vary based on the surgical approach. Approximately 70% of patients undergoing THA at HSS follow posterior lateral precautions. As advances in minimally invasive surgery continue with the emphasis on accelerated recovery and reduced LOS, anterior approach has gained traction with many surgeons. Moreover, some surgeons are relaxing their prescribed precautions for the posterior-lateral approach due to decreased risk with modern large head implants and improved surgical techniques [14]. The risk of instability decreased to less than 1% due to improvements in implant technology and soft tissue repairs [15]. Gromov and colleagues reported almost half of all dislocations in the first 90 days post-op were due to falls or unexpected twists [16]. Research demonstrates that placing patients on modified restrictions compared to those on traditional precautions did not result in an increase in dislocations for patients at 3 months status post THA [17]. This growing body of evidence on the safety of modified precautions is encouraging surgeons to move away from posterior-lateral precautions and prescribe modified hip precautions or "pose avoidance." The only pose to avoid with modified precautions or "pose avoidance" is the one in which patients are instructed not to combine the movements of hip flexion, internal rotation, and adduction which is depicted in Fig. 34.2a, b.

Fig. 34.2 (**a**, **b**). Pose Avoidance position precautions. (**a**). DO NOT rise from chair or commode with knees touching. (**b**). DO NOT reach back behind your leg to the outside of your ankle to shave leg or fix a sock/shoe

Since 2007, the HSS clinical pathway included day of surgery mobilization. Similarly to TKA, a variety of postoperative pain management pathway options can be utilized based on surgeon preference. The THA clinical pathway has been modified in 2017 and categorized into three levels ranging from 30 hours to 71 hours based on patient complexity. This allows for a more individualized approach to patients to support the care process required for each patient. Changes in the multimodal approach for anterior THA have allowed this select population to be discharged on the day of surgery. This has been successful for the patients who meet specified criteria for ambulatory THA, have a willingness to go home the same day and have effective pain control.

In evaluating our patient statistics, you must consider the large patient volume at HSS. At HSS, we have more than 25 orthopedic surgeons performing THAs on a diverse range of patients with varying preoperative functional levels. HSS performs more than 4500 primary unilateral THA surgeries per year. Our data reflect averages for all patients undergoing primary THA. Specific surgeon's statistics may differ, as well as specific controlled variables.

The most difficult functional activity for THA patients is transferring in and out of bed. This maneuver is reiterated in preoperative class and the preoperative screening so the patient has the opportunity to practice prior to surgery. In our experience, we have found patients have an easier time transferring in and out of bed on the surgical side, although modifications may be made as long as the patient can adhere to the precautions during the transfer. In addition, a detailed THA video and web-based microsite are provided to patients which reviews all functional activities, activities of daily living (ADL) training with equipment, and therapeutic exercises post surgery. An occupational therapy consult is ordered for patients that are discharged home to allow for ADL, equipment training, and home preparation.

The majority of patients undergoing primary THA, regardless of being cemented or uncemented, are allowed

progressive weight-bearing as tolerated (WBAT). All patients initiate ambulation with a rolling walker and progress to a standard cane as tolerated. Physical therapy exercises during the hospitalization include basic and an advanced home exercise program including:

- Ankle pumps
- Standing hip extension (except for anterior approach)
- Quadriceps sets
- Standing hip abduction
- Gluteal sets
- Standing knee flexion with 0° hip flexion
- Sitting hip flexion (<90° if traditional posterior-lateral precautions)
- Sitting knee extension
- Heel slide supine (<45° if traditional posterior-lateral precautions)

Straight leg raise (SLR) is an advanced exercise and usually instructed 4–6 weeks after surgery due to the increased joint reaction force across the hip joint [18]. Moreover, surgeons who perform the anterior approach prescribe avoiding repetitive hip flexion movements due to the risk of patients developing tendonitis.

Our data have shown that patients who initiate mobilization within 10 hours of surgery achieve functional independence earlier compared to those who initiate mobilization the following morning after surgery. Our rehabilitation guidelines include two physical therapy sessions with an additional ambulatory session with the nursing staff. Patients are seen by physical therapists until independence with functional goals for discharge home is achieved.

In 2017, 97% of eligible patients following unilateral THA were seen on POD# 0. Therefore, we no longer track differences between POD # 0 and POD #1 in time to PT clearance as mobilizing on POD # 0 has become standard of care at HSS. PT milestones are now expressed in hours versus days since our length of stay continues to decrease. In order to successfully achieve day of surgery mobilization by PT for all patients undergoing unilateral THA and TKA, PT staffing hours were extended to 9 pm in the acute care setting to capture all available patients. Data in Table 34.1 demonstrate improvement in achievement of functional milestones since implementing day of surgery mobilization compared to our current pathway which categorizes patients in three different hourly pathways.

Patients are instructed in precautions based on the surgical approach and the specific surgeon's guideline (Table 34.2). Precautions are generally adhered to for 6–8 weeks for traditional posterolateral and anterior hip precautions. After the precautions are lifted at 6 weeks, patients are instructed in an exercise program to include lower extremity strengthening, balance and specific exercises which will allow the individual to gain hip flexion and external rotation to perform functional activities. For modified precautions, patients are generally instructed to avoid this combined pose as much as possible as it is the combination of extreme ROM that may increase the risk of dislocation.

Table 34.1 Improvement in achievement of functional milestones 2012–2018 since implementing day of surgery mobilization

Day mobility initiated	2007 72-hour pathway	2012 51-hour pathway	2017 combined pathway average (Levels 1,2,3)
	Day achieved	Day achieved	Day achieved
	Independence with Cane	Independence with Cane	Independence with
Day of surgery	3.25	2.41	35.5 hours or 1.48 days unassisted with cane 41 hours or 1.71 days unassisted with RW
POD # 1	3.78	2.55	n/a

Accessed from Hospital for Special Surgery, Rehabilitation Department, Functional Milestone Database, and EMR

Table 34.2 THA precautions based on the surgical approach

Posterior lateral approach – traditional precautions	Posterior approach Modified precautions/pose avoidance	Anterior approach – traditional precautions	Anterior approach – no precautions
No hip flexion >90° No internal rotation (IR) Past neutral No adduction	No combination of hip flexion >90, no IR and no adduction	No hip extension with external rotation	None

Patients should begin outpatient physical therapy approximately 1-2 weeks after surgery to allow time for healing. The goals for outpatient physical therapy are to minimize gait impairments, restore balance and ROM, and allow the patient to return to functional activities without adaptive equipment. The most challenging tasks for most patients after surgery are putting on socks and shoes and cutting toenails. Typical hip ROM demands for tying shoes is 120° hip flexion, whereas functional stair training only requires 36° of hip flexion to descend a step and 67° of hip flexion for ascending a step [19]. Progressive stretching and ROM is emphasized to allow the patient to be independent in these functional activities. Hip abductor strengthening is critical to improve normal pelvic alignment during gait and stair negotiation. Gluteus medius strength can be weak after surgery for up to 2 years. Hip abductor strengthening can be done in a position of comfort for the patient and is more functional in a weight-bearing position without increasing strain or activation of the gluteus medius [20]. In addition, bilateral balance activities progressing to single leg balance exercises are initiated. It is important to note that if patients have had prior spinal fixation, they may require greater hip flexion to assume a functional position such as sitting compared to

someone without spinal fixation. This is important to consider when deciding on treatment interventions for your patients as they may be at a higher risk of dislocation since they may need greater than 90 degrees of hip flexion due to an inflexible spine [21]. A series of objective tests, including functional reach and timed up and go, have been determined valid and reliable with normative values that will enable the clinician to compare postoperative joint replacements to older/normal individuals [22, 23].

Rehabilitation Following Spine Surgery

Spine surgery can often vary from a minimally invasive microdiscectomy to a multilevel fusion. Our goal is to promote frequent and gradual increase in mobility with this patient population. Since each patient's pain and functional level may fluctuate, each patient's baseline of postoperative progression will vary. Patients may be mobilized within 2 hours of surgery based on the complexity of the surgery and if the anesthesiologist medically clears the patient.

Bracing is often surgeon specific and recommended for those individuals who may not adhere to proper body mechanics following surgery. Bracing is typically recommended during movement activities. Normally, sitting time is limited to 15–30 minutes to minimize soreness and compression on the spine [24] (Fig. 34.3). An occupational therapy consult may be recommended for ADL training, if the patient presents with functional impairments and ADL deficits.

Patients are instructed in safe and proper body mechanics after any type of spine surgery. Log rolling is typically instructed for cervical, thoracic, and spine procedures to minimize any undue rotational stress on the spine. In addition, patients are instructed in modifications to bending, lifting, and twisting. Patients may be instructed, depending on the surgery, on how to bend at the hips and knees for dressing and to minimize excessive trunk flexion. Patients are instructed to minimize lifting and unnecessary weight, in addition to minimizing torque at any level of the spine. Our goal is to progress the patients to a functional level of independence for ADLs but they may require assistance or the use of adaptive equipment if limited with functional tasks.

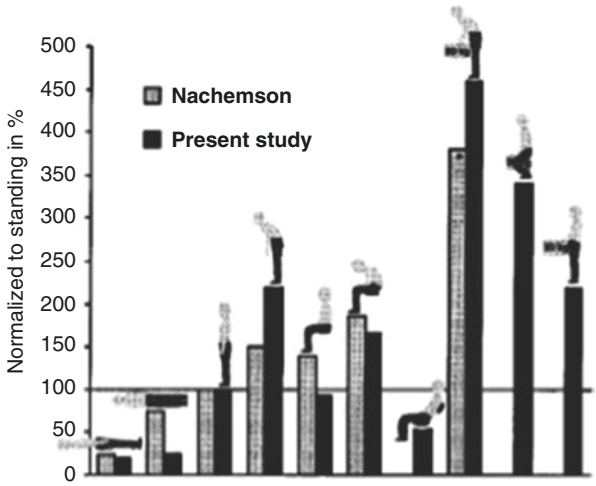

Fig. 34.3 A comparison between data of Nachemson∗ and those of the Wilke study (see source line) (both for 70-kg individuals) regarding intradiscal pressure in common postures and activities, normalized to standing. Lifting weight = 20 kg in the current study; ∗lifting weight = 10 kg in Nachemson study (∗See Simmonds et al. [25]). (Used with permission of Wolters Kluwer from Wilke et al. [24])

Depending on the spine surgery, assistive devices for ambulation typically coincide with the complexity of the surgery, deviations, support required, comfort level, and prior level of function. One-level microdiscectomy or laminectomy surgeries may not require any device, whereas multilevel fusions may require rolling walkers for in-hospital and home use.

Postoperative outpatient physical therapy is surgeon and surgery specific. Overall, all patients may benefit from a core stabilization program while protecting the spine. Our goals for outpatient therapy are to emphasize activity modification and minimize repetitive loading of the spine while improving core strength in a static and then dynamic positions.

Summary

A cohesive interdisciplinary team and care plan needs to be established in order to design and implement an effective clinical pathway. Critical factors that delay LOS need to be identified and modified in order to design a pathway that optimally progresses patients to the highest level of function safely and expeditiously.

Preoperative planning and preoperative education are essential steps that will allow the organization to individualize the clinical care plan for each patient. Formalized education programs will allow the education material to consistent and comprehensive and will prepare the patient for the upcoming surgery, answer questions, and reduce anxiety.

It is imperative that the interdisciplinary team, particularly the surgeons, anesthesiologist, nursing, and rehabilitation specialists, discuss rehabilitation goals in the acute phase while concomitantly reducing pain and side effects of opioids. Once this is achieved, early mobilization is imperative to enhance the patient's recovery. As seen since the inception of the revised HSS THA clinical pathway in 2007, in 2012, and again in 2017, patients are achieving independence with a cane earlier as we continue to increase earlier mobilization while minimizing pain.

Lastly, tracking data is critical to evaluate the effectiveness of the pathway and identify variables and opportunities for improvement. The HSS functional milestone tool is a

valid and reliable tool which has been utilized in modification of clinical pathways as surgical and anesthesia trends have evolved.

Summary Bullet Points

- Preoperative education is essential to establish realistic patient expectations.
- Early mobilization after surgery allows the patient to achieve functional milestones earlier.
- Communication with the interdisciplinary team is crucial to ensure the patient is following critical steps in the rehabilitation guideline.
- A functional tracking tool will enable you to evaluate outcomes and make appropriate modifications to your plan of care.
- Rehabilitation therapists need to execute specific therapeutic principles to address functional deficits of the patient.

Case Study: Right Total Hip Arthroplasty

The patient is a 70-year-old female who presented with intermittent longstanding right hip pain that has significantly worsened over the past 6 months. Her hip pain is constant at this point and worsens with sit to stand transfers and disrupts her sleep at night. Pain radiates into her groin, down her thigh, and into her knee. She also reports balance issues. Referred for RTHR.

- PMH: Anxiety, arthritis, depression, high cholesterol, osteoporosis
- PSH: Cholecystectomy, foot arthrodesis, LTHR 2 years ago
- Social hx: Lives in a private house alone, supportive son nearby and available to assist. Discharge plan is home with home care services and son available for support as needed.
- RAPT score = 9 at pre-admission phone call. Plan for home care services at discharge.
- Chart Review Findings: Patient underwent a RTHR starting at 2:09p ending at 3:15p. Implant: Ceramic femoral head with polyethylene acetabular cup. Anesthesia: Spinal with bupivacaine. Placed on Clinical Pathway for Total Hip Arthroplasty Level #1 or a rapid care pathway for d/c goal <30 hours.

Patient was transferred to PACU at 3:30p and PT orders placed for day of surgery mobilization with modified/pose avoidance restrictions. Pt. presented for evaluation at 7:50 pm and nursing stated patient was ready for PT. VSS at HR 83 bpm, BP 139/78, SaO2 = 99%. BMI = 28.71%. After chart review, PT assessment was performed. Note: during first session patient dangled × 5 minutes at bedside. She reports feeling slightly lightheaded which passed with increased sitting time. Once on her feet this is the timeline and pertinent findings (Daily PT Documentation):

Day/Time	POD #0 at 7:50 pm (Initial Evaluation Note)	POD#1 at 8 am (Treatment note)	POD #1 at 1 pm (Discharge Note)
Lines and tubes	IV hep locked, O2, telemetry	IV hep locked	IV hep locked
Strength	Able to initiate heel slide supine, distal strength 5/5 EHL, TA, GS UE Strength: grossly 5/5	Able to initiate heel slide supine	Hip flex 3-/5 sitting
Pain: /10 Numeric Scale	5	3	2
Bed mobility	Min assist for RLE support	CG for guidance of RLE	Independent; able to move RLE on and off bed independently
Transfers	CG assist	Supervision	Independent
Gait	5′ × 2 with min assist	100′ with RW with CG assist	150′ with RW
Complaints during session	Lightheaded	No complaints	No complaints
Stairs	NA	Up and down 4 stairs with handrail and cane with CG and verbal instructions	Up and down 4 stairs × 3 with handrail and straight cane; supervision 1st trial with verbal instruction, then demonstrated independence
Education	Modified/pose avoidance precaution; glut sets, quad sets, reviewed car transfers	Modified/pose avoidance precaution, glut sets, quad sets, reviewed car transfers	Independent in verbalizing pose to avoid and glut set, quad set, and ankle pumps
Ther ex	Ankle pumps, quad and glut sets 10×	Bed therex, heel slides, supine hip ER to comfort, seated knee extension, seated hip flexion	Performed standing hip flexion, standing hip abduction, standing hip extension, standing knee flexion. All 3 × 10 repetitions for HEP
Abbreviations	CG: contact guard Min: minimal RW: rollator walker HEP: Home exercise program		

Patient met all functional goals and cleared PT; able to be d/c from hospital at 23 hours from admission, and 7 hours shorter than the pathway due to good pain control and functional progress. This occurred despite initial symptoms of being lightheaded during the first PT session.

This case study illustrates that day of surgery mobilization helps patients achieve functional independence with an assistive device in fewer than 24 hours. This patient did not undergo general anesthesia and did not have a PCA or a foley placed which allows for more ease of mobilization on the day of surgery as the patient was not nauseous and the pain was well-controlled. This patient was discharged home with home care services as planned. Postoperative course was as expected.

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35

Introduction of Clinical Pathways in Orthopedic Surgical Care: The Experience of the Hospital for Special Surgery

Susan Flics, Shivi Duggal, Katarzyna Kujawa, and Charles N. Cornell

Objectives

- To document the foundation for and the success of the adoption of clinical pathways for the care of patients undergoing routine orthopedic procedures.
- To describe the HSS experience which illustrates the benefit given to patients and hospitals through the adoption of clinical pathways for the care of total joint replacement patients.
- Discuss the potential value of the adoption of clinical pathways for complex surgery of the spine and to address their increasingly important role in the challenging economic environment associated with health care reform.

Key Points

- Clinical pathways are structured multidisciplinary care plans which address specific clinical scenarios which help to standardize and coordinate care.
- Clinical pathways are evidence-based, incorporating proven best practice but ideally can be adopted to any given hospital environment and culture.
- Clinical pathways aim to optimize the quality and efficiency of care. These care plans must address pre-hospital preparation, in-hospital care, and post-hospital discharge.
- The patient experience can be optimized, leading to improved overall patient satisfaction. The care plan must be focused on the patient experience primarily. Managing patient expectations through pre-hospitalization education and counseling are key elements of success.
- Adoption of clinical pathways demands physician championship which is best achieved by recording and providing feedback on outcomes following adoption of the new care plans.
- Following implementation, all clinical pathways must be routinely monitored for success and for modification to ensure that best clinical practices are represented and that continuous process improvement is assured.

Introduction

The adoption of clinical pathways in patient care has grown from the necessity of providing consistently high quality of care for an increasing demand for clinical services. Clinical pathways are structured multidisciplinary care plans that detail the essential steps in the care of patients with specific clinical problems. Clinical pathways provide hospitals with a consistent template for patient care by creating a predetermined standardized approach to care that should be adhered to by each member of the health care team. Clinical pathways are especially suited to the high volume and elective nature of much of orthopedic surgery. In our specialty quality and efficiency must be optimized. Toward that goal, clinical pathways are used as standard protocols [1]. Each process,

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in a clinical pathway, is followed in order to ensure that the desired end results are achieved. The pathway also ensures that each patient is receiving optimum levels of care pre, intra-, and post-operatively. Clinical pathways are evidence-based using the common international experience but must be adapted to the culture of any given hospital. Clinical pathways are effective because they standardize care, help develop measures for prevention of patient discomfort and harm, and provide ongoing performance measures that promote effective and useful change in practice.

In the United States, the demand for joint arthroplasty has steadily been increasing, which in turn has been placing pressure on hospitals to provide efficient care delivery models for these procedures. The demand for total knee replacements is predicted to increase by 673% in 2030 [2, 3]. In order to provide this high volume, hospitals have to develop and adopt new strategies which focus on quality, safety, and efficiency in order to maintain positive financial margins for the delivery of these services. Due to the high volume and expenditure associated with total joint replacement in the Medicare population, the centers for Medicate and Medicaid Services (CMS) introduced in 2013 a bundled payment program for these procedures. The premise behind this change was that bundled payment programs (BPCI and CJR) would lead to better coordination of care with higher quality resulting in cost savings to CMS [4, 5]. These payment programs define the episode of care to include the hospitalization as well as a period of 90 days following discharge. Costs of post-acute services, such as home care and subacute or acute rehabilitation facilities stays, are considered part of the episode. Therefore all related post-hospital care prescribed and any related complications requiring transfer to a higher level of care or readmission become the responsibility of the hospital and treating physicians. To remain profitable, hospital processes must ensure a minimum of complications and readmissions, an efficient length of stay, responsible use of post-discharge services, and high patient satisfaction. Clinical pathways introduce a process, which standardizes care among all caregivers. Practice is standardized into a team approach that allows for better coordination of care, communication and process improvement based on the post-implementation experience. Clinical pathways have been shown to be essential in this reimbursement model because they reduce length of stay without compromising patient-reported outcome ratings, satisfaction, or complication rates [3–12].

Since the 1990s Hospital for Special Surgery has adopted the use of clinical pathways for patients undergoing total hip and knee replacement surgery [13]. These pathways include standardized patient orders that ensure the most important elements of care are routinely addressed. Over the years, modifications of the Hospital for Special Surgery's clinical pathways have been initiated in response to clinical advances, hospital processes, and third-party payer demands. For example, the original clinical pathways were designed to improve the patient experience focusing primarily on improvements in pain management and postoperative physical rehabilitation [13, 14]. In spite of early success in achieving these goals, it became clear by 2007 that the pathways needed modification to help reduce the length of stay to accommodate a large increase in the volume of these procedures in the setting of a fixed bed capacity. Since 2011, they have been modified to help address the introduction of bundled payments with an emphasis on the preoperative period and increasingly shortened length of stay with discharges primarily to the home environment. One of the advantages of standardized pathways is that they lend themselves to evaluation and provide simple groundwork for modification based on their own results. Evaluation of our initial clinical pathway results directed the changes needed to address diminishing length of stay, avoidance of discharge to skilled nursing and rehabilitation facilities with a focus on avoidance of complications while improving patient satisfaction with the experience [3].

The Key Elements of Clinical Pathways Addressing Total Joint Arthroplasty

The success of total joint replacement is ultimately judged by the patient experience. Total joint arthroplasty intends to provide improved quality of life. With that specific goal, the surgical care plan must be safe, predictable, and efficient. The experience might be compared to air travel. A passenger books a flight expecting a predictable outcome with little to no expectation for failure. Air travel is obviously complex requiring a detailed approach to the delivery of a safe and efficient service. The happy passenger is usually unaware of the planning and complex processes involved. The processes used by the airline industry provide a model for us in arthroplasty. Each surgical procedure should be planned with optimal preparation of the patient in the pre-hospital phase, executed with best practice during the hospital stay and a detailed plan for the postoperative recovery ensuring the desired restoration of pain-free mobility and quality of life expected. As such, clinical pathways must address preoperative preparation, in-hospital care, and post-hospital rehabilitation period.

Elements of Pre-Hospital Preparation for Total Joint Replacement

Preoperative preparation of patients for total joint surgery is perhaps the most critical element of a successful outcome. It was our experience prior to adoption of our current clinical

pathway that many phases of the preoperative process failed to address the complex issues that arose during the hospital stay. In particular, inadequate preparation of the patients with medical comorbidities predictably leads to postoperative complications. We are now convinced that meticulous preparation of patients, especially those with complex medical histories, is required before surgery can proceed. We have developed guidelines for patients with cardiovascular disease and diabetes mellitus which are detailed in the prior chapters of this text. We also established a complex case panel to which our surgeons can refer their complex cases to help develop plans for preparation and execution of surgery in especially high-risk scenarios. We have established a Perioperative Medical Service that provides for preoperative evaluation and preparation of all scheduled arthroplasty patients with the goal that each is medically optimized before the day of surgery (see Chap. 33). We attribute our recent improvements in the incidence of infection, perioperative cardiovascular and thromboembolic complications, in part, to this process.

Additionally, addressing each patient's psychosocial readiness for surgery has been extremely helpful in improving the quality and efficiency of care. Preoperative education of arthroplasty patients has become an accepted standard practice [13, 15–17]. A preoperative education program can effectively address what information patients need prior to surgery and helps to manage and organize the postoperative care. Patients should be encouraged to attend interdisciplinary preoperative total knee/hip arthroplasty educational classes prior to their surgery. The patient educational class describes in detail the expectations and outcomes that any patient should expect from a total knee/hip arthroplasty. The plan of care should be presented so that patients understand what is expected of them and the hospital staff during their perioperative period. In particular, information regarding all aspects of the process should be clearly explained and the daily in-hospital routine should be emphasized. In particular the approach to pain management and physical therapy should be clear, and the details for items such as DVT prophylaxis, hip precautions, pain management, and physical therapy should be covered. Of particular importance is to address patient expectations for their level of pain and physical mobility and dependence by the time of discharge. It was our experience that most patients had little understanding of the nature of recovery following arthroplasty and often anticipate extreme dependency and prolonged disability. By incorporating our experience into the educational curriculum [12] we have allayed patient and family fears regarding a prolonged post-op disability or dependency. This has allowed for acceptance by our patients of early plans for discharge to home rather than in-patient rehab or skilled nursing facilities. In addition to the education class, the hospital's Department of Case Management and the patients' surgeons develop a combined preliminary discharge plan for each patient which is discussed with the patients via phone during the week prior to the surgical admissions date. In this way, the discharge plan is firmly established weeks before the admission making the post-admission case management process more automatic and efficient.

Perioperative Pain Management

It is now clearly established that optimal pain management is a critical element in the quality and efficiency of care of orthopedic patients. Poorly controlled postoperative pain delays postoperative mobility, contributes to adverse outcomes, and results in poor patient satisfaction with their experience [18]. On the other hand, overmedication is also associated with side effects and morbidities that also negatively influence patient outcome [19, 20]. To address this new multimodal, pre-emptive pain management strategies have been developed which can be easily incorporated into total joint replacement clinical pathways. Multimodal and pre-emptive strategies to prevent postoperative pain have benefitted from recent advances in the understanding of neuronal plasticity and how undertreated acute pain can lead to chronic pain. Also, clarifying the role that local inflammation plays in injured tissue increasing the sensitization of nociceptors has led to drug therapies incorporating NSAIDs and COX-2 agents in pre-emptively controlling post-op pain. Blocking the pain signal by a variety of methods including narcotics, anti-inflammatories, and peripheral nerve blockade (multimodal) has improved postoperative pain management and has improved the overall quality and efficiency of care [21].

The pre-emptive pain management procedure involves preoperative administration of medications, which blunt or even prevent post-op pain and other side effects such as nausea. Pre-emptive pain management strategies usually call for administration of a COX-2 non-steroidal anti-inflammatory (NSAID) drug to reduce the development of post-op pain along with steroid medications which are extremely effective and safe in preventing post-op nausea [3, 18, 20]. Embedded in the latest HSS THR and TKR clinical pathways are a preoperative order set that calls for the administration of a COX-2 agent and oral steroid (dexamethasone 6 mg) to each patient 1 hour prior to surgery. In addition, the pathway established the anesthesia practice of administration of ondansetron (Zofran) intravenously to each patient during surgery to reduce the occurrence of postoperative nausea.

New strategies for pain management are rapidly emerging which are designed to rely less on the epidural or intravenous route focusing on locally applied pain management techniques. It is hoped that these will decrease the side effects and morbidity associated with neuraxial analgesia

while permitting more aggressive mobilization. Epidural anesthesia is being replaced by shorter acting spinal anesthesia combined with long acting blocks of sensory nerves to the operative site. In addition local injections of long-acting anesthetics and intraarticular infusion of pain medication compliment this approach [20, 22].

Post-mobilization and Physical Therapy: Fast-Track Rehabilitation

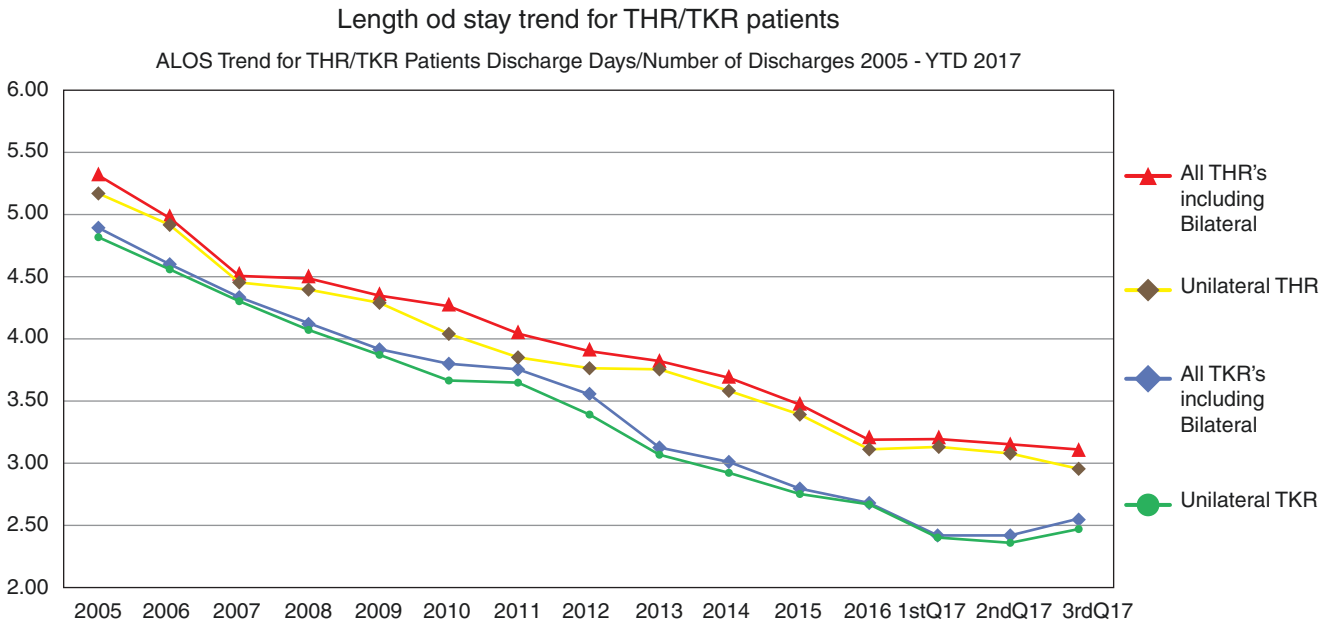
The traditional approach to rehabilitation following joint replacement has in most cases relied on transfer of patients from the acute hospital setting to in-patient rehabilitation facilities where intensive physical therapy is applied to ready patients for the home setting. This approach reduced the expectations for an early in-hospital recovery and thereby directly increased length of stay and the cost of care per beneficiary. It is not surprising that most health insurance programs currently seek to limit access to post-discharge rehab facilities. Since the coordination of transfer is also time consuming lengthening the acute hospital length of stay, it is also not surprising that hospitals delivering these procedures have sought means for early home discharge as well. Traditional approaches to physical therapy and mobilization have had to be modified to achieve more efficient hospital stays and earlier recovery. Although immobilization and bed rest have been known to contribute to postoperative complications, it has not been until recently that efforts to rapidly mobilize following total joint replacement have been implemented. Postoperative orthostasis, syncope, and falls have been relatively common in our own experience, and we believe the 24–48 hours of bed confinement that results from epidural analgesia contributes to this. New "Rapid Recovery" approaches to mobility and physical therapy have been implemented with great success [5, 11, 23–25]. Combined with our new multimodal pain management strategies early and rapid mobilization has become the norm. Patients are encouraged to stand and ambulate on the day of surgery and our Rapid Recovery protocols can include up to 3 visits per day from the physical therapists and mobility technicians. With the understanding that recovery of range of motion following total knee replacement is a gradual process, the emphasis of the post-op in-hospital program is gait training and mobility rather than focus on a range of motion prior to discharge. We have partnered with our local visiting nurse service to provide an accelerated in-home early PT program which front-loads a patient's therapy from a 4-week to a 2-week program to continue the pace of early recovery avoiding the need for a rehab hospitalization. We now aim for a 2-day length of stay for TKR and 1–2 days for THR. In addition, patients who are under 70 years of age, in excellent health with no risk factors and supportive home environments are offered very short stay options for these procedures (Box 35.1). Indeed, in 2017 HSS launched an ambulatory surgery THR program with an expected 8-hour hospital recovery time. In 2018, CMS removed TKR from the Medicare Inpatient Only List. As a result, HSS clinicians are examining all aspects of pathway guidelines to develop even a more streamlined approach to offer to a select group of TKR patients.

Box 35.1 The patient selection criteria for being considered for the Ambulatory THR pathway are shown. Careful patient selection for ambulatory pathways is essential for success

- Age 18–70 years (excluding government payers)
- Body mass index (BMI) less than 35
- If diabetic, A1C ≤ 7
- Low-risk patients
  - Exclude patients with history of MI, heart surgery, valvular heart disease (e.g., aortic stenosis), arrhythmias, OSA, opioid tolerance, and complications from anesthesia
- Not currently taking Coumadin
- Patient with support at home
- Patient/family agrees with same-day discharge plan
- Case must be scheduled as an ambulatory surgery and first or second case of the day

Successful Implementation of Clinical Pathways

Adoption of clinical pathways requires a multidisciplinary team approach. All disciplines involved in the care of the patient must be involved. In general, we have worked to establish the principles of care for each of the disciplines involved and then implemented these through the creation of standardized order sets which are now a part of our electronic medical record and computerized order entry. Physician and surgeon buy-in is critical to the success of this process and every effort has been made to involve them in the process. The most effective tool in physician recruitment is the generation of evidence that the pathways work leading to better quality of care, fewer complications, shorter length of stay, and improved patient satisfaction. At HSS we now have achieved an overall length of stay below 4 days with the highest patient satisfaction ratings as recorded by Press Ganey in our history (Fig. 35.1). We continually review the established pathways searching for improvements as our post-implementation experience develops. Our success is mirrored by the success in many other hospital settings [26]. Based on the success we



	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	1stQ17	2ndQ17	3rdQ17
All THR's including Bilateral	4.90	4.61	4.34	4.13	3.91	3.81	3.76	3.56	3.12	3.03	2.79	2.70	2.43	2.43	2.56
Unilateral THR	4.82	4.57	4.31	4.08	3.89	3.67	3.66	3.40	3.08	2.93	2.75	2.69	2.42	2.36	2.47
All TKR's including Bilateral	5.32	4.99	4.51	4.50	4.35	4.27	4.05	3.91	3.83	3.70	3.47	3.19	3.21	3.16	3.12
Unilateral TKR	5.19	4.93	4.45	4.40	4.31	4.05	3.86	3.77	3.76	3.59	3.41	3.12	3.14	3.08	2.97

Fig. 35.1 The average length of stay in days for total hip replacement and total knee replacement is displayed as a function of Year. Since 2005 the average length of stay has fallen significantly

have achieved with total hip and knee arthroplasty we have developed and adopted clinical pathways for both simple and increasingly complex spinal surgery.

One concern often voiced regarding efforts to shorten length of stay reflects a common belief that decreasing the hospital length of stay would increase the incidence of complications in patients with a need for re-admission. This belief has been proven to be inaccurate. Studies have shown that decreasing the length of stay to less than 5 days does not have any correlation with increased risks of complications or hip dislocation [8, 9]. Contrary to the dogma, decreasing the length of stay also benefits patients by allowing them to return to their natural environment, which is generally the patient's home. A patient's natural environment is usually safer and more comfortable for them, as patients have created this environment to reside in, as a niche. Patient in-home care, which provides physical therapy and visiting nurse services, allows the patient to recover at a pace comfortable to them and still be satisfied with the environment in which they are recovering. Many studies have also demonstrated that an increase in the length of hospital stay after total joint arthroplasty does not improve patient outcome. Instead it simply increases the cost of care and decreases patient satisfaction [4, 5, 8].

Patient satisfaction is a vital component to patient care. Satisfaction is a state of mind that allows patients, or individuals, to be pleased with the work they or others have performed. Patients who are satisfied with the surgical or medical procedures performed on them have a higher recovery rate with less probability of complications. Satisfied patients generally believe that their surgeons/physicians have provided the best possible care in an environment that values their safety and comfort. Studies have indicated that hospitals that create clinical pathways that decrease the patient's length of stay in hospitals have a higher number of satisfied patients [8, 27]. Patients who are satisfied have a higher rate of compliance with prescribed medications as well as other instructions given to them. This is particularly important in total joint arthroplasty to avoid complications such as falls and dislocation of the prosthetic joint and to ensure that the proper approach to physical therapy and rehabilitation is followed.

Adoption of clinical pathways can be met with skepticism and resistance from any member of the multidisciplinary team involved in patient care. Because clinical pathways standardize care, they reduce reliance on individual decision-making or traditional approaches to care. Every effort must be made in adopting new clinical pathways to educate and inform the multidisciplinary team of the evidentiary basis on which the

principles of the new pathway are based. Physician, nursing, and administrative champions must work together to develop and institute new pathways. The process should be communicated in a completely transparent manner. The thought processes involved should be clearly documented and every member of the patient care team must be trained and oriented to the new process. Following implementation documentation of important clinical indicators should be monitored and regular reports of outcome must be communicated back to the hospital staff. The pace of implementation must be geared to the tolerance of the staff at each individual hospital. Often implementation should be conservative with realistic expectations. As success is garnered more progressive modifications to the pathway based on real outcomes can be pursued. It is critical that the clinician champions involved in this process be sensitive and realistic as well as willing to devote their time and energy to the process.

Summary Bullet Points

- In high-volume clinical settings, adoption of standardized care plans known as clinical pathways can improve patient outcomes and safety and provide for more efficient and satisfying care.
- The creation of clinical pathways should be multidisciplinary involving all members of the healthcare team. Each hospital should design clinical pathways based on their unique environment and should be specific to patients undergoing particular medical procedures.
- Clinical pathways provide hospitals with a way to gather performance and quality data to aid in decreasing the incidence of complications, shorten length of stay, improve budget planning and much more.

Summary

Hospital for Special Surgery has benefitted from the fact that it is a hospital dedicated solely to the care of musculoskeletal disease. This focus has allowed the hospital to develop specialized care plans and a patient-centered approach to care that would be a greater challenge in other more general hospital settings. However, this specialization has led to the development of approaches to care that can benefit patients in any hospital setting. The adoption of clinical pathways has led to safer and more efficient care that has reduced perioperative complication and hospital length of stay and significantly improved patient satisfaction as well as the hospital's reputation as a center of excellence. This experience has also been achieved in many hospital settings throughout the World. It is now clear that hospitals, as well as patients, benefit from the creation and implementation of clinical pathways.

The procedures adopted in clinical pathways must be created through the cooperation of all members of the health care team. Physician champions are especially important to help educate and train their colleagues and to provide the convincing evidence that the pathways are successful in improving overall care. Each hospital must customize the clinical pathways to their own environment and subspecialty focus. Following implementation, the success of the pathway must be routinely monitored to encourage continued participation of the health care team as well as to allow modification of the pathways based on evidence and experience. Surgical procedures such as total joint arthroplasty and spinal reconstruction are extremely amenable to adoption of standardized approaches to care and the implementation of clinical pathways in these subspecialties has been met with success throughout the World.

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36

Achieving Value in Orthopedic Surgery: Clinical Pathways, Bundled Payment Programs, and Proactive Risk Assessment for Elective Orthopedic Procedures

Alana E. Sigmund and Catherine H. MacLean

Objectives

- Promote an understanding of the value imperative for musculoskeletal disease.
- Describe what bundled payments are and how they impact value.
- Facilitate an understanding of risk factors for complications and readmission.
- Provide a framework for assessing risks of complications and readmissions across the orthopedic surgical episode of care.

Key Points

- Bundled payment models hold providers accountable for both the quality and cost of care provided to patients.
- Proactive risk assessment can improve quality and reduce costs of care.
- Identification of factors that affect key outcomes within a care episode facilitates the implementation of (1) strategies to reduce or eliminate modifiable risks and (2) specialized care plans to manage the risks.
- Numerous risk factors may impact patient outcomes.
- Opportunities exist before, during, and after the surgical admission to mitigate operative risk.
- Key time points to assess risk include the following: at the operative consultation, at the medical clearance, immediately postoperatively, before discharge, and after discharge for high-risk patients.
- A variety of validated tools exist to assess risk in different settings and for different patients.

Introduction

Recognition that health care in the United States is at once of suboptimal quality [1, 2], expensive [3], and wasteful [4] has driven interest in achieving "high-value care." Musculoskeletal care is of particular interest to payers and policy makers because it accounts for a significant proportion of all health-care spending at $183 billion annually [3]. It is the leading and fastest-growing health-care expenditure segment for employers [5]. These costs are expected to increase substantially over the coming decades as the baby boom generation ages through mid- to late-life and the effects of the US obesity epidemic on the development of osteoarthritis unfold [3, 6, 7]. Currently, about one million Americans undergo total knee or hip arthroplasty each year and it is estimated that annual usage will grow to four million in the next 20 years [8]. Assuming average procedure costs of $25,000 across all payers, this equates to $25 billion annually [6, 9]. At the same time, the $86.7 billion in annual expenditures for back and neck pain accounts for the third greatest medical expenditures following only those diabetes and ischemic heart disease [3].

Health-care value describes the relationship between the quality and cost of the care delivered [10]. Unfortunately, there is no standard method to measure value and no established value unit that can be used to compare value across therapeutic options, providers, or conditions [11]. Instead, value assessments are typically a qualitative consideration of performance on a set of available quality metrics and

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the cost of care provided to patients with certain diseases or who have undergone specific procedures. Value can be improved by improving quality, reducing costs, or doing both. At HSS, we consider high-value care to be that which produces the best possible patient outcomes in the most cost-efficient way.

Bundled Payment Models

A number of different payment models have been developed to promote high-value care. These range from pay-for-performance programs that focus entirely on health-care quality to population-based risk contracting, which focuses primarily on costs of care, though generally it also includes some quality metrics. Bundled payment programs fall somewhere in between.

These programs, also known as episode payment programs, "bundle" into a single payment, a defined set of services over a defined period of time for a defined disease, condition, or procedure. Services included in a bundle typically include the professional fees of all the clinicians involved in the care and facility fees for all the different facilities that might be used during the bundle period. Which care and for how long varies across bundles. For example, the Centers for Medicare and Medicaid Bundled Payment for Care Improvement (BPCI) and Comprehensive Care for Joint Replacement Model (CJR) include most health care provided to patients who undergo lower extremity total joint replacement starting at the admission for the procedure through 90 days after [12]. Included are professional fees for treating surgeons, anesthesiologists, and hospitalists; facility fees for the hospital and any post-acute care facilities such as skilled nursing or acute inpatient facilities; readmissions; outpatient care; and indeed most medical care provided. While some conditions and procedures that are clearly not related to the arthroplasty are excluded (e.g., parasitic infections, malignancies, and cataract surgery), others that are unlikely to be related are included (e.g., hypertension, diabetes, and screening colonoscopy) [13].

Other bundled payment programs may focus on a procedure including only services directly related to it and sometimes only ones provided by the index providers. For example, some employer-based bundles are limited to all professional and facility fees related to the index procedure and a defined set of complications specifically related to the procedure (e.g., peri-prosthetic fractures after total joint replacements) when those complications are treated at the index facility.

Bundles are cost saving by design because the predefined payment amount is set to be lower than the usual cost to provide the included services on a fee-for-service basis. Some bundled payment programs, such as BPCI and CJR, include a gain-sharing arrangement such that payers will share with the bundle organizing provider entity, the cost of care savings beyond a predefined target price (upside risk). Bundles may also include downside risk to providers such that when the episode cost goes above the target price, the provider entity would need to repay the payer the difference. For both BPCI and CJR the bundle entity face downside risk after an initial period of upside risk only. In contrast the BPCI Advanced program will contain up- and down-side risk from program initiation [14].

Strategies to promote cost-efficient care within bundles include using less expensive inputs (e.g., lower-cost drugs or devices); coordinating services to reduce duplication (e.g., across providers and sites of service); eliminating unnecessary services (e.g., SNF for patients safe to go home); and avoiding costly complications (e.g., readmissions).

Quality incentives can be built into bundles in a variety of ways. Bundled rates that cover all care delivered within the episode incent providers to prevent costly complications. Additionally, bundled payment programs may include specific quality criteria that impact payment. For example, the CJR program includes three quality measures that may impact the target price, and hence the available gain share by up to 1.5% [12]. These measures include the risk-stratified readmission rate, a measure of patient experience, and a measure of collecting and reporting patient-reported outcome data (Table 36.1).

Table 36.1 Quality measures used in Comprehensive Care in Joint Replacement (CJR) model

Quality Measure	Weight in Composite Quality Score
Hospital-level risk-standardized complication rate following elective primary THA and/or TKA complications measure (NQF #1550)	50%
HCAHPS survey measure (Revised from NQF #0166) 6 multi-item measures (communication with doctors, communication with nurses, responsiveness of hospital staff, communication about medicines, discharge information, and care transition) 4 single-item measures (cleanliness of the hospital environment, quietness of the hospital environment, overall rating of the hospital, and recommendation of hospital)	40%
THA/TKA patient-reported outcome and limited risk variable voluntary data submission.	10%

THA total hip arthroplasty, *TKA* total knee arthroplasty, *NQF* national quality forum

Proactive Risk Assessment

Regardless of whether patients are being treated within bundled payment arrangements, evidence-based care that is coordinated across the entire care episode will produce the best outcomes most cost-efficiently [15]. This chapter will describe considerations and approaches to proactive risk assessment throughout the care episode. Details on clinical pathways can be found in Chap. 35.

Reasons to Assess Risk

At the highest level, risk assessment is performed to optimize health outcomes. Within the context of a bundled or other risk-based payment mechanism, it is key to reducing unnecessary health-care spending. Proactive identification of factors that affect key outcomes within a care episode facilitates the implementation of (1) strategies to reduce or eliminate modifiable risks and (2) specialized care plans to manage the risks. Key outcomes within a care episode include: health improvement; patient satisfaction; complications during the hospitalization; complications after discharge; and discharge disposition. Each of these outcomes impacts the value of the episode affecting quality and cost to varying degrees. Examples of risk parameters that impact these outcomes are detailed in Table 36.2.

Although risk assessment should be continuously performed across orthopedic care episodes, there are five key time points when structured risk assessments should be performed: at the surgical consultation, during medical clearance, immediately after the procedure, before discharge from the hospital, and after discharge for selected patients. Care systems and processes should be put in place to ensure that risk is routinely assessed and acted upon at each of these time points.

Table 36.2 Outcomes that pro-active risk assessment seeks to inform and examples of risk parameters which inform them

Outcomes	Risk parameters
Health improvement	Preoperative pain, functional and mental health status Preoperative patient activation status
Patient satisfaction	Preoperative mental health Preoperative patient activation status
Complications during index hospitalization	Preoperative health status Intraoperative course
Complications after discharge	Preoperative health status Intraoperative course Complications during hospitalization Length of stay
Discharge disposition	Age Preoperative functional status Home support Home environment

Surgical Consultation

Presurgical risk assessment starts at the initial consultation with the surgeon. In order to make a decision on whether a procedure should be performed, the surgeon needs information to understand the likelihoods of surgical success, complications, and patient satisfaction. Surgical recommendations have traditionally been based on a qualitative assessment of elements in the history, exam, laboratory, and radiographic studies. An expanded, patient-centered perspective should also consider factors that affect whether patients will achieve their pain, functional status, and quality of life goals – and whether the patient will be satisfied with the outcome of their procedure. Quantitative assessments of pain, function, quality of life, mental health, patient expectations, and the degree of patient activation based on validated survey instruments can inform this perspective [16–20].

When determined that a procedure is indicated, a more comprehensive risk assessment and mitigation strategy should be immediately implemented. All patients should be referred to an internist skilled in perioperative management for medical clearance and further risk assessment. Patients with special high-risk problems should also be referred to the appropriate clinicians for evaluation and treatment. Examples include referring patients with a history of chronic opioid use to pain management specialists and patients who are morbidly obese to a weight loss specialist.

To ensure that the eventual discharge destination is the one safest for the patient and also most cost-effective, assessment and recommendation regarding discharge disposition should be initiated at the time of the surgical consultation. Beyond selecting the right disposition, knowledge of the disposition site facilitates advance planning and shortened length of the hospital stay. Factors including age, preoperative functional status, home support, and home environment should be considered. The Risk Assessment Prediction Tool (RAPT), a validated six-item patient survey [21], can inform the disposition recommendation. This tool has been demonstrated to accurately predict eventual discharge disposition for patients undergoing total joint replacement and spine surgery [22, 23].

Medical Clearance and Risk Optimization

Once the benefits and risks of surgery have been considered and a decision for an orthopedic procedure made, a comprehensive medical clearance involving evaluation of all organ

systems should be performed before all elective orthopedic procedures. Modifiable risk factors should be optimized preoperatively and a care plan developed that will optimize outcomes given the presence of risk factors, whether or not they can be modified. The discharge disposition recommended by the surgeon should be considered and reinforced with the patient or if appropriate modified in consultation with the surgeon. As detailed in Chaps. 1 and 2, medical evaluation, risk assessment, and optimization should be directed to the specific needs of individual patients.

As detailed in Table 36.3, various clinical risk factors are associated with undesired outcomes including medical complications, surgical complications, or the need for additional care, such as readmission or increased length of stay. A useful approach, especially when designing a preoperative screening program, can be to view risk factors along a continuum, in which some risk factors are completely modifiable prior to surgery, and others, such as ischemic heart disease, cannot be reversed, but can be optimized prior to surgery. Finally, risk factors that are not easily categorized may be well-managed with a pathway-based approach designed to reduce the risk of a particular clinical endpoint, such as readmission or infection [24, 25].

Obesity and Malnutrition

In a retrospective study of 98,410 primary TKA patients in the National Inpatient Sample with morbid obesity, defined as a body mass index (BMI) ≥40, those with a (BMI) of 40 or greater were at increased risk for postoperative infection (OR 1.3 CI 1.1–1.7), wound dehiscence (OR 1.3 1–1.7), and genitourinary complications (OR 1.3, CI 1.1–1.5) [26]. In a study, 42 patients with a BMI greater than 50 were found to have a postoperative complication rate close to 50%, although this group of patients did have clinically relevant improvement on the Harris Hip score [27]. In a small study, which identified obese patients preoperatively, 13 patients with average BMI of 47 were referred to a weight loss clinic prior to hip arthroplasty. Among these, 6 patients participated in a weight loss program, with an average BMI decrease to 43.3. Surgical outcomes were not followed in this group, but the rate of attrition in following up for an obesity management visit was a notable obstacle in this study [28]. In an attempt to understand if reversing obesity would also reverse the associated surgical risk, a systematic review and meta-analysis was performed to determine if bariatric surgery had a positive impact on outcomes after total joint arthroplasty. The 5 studies included compared 657 patients who underwent bariatric surgery to 22,691 obese patients who had not, but no difference in outcomes such as wound infection revision surgery and mortality were observed [29].

A study of malnourished patients undergoing total joint arthroplasty (TJA) may shed some light on why bariatric surgery did not mitigate surgical risk for patients with obesity planning joint surgery. In this study, 2161 patients undergoing TJA were classified as malnourished if they had a low transferrin or albumin, and obesity if their BMI was 30 or greater. The malnutrition rate in this cohort was 8.5% and notably, obesity was present in over 40% of malnourished patients. Patients who were malnourished experienced a complication rate of 12%. By comparison, obese patients had a complication rate of only 3.2%. The incidence of complications was much higher in patients who were both malnourished and obese, at 10.4% [30]. Addressing a malnourished state may be at least as important as addressing excess weight itself in many obese patients.

In a small study examining the impact of a protein supplement in elderly, malnourished patients undergoing hip fracture surgery, a trend was noted toward fewer complications in the intervention group, but it is likely that a larger sample size would be needed to draw a conclusion regarding the role of protein drinks prior to surgery [31].

Smoking

In a 2011 meta-analysis of patients undergoing hip and knee arthroplasty examining "all complications" and "death" as outcomes found, all examined complications were elevated in smoking cohorts including mortality, infection, and revision (OR 1.24 CI 1.01–1.54). The OR for death was 1.69 CI 1.08–2.64 [32]. In another study of nearly 80,000 hip and knee arthroplasty patients, smokers were compared with non-smokers in a multivariate analysis, and smoking was found to increase the risk of wound complications at 1.8% compared with 1.1% for non-smokers ($p < 0.001$). Of note, former smoking was also a risk factor for adverse outcomes, calling into question whether or not smoking cessation interventions would impact adverse outcomes related to smoking [33]. In a systematic review that addressed this discrepancy, it was noted that intensive preoperative behavioral interventions increased smoking cessation and reduced complications if patients stopped smoking 4–8 weeks prior to the surgery [34].

Substance Abuse

In a 1994 Australian study of 120 consecutive patients admitted to an orthopedic surgery service, 34% of acute admissions and 39% of elective admissions reported hazardous drinking on an AUDIT risk scoring tool, and use of a similar tool showed that drinkers were at risk for in-hospital complications, such as verbal abuse, agitation, and sleep disturbances. Those with AUDIT scores ≥8 had complications at a rate of 47% and those with a score <8 had a rate of complications at 22% [35–37]. It is not currently clear what role alcohol cessation plays prior to orthopedic surgical admission with respect to managing cost, due to lack of data on this subject, but established alcohol abuse should be managed preoperatively with a referral for cessation counseling.

Table 36.3 Important Risk Factors Prior to Orthopedic Surgery and Possible Adverse Outcomes

	MACE	Pulmonary Edema	Complete Heart Block	CVA	Surgical Site Infection	Other postoperative Infection	Venous Thromboembolic Disease	GU complications	Postoperative Anemia	Delirium	Dislocation/ Fracture	Hematoma/ Seroma	Respiratory Failure	Aseptic Loosening	Renal Complication	GI complication	Neurologic Complication	Increased LOS	Readmission
Ischemic Heart Disease	x	x	x																x
Elevated Serum Creatinine	x	x	x					x											x
History of CVA	x	x	x	x															x
Congestive Heart Failure	x	x	x																x
Diabetes	x	x	x		x	x	x		x						x				x
Morbid Obesity	x				x		x	x	x	x	x	x	x	x			x		x
Malnutrition	x				x	x						x			x		x	(Hypoalbuminemia)	(Hypoalbuminemia)
Vitamin D Deficiency					x														
Smoking	(Death)				x									x					x
Anemia	x				x			x	x										
Opioid Use							x	x		x						x		x	
Substance Abuse		Intubation				x	x		x	x				x	x	x		x	
Dementia										x									x
Frailty	x	(Pulmonary Complication)			x	x	x		x						x			x	x

MACE – Major Adverse Cardiac Events - Myocardial Infarction, Cardiac Arrest/Death, Revascularization

Known adverse effects of withdrawal such as delirium tremens and seizure can be avoided with this strategy with a supervised preoperative alcohol cessation strategy.

In a prospective study of 583 patients undergoing spine surgery, preoperative opioid use was significantly associated with increased intra- and postoperative opioid use ($p < 0.05$) [38]. Fifty-four patients requiring preoperative opiates undergoing total hip arthroplasty were found to have significantly higher daily opioid use ($P < 0.05$ on postoperative days 0, 1, and 3) during their inpatient stays. This effect persisted at 6 and 58 weeks ($p < 0.05$) [39]. Similar results were recently found for patients undergoing unicompartmental knee arthroplasty [40]. In a quality-intervention study, 121 patients undergoing carpal tunnel release were followed after they received an opioid-education handout. The post intervention group had at least 35% reduction in opioid use after the surgery [41]. A double-blind trial of patients with depression undergoing spine surgery assigned patients to either duloxetine or placebo and found no difference in opiate use between groups postoperatively [42]. Patients with prior opiate use would likely benefit from preoperative opiate use mitigation and education prior to orthopedic surgery.

Risk factors that are targets for optimization include risk factors such as a high-risk surgery, congestive heart failure, ischemic heart disease, history of CVA, insulin-dependent diabetes, and serum creatinine greater than 2 [43]. While these factors cannot be completely reversed prior to surgery, optimal management can mitigate the peri-operative risk.

Ischemic Heart Disease

The management of ischemic heart disease prior to any surgery, including orthopedic surgery, is the subject of multiple guidelines, most recently including the Canadian Cardiovascular Society (CCS) in 2017 [44] and the American College of Cardiology/American Heart Association (ACC/AHA) in 2014 [45]. These guidelines differ in many ways, and it is likely that clinical trials will be required to resolve the differences in the recommendations. For example, the CCS guidelines cite literature that suggests an elevated B-type natriuretic peptide level increases surgical risk and should prompt postoperative troponin monitoring, but the ACC/AHA recommendations do not support this practice [45]. Areas of agreement include the continued use of the Revised Cardiac Risk Index [43] tool, continuation of beta-blockade therapy for patients with ischemic heart disease or multiple risk factors for ischemic heart disease through the peri-operative period and the continuation of aspirin in patients with prior coronary artery stent placement planning elective surgery [46]. Decisions regarding stress testing, B-type natriuretic peptide testing, and postoperative troponin monitoring should be made in conjunction with the patient's cardiologist or internist.

Congestive Heart Failure

Both the CCS [44] and ACC/AHA [45] guidelines agree that congestive heart failure is a risk factor for adverse outcomes postoperatively for non-cardiac surgery, but do not suggest specific management or testing prior to surgery. A 2015 study of 28,263 patients with and without CHF ($n = 7990$) undergoing elective surgery found that use of beta-blockers was associated with a decreased risk of major adverse cardiac events (MACE) after non-cardiac surgery HR 0.78 CI 0.67–0.90 as well as all-cause mortality HR 0.90 CI 0.70–0.92 [47]. This therapy should be continued perioperatively for arthroplasty patients in conjunction with the patient's cardiologist or internist.

Stroke

A history of ischemic stroke is not a modifiable risk factor, but risk is likely best managed by delaying an elective surgery until at least 9 months after the ischemic event; a nationwide cohort study conducted in Denmark showed that risk of MACE stabilized, although did not normalize 9 months after the ischemic stroke [48]. In a study including a large number of emergency orthopedic surgeries, a similar cohort of patients who had prior ischemic stroke were found to be at higher of MACE postoperatively, particularly 4–14 days after their stroke compared with 1–3 days after the stroke with a complication rate of 29% versus 21% in prompt-surgery patients ($p = 0.029$) [49], underscoring the role of prompt orthopedic intervention [50]. Collaboration with the patient's neurologist and cardiologist is appropriate preoperatively to determine appropriate medical management leading up to the time of surgery.

High-Risk Surgery

The risk conferred from the type of surgery planned is best assessed in collaboration with the surgeon, internist, and anesthesiologist to minimize blood loss and time under anesthesia. A recent administrative database study examining patients who underwent removal of infected hip hardware had a 30-day readmission rate of 11.1% and 30-day mortality of 2.6%, rivaling rates of carotid endarterectomy, prostatectomy, and kidney transplant [51]. Similarly, hip fractures are associated with a particularly elevated mortality rate ranging from 14% to 36% within 1 year of surgery in a study examining surgeries through 2013 [52]. Timing may have a role in mitigating the risk of surgery: in one study of over 40,000 surgical patients, 30-day mortality was 7%; however, those who underwent surgery within 24 hours of injury were at significantly lower risk [50].

Diabetes Mellitus

In a study of approximately 6,000 patients with diabetes undergoing arthroplasty, patients with a hemoglobin A1c of 7% or higher were compared with patients with a lower

value and were noted to be at increased risk (OR 1.22 CI 1.01–1.47) for any complication including return to the operating room, urinary tract infection, infection of any kind, and acute renal failure. In this study, patients with HgA1c ≥7% also had increased 90-day mortality (IOR 1.37 CI 0.82–2.29) [53]. Some centers have implemented cut-off hemoglobin A1c values to address this issue [54], and some have implemented a cut-off as part of an overall pathway program [25]. Hemoglobin A1c screening may not be the only valuable approach in managing the additional risk a patient with diabetes has with respect to surgery. In a retrospective review of patients with average HgA1c of >6.7% or postoperative blood glucose of >200 mg/dL, both groups were at higher risk of postoperative wound complications following elective total joint arthroplasty. The OR for wound complication in patients with mean postoperative glucose >200 mg/dL was 3.75 (1.25–11.22) and 9.0 (CI 1.1.4–71.20) in patients with Hga1c >6.7%, emphasizing the importance of adequate pre- and postoperative glucose control in addition to preoperative levels [55].

Serum Creatinine >2 or Chronic Kidney Disease

Chronic kidney disease (CKD) has been recognized as a risk factor prior to surgery within the Revised Cardiac Risk Index [43]. In a retrospective analysis of patients with CKD undergoing total hip arthroplasty, the prevalence was found to be 6.1%, and patients with this finding were noted to have increased risk of 90-day readmission OR 1.3 (CI 1.1–1.6), mortality 1.5 (CI 1.2–1.8) and superficial surgical site infection (OR 1.3 CI 1.1–1.6) [56]. Similar results were found examining patients with CKD undergoing total knee replacement [57]. End-stage renal disease (ESRD) has been noted to be a risk factor prior to hip hemiarthroplasty in displaced femoral neck fracture patients [58]. In a retrospective case-control study of ESRD patients undergoing elective total knee arthroplasty, patients had increased risk of prolonged hospital stay (7.2 versus 4.4. days, $p = 0.002$) and transfusion rate (60% vs 10% p.001) but with similar improvements in pain scores [59].

In posterior lumbar interbody fusion, stage 3–4 CKD was found to significantly ($p < 0.05$) adversely impact recovery when measured by Japanese Orthopedic Association Scores at 2-year follow up to assess back pain [60]. A retrospective review of patients undergoing spine surgery in patients on hemodialysis examined patients judged to have destructive spondyloarthropathy (DSA) associated with chronic renal replacement. In this study, it was noted that limiting patients only with DSA to spinal fusion and patients without to decompression, patients achieved neurological and functional improvement [61]. Patients with chronic kidney disease should plan surgery in conjunction with their nephrologist, and dialysis should be timed shortly after the procedure.

Postsurgical Risk Assessment

Immediately after surgery patients should be reassessed for risks of postsurgical complications including poor pain control, fluid/blood abnormalities, infection, and VTE. Intraoperative factors associated with complications include procedure type, total operative time, and blood loss. Management of these risk factors is described in detail in Chaps. 6, 7, 8, 9, 10, and 11.

Surgery-Specific Complications

Surgery-specific complications include cardiac events, VTE, and ileus. Intermediate and high-risk surgeries such as arthroplasty and many spine procedures place patients at increased risk for adverse cardiac outcomes. In the VISION study, more than 20,000 patients undergoing noncardiac surgery underwent high-sensitivity serum troponin testing in the first 3 days after surgery and were followed for the outcome of death within 30 days of surgery. Patients with increased high-sensitivity troponin serum values were at increased risk for 30-day mortality. It is not yet clear, however, what management strategy is cost-effective in patients with elevated high-sensitivity serum troponin values and if any management will reduce the risk of 30-day mortality in these patients [62].

The rate of venous thromboembolic (VTE) disease may range from 1.1% to 4% for hip and knee arthroplasty patients [63, 64] and from 0.0% to 2% for spinal surgery patients [65, 66]. Attempts to use risk stratification tools to evaluate hospitalized orthopedic surgery patients for VTE disease have had mixed results [67, 68]. Tests such as computed tomography of the chest with intravenous contrast have disadvantages, such as cost, contrast, and radiation exposure [69, 70]. Approaches such as end-tidal CO_2 measurement and following postoperative tachycardia are evidence-based approaches that have shown promise as possible tools in deciding to pursue further more costly evaluation such as computed tomography of the chest with intravenous contrast [71, 72].

In spinal orthopedic patients, the rate of ileus ranges from 26 per 1000 patients in posterior lumbar fusion to 74.9 per 1000 patients in anterior lumbar fusion; interbody fusion obstruction rates may also be as high as 70 per 1000 patients [73]. Among patients who undergo total hip or knee arthroplasty, the rate is 7 per 1000 patients [74]. Regardless of the procedure, postoperative ileus was associated with higher costs from prolonged length of stay, readmissions, and visits to the emergency department [73, 75]. Risk factors for ileus include male gender for both spinal fusion and TJA [73, 74]. Additional risk factors for spinal fusion patients include three or more levels, alcohol abuse, anemia fluid/electrolyte disorders, weight loss, gastroesophageal reflux disease, and posterior instrumentation [73, 76]. Additional risk factors for postoperative ileus after TJA include older

age and hip arthroplasty (as compared to knee) [74]. History of prior abdominal surgery has been reported to be a risk factor for TJA [74] and protective against postoperative ileus for patients who underwent interbody spinal fusion [76].

Operative Time

For total hip and knee arthroplasty, operative time greater than 120 minutes is associated with an increase in overall complications and surgical site infections [77]. Likewise a retrospective review of 98 patients who had undergone a posterior decompression and lumbar arthrodesis with instrumentation found that complication rates increased with longer operative time [78].

Blood Loss

Blood loss varies with different orthopedic procedures. Total joint arthroplasty, orthopedic tumor, and pelvic surgeries are associated with significant blood loss. Patients with significant blood loss are at risk for hemodynamic instability, major cardiac events, and surgical site infections [79, 80].

Pre-Discharge Risk Assessment

Prior to discharge, risk for complications in the post-acute care period should also be assessed and plans to mitigate them implemented. A number of readmission risk screening tools have been validated for the general hospitalized population. For example, the LACE index [81] considers *L*ength of stay, the *A*cuity on admission, the degree of *C*omorbid illness (as measured by the Charlson Comorbidity Index), and the number of times the patients has been to the *E*mergency department in the last 6 months. The HOSPITAL score [82] is calculated by points assigned for *H*emoglobin <12 g/dL, discharge from the *O*ncology service, or Sodium <135 mEq/L at discharge; having a *P*rocedure during the hospital stay; and *I*ndex admission *T*ype: non-elective, number of hospital Admissions in the previous year, and *L*ength of stay ≥5 days. The fact that some of the variables included in the LACE index and HOSPITAL score would not occur in an elective orthopedic population (e.g., acuity on admission should be normal, patients would not be on oncology services, and the index admission type would not be non-elective), raises questions as to the applicability of these tools in this population. Also developed for the general hospital population by the Society of Hospital Medicine, the 8Ps Risk Assessment Tool [83] may be more readily used to assess readmission risk after elective orthopedic procedures as it simply identifies risk factors that can be addressed if present: *P*olypharmacy; *P*sychological problems; *P*rincipal diagnosis or reason for hospitalization related to cancer, stroke, diabetic complications, COPD, or heart failure; *P*hysical limitations; *P*oor health literacy; *P*oor social support; *P*rior unplanned hospitalization in prior 6 months; and *P*alliative care.

Two separate analyses of the National Surgical Quality Improvement Project (NSQIP) database have evaluated the risk of readmissions after orthopedic procedures. Across total knee or hip arthroplasty, posterior lumbar fusion, anterior cervical discectomy and fusion, or total shoulder arthroplasty, the all-cause 30-day readmission rate was 3.8%; 3.6% had an unplanned readmission, and 2.4% had an unplanned readmission related to surgery (URRS) [84]. The most common reason for readmission was surgical site complications followed by venous thromboembolism and bleeding. Independent predictors of URRS were current smoking, any inpatient complication, and non-home discharge. In an evaluation focused on total hip and knee arthroplasty, the 30-day readmission rate was 4.5% and the most common reasons surgical site infection, graft or prosthesis failure, and venous thrombus embolism [85]. In contrast to the other study, this one concluded that readmissions after surgery were mostly associated with post-discharge complications related to the procedure and not with inpatient complications.

In a recent study examining the safety of same-day discharges, investigators studied the National Surgical Quality Improvement Program Registry. 1236 underwent a same-day procedure. "When procedures were assessed individually, the only difference identified was that the same-day total knee arthroplasty cohort had an increased return to the operating room compared with the inpatient total knee arthroplasty cohort (p = 0.046). Body mass index of >= 35 kg/m^2 (p = 0.035), insulin-dependent diabetes (p = 0.041), non-insulin-dependent diabetes (p = 0.013), and age of >= 85 years (p = 0.039) were associated with 30-day readmission following same-day surgical procedures. Infection was the most common reason for reoperation and readmission following same-day procedures" [86]. In another study examining 2437 Medicare patients undergoing total joint arthroplasty, Hendrich Fall Risk score of ≥6 either before or after the patient's surgery was associated with 2.84 OR (CI 1.70–4.76) unplanned 3-day-readmission, length of stay >3 days (4.9.6 vs. 36.6%), and a location other than home for discharge (20.8 vs. 35.8%) [87].

In a study of 1631 patients that underwent elective spine surgery, 1444 patients were discharged home and 187 were discharged to an inpatient facility. 4% of 65 patients were readmitted and there were no differences in readmission rates between the home and rehab groups. Readmissions from rehabilitation facilities were 80% related to medical complications and readmissions from home were 67% surgical (wound) issues [88].

Post-Discharge Risk Assessment

Risk assessment should continue after discharge for high-risk patients. Patients identified as high risk prior to discharge should be proactively assessed for problems at specified time

points based on risk. Assessment can occur via telephone call from a clinician, through electronic communication (email or text message), and at office visits including the postoperative visit. The frequency of contact should be based upon the risk factor and the likelihood that contacting the patient will make a difference. Pre-discharge risk assessment tools can be used to identify patients who should be contacted proactively. Additional consideration should be given to patients with specific conditions associated with a high risk of readmission (Table 36.4) [89].

Summary

Bundled payment models hold providers accountable for both the quality and cost of care provided to the patients. Proactive risk assessment can improve quality and reduce the costs of care. Numerous risk factors may impact patient outcomes. Personalized care plans aimed at reducing or eliminating risks are key to improving patient outcomes. Opportunities to provide personalized risk modification exist before, during, and after the elective surgical admission. A variety of validated tools exist to assist providers in assessing risk in patients planning an elective procedure.

Table 36.4 Odds of readmission within 30 days for top 15 risk factors among 981,400 Medicare beneficiaries who underwent primary TKA or THA between 7/2013 and 6/2016

Risk factor	Odds ratio (95% CI)		Frequency (%)
Dialysis status	1.83	(1.60–2.09)	0.2
Severe hematological disorders	1.44	(1.28–1.61)	0.4
Chronic obstructive pulmonary disease (COPD)	1.39	(1.35–1.42)	12.6
Number of procedures (two vs. one)	1.37	(1.28–1.46)	2.1
Renal failure	1.35	(1.32–1.39)	13
Morbid obesity	1.35	(1.31–1.40)	8.4
Major psychiatric disorders	1.35	(1.30–1.41)	4.7
Congestive heart failure	1.25	(1.21–1.29)	8.3
Protein calorie malnutrition	1.20	(1.10–1.31)	0.7
Hemiplegia, paraplegia, paralysis, functional disability	1.19	(1.10–1.28)	1.1
Coronary atherosclerosis or angina	1.19	(1.16–1.21)	25.4
Hypertension	1.19	(1.16–1.23)	80.5
Decubitus ulcer or chronic skin ulcer	1.19	(1.13–1.25)	2.4
Dementia or other specified brain disorders	1.19	(1.15–1.24)	4.1
Metastatic cancer or acute leukemia	1.18	(1.05–1.33)	0.5

Data from the 2017 Procedure-Specific Measures Updates and Specifications Report: Hospital-Level 30-Day Risk-Standardized Readmission Measures Isolated Coronary Artery Bypass Graft (CABG) Surgery – Version 4.0, Elective Primary Total Hip Arthroplasty (THA) and/or Total Knee Arthroplasty (TKA) – Version 6.0. Prepared by Yale New Haven Health Services Corporation/Center for Outcomes Research & Evaluation (YNHHSC/CORE) for the Centers for Medicare and Medicaid Services, March 2017

Summary Bullet Points

- Recognition that health care in the United States is at once of suboptimal quality, expensive, and wasteful has driven interest in achieving "high-value care."
- Bundled payment models, which lump together payments for a care episode, incent providers to deliver efficient care and to avoid costly complications and readmissions.
- To reduce complications and readmissions, proactive risk assessment should occur throughout the care episode.
- Key time points to assess risk include the following: at the time of surgical consultation, at the medical clearance visit, immediately postoperatively, before discharge, and after discharge for select, high-risk patients.

Case Study

AB, a 68-year-old white female, has a long history of osteoarthritis involving her bilateral knees and hands. Over the last 2 years, she has had increased pain, stiffness, and gelling of her right knee. She is able to walk two blocks before her right knee pain stops her from walking further. She does not use a walking aid. She has had two previous corticosteroid injections in her right knee with moderate improvement for several months. She has also previously participated in physical therapy with right quadriceps strengthening with limited improvement in her knee pain. She now takes naproxen 500 mg BID and acetaminophen 1000 mg TID. Her goal for surgery is to walk one mile without pain. Her preoperative pain score is 7/10; her PROMIS global health score 40; her KOOS-JR 50. Her other medical history includes obesity with a BMI of 41 and type II diabetes with a HgA1c of 9.1 at her preoperative visit. She lives with her husband and adult son in a one-floor home with no steps. Her RAPT score was 10 indicating low need for post-acute services. In preparation for surgery, she was seen by a weight loss specialist and internist with a goal to reduce her BMI by 5% and her HgA1c to ≤8 over a 3-month period through diet and medications. She also completed a preoperative physical therapy assessment including a home environment assessment. When she was admitted for surgery, her BMI was 39 and her HgA1C was 7.9. A plan to discharge to home was made before admission, which included family education. In the OR, she received regional anesthesia; total OR time was 60 minutes. Her procedure was performed with-

out complications. Postoperatively her blood glucose was 150 mg/dL. Her risk was reassessed immediately after her procedure and she was placed on aspirin for VTE prophylaxis. She was up and walking 12 hours after surgery. On postoperative day (POD) 2, her risk for readmission and complications was reassessed. Her RAPT score remained 10; her LACE score was 3, indicating low risk for readmission. Discharge education emphasized keeping her blood sugar under control and carefully managing her wound to avoid infection. She was discharged to home without home services on POD 2. She received videophone calls from a nurse on post-discharge days 1, 8, and 15 with particular attention to her wound and diabetes management. She was also contacted by a physical therapist via videophone calls on days 2, 7, and 14. She returned to her surgeon for a follow-up visit 6 weeks after her procedure, doing well. One year later she reported improvement in her pain and function with pain 2/10 and KOOS-JR = 85. She is able to walk two miles without pain.

Obesity and poorly controlled diabetes put this patient at risk for surgical complications. This risk was reduced through a preoperative weight loss program and medical management of her diabetes. Although her RAPT score indicated that she was safe to discharge home, through preoperative assessment of her home environment and after-care education, she and her family gained confidence in the plan to discharge to home. While her intra-operative course was uneventful, her risk for postoperative complications was nonetheless assessed and she was put on aspirin for VTE prophylaxis. Since diabetes and obesity put this patient at increased risk for surgical site infections, she received focused education prior to discharge about wound care and the importance of keeping her blood sugar under control. After discharge she was monitored by video-telephone calls through which her diabetes and wound were monitored. One year after surgery her pain and function had improved greatly and she had exceeded her goal to walk at least one mile. This is a high-value case because substantial improvements in pain and function were achieved; complications were avoided; and unnecessary services – such as discharge to a skilled nursing home – were avoided. Continuous, proactive risk assessment throughout this surgical episode facilitated achieving this value.

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Bioethical Considerations in Perioperative Orthopedic Medicine

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Objectives

- To understand the basic concepts of bioethics and their importance in perioperative decision-making
- To examine common ethical problems that arise in the perioperative setting
- To apply a bioethics framework to selected issues, including informed consent, competency, capacity, and refusal of care
- To present an approach to the initial management of these problems, including when consultation with a clinical bioethicist is appropriate

Key Points

- Surgical patients are a vulnerable population, and it is critical that perioperative clinicians consider principles of bioethics in the decision-making process.
- Surgical patients are particularly vulnerable when they are also the subjects of clinical research, and deserve special protection during this time.
- Understanding the core principles of bioethics is a helpful guide to the clinician during perioperative decision-making.
- Perioperative clinicians need to have a clear understanding of competency, capacity, and the nature of informed consent.
- It is part of the professional duty of all clinicians to understand when care violates the basic principles of bioethics and to actively intervene to correct it.

Introduction

A study of perioperative medicine raises many issues which are central to bioethics. This chapter reviews the important ethical challenges which arise in this clinical setting, beginning with a summary of the fundamental concepts which guide bioethical analysis.

Basic Concepts of Bioethics

Morality refers to the set of behaviors that govern how one should act – how human character should be expressed in a given set of circumstances [1]. In the setting of good and bad character, and behaviors which are right and wrong, ethics answers the question "what ought to be done?" [2]. Bioethics is the study of how principles of morality are used to guide decision-making in medicine. As a medical discipline it arose in lockstep, indeed an inseparable companion, with the technological advancements in medicine.

Defining which actions are good or bad seems at first a subjective assessment, about which most might feel that they "know it when [they] see it" [3]. From a philosophical perspective, however, there are several ways to develop a consensus not only about how we feel, but why. Two leading approaches are known as consequentialism and deontology [4]. Consequentialists judge the rightness or the wrongness of

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Table 37.1 Basic principles of medical ethics

Autonomy	Respect for autonomous decision-making
Nonmaleficence	Avoidance of harm
Beneficence	Prevention of harm
Justice	Fair distribution of benefits, risk, and cost

Data from Beauchamp and Childress [4]

an action by its outcome. An action would be considered as right if it resulted in the best outcome to the largest number of people. For example, using the logic of a consequentialist, breaching patient confidentiality would be justified if the overall benefits outweigh the harms. In contrast, deontology holds that regardless of the outcome, certain actions are inherently right or wrong, and that the right action should always be chosen. According to this point of view, for example, the breaching of patient confidentiality is simply wrong and never the appropriate choice, regardless of the circumstances. When faced with a difficult decision, clinicians may employ a hybrid approach melding both conceptions to varying degrees.

Owing to their complexity, the ethical challenges arising in modern medicine have incited the development of a third, principle-based approach to ethical analysis. The core elements (principles) that compromise this approach are shown in Table 37.1. Founded on four principles – autonomy, beneficence, nonmaleficence, and justice – this construction for clinical decision-making has become enormously influential in the practice of medical ethics [4].

Beneficence

Beneficence is the act of doing what is good and right, and is predicated on the intent of the clinician to always strive for the best interest of their patient. While making the right choice can be built into an algorithm or checklist, it is important to explicitly state that intending to be good is an essential quality of the clinician.

Nonmaleficence

While nonmaleficence is a corollary of beneficence, it is not the same thing. A maleficent act is one which is wrong, evil, or results in intentional harm. To act with nonmaleficence is to strive never to have a wrong intent, and to the extent possible minimize unintentional harm.

Justice

In bioethics, justice refers to the equal distribution of risks, benefits, or resources across a population. The application of justice means, for example, that the trial of a new drug should not be performed in a population which cannot have access to the drug after its development.

Autonomy

Respect for the autonomy of the individual implies that the clinician will strive not only to act in accordance with their patient's wishes, but to promote them as much as possible. Protecting the autonomy of the patient may also include recognizing when they lack the capacity or competence to act in their own best interest and implementing safeguards which guide decision-making in such situations.

Professional Duty

All professionals are engaged in a social contract which provides them with certain privileges not granted to the lay public (such as the ability to self-regulate training and practice), with the understanding that they must exercise them in an ethical way. As professionals, clinicians have a fiduciary responsibility to act in the interests of their patient, which is distinct from the commitment to beneficence and nonmaleficence.

Capacity and Competency

Capacity and competence are fluid concepts which can change throughout the perioperative period, in the critical care unit, and with exposure to anesthetic and pain medication. Related but distinct concepts it is important to remember that consent implies the patient understands the risks, benefits, and alternatives of treatment (including refusal) and agrees to proceed. However, the patient must have the capacity to decide, thus consent does not exist without the capacity to give it [5].

A person can be said to have the capacity to make decisions when they demonstrate they understand the proposed treatment; appreciate their current situation and what may happen if treatment is refused; can explain their choice with reason; and are able to communicate. The clinician can better assess the patient's capacity by asking them questions in such a way as to encourage them to imagine and verbalize the alternatives [6].

Capacity is often used synonymously with competence; however, there is a real distinction for the clinician. Evaluating capacity is clearly within the capabilities of the clinician; however, determining competence is a legal determination more properly made by a court [7].

When a person is unable to make decisions for him- or herself, a surrogate can be designated to act as the patient's representative, and make decisions based on their understanding of the patient's wishes. The anticipation of such circumstances is important and involves the use of an advanced directive (also called a durable power of attorney for healthcare or healthcare proxy), which gives legal decision-making power to a surrogate of the patient's choice during a period of incapacity.

Vulnerable Populations

A vulnerable population could be considered any group with an increased risk for harm based in their inherent characteristics when compared to others in similar circumstances.

As such they deserve additional protection [8]. Examples include people who are disadvantaged by such factors as poverty, ethnic background, or by gender discrimination; people with cognitive or behavioral problems such as dementia or serious psychiatric illness; and those with chronic physical problems requiring extensive support.

Common Ethical Problems That Arise in the Perioperative Setting

Informed Consent

To the moral philosopher, the concept of autonomy is a reference to personal self-governance. To respect someone as an autonomous agent, one must recognize the person's capacities and perspective, including his or her right to hold certain views, make choices, and take actions based on personal beliefs. It is important not to conflate autonomy with other related concepts such as voluntariness, privacy, or freedom to choose which are sometimes associated with informed consent in the literature. In the clinical environment, informed consent is a necessary legal requirement for the initiation of therapy. It is part of the clinician's professional responsibility to have an understanding of autonomy and informed consent, and be able to engage with patients in a way that incorporates that understanding. It is critical to remember that the consent form and informed consent are not the same thing. An informed consent discussion is necessary, and while a signed document is often expected, it is only a record of that process.

When obtaining informed consent, the clinician is responsible for explaining – in language that the patient can understand – the nature of their condition, its natural history if left untreated, recommendations for treatment, and the potential risks and benefits of that treatment. This can be a complicated task given the logistics of a busy operative practice, especially when confronted with many patient factors, including language proficiency, education level, religious and social mores, and the effects of the patient's medical condition and its treatment [9].

Capacity, Competency, and Advanced Directives

For patients to be able to give their consent to a procedure they must have the capacity to understand the issues at hand. Clinicians often confuse the terms Capacity and Competency. Competence is typically considered a legal term and, as such, may differ by jurisdiction. Competence is determined by a court of law and is, hopefully, not a part of routine patient care. Capacity is a medical term that addresses a patient's ability to understand. When the capacity of a patient comes into question, the determination of capacity is made by the doctors caring for the patient. Often this will be done by requesting a consultation from a psychiatrist. Having a psychiatric evaluation can also be of significant additional help in determining if depression is having an undue influence on a patient's decisions regarding their care.

Determinations of capacity are perhaps best seen as assessing the following: Can the patient understand the proposed treatment or care options? Can the patient apply that information to the particular context? Is the patient able to consider the decision in light of their personal beliefs and values? Can the patient clearly communicate these choices? [10, 11]. Capacity is considered fluid and may change quickly, especially in sick patients. It is decision-specific with easy decisions requiring less capacity than complex ones.

When patients have diminished capacity it sometimes becomes necessary for others to make decisions for them. There are many ways that this can be accomplished while protecting the autonomy of those made vulnerable by lack of capacity. When there is an appointed healthcare proxy, the patient has already decided who will make decisions. In circumstances when no formal proxy declaration has been made, one must turn to the patient's family. Typically, surrogate decisions should be made according to the following order of authority: considered first are decisions based on the known preferences of the patient. When those are not known for the particular circumstance, a decision based on substituted judgment (i.e., what the surrogate believes is most consistent with the beliefs and values of the patient) is next in order. Finally, when these standards cannot be applied (e.g., when a patient never had capacity or when there is no one who knows what their preferences or beliefs were), it is appropriate to use a best interest standard, which attempts to guide decision-making based on what choices a reasonable person would make. These concepts about surrogate decision-making seem appropriate and sound. Our culture and legal system are comfortable with them. Nonetheless there is research calling into question a number of these tenants suggesting that, as people age or face significant illness and confront their mortality, they can gain new insight and change their minds [12, 13].

Patients can plan for such decision-making through the invocation of an Advance Directive and Living Wills. Further the appointment of a healthcare proxy can facilitate surrogate decision-making and help assure that a patient's personal values are protected. Advanced directives and Do Not Resuscitate (DNR) in the perioperative period and in the setting of anesthesia and surgery need particular scrutiny. The recommendations for how best to provide care for these patients have evolved over recent decades, and perioperative healthcare teams should be aware of the current recommendations [14].

Resuscitation procedures and anesthesia procedures have much in common. When a patient with a DNR order is to have

surgery, that patient is simultaneously making a positive request for care while asserting a negative right to be left alone [15]. He or she wants anesthesia, but just does not want to be resuscitated if he or she suffers a mortal event. Many people with DNR orders see resuscitation as a potential road to prolonged suffering, with little hope of weaning from a ventilator, or to a life with a serious neurological deficit. Furthermore, they often do not see a problem or conflict arising from their requests. In contrast, the healthcare team may foresee major confusing problems [16]. Fully appreciating how DNR requests avoid unnecessary suffering, members of the healthcare team do not want to cause the patient's death by being limited in their capacity to respond to unforeseeable but easily reversible problems (such as the need to secure the airway or to give vasopressors or antiarrhythmic agents), frequently encountered in even routine circumstances. Thus, anesthesiologists want to be able to care for patients without having their hands tied.

There are also many other problems that can arise that are not easily foreseeable. An episode of rapid atrial fibrillation or supraventricular tachycardia causing profound hypotension can revert to normal sinus rhythm on its own even in a patient who proscribed defibrillation or cardioversion. Such a problem left untreated for just a few minutes could cause the patient to suffer precisely the outcome (alive but neurologically profoundly damaged) that he or she wanted to avoid by forbidding resuscitation.

In previous decades the most common way of resolving these conflicting imperatives was to temporarily "suspend" the DNR order before going to the operating room. Yet such automatic practices do not fully address the concerns and rights of these patients. While many healthcare teams still do this, the practice is contrary to current guidelines and against the law in some jurisdictions. The current guidelines of the American Society of Anesthesiologists and the American College of Surgeons recommend a reconsideration of DNR orders before surgery [17, 18].

The ASA guidelines suggest the following three approaches:

> "1. Full Attempt at Resuscitation:
> The patient or designated surrogate may request the full suspension of existing directives during the anesthetic and immediate postoperative period, thereby consenting to the use of any resuscitation procedures that may be appropriate to treat clinical events that occur during this time."
> "2. Limited Attempt at Resuscitation Defined with Regard to Specific Procedures:
> The patient or designated surrogate may elect to continue to refuse certain specific resuscitation procedures (for example, chest compressions, defibrillation, or tracheal intubation). The anesthesiologist should inform the patient or designated surrogate about which procedures are essential to the success of the anesthesia and the proposed procedure and which procedures are not essential and may be refused." (Depending on the type of anesthesia or surgery, certain procedures may not be necessary. For example, intubation may not be needed for monitored anesthesia care, and vasopressors may not be needed for a slowly dosed epidural.)
> "3. Limited Attempt at Resuscitation Defined with Regard to the Patient's Goals and Values:
> The patient or designated surrogate may allow the anesthesiologist and surgical team to use clinical judgment in determining which resuscitation procedures are appropriate in the context of the situation and the patient's stated goals and values. For example, some patients may want full resuscitation procedures to be used to manage adverse clinical events that are believed to be quickly and easily reversible but to refrain from treatment for conditions that are likely to result in permanent sequelae, such as neurologic impairment or unwanted dependence upon life-sustaining technology."[1]

In instances when a patient does not want a full reversal of their DNR status, the last of these options is preferred. When DNR status has been changed for the perioperative period, it is appropriate to maintain the changes until after discharge from the Post Anesthesia Care Unit.

Clinical Ethics Consultation

Making decision in the context of modern medicine's complexities is often challenging with ethical issues arising in virtually any clinical setting. A partial list of the challenges where clinical ethics consultation might be needed is shown in Box 37.1.

Box 37.1 Reasons for Perioperative Ethics Consultation

- Informed consent
- Confidentiality
- Decisional capacity
- Surrogate decision-making
- Refusal of treatment
- Clarifying the goals of care
- Conflict concerning discharge
- Medical futility
- Withdrawing or withholding care
- End-of-life decision-making, palliative care
- Demands for non-indicated medical care
- Truth-telling
- Family conflict or conflicts among team members
- Religious objections to treatment
- Protection of vulnerable populations
- Duality of purpose (intersection of clinical care with a second purpose, e.g., research, product development)

[1] Excerpted with permission of the American Society of Anesthesiologists from Ref. [17]. A copy of the full text can be obtained from ASA, 1061 American Lane, Schaumburg, IL 60173–4973, or online at www.asagq.org.

The goal of ethics consultation has been described as follows: to "support informed, deliberative decision making on the part of patients, families, physicians, and the health care team. By helping to clarify ethical issues and values, facilitating discussion, and providing expertise and educational resources, ethics consultants promote respect for the values, needs, and interests of all participants, especially when there is disagreement or uncertainty about treatment decisions" [19]. A simple rule guides the need for ethics consultation: if you think you need one, you probably do.

Ethics consultations may be carried out by a full committee, a small team, or an individual consultant. Although more unwieldy and difficult to mobilize, the ethics committee format has the advantages of the diverse perspectives of an interdisciplinary group of individuals with backgrounds in medicine, nursing, social work, and the clergy; representatives of the lay community are often added to help ensure the deliberations include the patient's perspective. Specific rules of engagement that apply to ethics consultation have been enumerated by the American Medical Association [19]:

1. To balance the concerns of all stakeholders, focusing on protecting the patient's needs and values.
2. To serve as advisors and educators rather than decision-makers.
3. Patients should be informed when an ethics consultation has been requested. Whether or not the patient or their family chose to participate should be respected.
4. The rights and privacy of all participants must be insured (i.e., preservation of confidentiality).
5. Those who perform ethic consultation should have appropriate expertise or training.
6. Policies and procedures governing ethics consultation services must be in keeping with medical staff bylaws, including accountability and documentation standards.
7. Ensure that all stakeholders have timely access to ethics consultation.[2]

Hospital-based ethics committees may play a number of important roles among which include establishing patient prognosis, educating both patients and caregivers, and the development of hospital policy; its most important function is making healthcare-related recommendations in difficult circumstances [20].

[2]Used with permission of the American Medical Association. American Medical Association. Opinion 10.7.1 Ethics Consultations. AMA Code of Medical Ethics. https://www.ama-assn.org/delivering-care/ethics/ethics-consultations. Published 2016. Accessed September 25, 2019. © Copyright American Medical Association 2016. All rights reserved.

Summary

Perioperative medicine is a unique microcosm of clinical care and involves processes designed to safely and efficiently deliver interventional care for specific types of medical condition. Effective implementation of these practices requires the standardization of surgical, medical, nursing care as well as social support. During surgery, perhaps more so than in any other aspect of healthcare, we ask the patient to completely surrender self-control with confidence that a team of individuals will help them overcome a specific disease process. It is an immense investment of trust by the patient and an equally significant acceptance of responsibility by the perioperative team. Systems which balance medical expertise, safety, and efficiency yet respect the individuality of the patient must be developed carefully, monitored, and constantly reassessed. Bioethics provides the best means by which healthcare systems can achieve this goal.

Summary Bullet Points

- Bioethical analysis can be guided by assessing each clinical situation from the perspective of the autonomy of the patient; justice in the provision of care; and the extent to which the clinician's actions are beneficent and nonmaleficent.
- Clinicians in perioperative medicine should understand issues related to informed consent, capacity, competence, advanced directives, and the right to refuse care.
- Clinicians in perioperative medicine have a professional duty to recognize when care violates the basic principles of bioethics, and to actively intervene to correct it.

Case Study

Refusal of Care and "Do Not Resuscitate" Orders

The patient was a woman in her late 60s with advanced adenocarcinoma of unknown origin, metastatic to her hip producing extreme, unremitting pain. A journalist whose expertise was in healthcare, she had a supportive husband and two adult children, though the latter lived thousands of miles away. With a DNR ordered established she believed she had about 6 months to live; her oncologist thought it was half of that time.

The patient was strongly desirous of undergoing surgery for the relief of pain. She nonetheless did not want to reverse her DNR order as she did not want her life to

be extended in the event of major neurologic injury with surgery. Furthermore, she did not want to be intubated nor to have chest compressions or defibrillation under any circumstances. She was willing to receive medications to support her blood pressure if needed. Indeed her primary goal of surgery was to end her life pain-free and sufficiently cognitively intact to say goodbye to her children in a meaningful way.

She proceeded to surgery with an anesthetic plan of sedation and an epidural with invasive monitoring that included an arterial and a pulmonary artery catheter. The surgeon determined that he would have to cement a hip prosthesis and, in anticipation of potential embolization during seating of the femoral prosthesis, large vent holes were placed in the canal. Despite the gentle seating of the prosthesis, within moments the patient's blood pressure dropped to near zero with flattening of the radial and pulmonary artery catheter waveforms signifying massive embolization. Vasopressors were immediately administered to no effect. With virtually no blood pressure the patient stopped breathing though remained in normal sinus rhythm. Because the duration of episodes of cement reaction such as this is unpredictable, the anesthesiologist feared that doing nothing more could very well leave the patient alive but neurologically damaged, precisely the outcome she wanted most to avoid. Chest compressions were begun, restoring a blood pressure and spontaneous ventilation and allowing for completion of the surgery. Postoperatively, with normal vital signs and breathing spontaneously, the patient did not wake up after arrival in the PACU. With the surgical team emotionally drained and devastated, the anesthesiologist discussed the outcome of surgery with the patient's husband who wept.

By the next morning the patient's mental status and neurological status had normalized and she lived for another 2 months. Her children came to be with her. Her anesthesiologist visited with her at her home where the patient and her family expressed their profound gratitude.

Discussion

This case demonstrates the benefits of allowing the perioperative team to use their best judgment to determine which procedures to use in order to achieve an outcome most consistent with the patient's goals and values. It should also be appreciated for the cautionary tale that it is as the outcome, while optimal under the circumstances, was far from assured. Decisions such as these are, by definition, made in the moment with no promise concerning the outcome. Taking patients to the operating room with a DNR order in force is fraught with moral hazard. No one should underestimate the suffering that poor outcomes can visit upon all involved.

Among the healthcare team, the burdens of poor outcomes in these circumstances are disproportionately borne by the anesthesiologist. It is the anesthesiologist who will make most of the split-second decisions concerning which treatments to pursue or withhold when the patient has chosen a limited resuscitation. If the patient has chosen to limit specific treatments and interventions, it is the anesthetic management (the techniques chosen, the drugs administered, fluids, etc.) that will determine outcomes as conversations pertaining to the limiting of resuscitation typically do not include limitations on surgical procedure. Indeed something as routine as an obstructed airway under sedation during a regional anesthetic can present a moral crisis when it does not respond to the usual simple measures. When such problems arise, moments are pivotal, the needs immediate, the decisions critical, and the consequences monumental. They are circumstances that will be re-lived over and over by providers and the patient's family. Sources of blame (and self-blame) exist on all sides and include not just what was done (or not done), but also a re-visiting of the adequacy of the preoperative counseling with regard to the range of possible outcomes and ultimately the choices made.

Finally the ASA guidelines on DNR in the OR recognize that some anesthesiologists may have views that cannot be reconciled with the limitations that might be imposed and allows for them to withdraw from participation "in a non-judgmental fashion" in a given patient's care. Similar considerations for other members of the team would seem appropriate even if their professional societies have not yet addressed this issue.

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