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PERIOPERATIVE MEDICINE SUMMIT
USING EVIDENCE TO IMPROVE QUALITY, SAFETY, AND PATIENT OUTCOMES

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Foreword:

Why perioperative medicine matters more than ever

More than 33 million surgeries are performed annually in the United States at a cost of $450 billion. Each year approximately 1 million patients sustain medical complications after surgery, such as myocardial infarction, heart failure, stroke, pneumonia, respiratory failure, venous thromboembolism, delirium, or renal failure. These complications cost the US health care system $25 billion annually.[1]

The portion of the US population older than 65 is estimated to double in the next 2 decades, from 35 million to 70 million people. This growth, due in part to increasing longevity among the elderly, is expected to lead to a 25% increase in the number of surgeries, a 50% increase in surgery-related costs, and a 100% increase in complications from surgery.[1,2] In other words, a large surgical burden is in store in the coming years, so large that some see it as an impending crisis for the US health care system.

To prepare health care providers to better deal with this growing surgical burden, we decided to hold the "1st Perioperative Medicine Summit: Using Evidence to Improve Quality, Safety and Patient Outcomes" on September 22–23, 2005, in Cleveland. We invited experts both from within The Cleveland Clinic and from across the nation to provide state-of-the-art lectures on a broad range of topics essential to the practice of perioperative medicine. More than 200 clinicians attended the summit and left armed with evidence-based risk assessment tools, guidelines, and recommendations. We believe that they are now better equipped to assess preoperative risk and to prevent and manage postoperative medical complications.

This CME-certified supplement to the *Cleveland Clinic Journal of Medicine* represents the proceedings of the summit, consisting of review articles developed directly from lectures and panel discussions presented at the summit. We are pleased that more than 32,000 physicians across the United States are receiving this supplement, as we hope it will increase the summit's impact in this critical area of medicine.

We hope you find this supplement useful and will consider attending our 2nd Annual Perioperative Medicine Summit, to be held September 18–19, 2006, at the InterContinental Hotel and MBNA Conference Center on The Cleveland Clinic campus. We are very excited about the upcoming summit, which will be held in conjunction with the newly formed Society for Perioperative Assessment and Quality Improvement (SPAQI). Details on the upcoming summit can be found on the inside back cover of this publication and at *www.clevelandclinicmeded.com/perioperativemed.htm*.

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The preoperative evaluation and use of laboratory testing

FRANKLIN A. MICHOTA, JR., MD

A thorough preoperative evaluation requires a medical consultant's time and skill. The primary elements of the evaluation are a comprehensive history, a focused physical examination, and effective communication with the surgical team.

Preoperative laboratory testing can be a valuable tool in the preparation of the evaluation, but should be conducted on a selective rather than routine basis. When laboratory testing is ordered without being justified by a specific sign, symptom, or indication, the clinical benefits are minimal and the costs are high.

This article outlines the specific components of the preoperative evaluation and offers guidelines for the use of laboratory testing.

ROLE OF THE MEDICAL CONSULTANT

Contrary to dogma, the role of the medical consultant is not to "clear" the patient for surgery, which would suggest that no problems will occur. Instead, it is to make a precise medical diagnosis, evaluate the extent of organ disease, optimize medications, assess and describe physiologic limitations, and ensure adequate postoperative care and follow-up care. Recommendations for anesthesia should be left to the anesthesiologist.

PREOPERATIVE EVALUATION

The purpose of the preoperative evaluation is to provide information for the surgeon, anesthesiologist, or perioperative team that will assist in determining the best plan of action for the patient. The preoperative evaluation entails a thorough review and documentation of the patient's history as well as a complete review of systems. The evaluation should incorporate drug history, surgical and anesthetic history, alcohol and tobacco use, allergies to drugs and latex, bleeding history, functional class, and physical examination.

Drug history

Ask patients which medications they are taking, including all prescription medications, over-the-counter drugs, and alternative or herbal therapies. Unless specifically asked, patients often do not mention herbal therapies.

Herbal therapies. Tsen et al[1] found that 22% of patients were taking herbal therapies at the preoperative visit, most commonly echinacea, ginkgo biloba, St. John's wort, garlic, or ginseng. Additionally, Harnack et al[2] reported that 61% of 376 adults surveyed in a large metropolitan area had used herbal products within the past 12 months.

All herbal therapies have properties that may affect surgical outcome (Table 1). Herbal therapies to be avoided preoperatively are the "three Gs": ginseng, garlic, and ginkgo biloba. Each of these herbs inhibits platelet activity, which increases the potential for bleeding. Patients should therefore be advised to not take any of these three therapies close to the time of surgery (see article on perioperative medication management, page S82 of this supplement, for specific recommendations on when to stop these therapies).

Latex allergy

Although latex allergy is uncommon in the general population, it occurs in about 5% to 10% of patients in high-risk groups. High-risk groups for latex allergy include patients with spina bifida, those with chronic urologic problems who frequently undergo bladder catheterization, patients with a history of atopic dermatitis, and health care workers.

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Functional class

The Duke Activity Status Index, a brief self-administered questionnaire, is a useful tool for determining and documenting the degree of physiologic stress that patients can handle.[3] The index includes a number of common physical activities ranging from running to being bedbound, and places the patient into one of four functional classes based on the single most difficult activity that he or she can perform (Table 2). A metabolic equivalent is listed for each functional classification.

The risk of perioperative cardiovascular complications is low for patients reporting that they can tolerate 4 or more metabolic equivalents of activity, but most patients do not participate in regular physical activity.

Occasionally, further questioning or observation will reveal a discrepancy between the patient's reported level of activity and actual level of activity. For instance, a patient who reports mowing the lawn every week may be riding a lawn tractor rather than pushing a mower. Another patient may say that he plays tennis three times a week but is observed to have trouble getting out of a chair and onto the examining table.

In a study of 600 consecutive outpatients undergoing preoperative evaluation for 612 major noncardiac procedures, Reilly et al[4] confirmed the validity of self-reported exercise tolerance in predicting perioperative risk.

Physical examination

The physical examination should be focused and should constitute less than 15% of the preoperative medical evaluation, since little that is uncovered during the physical examination would not have already been predicted by talking with the patient and learning about active symptoms.

Nevertheless, important information can be gleaned from the physical examination. One of the most obvious tasks is visual examination of the planned incision site for abnormalities. Other signs not to be missed are lack of range of motion in the neck, poor teeth, gum abscesses, irregular pulses or bruits, signs of edema, petechiae, hemorrhage, clubbing of fingers, and organomegaly.

Communicating findings with the clinical team

An important part of the preoperative evaluation is communication with the surgeon, anesthesiologist, and overall perioperative team.

Summarize your preoperative evaluation by listing the diagnoses and functional class in a quantitative way and by outlining the perceived risks for perioperative complications. This information should be the basis for determining whether to proceed with surgery or perhaps to do a less invasive procedure with shorter operating time.

TABLE 1
Potential effects of preoperative use of common herbal therapies

Echinacea	Immunostimulant; hepatotoxicity
Ginseng	Platelet inhibitor; hypoglycemia
Garlic	Platelet inhibitor; preload reduction
Ginkgo	Platelet inhibitor; alters vasoregulation
St. John's wort	Upregulates P450; drug-drug reactions
Ephedra	Alters vasoregulation; hypertension; ventricular arrhythmias
Kava	Potentiates sedation; drug-drug reactions

The preoperative evaluation should include general recommendations in relation to further cardiac risk stratification, medications, prophylaxis for venous thromboembolism or subacute bacterial endocarditis, and postoperative care issues.

ROLE OF LABORATORY TESTING

Preoperative laboratory testing should be selective, not routine. A routine test is a screening test for which an abnormality would be unexpected.[5–10] All preoperative testing should be justified based on a specific sign, symptom, or diagnosis.

Normal laboratory test results obtained 4 to 6 months before surgery may be used as preoperative tests, provided there has been no change in the clinical status of the patient, according to MacPherson et al.[11] They found that less than 2% of test results conducted 4 months before surgery had changed at the time of the clinical evaluation.

Abnormal test results

Two standard deviations from the mean, or 2.5% above or below the cutoff point for the reference range of a particular preoperative test, is considered abnormal for continuous variables. When a single laboratory test is conducted in a population without known disease, 5% of subjects can be expected to have an abnormal value; when a chemistry panel of 20 tests is ordered, the likelihood of one abnormal result rises to 64%.[9]

Remarkably, clinicians ignore 30% to 60% of

TABLE 2
Functional class: Duke Activity Status Index

Functional class	Metabolic equivalents	Activity
I	> 8	Run, swim, play tennis, ski
II	4–5	Yardwork, climb stairs, walk up a hill
III	< 4	Light housework, grocery shopping, walking
IV	< 4	Bedbound, limited activities of daily living

Adapted from reference 3.

abnormalities found on routine preoperative tests.[12] Ignoring abnormal test results can have legal ramifications, so reviewing the results of tests ordered is obviously important.

Diagnostic abilities of tests

The true diagnostic abilities of the tests ordered should be understood. For example, the sensitivity of an electrocardiogram for detection of coronary artery disease (CAD) is 0.27, and its specificity is 0.81. Assuming a prevalence of CAD of 20% would yield 162 positives in 2,000 patients being screened, of which 108 would be false, leading to possible subsequent unnecessary testing. On the other hand, the diagnosis would be missed in 146 patients who would be sent off to surgery despite having occult CAD.

Clinical value of testing: More is usually not better

A mistaken belief exists that voluminous information obtained from preoperative laboratory testing, regardless of how extraneous, enhances the safety of care. In reality, considerable data suggest that these tests are not needed. Additionally, the cost for preoperative evaluation is great: 10% of the more than $30 billion spent on laboratory testing each year is for preoperative evaluation.[8]

The clinical benefits of laboratory tests have been evaluated in several studies. Korvin et al[13] reviewed the test results of 1,000 patients who each underwent 20 chemical and hematologic tests during admissions screening, for a total of almost 20,000 tests. Of the 2,223 abnormal results found, 675 had been predicted on clinical assessment, 1,325 abnormalities did not yield new diagnoses, and 223 led to 83 new diagnoses in 77 patients. None of the diagnoses, however, was found to be unequivocally beneficial.

Kaplan et al[7] studied randomly selected test result samples of 2,000 patients who had undergone routine laboratory screening before having elective surgery. Of 2,785 preoperative admissions tests studied (1,828 not indicated), 96 were abnormal, 10 were unanticipated, and only 4 were clinically significant.

Turnbull and Buck[14] also reviewed the results of routine tests conducted before elective surgery. Of 5,003 tests ordered, 225 had abnormal results, 104 were judged clinically relevant, and only 4 may have resulted in clinical benefit. A similar analysis by Rucker et al[15] of 905 surgical admissions, 872 of whom had chest radiographs, who were screened for the presence of clinical risk factors revealed that 368 had no risk factors, and only one serious abnormality was found in these 368 patients. Of the 504 patients with identifiable risk factors, 22% had serious abnormalities, all of which had been predicted previously by the history and physical examination.

Lawrence et al[16] conducted a cost analysis of routine urinalysis before total knee replacement surgery. Assuming the incidence of wound infection to be approximately 1%, that 10% of urinalysis results reveal infection, and that each positive urinalysis result increases the risk of total knee replacement wound infection by about 1%, routine urinalysis was found to potentially prevent wound infection in 0.001% of patients annually at a cost of $1.5 million.

TESTING GUIDELINES

Recommendations for tests should be based on a sign, symptom, or diagnosis for which abnormalities would likely be expected. Tests to consider include a chemistry profile, complete blood count, coagulation profile, aspartate transaminase/alanine transaminase (AST/ALT), and urinalysis (Table 3).

Chemistry profile. Some clinicians have advocated a chemistry profile to check renal function before major surgery in all patients older than 50 years[9] because renal insufficiency is a potent predictor of postoperative complications in both cardiac and noncardiac surgery.[17,18]

Coagulation profile. A coagulation profile (including prothrombin time and partial thromboplastin time) is generally ordered because we believe it is safer to know whether or not a patient has proper clotting ability. Yet most scientific evidence shows that ordering these tests does not add clinical value unless the patient has a history of abnormal bleeding. Abnormal coagulation times in asymptomatic patients usually lead to additional testing that does not change the operative management or outcome.

Liver function tests. Signs of chronic liver dis-

ease or alcohol use are obvious indications for AST/ALT tests. Albumin may be measured because we believe that it is a potent predictor of perioperative complications in older patients having major surgery. This laboratory value, however, probably is not often found to be abnormal in an unanticipated fashion.

Electrocardiography. Some clinicians have also advocated ordering an electrocardiogram before major surgery for all patients older than 50 years. Yet electrocardiographic results do not generally alter the perioperative plan, except for patients with a history of cardiac problems.

Pulmonary function tests. The American College of Physicians promulgates guidelines for the use of pulmonary function tests, but these tests (like radiographs) are probably of little clinical utility except for patients being assessed prior to coronary artery bypass graft surgery or lung resection. Order these tests infrequently unless the patient has signs of pulmonary disease.

TABLE 3
Guidelines for preoperative laboratory testing

Test	Indications
Chemistry profile	History of hypertension, diuretic use, COPD or obstructive sleep apnea, diabetes, renal disease, chemotherapy
Complete blood count	History of fatigue, dyspnea on exertion, liver disease, blood loss, signs of coagulopathy, tachycardia
Coagulation profile	History of VTE, warfarin use, signs of coagulopathy, chronic liver disease
AST/ALT	Signs of chronic liver disease, hepatitis, alcohol abuse
Urinalysis	Signs of cystitis, genito-urologic procedure
Electrocardiogram	History of hypertension, diabetes, tobacco use, hyperlipidemia, CAD, arrhythmia, CHF, family history or signs of heart disease, syncope
Echocardiogram	Uncharacterized murmurs, signs of cor pulmonale, decompensated CHF
Chest radiograph	Signs of pulmonary disease
Pulmonary function tests	Signs of pulmonary disease, lung resection, CABG
Carotid duplex ultrasound	Carotid bruits, signs of stroke or transient ischemic events

COPD = chronic obstructive pulmonary disease; VTE = venous thromboembolism; AST/ALT = asparate aminotransferase/alanine aminotransferase; CAD = coronary artery disease; CHF = congestive heart failure; CABG = coronary artery bypass graft surgery

CONCLUSIONS

A thorough preoperative evaluation is an important first step in achieving a good perioperative outcome. The evaluation should concentrate on a comprehensive history and a focused physical examination. Laboratory tests should not be "routine" but should instead be selected based on a specific sign, symptom, or diagnosis.

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The surgical burden:

How to prevent a crisis in perioperative medicine

MICHAEL F. ROIZEN, MD

Three major issues are at the forefront of the current surgical burden in the United States: patients are given too little responsibility for their health, the aging population has a desire for functional recovery, and too few specialists and registered nurses are trained in anesthesia and perioperative medicine. This combination of factors has led to an imbalance of supply and demand for perioperative care.

This article will focus on the preoperative evaluation as a means to improve efficiencies in perioperative care that result in desirable outcomes while decreasing the institutional costs associated with surgery.

REASONS FOR THE BURDEN

Too little patient responsibility

Patients currently accept too little responsibility for their own health, in part because physicians have not motivated them adequately to stay healthy. An example is the poor rate of control of hypertension in the United States; only 34% of patients diagnosed with hypertension are able to achieve adequate blood pressure control.[1] Achieving more optimal control is hypothesized to require the same process changes involved in the optimal preventive maintenance of a car:

- Removal of inconvenience and cost (eg, free pills delivered through the mail)
- Ability to monitor and setting of ideal goals (eg, blood pressure measurement device for home use and accountability via wireless transmission of results)
- Emotional attachment (to one's body) and education from the "mechanic" (physician or nurse) that emotionally grabs the patient as to the importance of the health goal.

Aging population

Meanwhile, the population is aging and people desire functional recovery. Yet this desire comes at a price: medical care expenditures increase threefold for every extra decade of life.[2,3]

Imbalance in need and supply

The imbalances in need and supply that contribute to the surgical burden are numerous. Few institutions in the United States have perioperative assessment or preoperative anesthesia consultation and evaluation facilities. Across the nation, there are too few critical care beds, nurses, physicians, and health care dollars.

The burden will be compounded by an expected epidemic of diabetes. In 2000, the number of people with diabetes stood at 171 million worldwide; the World Health Organization projects that by 2030, that number will jump to 366 million.[4] Health issues such as diabetes and obesity create a significant cost burden, including the cost of procedures such as bariatric surgery.

AVERTING A CRISIS: PROPOSED SOLUTIONS

One proposed solution to address the surgical burden is to implement bypass processes in which the healthiest patients are excluded from routine preoperative evaluation. Although this approach may be acceptable at the level of an individual institution, in my opinion it is unacceptable from a societal perspective because the perioperative period is an ideal time to motivate patients to adopt healthier behaviors.

Another potential solution is to work with other providers such as nurse practitioners and medical assistants to gather patient information. The use of information systems is enhancing medical care, but ultimately the most significant factor to minimize the surgical burden will be to make patients healthier.

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Disclosure: Dr. Roizen reported that he owns stock in and earns book royalties from RealAge Inc.

TABLE 1
Cost-benefit analysis of the preoperative visit

Costs of a preoperative visit	**Minutes**	**Dollars**
Physician time	20	67.00
Paperwork/computer time	10	5.00
Secretary scheduling	20	3.00
Facility costs*	40	16.00
Total cost		**91.00**
Benefits of a preoperative visit	**Time savings**	**Dollar savings**
Avoided laboratory costs†	—	27.00
Reduction in operating room time‡	8 min	64.00
Reduction in cancellations§	—	9.00
Reduction in hospital stay¶	0.33 days	105.00
Total cost savings		**205.00**
Net savings per patient		**$114.00**

*Based on $1 million cost, 8-year depreciation, and 60 patients/day.
†Based on $100 charge paid at 30%, less $3 for unspecified costs.
‡At $8.00/minute.
§Calculated as 2% of (60 min × [cost per hour ÷ minutes per hour]).
¶At $950/day paid at 30%.
Modified from Fischer[5] based on personal communications with Stephen P. Fischer, MD.

Preoperative clinic: Savings to the institution

In 1996, researchers at Stanford University assessed the cost-benefit ratio of the preoperative visit and found that it resulted in a net savings of $114 to the institution (Table 1).[5] The savings did not appear in the preoperative clinic's balance sheet; rather, they were realized by the entire institution as a result of a reduction in hospital days, fewer cancellations, and minutes saved in the operating room. This finding reinforces the benefit of implementing this type of program on an institution-wide basis rather than in an independent internal medicine clinic or an anesthesia preoperative clinic.

New paradigms in patient evaluation

The American Society of Anesthesiologists (ASA) Task Force on Preanesthesia Evaluation issued its Practice Advisory for Preanesthesia Evaluation in 2002, which has generated some new ideas about patient evaluation.[6] The advisory focuses on the timing of the evaluation, the choice of tests, and a recommendation that no tests beyond a physician evaluation be ordered for patients undergoing minimally invasive surgical procedures as long as the patient's primary care physician judges that he or she cannot further optimize the patient's condition.

TABLE 2
When to perform the preoperative evaluation: American Society of Anesthesiologists advisory

Surgical invasiveness	**Severity of disease**	**Timing**
High	Any	Prior to day of surgery
Any	High	Prior to day of surgery
Not high	Low	On or prior to day of surgery

Adapted from reference 6.

Serum albumin levels. The ASA advisory recommends that albumin levels be obtained for all patients. Serum albumin levels are highly predictive of postoperative mortality.[7] An albumin level of 1.9 g/dL or less is associated with a 6-month mortality greater than 50%, regardless of the absence or presence of other risk factors. If a patient cannot achieve an albumin level greater than 2.1 g/dL with alimentation (either oral or hyperalimentation), discussion about end-of-life care and related issues is in order.

Procedure invasiveness. The ASA also recommends that if surgery is highly invasive, or the patient's disease is severe, the patient should be seen prior to the day of surgery. The advisory states that patients who do not fall into those categories can be bypassed for a preoperative evaluation (Table 2).[6] Seeing these patients in advance may still have value, however, to encourage them to adopt healthier lifestyle choices. Patients are rarely more motivated to adopt healthy behaviors than when they come in before an operation.

The data support preoperative laboratory testing only with highly invasive procedures. With moderately invasive procedures, the benefit of laboratory tests is unclear. No data demonstrate that preoperative laboratory tests are of value with minimally invasive procedures. Because of the quality of anesthesia and perioperative care, noninvasive procedures such as a colonoscopy are not much riskier than getting a haircut.

One of the largest studies evaluating medical testing and noninvasive procedures was conducted in patients undergoing cataract surgery. Schein et al[8] studied 18,189 patients undergoing cataract surgery to determine whether routine medical testing (electrocardiography, complete blood count, and measure-

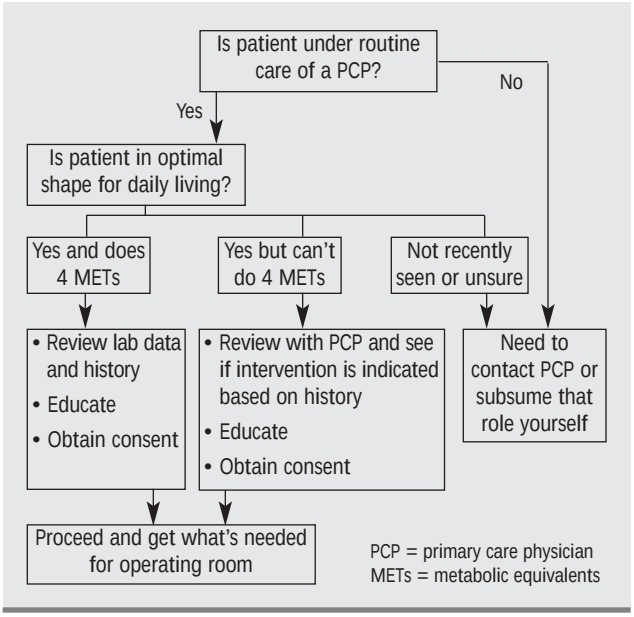

FIGURE 1. Algorithm for the preoperative evaluation of patients undergoing minor surgery. Management relies on whether the patient is in optimal shape for daily living and on his or her exercise intensity as measured in metabolic equivalents.

ment of serum levels of electrolytes, urea nitrogen, creatinine, and glucose) is associated with a reduction in intraoperative and postoperative medical complications. All patients received a physical examination and their medical histories were recorded, whether or not they received the medical tests. There were no significant differences in the rates of intraoperative events, postoperative events, hospitalizations, or deaths between patients who underwent routine testing and those who did not. Lira et al[9] obtained similar results and concluded that it is more efficient not to request preoperative tests for patients undergoing cataract surgery unless indicated by patient history or physical examination.

These study results should not be extrapolated to mean that no laboratory tests are ever needed for patients undergoing noninvasive surgery. Rather, they indicate that no laboratory tests are necessary if the patient's primary care physician has seen the patient and determined that he or she cannot further optimize the patient's condition. The underlying message is that preoperative assessment is best performed by physicians rather than by laboratory tests.

'RULE OF THREES'

Following the "rule of threes" should ensure that no important component of the preoperative evaluation is overlooked. This rule states that three aspects in each of three evaluation areas—the physical examination, the acute history, and the chronic history—are judged important in the evaluation. These aspects relate to nonsurgical procedures as well as to surgery.

Physical examination

Airway evaluation is the first key aspect of the physical examination, since airway problems during anesthesia are a leading cause of morbidity and increased cost.

Cardiovascular health is the second important aspect, and includes blood pressure, heart rate, and pulses.

Patient satisfaction is the third key component and is predicated on the notion that patients expect the physician to do certain things during the examination, and if the physician doesn't, patients can lose faith in the physician and the institution. For example, patients expect to have a stethoscope applied to their chest, even though a history of lung disease or symptoms is more meaningful than applying a stethoscope. Patients may lose confidence in the system, however, if the physician doesn't apply the stethoscope, and this unmet expectation risks degrading the patient's perception of the overall quality of care.

Acute history

Exercise tolerance. The first key aspect of the acute history demonstrated to be of value is exercise tolerance (ie, can the patient do 4 metabolic equivalents [METs] of activity, which is equal to climbing two flights of stairs or walking more than four blocks without stopping?). An inability to perform 4 METs of activity should arouse suspicion of congestive heart failure or coronary disease.

The METs criterion comes primarily from two studies. The first, by Reilly et al,[10] found that the complication rate for noncardiac surgery in 600 elderly patients nearly doubled if they were able to do less than 4 METs vs 4 METs or more of activity (20.4% vs 10.4%, respectively; $P < .001$). Those results were replicated by Sgura et al.[11] Eleven other studies have verified that the 4-MET rule can be used to predict complication rates in vascular surgery, bariatric surgery, and other forms of surgery.

An algorithm that incorporates patients' level of activity in METs (Figure 1) can be useful in determining the recommended level of preoperative evaluation for patients undergoing minor surgeries or procedures.

Medications. The second key consideration is medications, including supplements, and why they are being taken.

Acute problems. The third aspect focuses on acute problems and when the patient last saw a physician.

Chronic history

The three important aspects of the chronic history are the history of hospitalizations and surgeries, family history, and social history.

ECONOMIC CONSIDERATIONS

Approximately 33 million surgeries are performed each year in the United States, at an annual cost of $450 billion.[12] These numbers and costs will only rise in the years ahead, owing to the aging population and growing surgical burden discussed above.

Because of this huge volume of patients who undergo surgery, the preoperative evaluation, when considered across the full population of surgical patients, constitutes one of the single most expensive aspects of US medicine. Nevertheless, the preoperative evaluation saves economic resources in the long run, as demonstrated by the Stanford University study discussed above.[5] Even greater cost savings could be realized, as up to 40% of preoperative testing currently performed by many institutions could be eliminated without significantly increasing the risk of adverse outcomes.[13,14]

Selective ordering of tests

Unnecessary laboratory tests can be eliminated by considering whether the patient's condition and the proposed therapy or corrective procedure warrant a specific laboratory test. In a trial of 3,866 patients, Charpak et al[15] established and implemented a protocol at a teaching hospital in Paris, France, for selective ordering of preoperative chest radiographs, based on the patient's clinical status, medical history, and scheduled surgery. Five internists, four anesthesiologists, and three surgeons agreed on the protocol, and 11% of the tests were still ordered without indication. Unfortunately, 42% of the indicated tests also weren't ordered.

New pathways may be necessary

Deming and Juran said it best for the automobile industry in the 1960s when they attributed repeated breakdowns in productivity and accuracy to the system, not the worker. Likewise, if unnecessary tests are still being ordered and appropriate tests are not despite the efforts of internists, surgeons, and anesthesiologists to educate themselves, then something is wrong with the system of preoperative evaluation and a new system is needed.

Examples of new systems-based solutions are emerging. For instance, clinicians at the University of Chicago found that use of an interactive system that suggests appropriate tests for patients after the patient enters his or her personal medical data safely eliminated 81% of glucose testing costs and more than 50% of overall testing costs (personal communication). Another example involves radical retropubic prostatectomy (RRP), which has traditionally required a 5-day hospital stay. Alternate clinical pathways for RRP were initiated at the University of Chicago and included epidural anesthesia with or without spinal anesthesia followed postoperatively by intramuscular methadone, acetaminophen, and ibuprofen for pain control. Mean hospital stay was reduced from 4.9 days to slightly more than 1 day without a change in satisfaction with analgesia or overall satisfaction, and the readmission rate declined.[16,17]

PHARMACOLOGIC PROPHYLAXIS

A few simple pharmacologic measures instituted preoperatively can result in a substantial reduction in perioperative risk. Following is a brief introduction to the use of these therapies in the preoperative setting, each of which will be explored in greater depth in subsequent articles in this supplement.

Beta-blockers

The first large study focusing on prophylactic beta-blocker use prior to surgery was the Multicenter Study of Perioperative Ischemia (McSPI),[18] which demonstrated that preoperative beta-blocker use reduced the risk of postoperative myocardial ischemia. This study and others support the preoperative use of beta-blockers in patients with risk factors undergoing noncardiac surgery.

Aspirin

Routine discontinuation of aspirin therapy prior to noncardiac surgery is being questioned, given that the McSPI database demonstrated that taking a single aspirin daily for 3 days prior to surgery reduces the risk of adverse outcomes in cardiac surgery patients.[19] Two other ongoing studies are assessing the effect of aspirin prior to surgery on outcomes following cardiac surgery and vascular surgery.

Statins

Giving a statin prior to high-risk, highly invasive surgery can decrease the perioperative risk, even if therapy begins as little as 3 days prior to surgery.[20,21]

Immunizations

Immunizations against pneumococcus and influenza have been shown to decrease the length of hospital stays and decrease readmission rates over a 6-month period.[22]

SUMMARY

Preoperative patient evaluation can minimize the surgical burden and help prevent a crisis in perioperative medicine. Relieving the surgical burden involves a shift from practicing medicine to practicing preventive care in the preoperative environment, as well as motivating patients to adopt healthier behaviors over the long term.

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Anesthetics and anesthesia techniques:
Impacts on perioperative management and postoperative outcomes

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Inhaled and intravenous anesthetic agents have diverse effects on the nervous, cardiovascular, and respiratory systems, as do local anesthetics administered neuraxially. New evidence suggests that they also alter the inflammatory response. This article provides an overview of how anesthetic agents and their method of administration differentially affect perioperative management and long-term postoperative outcomes.

QUALITIES OF GENERAL ANESTHESIA

General anesthesia involves the use of inhaled or intravenous anesthetic agents and has four broad objectives or components:

- Unconsciousness (also referred to as hypnosis)
- Analgesia (insensitivity to pain)
- Attenuation of sympathetic nervous system responses to the noxious stimuli of surgery
- Skeletal muscle relaxation.

INHALED ANESTHETIC AGENTS

Inhaled anesthetics, also known as volatile agents, include desflurane, enflurane, halothane, isoflurane, and sevoflurane. These fluorinated hydrocarbons are simple molecules with the ability to exert potent physiologic effects at very low concentrations. They are general anesthetics and are often used in conjunction with intravenous agents as well as with skeletal muscle relaxants.

The inhaled anesthetics act by making cells more porous to chloride ions via interactions with protein channels in the lipid membrane. It is unknown whether increased ionic movement occurs because the drugs are incorporated within the lipid membranes, making them more fluid and causing conformational change of the ion channels, or whether the drugs interact with receptors in or near the protein channels, changing the channel conformation.

Effects on the central nervous system

Within the central nervous system, inhaled anesthetics interrupt transmission of excitatory and inhibitory pathways, causing amnesia and hypnosis. The cerebral cortex is affected, as are the more primitive areas of the brain, including the hippocampus, thalamus, and brainstem reticular formation. At high concentrations, the drugs penetrate the spinal cord and inhibit transmission at synapses, causing muscular paralysis and altering descending input from the brain.

Cardiovascular effects

The cardiovascular effects of inhaled anesthetics are direct and can be significant, with impacts on the following:

Contractility and diastolic function. All inhaled anesthetics alter the heart's ability to regulate calcium intracellularly, resulting in depressed contractility and diastolic dysfunction.

Heart rate. Some inhaled agents, like halothane, when used in high concentrations, cause profound bradycardia. High levels of desflurane, on the other hand, sometimes cause tachycardia, which is often seen in young, healthy patients.

Blood pressure. All the inhaled agents reduce arterial blood pressure, either through lowering systemic vascular resistance, contractility, and cardiac output, or by reducing left ventricular afterload.

Ischemia. Ischemia is of concern during general anesthesia, and many patients develop silent ischemia postoperatively. The strongest predictor of ischemia during surgery, however, is preexisting ischemia, a factor often more important than the surgical procedure itself or the anesthetic used.

Arrhythmias. Inhaled agents reduce sinoatrial

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node discharge, which can result in bradycardia and atrioventricular conduction abnormalities. Often, elderly patients without a documented history of cardiac disease but who report occasional "fluttering in the chest" or "strange rhythms" develop arrhythmias during anesthesia, which disappear as the agents wear off.

These drugs can have proarrhythmic or antiarrhythmic effects after myocardial ischemia and infarction: some induce arrhythmia but others may be protective. They also can prolong QT intervals, putting patients who have prolonged-QT syndrome at risk for torsade de pointes.

Several procedures, including many gynecologic and otolaryngologic surgeries, require local anesthetics and epinephrine to reduce blood loss. Combining inhaled anesthetics with epinephrine increases the risk of inducing ventricular tachycardia.

Myocardial protection. In addition to adverse cardiovascular effects, inhaled anesthetics can exert myocardial protective effects as well. All of the inhaled agents are weak coronary vasodilators. Isoflurane and other inhaled agents, despite what was once believed, do not cause coronary steal syndrome.[1] Instead, they appear to be cardioprotective against both reversible and irreversible ischemic insults, via several mechanisms:

- Reduced myocardial oxygen demand, owing to these agents' depressive effects
- Reduced release of reactive oxygen species after ischemia or an infarct has occurred
- Anesthetic preconditioning, in which cells are conditioned to tolerate ischemia through the reduced release of reactive oxygen species and through direct effects in the mitochondria of myocytes.

Pulmonary effects

Bronchodilation. Inhaled anesthetics are potent bronchodilators and theoretically help patients with chronic obstructive pulmonary disease or asthma. Bronchodilation occurs as a result of smooth muscle relaxation caused by depressed contractility, as also occurs in cardiac muscle. These agents also directly affect bronchial epithelium and indirectly inhibit local neural pathways within the lungs and spinal cord, resulting in reduced bronchoconstriction.

In reality, however, the manipulation of the airway required to administer general anesthesia can result in bronchospasm in patients with severe reactive airway disease, even if they are premedicated with steroids and inhalers, and inhaled anesthetics may actually serve to stop the attack of bronchospasm.

Reduced functional residual capacity. At the same time, inhaled anesthetics also reduce functional residual capacity, increasing airway resistance. Patients with reactive airway disease have increased morbidity and mortality from anesthesia, which may be partially explained by this reduced functional residual capacity and the harm caused by mechanical ventilation.

Reduced clearance of mucus and foreign bodies. Inhaled anesthetics reduce ciliary movement, hampering the clearing of mucus and foreign bodies from the lungs.

Reduced surfactant production. Inhaled anesthetics impair the ability of type II alveolar cells to produce phosphatidylcholine, the main component of pulmonary surfactant.

Effects in spontaneously breathing patients. In patients who are spontaneously breathing, inhaled anesthetics can reduce both tidal volume and minute ventilation and cause tachypnea, resulting in increased "work of breathing."

INTRAVENOUS ANESTHETIC AGENTS

Intravenous anesthetics are typically used to induce anesthesia, while inhaled agents are used to maintain general anesthesia afterwards. The exception is for children, in whom induction can be achieved with the inhaled agents halothane or sevoflurane alone.

Profiles of three representative agents

Three common intravenous anesthetics are propofol (an alkylphenol), thiopental (a barbiturate), and etomidate (an imidazole). Despite having different chemical structures, they all interact with GABA receptors in the brain and potentiate chloride movement, which may explain their ability to cause amnesia and hypnosis for short periods after administration.

Propofol is the most widely used anesthetic worldwide. It has both hypnotic and mild analgesic properties. It is antiemetic at low doses and has been also used for this purpose in patients undergoing chemotherapy.

Propofol causes mild cardiovascular changes: continuous infusion reduces both myocardial blood flow and oxygen demand. It decreases systemic blood pressure through vasodilation and direct myocardial depression, reduces cardiac output, stroke volume, and systemic vascular resistance, and causes minimal conduction changes.

Like the inhaled agents, propofol has bronchodilatory effects.

Thiopental and other barbiturates cause sedation,

loss of consciousness, hypnosis, and significant cardiac and respiratory depression. They have no analgesic properties.

Barbiturates cause blood to pool in veins as a result of venous dilation; they also reduce cardiac output through negative inotropy, increased capacitance, and decreased central sympathetic tone. Barbiturates also increase heart rate via baroreceptor actions. These drugs must be used cautiously in patients with cardiac disease who may not be adequately prepared with beta-blockers.

Etomidate causes minimal cardiac depression, so it is commonly used in cardiology for cardioversions and other procedures. It also causes minimal respiratory depression; patients may continue to breathe despite being completely unconscious unless a muscle relaxant is also given.

Etomidate has no analgesic properties. For invasive procedures, a narcotic or a beta-blocker is needed to attenuate the sympathetic nervous system responses.

LOCAL ANESTHETICS

Local anesthetics come in two classes: esters (eg, chloroprocaine, cocaine, tetracaine) and amides (eg, bupivacaine, lidocaine, ropivacaine). They vary in their half-lives and how they are used, and are widely administered for field blocks, peripheral nerve blocks, and neuraxial blocks (both spinal and epidural).

Cardiovascular effects

Many "complications" of neuraxial anesthesia (as well as of general anesthesia) are actually expected physiologic responses to particular drugs. For example, administering a local anesthetic neuraxially results in sympathectomy, which may slow the heart rate, reduce systemic vascular resistance, and lower arterial blood pressure. These responses are predictable for patients with or without cardiac disease.

Preblock hydration (ie, with up to 2,000 mL intravenous fluids, such as a colloid or crystalloid) does not prevent hypotension or otherwise adequately protect patients with cardiovascular disease who are about to undergo a neuraxial block.[2] In such patients, intravascular volume loading only transiently increases stroke volume and cardiac output because the fluid redistributes quickly. In these cases, pharmacologic cardiovascular protection is needed.

Respiratory effects

Local anesthetics administered neuraxially result in an unchanged tidal volume, while vital capacity decreases slightly.

Administering an unintentionally high spinal anesthetic can result in respiratory arrest. There is a misconception that this occurs because of phrenic nerve dysfunction or respiratory muscle paralysis. However, this is not possible because of the small volume of drug being administered and the large anatomic distance from the brainstem. Respiratory arrest is actually caused by brain hypoperfusion: when fluids and drugs to increase blood pressure are administered, the patient's apnea resolves.[3]

Gastrointestinal effects

Nausea and vomiting develop after neuraxial administration of local anesthetics in many patients, probably as a result of hypotension caused by the sympathetic blockade and the resultant reduced arterial blood pressure as well as the unopposed parasympathetic response of increased peristalsis.

Hepatic blood flow is reduced as a result of spinal anesthesia, which can be dangerous for patients with liver disease. Many physicians hope to avoid problems by using a neuraxial block instead of a general anesthetic, but any neuraxial block reduces both hepatic blood flow and hepatic oxygen uptake.

Epidural vs spinal administration

Compared with spinal anesthesia, epidural anesthesia involves administration of larger volumes of local anesthetics over longer periods of time (such as for lower extremity revascularization procedures). Despite perceptions to the contrary, the onset of reduced arterial blood pressure is *not* more gradual or of less magnitude with epidural anesthesia as opposed to spinal anesthesia.

LOCAL VS GENERAL ANESTHESIA: EFFECT ON POSTOPERATIVE CLINICAL OUTCOMES

In the perioperative period, outcomes are influenced by anesthetics, the techniques used to deliver them, and patients' preexisting medical conditions. Although the long-term effects of anesthetics on outcomes have not been well studied, some data are beginning to emerge.

Local anesthesia improves cardiovascular outcomes

Three published studies have examined the outcomes of patients who received either epidural anesthesia and analgesia or general anesthesia without a regional block.

Christopherson et al[4] reported a study of 100 patients scheduled to undergo lower extremity revascularization procedures who were randomized to epidural anesthesia followed by epidural analgesia or to general anesthesia followed by intravenous

patient-controlled analgesia. The postoperative revascularization rate was significantly higher in patients who received general anesthesia (20%) than in those who had epidural anesthesia (4%). No differences were found between the groups in postoperative myocardial infarctions or deaths. The institutional review board stopped the study early, citing a clear relative benefit of epidural anesthesia.

In another randomized trial, Tuman et al[3] compared postoperative epidural analgesia or on-demand narcotic analgesia in 80 patients who underwent lower extremity revascularization under general anesthesia. In the patients randomized to epidural analgesia, epidurals were placed intraoperatively. The group that received epidural analgesia had fewer thrombotic events as well as fewer cardiovascular, infectious, and overall postoperative complications. Length of stay in the intensive care unit was also reduced in the epidural analgesia group.

Yeager et al[5] randomized 53 high-risk patients who were about to undergo major noncardiac surgery to receive either epidural anesthesia and postoperative analgesia or standard anesthetic and analgesic techniques without an epidural. Patients who received epidural anesthesia and analgesia had a reduced postoperative complication rate, a lower incidence of cardiovascular failure, fewer major infectious complications, and fewer deaths. Hospitalization-associated costs were also 40% lower in the group that received epidurals.

Local anesthesia reduces blood loss

Compared with general anesthesia, epidural anesthesia is associated with less blood loss in patients undergoing total hip replacement or urologic procedures such as transurethral resection of the prostate or radical retropubic prostatectomy. Reduced blood loss probably results from the fact that sympathetic blockade reduces arterial blood pressure, redistributing blood flow from the surgical site.[6] Central venous pressure is also reduced, as epidurals are performed without the positive pressure ventilation inherent in general anesthetic procedures.[7]

Local anesthesia reduces thromboembolic risk

Surgery enhances coagulation, and epidural and spinal anesthesia can help avoid this phenomenon. Local anesthetics directly inhibit platelets as well as reduce platelet-fibrinogen actions.[8] In addition, sympathetic blockade increases lower extremity blood flow.[9]

In a meta-analysis of 13 randomized trials comparing local and general anesthesia in patients undergoing hip fracture repair, Sorenson and Pace[10] demonstrated a 31% reduction in the incidence of deep venous thrombosis and pulmonary embolism in patients receiving spinal or epidural anesthesia.

Similarly, Sharrock et al[11] retrospectively examined more than 15,000 patient records from one institution before and after the hospital transitioned from general anesthesia to epidural anesthesia for patients undergoing total hip and total knee arthroplasty. They found that the incidence of pulmonary embolism declined from 0.4% before the shift to epidural anesthesia to 0.1% after the shift.

DEPTH OF ANESTHESIA CORRELATES WITH POSTOPERATIVE OUTCOME

Recent inquiries into the relationship between anesthesia and postoperative outcomes have begun to focus on an issue specific to general anesthesia—the patient's intraoperative level of unconsciousness or their "depth" of anesthesia.

Two methods of measuring anesthesia depth

Until recently, depth of anesthesia was estimated only by observing patient physiologic responses (heart rate, blood pressure) to surgical stimuli and respiratory patterns as well as ocular position and pupillary diameter. Now, two currently available methods of measuring the depth of anesthesia use processed electroencephalic (EEG) information and convert the data into a unitless scale ranging from zero (no EEG activity) to 100 (fully conscious).

The bispectral index monitor gathers EEG data from the frontal cortex only but assumes uniform global data.

The patient state index monitor gathers EEG data from the front, back, and top of the head.

Data supporting a correlation with outcomes

The first studies suggesting a correlation between depth of anesthesia and patient outcomes were reported in abstract form. Weldon et al[12] used the bispectral index monitor to evaluate 907 patients while they underwent major noncardiac surgery of at least 2 hours' duration. They found that deeper maintenance anesthetic levels were associated with higher 1-year postoperative death rates in patients aged 40 years or older. Similarly, in a study of more than 5,000 patients, Lennmarken et al[13] found that the risk of death within 1 year after surgery increased nearly 20% for every hour that a patient had a bispectral index monitor score of less than 45 (indicating deep hypnotic time) during the surgery, although the total duration of surgery or anesthesia did not affect mortality. Other risk factors for death included male gender, *lower* body mass index, and higher American Society of Anesthesiologists Physical Status score

(indicating poorer health) at the time of surgery.

More recently, Monk et al[14] evaluated more than 1,000 patients who underwent noncardiac surgery and found that increased cumulative deep hypnotic time (bispectral index monitor score < 45) was a significant independent predictor of death within 1 year of surgery.

IS INFLAMMATION THE KEY TO POSTOPERATIVE RESPONSE?

Studies indicating that the depth of anesthesia is proportional to mortality raise the question of why this is so. We are increasingly recognizing the importance of inflammation in this process.

We now understand that inflammation is a driving force in many disease states, including atherosclerosis. In response to injury—such as a surgical procedure—tissue responds with vasodilation, increased vascular permeability, chemotactic peptides, and white blood cells. This starts the inflammatory cascade, mediated by plasma proteases, lipid mediators, peptides, amines, cytokines, and the leukocytes themselves.

Of particular interest are cytokines, which include the interleukins and tumor necrosis factor. Cytokines are released into the circulation from the site of injury during surgery, and are also elevated in patients with cancer or atherosclerosis.

An inflammatory role for anesthetics?

It is possible that anesthetics themselves may augment the cytokine inflammatory response, and this response may be dose-related, such that a deeper level of anesthesia may trigger a greater response. Two types of cytokines exist—some are proinflammatory while others are anti-inflammatory—and anesthetics may alter their balance, possibly resulting in more complications, more infections, and a greater risk of death.

After surgery, lymphocyte levels and activity are reduced, a phenomenon that can be caused by intraoperative hypothermia as well as by a direct effect of volatile anesthetics. This may also predispose patients to poorer postoperative outcomes.

In addition, in patients who undergo total intravenous general anesthesia (eg, propofol without an inhalation agent), cytokine levels and other inflammatory responses postoperatively are significantly lower than in patients who receive a general anesthetic with an inhalation agent.[15]

SUMMARY

Inhaled and intravenous anesthetic agents have diverse effects on the nervous, cardiovascular, and respiratory systems. Spinal and epidural anesthetics also produce significant physiologic changes.

Some evidence points to improved immediate postoperative outcomes (in terms of cardiovascular outcomes, blood loss, and venous thromboembolism) for certain types of surgical procedures with epidural and spinal techniques relative to general anesthesia. Evidence is just beginning to emerge, however, on the relation between specific anesthetics and anesthetic techniques and long-term clinical outcomes. A proposed relationship between anesthetics, inflammation, and long-term outcomes has attracted increasing research interest but has yet to be well defined.

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Cardiac risk stratification before noncardiac surgery

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Cardiac risk stratification prior to noncardiac surgery can serve a number of goals: (1) to determine the patient's current health status, (2) to establish a surgical-risk profile, (3) to decide whether further cardiac testing is indicated, and (4) to identify actions or recommendations that might reduce the patient's perioperative risk.

This article discusses the elements of cardiac risk evaluation in noncardiac surgical patients, reviews cardiac risk indices and clinical guidelines, surveys options for cardiac testing in preoperative risk assessment, and explores the pros and cons of invasive prophylactic measures to reduce perioperative cardiac risk. Prophylactic medical therapy is discussed in the next article in this supplement.

This discussion applies, of course, to patients undergoing nonurgent surgery. For patients undergoing urgent nonelective surgery, preoperative risk assessment is moot because there is little time to perform testing and the results are not likely to influence the surgical approach. In fact, no test should be performed unless the result will change patient management.

DETERMINING CURRENT HEALTH STATUS

Health interview

The most important element of cardiac risk evaluation is the health interview because information on the patient's history and current status will serve as the basis for most of our decisions and actions.

History. A history of cardiovascular disease—particularly myocardial infarction (MI), angina, congestive heart failure (CHF), arrhythmia, or valvular disease—is obviously significant. In such cases, ascertain the type of diagnostic and therapeutic procedures the patient has already undergone, when and where they were performed, and the specific results.

There is little value to knowing that the results of a previous test were "okay." With regard to stress testing, we need specific information on, for example, the patient's peak heart rate, peak systolic pressure, and rate pressure product (RPP). The "ischemic threshold" is a very reproducible value in an individual patient. It is important to anesthesiologists because a patient is less likely to experience ischemia during surgery if the anesthesiologist can keep the RPP from exceeding this threshold. If the patient previously underwent a thallium stress test, we need to know about any reperfusion abnormalities, including the number of segments involved and their distribution. Important findings on echocardiography include wall-motion abnormalities, ejection fraction, and valvular anatomy and function. If the patient has undergone cardiac catheterization, knowledge of the presence of left main coronary artery disease or triple-vessel disease is not only vital before surgery but is also an independent indication for revascularization even if surgery had not been planned. Finally, we need to know if the patient has undergone revascularization procedures.

Current medical status. Significant risk factors for cardiac disease are diabetes, hypertension, hyperlipidemia, and cigarette smoking. The presence of other concomitant conditions—eg, peripheral vascular disease, cerebrovascular disease, chronic renal insufficiency, and chronic obstructive pulmonary disease (COPD)—may place patients at a higher risk for cardiac disease and perioperative complications than they otherwise would be.

Another important issue is the patient's functional status. Key factors include chest pain and shortness of breath as well as the patient's functional capacity. I specifically ask patients how many blocks they can walk and how many flights of stairs they can climb

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without stopping. Do not underestimate the severity of risk in home-bound patients who report no chest pain or shortness of breath; the amount of stress that they will experience during surgery (other than a minor procedure) will probably exceed the amount they exert during activities of daily living.

Age. Age may serve as a marker for decreased cardiac reserve or subclinical disease, but by itself has only minor significance.

Physical examination

If the patient provides thorough and honest answers during the health interview, the typical physical examination will usually serve only to confirm what is already known about the patient's current status. Potentially important findings include the following:

- Vital signs (arrhythmias, uncontrolled hypertension)
- A murmur (aortic stenosis, in particular)
- A third heart sound, jugular venous distention, or rales (heart failure).

Electrocardiography

Electrocardiography (ECG) is typically performed prior to surgery, but it rarely changes the management approach. For example, detecting a conduction defect, bundle branch block, left ventricular hypertrophy, or nonspecific changes in ST-T waves on ECG will not have any impact on surgical decisions. Finding Q waves in a patient with a history of an MI only confirms it. At best, an ECG will detect evidence of a recent silent MI, but this is rare. Finally, most arrhythmias are discovered on physical examination prior to ECG.

RISK STRATIFICATION

Based on the history, physical examination, and ECG, patients can be categorized as being in a low-risk, intermediate-risk, or high-risk group.

High-risk patients should be considered for further therapy and evaluation, including invasive testing. A noninvasive test in such a patient often adds little to what is already known. Moreover, a negative result on a noninvasive test is not as reliable in a high-risk patient because the result is more likely to be a false negative in this setting.

Intermediate-risk patients are numerous and their risk can be refined either up or down depending on the rigor of further evaluation. One option for such patients is additional testing; another is to proceed with surgery after initiating a trial of prophylactic medical therapy.

Low-risk patients can proceed to surgery without any further cardiac evaluation.

PUBLISHED GUIDELINES

Many cardiac risk indices and recommendations have been published over the years, but the most prominent are the guidelines developed jointly by the American College of Cardiology and the American Heart Association (ACC/AHA) in 1996[1] (and updated in 2002[2]), guidelines published by the American College of Physicians (ACP) in 1997,[3] and the Revised Cardiac Risk Index.[4]

ACC/AHA guidelines

These guidelines[1] were generally built around three major considerations in assessing risk: (1) the patient's clinical predictors, (2) the patient's functional capacity, and (3) the individual risks of specific types of surgery (Figure 1).

Clinical predictors. The three classifications of clinical predictors are major, intermediate, and minor. Most patients have intermediate or minor predictors.

Major clinical predictors are unstable coronary syndromes (including a recent [< 30 days] MI or class III or IV angina), decompensated CHF, significant arrhythmias, and severe valvular disease. (Note that the ACC/AHA defines "recent" as within 30 days, unlike older guidelines in which the time frame ranges from 3 to 6 months. The reason for this change is that now most patients with a recent MI routinely undergo various tests to stratify risk or therapeutic interventions during their hospitalization for the MI.) Patients with major clinical predictors should probably not undergo any elective surgery without further evaluation and treatment, be it angiography and revascularization, noninvasive testing, or just medical therapy and risk factor modification.

Intermediate clinical predictors include class I or II angina, a history of MI beyond the preceding 30 days, compensated or previous CHF, diabetes, and chronic renal insufficiency. Patients with intermediate predictors should be evaluated for exercise capacity by assessment of metabolic equivalents (METs) for oxygen consumption (Table 1). Patients undergoing low-risk surgical procedures do not require any further testing; however, a low METs score (≤ 4) indicates a potential need for noninvasive testing prior to intermediate- or high-risk surgeries. Further assessment of patients with a moderate or good score depends on the degree of surgical risk.

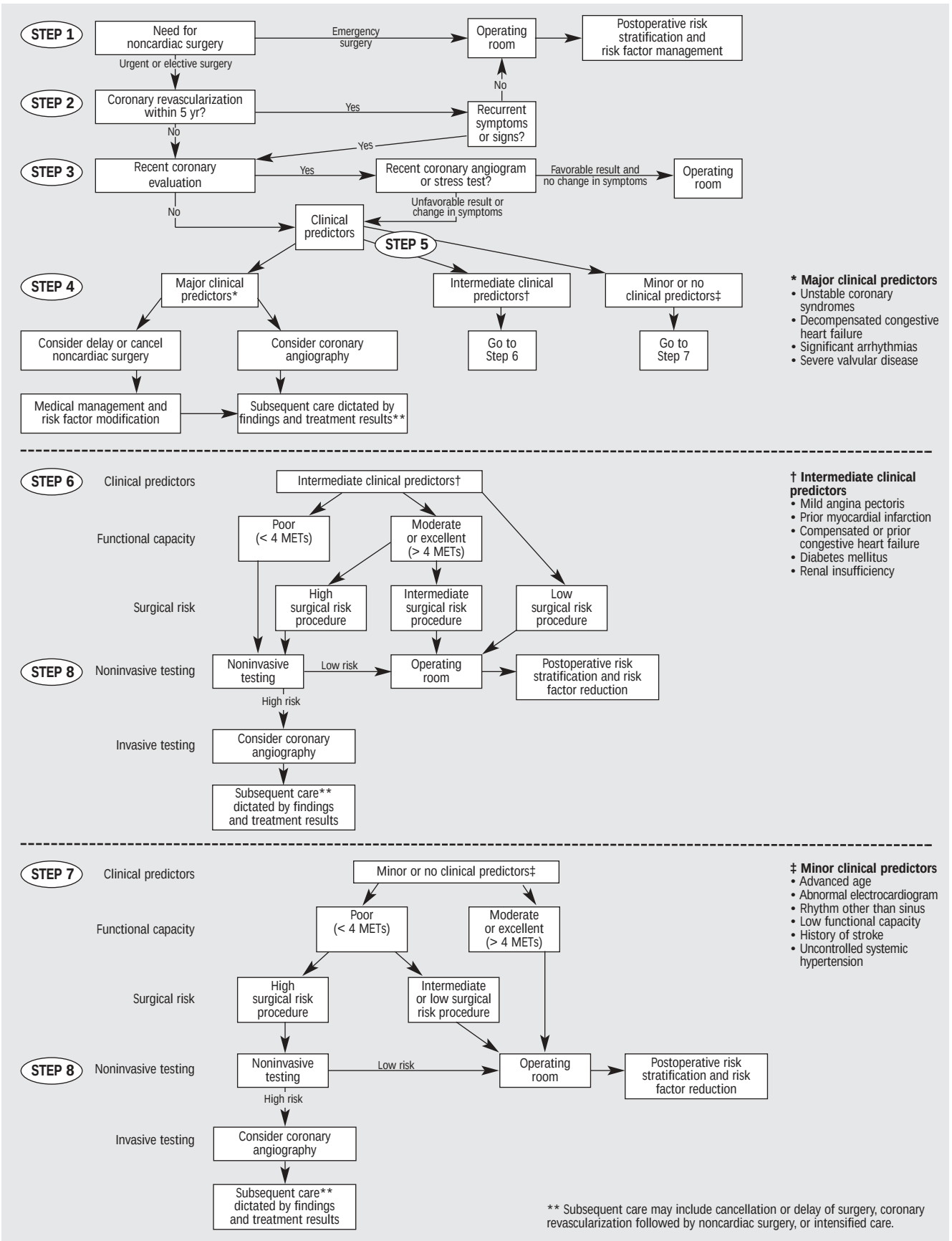

FIGURE 1. Stepwise approach to preoperative cardiac assessment. METs = metabolic equivalents. Reprinted from reference 2, copyright 2002, with permission from the American College of Cardiology Foundation.

Minor clinical predictors are advanced age, nonspecific ECG abnormalities, nonsinus rhythm, cerebrovascular disease, and uncontrolled hypertension. Patients with minor predictors also should undergo a METs assessment. Those with a moderate or good score can proceed to surgery, while others may or may not be candidates for noninvasive testing or medical therapy, depending on the surgical risk.

Surgery-specific risk. Different types of surgery are classified simply as high-, intermediate-, and low-risk.

High-risk surgeries are those associated with a predicted cardiac complication rate greater than 5%. These include major emergency surgery, procedures to correct aortic disease or significant peripheral vascular disease, and other prolonged procedures that involve significant fluid shifts, fluid administration, or blood loss. Most patients undergoing high-risk surgery should either undergo noninvasive testing or receive medical therapy, depending on their clinical predictors.

Intermediate-risk surgeries (expected cardiac complication rate of 1% to 5%) include carotid endarterectomy (which is classified separately from other vascular procedures because newer surgical techniques have lowered its risk), major head and neck operations, major joint replacement, repair of hip fracture, and intraperitoneal, intra-abdominal, and intrathoracic procedures. Open or radical prostatectomies are included in this list. Patients with adequate functional capacity (and no major clinical predictor) can undergo intermediate-risk surgery without further testing.

Low-risk surgeries (expected cardiac complication rate < 1%) are those that do not involve invasion of a body cavity, such as endoscopic procedures and superficial excisions. The risk of complications associated with these procedures is generally lower than the risk of preoperative cardiac testing and subsequent intervention, so adherence to the dictum "first do no harm" calls for allowing patients to proceed to these types of surgeries without testing.

Exercise capacity. The METs classification is used to determine exercise capacity. It is a fairly subjective evaluation. I consider a patient to be at risk if he or she cannot perform tasks that are assigned a METs value of 4 or less (Table 1). I generally ask patients how many blocks they can walk and how many flights of stairs they can climb without stopping. I consider patients to be at low (or at least acceptable) risk if they can walk at least three blocks and climb one flight of stairs without difficulty.

However, patient self-reports of exercise capacity are not always reliable, so when there is doubt, you can walk the patient up and down the hall or stairs to see firsthand what the patient can do.

TABLE 1
Estimated energy requirements for various activities

• 1 MET	• 4 METs
– Take care of self	– Climb 1 flight, go uphill
– Eat, dress, toilet	– Walk on level ground 4 mph
– Walk indoors	– Do heavy housework (scrub floors, move furniture)
– Walk 1 to 2 blocks (level) at 2 to 3 mph	– Do moderate recreational activities
– Do light work around the house (dust, wash dishes)	– Participate in strenuous sports
• 4 METs	• ≥ 10 METs

MET = metabolic equivalent

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ACC guideline shortcut for noninvasive testing. In general, noninvasive testing is indicated in the presence of two of the following three negative factors: intermediate or major clinical predictors, high-risk surgery, and poor exercise capacity.

ACP guidelines

The two main elements of the ACP guidelines[3] are the Detsky modified cardiac risk index and a list of "low-risk variables." Patients are first evaluated according to the Detsky criteria, and if they are found not to be at high risk, they are then evaluated according to the low-risk variables criteria.

Detsky index. This cardiac risk index was developed by Detsky et al and published in 1986.[5] A score of 20 points or more indicates high risk; point values are assigned for each of the following conditions:

- MI within 6 months (10 points)
- MI more than 6 months earlier (5)
- Class III angina (10)
- Class IV angina (20)
- Alveolar pulmonary edema within the previous week (10) or ever (5)
- Suspected aortic stenosis (20)
- Arrhythmias (5)
- Poor general medical condition (5)
- Age greater than 70 years (5)
- Surgery on an emergency basis (10).

Low-risk variables. "Low-risk variables" is a confusing term because the presence of these variables

actually indicates *higher* risk; it is the *absence* of these variables that indicates low risk.

There is significant overlap between the sets of so-called low-risk variables. Both Eagle et al[6] and Vanzetto et al[7] included in their lists age greater than 70 years, a history of angina, the presence of diabetes, and demonstration of Q waves on ECG. In addition, Eagle et al included a history of ventricular ectopy, and Vanzetto et al included a history of MI, demonstration of ST-segment ischemic abnormalities on resting ECG, hypertension with severe left ventricular hypertrophy, and a history of CHF.

Patients with fewer than 20 Detsky points who have 0 or 1 low-risk variable are considered to be at low risk (< 3% chance of complications), and those with 2 or more variables are considered to be at intermediate risk (3% to 15% chance of complications).

Evaluation steps. Patients who are young, who are undergoing minor surgery, who have no systemic disease, and who require emergency surgery can go directly to the operating room without further testing. For other patients, the next step is to incorporate the Detsky index. A Detsky score of 20 or more is comparable to a major clinical predictor in the ACC/AHA scheme, and it is an indication for further evaluation or treatment prior to surgery.

However, most patients have a Detsky score of 15 points or less, and at this point we consider the aforementioned low-risk variables. Patients with none or only one of these variables can proceed directly to surgery without testing. Likewise, patients with two or more low-risk variables who are undergoing *nonvascular* surgery require no further testing, but those with two or more low-risk variables who are scheduled for *vascular* surgery should undergo further noninvasive testing with either dipyridamole-thallium imaging or dobutamine stress echocardiography; also, we should determine their eligibility for beta-blocker therapy if needed. Patients whose imaging results are negative can proceed to surgery, but those with positive results are considered high-risk.

Once a patient is classified as high-risk (> 15% chance of complications) at any point during the evaluation process, we must postpone surgery until we determine the nature of the risk. Patients who have ischemic heart disease should be evaluated to determine if they are suitable candidates for coronary revascularization. If so, reevaluate after revascularization; if not, consider switching to a less risky procedure or canceling surgery.

Patients whose high risk is associated with CHF, arrhythmia, valvular disease, or modifiable risk factors should undergo a trial of optimal medical management and subsequent reassessment of their cardiovascular risks. Again, if optimal treatment or risk factor modification fails, consider switching to a less risky procedure or canceling surgery.

Differences between the ACC/AHA and ACP guidelines

The ACP guidelines are purely evidence-based; without evidence, the ACP makes no recommendation. The ACC/AHA, on the other hand, uses the best evidence available; when evidence is insufficient or lacking, it relies on expert consensus panels to make recommendations. Also, the ACP does not consider exercise capacity and the ACC/AHA does. Likewise, the ACC/AHA uses surgery-specific risk while the ACP divides surgery into vascular and nonvascular categories. In sum, the ACC/AHA tends to recommend more testing than does the ACP.

Other risk assessment systems

In 1999, Lee et al described their simple index, the Revised Cardiac Risk Index, which is based on a study of more than 4,000 patients aged 50 years or older who had undergone major elective noncardiac surgery.[4] They identified six independent predictors of major cardiac complications: (1) high-risk surgery, (2) preoperative treatment with insulin, (3) preoperative serum creatinine level greater than 2 mg/dL, (4) history of ischemic heart disease, (5) history of CHF, and (6) history of cerebrovascular disease.

An absence of these risk factors was associated with a 0.4% to 0.5% risk of a major cardiac complication, and the presence of one risk factor carried a risk of 0.9% to 1.3% (low risk in both cases). The risk was 4% to 7% for patients with two risk factors (intermediate risk) and 9% to 11% for those with three or more risk factors (high risk).

The shortcoming of this system is that the authors did not make any specific recommendations as to what to do with this information; however, subsequent publications did use this index in an algorithm with beta-blockers,[8] as discussed in the next article in this supplement.

In 2005, Kertai et al published their "customized" version of the Revised Cardiac Risk Index,[9] which is based on a point total similar to that used for the Detsky index. The Kertai system is different in that it also subtracts points for use of prophylactic medical therapy (beta-blockers and statins).

NONINVASIVE TESTING

Once the risk assessment indicates that further testing is advisable, the next step is to decide which tests are

appropriate. Noninvasive testing is usually the preferred first step. The common noninvasive tests are resting two-dimensional echocardiography, exercise stress testing with or without imaging, pharmacologic stress testing with nuclear imaging, and pharmacologic stress testing with echocardiography. Some are more useful than others.

Echocardiography

An ejection fraction of less than 35% may predict postoperative CHF, but it is not a consistent predictor of ischemic events. Therefore, resting two-dimensional echocardiography should not be used preoperatively to evaluate CAD. It might be helpful in a patient with CHF or suspected valvular disease, but it usually does not provide any useful information beyond what we already know clinically.

Exercise stress testing

The dynamic tests measure a patient's functional capacity, which can be impaired by old age, deconditioning, myocardial ischemia, and decreased cardiac or pulmonary reserve. One problem with ordering an exercise test is that we do not know whether the cause of functional impairment is cardiac or noncardiac. Another problem is that most patients cannot complete the test; fewer than half of tested patients reach their target heart rate, so their results are inconclusive. Ischemia at a low level of exercise, however, is significant.

Pharmacologic stress testing with nuclear imaging

Most of these tests use a dipyridamole stressor and thallium contrast. The endpoints are the size and number of reperfusion defects; fixed defects are less important for short-term prognosis. The negative predictive value is good (> 95%), but the positive predictive value is poor (4% to 20%).[2,10] These tests should not be used in patients with COPD, as dipyridamole may cause bronchospasm, but they are preferred over exercise and dobutamine stress testing for patients with left bundle branch block because the other modalities can yield false-positive results.

Pharmacologic stress testing with echocardiography

These tests are usually performed with dobutamine as a stressor to identify wall-motion abnormalities. The use of dobutamine more closely simulates true exercise in that it increases oxygen demand. Evidence of ischemia at low doses of dobutamine usually indicates more severe disease. Again, the negative predictive value is good (> 93%), but the positive predictive value for serious events is low (7% to 25%).[2,10]

INVASIVE PROCEDURES

Positive findings on noninvasive testing call for prophylactic measures—either a trial of medical therapy (discussed in the next article in this supplement) or an invasive procedure.

Prophylactic CABG. Keep in mind the fact that coronary artery bypass graft surgery (CABG) carries significant risks of its own. Among patients overall, the average risk of perioperative mortality during CABG is about 1% to 2%,[11] the risk of nonfatal MI is 2% to 5%,[12] and the risk of stroke is 1% to 3%.[13] These rates, of course, are higher in high-risk surgical patients.

Nevertheless, observational studies over the years have shown that previous CABG was associated with a lower rate of mortality and nonfatal MI during noncardiac surgery. Among all patients who underwent noncardiac surgery, perioperative mortality was 0.9% for those who had previously undergone CABG and 2.4% for those who had not. The corresponding rates for patients who underwent high-risk noncardiac surgery were 1.7% and 3.3%. Rates of nonfatal MI were 0.7% vs 1.1% overall and 0.8% vs 2.7% during high-risk noncardiac surgery. The protective effect of CABG lasted approximately 4 to 6 years. There was no benefit with CABG in those patients who subsequently underwent a low-risk noncardiac procedure.[14,15]

Percutaneous coronary intervention. Likewise, it appears that percutaneous coronary intervention (PCI) may also lower the risk of perioperative mortality and nonfatal MI (compared with historical controls). Studies suggest that noncardiac surgery should be performed no sooner than 7 to 10 days after balloon angioplasty[16] and no sooner than 4 to 6 weeks after coronary stent placement.[17–20] However, the prophylactic benefit of placing stents is questionable. A compilation of results from four studies using bare metal stents showed that despite preoperative stenting, complication rates with subsequent noncardiac surgery were high: mortality, 6.9%; nonfatal MI, 5.4%; and hemorrhage, 6.9%.[17–20] Likewise, drug-eluting stents may not be advisable prior to noncardiac surgery because they delay endothelialization and may require a longer period of dual-antiplatelet therapy (at least 2 to 3 months for sirolimus-coated stents and 6 months for paclitaxel-coated stents).

CABG-PCI study. A multicenter Veterans Administration study of men who underwent prophylactic preoperative CABG or PCI showed that coronary artery revascularization before elective vascular surgery in patients with *stable* cardiac symptoms did not significantly alter outcome.[21] A few study limita-

tions notwithstanding, including the fact that both groups were treated with intensive medical therapy, the authors could not recommend prophylactic revascularization. On the other hand, revascularization may be appropriate for patients with unstable or more severe cardiac symptoms.

Pulmonary artery catheterization. Although pulmonary artery catheterization might detect hemodynamic disorders that could lead to a change in treatment, there is no evidence that it prevents perioperative cardiac morbidity or mortality.[22] It might benefit the type of patients who are usually excluded from these clinical trials—eg, those with a recent MI, pulmonary edema, CHF, chronic kidney disease, or valvular disease—who undergo major surgery.

SUMMARY

The history and the physical examination remain the most important elements in cardiac risk stratification of patients prior to noncardiac surgery. Indications for further cardiac tests and interventions are usually the same as in the nonsurgical setting. No test should be performed unless the results will affect patient management. In many cases, noninvasive testing is being replaced by prophylactic medical therapy, a topic explored in the next article in this supplement.

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Perioperative cardiac risk reduction:

Doing it right

ANDREW D. AUERBACH, MD, MPH

Various interventions to reduce the risk of cardiac complications during surgery have been proposed. This article evaluates the evidence for these preventive approaches, examines methods of incorporating new and conflicting evidence into a coherent clinical approach, and reviews systems for successfully implementing evidence-based interventions in the hospital.

APPROACHES FOR PREVENTING CARDIAC COMPLICATIONS

With revascularization reserved as a preventive measure for those patients at extremely high risk of cardiac complications, other less invasive preventive approaches should be considered.

Maintenance of normothermia

One preventive approach is maintenance of normal body temperature. In a randomized, controlled clinical study of 300 patients with or at high risk for coronary disease who underwent major abdominal or vascular surgery, supplemental warming care was associated with a significant ($P = .02$) reduction in perioperative morbid cardiac events compared with routine thermal care.[1] The risk of supplemental warming is low and the potential reward is high; in addition to the reduction in cardiac complications, patients randomized to normothermia in this study had a lower rate of surgical-site infections, less nausea, and better pain control.

Calcium channel blocker therapy

A recent meta-analysis[2] demonstrated a significant reduction in adverse coronary endpoints with the use of calcium channel blockers, compared with placebo, as preventive therapy in patients undergoing various types of surgery. This reduction in the risk of events, however, was driven entirely by a significant reduction in the incidences of ischemia and supraventricular tachycardia, with no effect of calcium channel blockers on perioperative myocardial infarction (MI) or death. The largest reductions in risk with calcium channel blockers occurred in patients undergoing thoracic surgery. In most of the studies in which a favorable effect of calcium channel blockers was observed, patients were on concomitant beta-blockade that was not adequately controlled for, which obscures interpretation of the meta-analysis. For these reasons, calcium channel blockers should not be considered first-line therapy as a preventive strategy.

Perioperative adrenergic modulation: Clonidine and other alpha-2 agonists

Adrenergic modulation includes not only beta-blockers but clonidine and other alpha-2 agonists. A trend toward a reduction in mortality was observed in recipients of alpha-2 agonists (most often clonidine) in a meta-analysis of 23 trials that included 3,395 surgical patients.[3] In patients undergoing vascular surgery, who represent a higher-risk group in which a positive effect is more likely to be uncovered, these agents were associated with significant reductions in the risk of mortality ($P = .02$) and MI ($P = .02$) relative to placebo.

Clonidine is a hospital-only drug; it has no first-line indications in long-term patient care, which is a deterrent to its use since transition to therapy outside the hospital is difficult. Transdermal delivery is an advantage to the use of clonidine in the surgical setting. The patch can be applied in the preanesthesia holding area and then removed when the patient is discharged.

Perioperative adrenergic modulation: Beta-blockers

As in the ambulatory setting, beta-blockers reduce ischemia, prevent MI, and reduce mortality from

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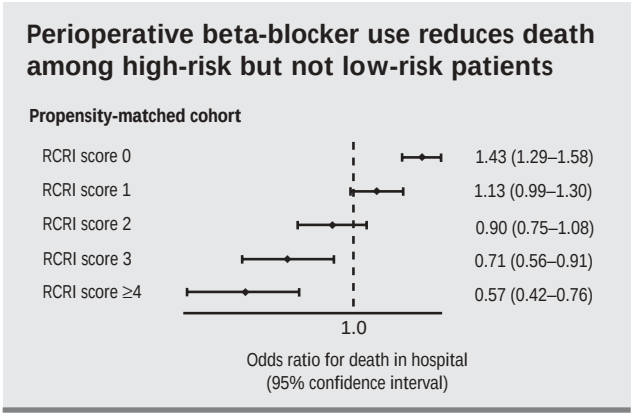

FIGURE 1. Adjusted odds ratio for in-hospital death associated with perioperative beta-blocker therapy in a review of patients undergoing major noncardiac surgery, according to patients' Revised Cardiac Risk Index (RCRI) score (the lower the score, the lower the cardiac risk).[13] Adapted, with permission, from Lindenauer PK, et al, N Engl J Med 2005; 353:346–361. Copyright © 2005 Massachusetts Medical Society. All rights reserved.

coronary artery disease (CAD) in the surgical setting.

In 2001, the Agency for Healthcare Research and Quality (AHRQ) ranked perioperative beta-blocker use for reduction of morbidity and mortality second only to venous thromboembolism prophylaxis in a ranking of patient safety practices according to the strength of supportive evidence.[4] Of note, perioperative beta-blocker use was rated higher than other well-established practices in surgical medicine, including antibiotic prophylaxis. This ranking of perioperative beta-blockers was based on four studies published from 1996 to 2001[5–8] showing that perioperative beta-blockade reduced the risks of death and MI. With beta-blocker prophylaxis, Mangano et al[5] found a 50% reduction ($P < .005$) in mortality at 2 years, Poldermans et al[6] reported a 90% reduction ($P < .001$) in cardiac death/MI at 28 days, Urban et al[7] found a 67% reduction in the risk of postoperative MI that did not reach statistical significance, and Boersma et al[8] reported a 70% reduction in the adjusted relative risk of MI.

Recent caveats. Since this AHRQ report, two randomized controlled trials in vascular surgery patients found metoprolol to have no effect on the incidence of major cardiac events.[9,10] Moreover, a meta-analysis of seven randomized controlled trials of beta-blockers in patients undergoing noncardiac surgery showed encouraging but not statistically significant beneficial effects on 30-day adverse outcomes.[11] As a result, the authors of the meta-analysis urged cautious interpretation of American College of Cardiology/American Heart Association guidelines[12] recommending perioperative beta-blocker treatment for varying groups of patients undergoing noncardiac surgery.

Greater benefit in high-risk patients. In 2005, a retrospective review of more than 600,000 patients undergoing major noncardiac surgery revealed that perioperative beta-blockers reduced the risk of in-hospital death among high-risk but not low-risk patients (Figure 1).[13] Among the patients with a Revised Cardiac Risk Index (RCRI) of 3, which indicates high-risk status, the risk of in-hospital death was reduced by 29% with beta-blockers compared with placebo. Among patients with an RCRI of 4 or greater, this risk was reduced by 43% with perioperative beta-blockade. This finding offers a potential explanation for the concentration of benefit of perioperative beta-blockers in patients undergoing vascular surgery, which is a higher-risk surgery.

A higher threshold for beta-blocker use? Most patients who are strong candidates for perioperative beta-blockers have indications for long-term beta-blocker therapy. The likelihood of an unexpected side effect from perioperative beta-blocker use is unclear, potentially reducing these agents' benefit-to-risk ratio in lower-risk patients. Because of the limited randomized data with beta-blockers in the surgical setting, as well as the reliance on observational data in making recommendations for their use, some have proposed raising the threshold for starting beta-blockers in surgical patients.

Statins

Observational data show a favorable effect of statin use on perioperative mortality, substantially paralleling statins' efficacy in the treatment of acute coronary syndromes. Statin therapy to reduce perioperative risk is intuitive, since most patients at risk for postoperative MI have long-term indications for statins.

Observational studies. Poldermans et al[14] found a 78% reduction in the adjusted risk of perioperative mortality among vascular surgery patients taking statins compared with those not taking statins. In an analysis of more than 600,000 patients undergoing noncardiac surgery,[15] statins reduced the risk of in-hospital death by 29%; the number needed to treat to prevent one death ranged from 30 in high-risk patients (RCRI ≥ 2) to 186 in low-risk patients. Kertai et al[16] found a 60% reduction in all-cause mortality and a 70% reduction in cardiovascular mortality with statin use, independent of beta-blocker use, over a follow-up of almost 5 years in a retrospective review of 530 patients undergoing surgery for abdominal aortic aneurysm. When modeling the effects of

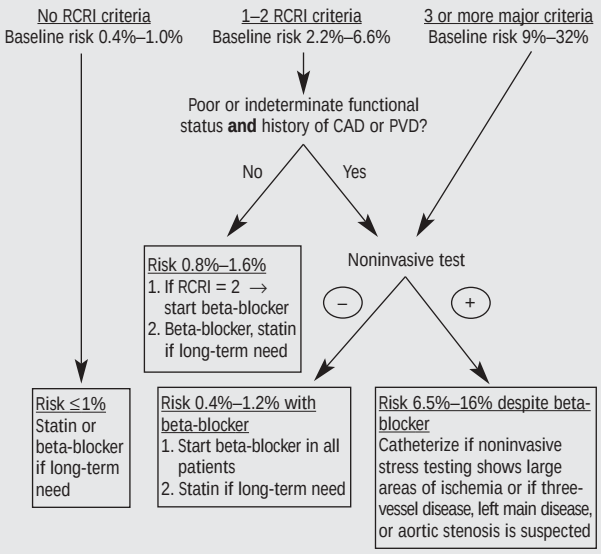

FIGURE 2. Algorithm for selection of patients for cardioprotective drug therapy and further testing before major noncardiac surgery. Adapted from reference 18.

different therapies, a synergism between statins and beta-blockers was suggested.[16]

Randomized trials. The one published randomized trial to date was a small study (N = 100) in which atorvastatin or placebo was started 1 month before vascular surgery.[17] Atorvastatin was associated with a 70% reduction in the combined endpoint of death from cardiac causes, nonfatal MI, unstable angina, and ischemic stroke. Liver function test abnormalities were more frequent in the atorvastatin group, but no patient had to discontinue therapy.

FORMULATING AN APPROACH TO CARDIAC RISK ASSESSMENT

Initial evaluation

In assessing the risk of cardiac complications, the initial evaluation should focus on finding new or unstable CAD, heart failure, or aortic stenosis.

During the evaluation, collect elements of the RCRI (see next section) and conduct a detailed review of symptoms. Listen for rales and bruits. Identify patients with unexplained or unstable symptoms and those who have a history of CAD or peripheral vascular disease plus poor or no exercise tolerance; in these patients, a preoperative electrocardiogram (ECG) is reasonable, to check for cardiac ischemia. Be aware that patients may report having angina or claudication in the past, but not recently, because they are no longer able to exercise or walk because of degenerative diseases.

If surgery is to be performed on an emergency basis, explain the risks and benefits of the surgery to the patient, surgeon, and family, and start cardioprotective agents (ie, beta-blockers) when able. Close postoperative monitoring (ie, telemetry, serial troponin measurements, and ECGs) is warranted following emergency surgery. The need for the intensive care unit should be decided on a case-by-case basis. Invasive intraoperative monitoring using right heart catheterization should be considered in selected patients, such as those with congestive heart failure or aortic stenosis.

TABLE 1
Revised Cardiac Risk Index (RCRI) criteria

History of coronary artery disease
History of transient ischemic attack or cerebrovascular accident
Creatinine >2 mg/dL
Diabetes mellitus
High-risk surgery (chest, abdominal, or pelvic vascular)

Use RCRI criteria to determine baseline risk

Use of the RCRI criteria to determine baseline risk is advised for selecting patients for further testing and/or beta-blockade before major noncardiac surgery (Figure 2).[18] Under the RCRI criteria, one point is awarded for each of the five criteria listed in Table 1; a risk class is then assigned based on the number of criteria present.

In the absence of RCRI criteria, which translates to an extremely low baseline risk of cardiac complications, beta-blockers or statins can be started if a long-term indication already exists for these agents. Because the presence of CAD is an indication for beta-blockade, patients whose lone risk criterion is CAD should be started on beta-blockers. Otherwise, secondary prevention should be practiced for a patient with an RCRI of 1.[18]

With an RCRI of 1 or 2, which corresponds to a baseline risk of 2.2% to 6.6%, noninvasive testing is recommended for patients with a history of CAD or peripheral vascular disease who have poor or indeterminate functional status. In patients with an RCRI of 1 or 2, a history of CAD or peripheral vascular disease, and normal exercise tolerance, beta-blockers should always be initiated, and statins can be started if needed long-term.[18]

Consider catheterization if large areas of ischemia are detected on noninvasive testing or if the patient has a high probability of three-vessel disease, left main disease, or aortic stenosis. Patients with three or more RCRI criteria have a 9% to 32% baseline risk of cardiac complications, and a noninvasive stress test is helpful to further stratify risk.[18]

IMPLEMENTING THE PRACTICE EFFECTIVELY

Know your systems

Understanding the systems in place at your institution is imperative for effective implementation of perioperative protective therapy. You should know the following:

- Which surgeons, anesthesiologists, and internists will be involved
- The final common pathway to the operating room
- How discharge medications are coordinated
- Who is available to screen patients, titrate drug dosages, and ensure continuity of medications.

Look at the preoperative clinic, preoperative holding area, operating room, and rehabilitation clinic/skilled nursing facility as opportunities to enter patients into the treatment algorithm. These are all potential places to start and titrate the dosage of beta-blockers, if deemed appropriate, and ensure that they are continued for the optimal duration of 30 days.

When to start therapy, and with which agent?

Starting beta-blocker therapy early, before admission, is optimal. The ideal time to start is when the patient is first referred for surgery, although a beta-blocker can still be initiated until the day of surgery—in the preanesthesia holding area, if necessary. The key to beta-blocker therapy is to start it soon enough to be able to titrate the dosage to reduce the heart rate to 55 to 65 beats per minute. In every clinical trial in which beta-blockers were shown to reduce cardiac complications in surgical patients, dosages had been titrated so that patients' heart rates were 55 to 65 beats per minute at the time of surgery.

With respect to the choice of beta-blocker, nonselective beta-blockers have the potential to induce bronchospasm and are associated with a greater likelihood of hypotension compared with selective beta-blockers, but agents within the class of beta-1-selective drugs (ie, atenolol, metoprolol) are roughly equivalent.

If a patient meets the criteria for beta-blockade but is receiving a calcium channel blocker, ask the patient's primary care physician to stop the calcium channel blocker for the surgery and switch to a beta-blocker.

Overcoming barriers

Effective implementation of protective agents is fraught with barriers. No one may want to take the responsibility for initiating protective agents, believing that someone else should do it. Objections may also take the form of "I have too many other things to think about." Strategies to overcome these objections should aim to put the task into the hands of someone who cares, make it so easy that there is no reason to object, and combine or simplify other tasks while adding the new one. For example, my institution recently rolled out a combined order set that encompasses deep vein thrombosis prevention, surgical infection prophylaxis, and perioperative beta-blocker use all in a single order, for use in all patients.

Consistent reinforcement through education is also crucial.

Finally, skeptics may claim not to believe the data. If this is the case, the contents of this review may appease them.

MOTIVATING YOUR HOSPITAL

A number of incentives can be used to motivate your hospital to adopt safety practices to prevent perioperative and postoperative cardiac complications. Not the least among these is the fact that operative mortality is reported publicly. Furthermore, perioperative beta-blocker use is a focus of national health care quality-improvement organizations such as the Surgical Care Improvement Project, the Leapfrog Group, and the National Quality Forum, and safety practices that are assessed by these groups are likely to be used as standards of care when hospital safety is graded by *Consumer Reports* and *U.S. News & World Report*.

Don't underestimate the challenge

Nevertheless, be aware that instituting patient safety practices is never easy. The difficulty is exemplified by two recent studies showing low utilization of perioperative beta-blockers.[19,20] One study found that 67% of ideal candidates for beta-blockade who underwent noncardiac surgery in one large US hospital did not receive perioperative beta-blockers.[19] The authors concluded that 62 to 89 lives could potentially be saved at their institution each year through full use of beta-blockade for eligible surgical patients. Even in Canada, where the efficacy of beta-blockers in the surgical setting is accepted almost universally by anesthesiologists, less than 10% of hospitals have a formal protocol in place for perioperative beta-blocker use, and less than 57% of surveyed anesthesiologists prescribed them regularly for this purpose.[20]

UCSF PERIOPERATIVE BETA-BLOCKER PROTOCOL

At my institution, the University of California, San Francisco, screening candidates for beta-blockade is conducted in the preoperative clinic for more than 95% of elective surgical cases. The eligibility criteria for beta-blockade are based on the algorithm mentioned previously (Figure 2). In eligible patients, oral metoprolol is started the day of screening or, in patients who are already receiving a beta-blocker, the dosage is titrated as needed. Postoperative dose titration is performed by physicians on the basis of the patient's heart rate. Metoprolol, 10 mg intravenously every 4 to 6 hours, is delivered in the telemetry unit in patients on NPO orders.

We have carry-through orders for discharge medications, in which beta-blockers are to be continued to day 7 or discharge, whichever is later, and continued indefinitely in patients with long-term indications for their use.

CONCLUSIONS

The preoperative evaluation represents a chance to screen patients for unstable symptoms that would require intervention even in the absence of surgery. It also represents an opportunity to initiate secondary prevention with beta-blockers and statins in appropriate patients.

Data to date indicate that perioperative adrenergic blockade appears to be effective in reducing morbidity and mortality in high-risk patients, but further data from randomized trials are needed to establish this definitively. The patients most likely to benefit from this therapy are those at the greatest cardiac risk (RCRI ≥ 2). Current evidence on statins in the perioperative setting is not robust enough to support their use in patients without a long-term indication for statin therapy.

The ingredients for an effective institutional approach to perioperative cardiac risk reduction are thorough knowledge of the key clinical players, identification of the final common pathway to the operating room, a coordinated "closing of the loop" at discharge, and a simple and well-integrated system for ordering perioperative protective therapy.

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Quality measurement:

Who is measuring outcomes and what are patients being told?

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Numerous outcomes and quality indicators are being measured in today's health care marketplace. These measurements are being performed by a variety of government agencies, health care purchasers and payers, not-for-profit organizations, and even individual health care institutions.

This article will review quality outcome measurements that are being collected and posted on public Web sites by the government, health care accrediting bodies, business groups, and insurance companies. It also will discuss new quality measures that these groups are planning as well as newer developments and trends in the quality measurement field.

ORGANIZATIONS MEASURING AND REPORTING QUALITY OUTCOMES

Medicare

The Medicare program, administered by the federal Centers for Medicare and Medicaid Services (CMS), has been collecting data for several years for 10 standardized quality measures covering three clinical conditions: acute myocardial infarction (MI), community-acquired pneumonia, and heart failure (Table 1). Although submission of data is optional, hospitals would stand to lose 0.4% of the 2005 market basket update for Medicare payments if they chose not to participate. As of January 2005, hospitals' performance in providing recommended treatments for these three clinical conditions has been reported on a public Web site.[1]

Challenges: The MI and vaccination examples. From a health care organization's standpoint, collecting and reporting these Medicare quality measures is not without its challenges. For example, withholding an angiotensin-converting enzyme (ACE) inhibitor or beta-blocker may be justified in certain patients with acute MI, yet this decision runs counter to the quality indicator for the treatment of acute MI. Convincing physicians to then document their valid reason for not performing an act is another hurdle, yet it affects the reporting denominator and thus an organization's performance rate if patients who should not get these drugs are not excluded.

Documenting whether or not a patient has received a pneumococcal vaccination provides another example. If patients present having already received their pneumococcal vaccination, is a note made that they have had it before? If this information is not excluded from the denominator, the reporting organization's performance rate is adversely affected.

The lag effect. Medicare quality measures may lag the latest science. For instance, angiotensin II receptor blockers were being used for treating heart failure once they were discovered to be effective alternatives in ACE inhibitor-intolerant patients, but until very recently CMS would only recognize and give credit for ACE inhibitor use. It took the CMS 9 months to revise this measure.

Future CMS measures. CMS is already reporting nursing home and home health quality data on its public Web site. We expect that the next target will be an expansion into the surgical arena, specifically measuring presurgical antibiotic prophylaxis and surgical site infection rates. CMS is also pilot testing a pay-for-performance reimbursement scheme for certain quality measures in 200 hospitals.

Joint Commission on Accreditation of Healthcare Organizations

As an accreditation requirement, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) requests the submission of data for

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TABLE 1
Medicare and JCAHO measures of quality

Acute myocardial infarction

- Aspirin given on arrival to emergency department
- Beta-blockers given on arrival to emergency department
- Aspirin prescribed at discharge
- Beta-blockers prescribed at discharge
- ACE inhibitors prescribed at discharge if heart failure is a secondary diagnosis
- Adult smoking cessation advice and counseling*
- Time to thrombolysis*
- Time to percutaneous coronary intervention*
- Inpatient mortality*

Community-acquired pneumonia

- Oxygen assessment on admission
- Screen for pneumococcal vaccination
- Appropriate antibiotic given within 4 hours of arrival to emergency department or hospital
- Blood cultures*
- Adult smoking cessation advice and counseling*
- Pediatric smoking cessation advice and counseling*

Heart failure

- Assessment of left ventricular function (echocardiogram)
- ACE inhibitor or ARB prescribed at discharge
- Discharge instructions specifically related to heart failure*
- Adult smoking cessation advice and counseling*

* JCAHO-measured indicators beyond those assessed for Medicare.
ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; JCAHO = Joint Commission on Accreditation of Healthcare Organizations

TABLE 2
JCAHO disease-specific certification areas

Acute coronary syndrome	Goucher disease
Allergic rhinitis	Hemophilia
Alzheimer disease	Hepatitis
Amyotrophic lateral sclerosis	High-risk pregnancy
Anticoagulation	HIV/AIDS
Arthritis	Hyperlipidemia
Asthma	Hypertension
Atrial fibrillation	Irritable bowel disease
Attention deficit disorder	Ischemic heart disease
Cancer	Lead exposure in childhood
Cellulitis	Low back pain
Chronic obstructive pulmonary disease	Lupus
Congestive heart failure	Migraine headache
Coronary artery disease	Multiple sclerosis
Cystic fibrosis	Obesity
Depression	Organ transplantation
Diabetes	Osteoporosis
Emphysema	Parkinson disease
End-stage renal disease	Sickle cell disease
Epilepsy	Sleep disorders
Gastroesophageal reflux disease	Smoking cessation
	Stroke
	Tuberculosis

JCAHO = Joint Commission on Accreditation of Healthcare Organizations

its quality "core measures," the results of which have been posted publicly since July 2004.[2] These core measures are the same as the CMS measures with nine additions—four more indicators for acute MI, three more for community-acquired pneumonia, and two more for heart failure (Table 1).

In addition to these three clinical areas, JCAHO has also developed pregnancy-related condition core measures. These include the rates of vaginal births after cesarean section, neonatal mortality rates, and the rates of third- and fourth-degree laceration.

Beyond these core measures, JCAHO offers certification in other areas. In addition to the regular hospital certification, it now offers ambulatory certification, office-based certification, network certification, and disease-specific certification. Disease-specific certification standards support a continuum-based approach for chronic condition management (Table 2) and signify that the services provided have the critical elements necessary for long-term success in improving outcomes.

As part of disease-specific certification, for example, JCAHO can offer an institution certification as a primary stroke center. In some regions of the country, emergency medical service units are considering routing stroke patients only to JCAHO-certified stroke centers.

The downside to disease-specific certification is that once achieved, it requires ongoing maintenance. JCAHO recertifies its disease-specific programs every 3 years. Organizations that seek this certification need to consider the ongoing costs for every disease for which they seek certification.

Purchasers and payers

The government and health care accreditation organizations are not the only entities that are requiring the collection and reporting of quality measures.

Insurers. The health insurer Anthem has for many years required annual reporting of certain measures and can include an option to renegotiate contracts if compliance falls below 70%. Specific areas of interest to Anthem are quality processes, behavioral medicine, obstetrical care, cardiac care, the hospital credentialing process, the emergency department's role in asthma and pneumonia care, joint replacement, cancer care, congestive heart failure, acute MI, and

TABLE 3
National Quality Forum hospital safe practices

- Create a health care culture of safety
- Provide adequate staffing
- Have methods in place to check for and prevent:
  - Surgical site infections
  - Pressure ulcers
  - Deep venous thrombosis
  - Tourniquet-based complications of ischemia and thrombosis
  - Malnutrition
  - "Wrong site, wrong surgery" errors
  - Central line sepsis
  - Contrast-induced renal failure
  - Aspiration
- Use anticoagulation services
- Document patient do-not-resuscitate orders
- Ensure health care workers use proper handwashing techniques
- Vaccinate health care workers against influenza
- Identify high-alert medications
- Dispense medications in unit doses
- Give perioperative beta-blockers to patients at risk for cardiac events
- Read back verbal orders immediately
- Ensure pharmacists are active in the medication use process
- Use only standardized abbreviations and dose designations
- Prevent mislabeling of radiographs
- Refer patients to appropriate health care facilities for high-risk elective surgeries or other specified care
- Staff general intensive care units with specialists in critical care medicine
- Properly prepare patient care summaries (ie, do not recall notes from memory)
- Transmit changes in patient care information in a timely fashion
- Have patients restate their informed-consent discussion
- Implement a computerized physician order-entry system
- Keep medication workspace areas clean, orderly, and well lit
- Standardize methods for medication labeling, packaging, and storage

patient safety. Beyond Anthem, other purchasers and payers are beginning to require the submission of data and are making compliance rates available to covered employers and employees.

The Leapfrog Group. The Leapfrog Group is a consortium of large private and public health care purchasers that has entered the quality-measurement arena in recent years.[3] This organization was launched in 2000 by the Business Roundtable, an association of Fortune 500 companies. Today, the Leapfrog Group consists of more than 150 public and private organizations that provide health care benefits to more than 34 million Americans and account for more than $62 billion in annual health care expenditures. The group encourages large employers to recognize and reward health plans and hospitals that make breakthrough improvements in patient safety and quality. It has identified a small subset of well-supported actions to improve quality and has adopted them as its quality measures. It is using preferential referral and other monetary market reinforcements to encourage compliance with its recommendations.

The three initial Leapfrog targets were:

- Computerized physician order entry. The Leapfrog Group believes that this development would eliminate 80% of preventable drug errors.
- Intensive care physician staffing. The belief is that ensuring the availability (either on site or by telemonitoring) of physicians who are subspecialty trained in critical care medicine would improve risk-adjusted outcomes, reducing mortality by as much as 29%.[4]
- Evidence-based hospital referral, with the expectation that outcomes would be improved and mortality reduced by greater than 30% if hospitals refined their practice methods and increased their volume for (and thus their experience in) seven complex surgeries.

The Leapfrog Group has moved beyond these three initial measures. In 2004, it added the remainder of the National Quality Forum's 30 "hospital safe practices."[5] Under these measures, health care organizations can receive a maximum of 1,000 points, with full compliance with a particular "safe practice" awarded a predetermined number of points. For example, the first safe practice, having a "culture of safety," is worth 263 points. Examples of other National Quality Forum safe practices are shown in Table 3. Health care organizations have to attest that the measures are being addressed and supported from a fairly high leadership level in their organizations. The points that organizations achieve are then posted on the Leapfrog Group's Web site.

The Leapfrog Group has not formally announced its 2006 initiatives at the time this is being written. It has been discussing a move toward assessing clinical decision support in physician offices, an initiative that would be developed in coordination with the federal government's Agency for Healthcare Research and Quality and CMS. Such an initiative would encompass electronic prescribing, electronic lab results management, and electronic care reminders.

Institute for Healthcare Improvement

The Institute for Healthcare Improvement is a not-

TABLE 4
Institute for Healthcare Improvement interventions: Six changes that save lives

Deploy rapid-response teams at the first sign of patient decline (these are similar to code teams except an attempt is made to reach the patient prior to code)
Deliver reliable, evidence-based care for acute myocardial infarction to prevent death from heart attack (eg, use of aspirin, beta-blockers, timely treatment)
Prevent adverse drug events by implementing medication reconciliation*
Prevent central line infections by implementing a series of interdependent, scientifically grounded steps called the "central line bundle"
Prevent surgical site infections by reliably delivering the correct perioperative care
Prevent ventilator-associated pneumonia by implementing a series of interdependent, scientifically grounded steps called the "ventilator bundle"

* Will also be a Joint Commission on Accreditation of Healthcare Organizations requirement.

for-profit group founded in 1991 that recently began an initiative called the "Save 100,000 Lives" campaign.[6] Its goal is to enlist 1,600 hospitals to commit to at least one of six evidence-based interventions (Table 4) and agree to submit their mortality data, the main measure of the campaign's success. The desired result is that participating organizations will report a decline in death rates, thus realizing the Institute's goal of saving 100,000 lives. Participation is free and voluntary.

Self-reporting: The Cleveland Clinic Outcomes Reporting Project

Rather than ceding control of outcomes reports by submitting data to the government, JCAHO, and various payers and purchasers, some health care organizations are reporting their own outcomes. The Cleveland Clinic has chosen this route, creating its own Web site devoted to quality measures that is updated continuously, and each clinical department also produces its own "outcomes booklet," a summary review of trends, approaches, and results.[7] Quality indicators for an orthopedic surgery department, for example, could include the percentage of patients with surgery less than 30 days from their initial diagnosis, the percentage of patients receiving magnetic resonance imaging or computed tomography scans within 12 months of surgery, and the percentage of patients requiring redo procedures within 12 months.

NEWER QUALITY MEASUREMENT TRENDS AND DEVELOPMENTS

Not only are the numbers and types of players involved in measuring and reporting outcomes growing, so too are some of the purchaser-provider incentives and reporting tools. Some of these newer developments are described below.

Pay-for-performance programs

The next wave in quality measurement is likely to be pay-for-performance schemes (see sidebar on next page), whereby a positive financial incentive for quality and/or efficiency is introduced. For example, copays may be waived if employees use hospitals or doctors with good quality scores. On the provider side, organizations may share in savings achieved by initiatives that increase quality and lower costs.

In one Midwestern city, a pay-for-performance program has recently been contemplated involving three entities: a large employer, the local hospitals, and a third-party payer. The employer asked the third-party payer to identify quality measures and monetarily incentivize the employees to seek out providers who scored well on those measures. The result was that payers were able to create a pay-for-performance scheme.

A few major pay-for-performance initiatives have already reported results. Here are their experiences:

• Bridges to Excellence involved several large employers, health plans, and provider groups in Boston, New York City, Cincinnati, and Louisville.[8] Five hundred physicians split $1 million in 2004 for initiatives that increased quality and lowered the cost of ambulatory care.

• The Integrated Healthcare Association of California involved six health plans, covering about 7 million enrollees.[9] Some 24,000 primary care physicians split $50 million in 2003. Some of their quality improvements included getting 35,000 more women to receive mammograms and immunizing 10,000 more children than the previous year.

• The CMS/Premier Hospital Quality Incentive Demonstration included 270 hospitals.[10] Hospitals deemed high performers on core measures shared $7 million per year, and the worst-performing hospitals bore financial penalties. A 7.5% median improvement occurred in the single composite quality score, and a 12% improvement was observed in a composite quality score for heart failure.

Health plan proposals vs insurer proposals. Health care organizations can be scored and reim-

Pay-for-performance: Commonly used terms

Because the development of more pay-for-performance proposals is likely, it's important to have an understanding of the terminology commonly used.

Value is simply quality divided by costs. To increase value, either increase quality or decrease costs.

Efficiency equates to costs. When payers or purchasers request increased efficiency, they are essentially asking for lower costs.

Provider refers to either the individual clinician or the hospital or health care organization.

Pay-for-performance proposals allow providers to earn bonuses for high scores on quality indicators.

Pay-for-value proposals allow providers to earn bonuses for high scores on quality and efficiency indicators.

Gain sharing allows providers to share in the cost savings they helped to achieve.

bursed using several methods. Health plan proposals for pay-for-performance schemes might focus on diseases and wellness, whereas an insurance company may look at a much wider range of practices to measure and presumably pay for. While an insurer's quality-measurement model is typically more comprehensive, it's also more complex.

A health plan's proposal might measure the following outcomes in several common clinical areas:

- In diabetes, the percentage of patients with office blood pressures less than 140/90 mm Hg, low-density lipoprotein (LDL) cholesterol levels less than 100 mg/dL, and hemoglobin A_{1c} levels between 7.0% and 9.0%
- In heart disease, the percentage of patients with office blood pressures less than 140/90 mm Hg and LDL cholesterol levels less than 100 mg/dL
- In hypertension, the percentage of patients with office blood pressures less than 140/90 mm Hg
- In the prevention arena, the percentage of women aged 52 to 69 years who have had screening mammograms, women aged 21 to 64 years who receive Papanicolaou smears, and patients aged 50 to 80 years who are screened for colorectal cancer.

In contrast, one insurance company is considering 16 measures in four categories. The types of measures being considered include efficiencies (cost vs expected cost), six process measures related to wellness (testing for hemoglobin A_{1c}, microalbumin, and lipids; diabetic eye examination; influenza immunizations; mammograms), and value-added offerings (eg, convenient office hours, patient satisfaction factors).

Many questions remain unanswered when considering these two types of proposals. Is performance and reward going to be based on an intermediate outcome (such as reducing LDL cholesterol below a certain level) or on the process (simply getting the lipid blood test ordered)? Should high-leverage wellness-type measures be rolled out after the plan has been initiated, or should the measures be worked into a more comprehensive plan from the start?

Patient incentives. One of the biggest questions is how to incentivize patients to participate in pay-for-performance schemes, such that they will comply with the indicated tests and medication regimens so that the health care organization can realize performance scores and receive reimbursement. Also, patients who choose not to comply may find it difficult to find a doctor under a pay-for-performance scheme, which could raise difficult social and public health issues.

APR-DRGs: severity-of-illness adjustment

APR-DRG stands for "All Patients Refined Diagnosis Related Group," an expansion of the long-standing DRG patient classification system. The adjustment is an attempt to enhance the accurate coding of comorbid conditions so that outcomes, as displayed on public report cards, can be compared fairly. APR-DRGs, developed by 3M Health Information Systems, are applied to all payers, not just Medicare. 3M identified four levels of severity of illness (minor, moderate, major, and extreme) for each DRG. This disease-severity index is used to develop a "risk of mortality" score. The Medicare Payment Advisory Commission supports adoption of this type of severity-of-illness scale, stating that such a system would help yield substantial improvements in payment accuracy.

Among the notable organizations using the APR-DRG severity-of-illness methodology are:

- The Agency for Healthcare Research and Quality. This federal agency selected the 3M index as the severity risk and adjustment method for use in its Inpatient Quality Indicators.
- HealthGrades. This health care rating and advisory Web site has announced that it will begin using APR-DRGs in addition to its own methodology. HealthGrades, together with 3M, will deliver a combined service for quality improvement.
- Premier. This alliance of not-for-profit hospitals and health systems will use APR-DRGs in its

prospective online benchmarking software.

• *US News & World Report*. This magazine uses APR-DRGs to rank America's best hospitals.

• State agencies. Some 33 state agencies are using APR-DRGs in their state performance reporting systems.

• Pay-for-performance demonstration projects. New Jersey is using APR-DRGs in its Gainsharing Initiative, a pay-for-performance demonstration project; CMS and Premier are using it in their Hospital Quality Incentive Demonstration; and other third-party vendors have purchased APR-DRG software to build their own pay-for-performance model.

• The Cleveland Clinic is using the APR-DRG tool for reporting outcomes data. This tool allows data to be analyzed at the level of the individual physician. Organizational leadership can then examine, on a physician-by-physician basis, such information as the number of patient cases, average length of stay, discharge rates, and severity of illness.

SUMMARY

Change is inevitable, but participation is optional. An array of quality measures is being used by various government entities, health care purchasers and payers, and other groups. Many of the quality-measurement initiatives have not only gained the attention of large employers, but are also beginning to pique the public's interest. Novel approaches to measuring and rewarding quality are also emerging, such as pay-for-performance schemes and the use of APR-DRGs. Health care organizations that participate in the quality-measurement process and provide input will benefit by the type of measures that are ultimately created. It is much better to be part of the development process than to have insurer- or employer-designed quality measures imposed on your institution. At the very least, health care organizations would be wise to serve as watchdogs to ensure that currently proposed quality measures truly measure high-quality care.

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Preoperative pulmonary evaluation:

Identifying and reducing risks for pulmonary complications

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Postoperative pulmonary complications are among the most common morbidities in patients undergoing major surgery. Yet despite the frequency and potential seriousness of these complications, preoperative patient evaluations often tend to focus more on cardiac, rather than pulmonary, risks.

This review discusses patient- and procedure-related risk factors that should be considered during preoperative pulmonary evaluation, as well as strategies for reducing the risk of pulmonary complications in surgical patients. In addition to this review, readers are referred to the upcoming American College of Physicians (ACP) guideline on preoperative pulmonary evaluation and its accompanying background papers, which are based on a systematic review of the literature. This will be the first set of evidence-based guidelines for preoperative pulmonary evaluation. As such, it is expected to help fill gaps in our current knowledge of perioperative pulmonary risks and management strategies.

THE STAKES: PULMONARY COMPLICATIONS ARE COMMON, SERIOUS, COSTLY

The major pulmonary complications that clinicians seek to prevent through proper preoperative evaluation and intervention include pneumonia, prolonged mechanical ventilation or respiratory failure, atelectasis, bronchospasm, and exacerbations of chronic obstructive pulmonary disease (COPD).

These complications are more widespread than is often perceived. Data from 3,970 patients in the Revised Cardiac Risk Index cohort who underwent major noncardiac surgery found rates of respiratory failure (2%) and pneumonia (1%) to be comparable with or slightly higher than rates of the two most common cardiovascular complications, pulmonary edema (1%) and myocardial infarction (1%).[1]

Additional studies[2,3] have shown that patients who develop a postoperative pulmonary complication have longer hospital stays than do patients who develop a postoperative cardiovascular complication. For example, a patient in the intensive care unit who develops pneumonia may require prolonged ventilation and have a lengthy and costly hospital stay.

PATIENT-RELATED RISK FACTORS: WHAT IS THE EVIDENCE?

Studies have evaluated potential associations between various patient-related factors and postoperative pulmonary complications, as detailed below. Among these, COPD, general health status, and age are the factors most clearly associated with increased risk and should be considered during a preoperative assessment.

Chronic obstructive pulmonary disease

COPD doubles the risk of postoperative pulmonary complications.[4,5] While clinical practice suggests that the severity of COPD influences postoperative pulmonary complication rates, the literature on this important point is limited. Physical examination findings can be helpful in assessing risk magnitude, as shown by Lawrence et al,[6] who found that decreased breath sounds, prolonged expiration, rales, wheezes, and rhonchi were each associated with a sixfold increase in pulmonary complications compared with the absence of any of these findings. This study was conducted in patients undergoing elective abdominal surgery, which is associated with a relatively high risk of pulmonary complications.

General health status

General health status is an important predictor of the

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risk of pulmonary complications and has been evaluated using the American Society of Anesthesiologists (ASA) physical status classification to describe current health status.

The ASA classification was designed to estimate overall mortality risk in patients undergoing surgery, but a number of studies have shown that it also predicts cardiovascular and pulmonary complications.[4,7,8] Patients who are graded higher than class 2 in the five-class ASA system (Table 1) have a twofold to threefold increased risk of postoperative pulmonary complications compared with those graded class 2 or lower.[9] Thus, as an integrated risk index, the ASA classification not only provides the anesthesiologist's assessment of a patient's overall physical status, it also predicts the likelihood of postoperative pulmonary complications.

Two large studies[10,11] that used multivariable analysis suggest that functional dependence (ie, inability to perform activities of daily living) is an independent risk factor for postoperative pulmonary complications. Although no statistically significant results have been reported, self-reported exercise capacity may also predict pulmonary complications.

TABLE 1
ASA physical status classification for surgical candidates

Class 1	Normal healthy patient
Class 2	Patient with mild systemic disease
Class 3	Patient with severe systemic disease
Class 4	Patient with severe systemic disease that is a constant threat to life
Class 5	Moribund patient who is not expected to survive without the operation

ASA = American Society of Anesthesiologists

Age

The role of patient age as a risk factor for postoperative pulmonary complications has been controversial. Although advanced age is associated with an increased risk of these complications, whether this increased risk is attributable to age or to the comorbidities associated with increased age is not clear. The pending ACP guideline and background papers are expected to better clarify the degree to which age may be a risk factor independent of comorbidities.

Obesity

Since decreased lung volume after surgery is one of the mechanisms that contributes to the development of postoperative pulmonary complications, obese patients who have a restrictive ventilatory pattern might be expected to have an increased risk for pulmonary complications. However, the literature has consistently found that no such association exists and that obesity is not a risk factor for postoperative pulmonary complications. Although distinguishing between obesity and other risk factors that are common among obese persons is difficult, studies that have used multivariable analysis have generally found no increase in pulmonary complications in obese surgical patients, even for morbidly obese patients or those undergoing bariatric surgery.[12–14]

Nevertheless, a common complication of obesity, obstructive sleep apnea, may be associated with an increased risk of postoperative pulmonary complications. This suggestion comes from a single study from the Mayo Clinic[15] that found unplanned intensive care unit transfers and length of hospital stay to be increased among patients with obstructive sleep apnea undergoing hip or knee replacement. However, pulmonary complications were not frequent enough in the overall study to allow detection of any potential association with obstructive sleep apnea. Further investigation is needed to determine whether such an association may exist.

Asthma

In contrast to COPD, well-controlled asthma is not a risk factor for pulmonary complications following surgery. A retrospective analysis from the Mayo Clinic found a low incidence of pulmonary complications among 706 patients with asthma undergoing various general surgeries.[8] Pulmonary complications and their incidences were as follows:

- Bronchospasm, 1.7%
- Respiratory failure, 0.1%
- Laryngospasm, 0.3%.

There were no deaths and only one clinically important postoperative complication in the entire study sample. The subgroup of patients whose asthma was not well controlled (based on recent inhaler use or a recent emergency room visit) had significantly higher rates of pulmonary complications than their counterparts with well-controlled asthma.

Other patient factors of interest

Cigarette smoking confers a modest increase in pulmonary complication rates even among patients without COPD.[16,17] The findings of the National Veterans Administration Surgical Quality Improvement Program also indicate that impaired sensorium, recent weight loss (more than 10% in the past 6

TABLE 2
Multivariable risk indices for postoperative pneumonia and respiratory failure (abbreviated)

Variable	Points for pneumonia	Points for respiratory failure
Surgery type/site		
AAA repair	15	27
Thoracic	14	21
Neurosurgery	8	14
Upper abdominal	10	14
Vascular	3	14
Neck	8	11
Emergency surgery	3	11
Weight loss	7	NA
Albumin < 3 g/dL	NA	9
BUN ≥ 30 mg/dL	3	8
Functional dependency	10	7
COPD	5	6
Age ≥ 70 yr	NA	6
Age ≥ 80 yr	17	NA

Risk class (point totals)	Risk for pneumonia*	Risk for respiratory failure*
Class 1 (10–15 points for pneumonia) (≤ 10 points for resp. failure)	0.24%	0.5%
Class 2 (16–25 points for pneumonia) (11–19 points for resp. failure)	1.19%	2.1%
Class 3 (26–40 points for pneumonia) (20–27 points for resp. failure)	4.0%	5.3%
Class 4 (41–55 points for pneumonia) (28–40 points for resp. failure)	9.4%	11.9%
Class 5 (> 55 points for pneumonia) (> 40 points for resp. failure)	15.8%	30.9%

AAA = abdominal aortic aneurysm; BUN = blood urea nitrogen; COPD = chronic obstructive pulmonary disease; NA = not assessed

* Development cohort.

Adapted from references 10 and 11.

months), and a history of stroke are modest risk factors for postoperative pulmonary complications.[10,11]

PROCEDURE-RELATED RISK FACTORS

Contrary to the case in cardiac risk assessment, procedure-related factors are more important than patient-related factors for predicting postoperative pulmonary complications. For this reason, the type of procedure planned will have a greater impact on risk than the risks inherent to the patient being sent to surgery. At the same time, most procedure-related risk factors are not modifiable, so identifying such a risk factor will not necessarily lead to a strategy to reduce risk. It does, however, allow physicians to stratify pulmonary risk for better planning and enhanced perioperative care.

Some of the best data to date on procedure-related risks for pulmonary complications have come from Arozullah et al, who developed and validated the first multivariable risk indices for postoperative pneumonia and respiratory failure.[10,11] These indices, analogous to those used for cardiac complications, were based on the strength of predictors for pneumonia and respiratory failure as identified in prospective cohort studies of more than 160,000 veterans who underwent major noncardiac surgery.[10,11] Table 2 summarizes these indices by listing the points these researchers assigned to various predictive factors for pneumonia and respiratory failure, as well as the rates for each complication according to patients' overall point totals. In this way, the indices can be used in clinical practice much as the Revised Cardiac Risk Index is used to assess risk for cardiac complications.

The cohort studies by Arozullah et al[10,11] found surgical site to be the most important risk factor in predicting postoperative pulmonary complications, with aortic and thoracic surgeries carrying the highest risk, followed by upper abdominal procedures, neurosurgery, vascular procedures, and neck surgery. These findings are in keeping with other studies to date.

Other procedure-related risk factors for postoperative pulmonary complications include emergency surgery and prolonged surgery of greater than 3 hours' duration. The impact of general anesthesia as a risk factor (when compared with spinal or epidural anesthesia) remains controversial. A large meta-analysis reported that among patients randomly assigned to one anesthetic type or the other, those receiving spinal or epidural anesthesia (alone or combined with general anesthesia) experienced lower rates of pneumonia and respiratory failure,[18] but sources of bias in this study have raised questions about the generalizability of its results.

ROLE OF PREOPERATIVE PULMONARY FUNCTION TESTING

Spirometry is indicated before surgery in all patients undergoing lung resection to estimate postoperative forced expiratory volume in 1 second (FEV_1) and suitability for resection.[19] However, in patients undergoing other high-risk procedures, such as abdominal,

aortic, or nonresective thoracic surgeries, the role of pulmonary function tests (PFTs) has been more controversial, with the controversy centering on the following two questions.

Do PFTs predict risk more accurately than clinical evaluation alone?

The answer to this question appears to be *no*, according to one of the few studies that has directly compared clinical evaluation and spirometry for predicting pulmonary complications. In an analysis of more than 2,000 patients who underwent elective abdominal surgery, Lawrence et al[6] compared adjusted odds ratios (ORs) for pulmonary complications among four variables:

- Abnormal physical examination, OR = 5.8
- Abnormal chest radiograph, OR = 3.2
- Goldman cardiac risk index (per point), OR = 2.0
- Charlson comorbidity index (per point), OR = 1.6.

In contrast, FEV_1, FVC, and FEV_1/FVC were nearly identical among patients with and without pulmonary complications, and no spirometric value was associated with postoperative pulmonary risk. Wong and colleagues[7] similarly reported that an ASA physical status of class 4 or greater conferred higher ORs for pulmonary complications than did abnormal spirometry. These results and others suggest that clinicians can identify high-risk patients based on clinical criteria and that the results of spirometry are unlikely to modify the clinical risk estimate.

Are there spirometry values below which surgery should be denied?

At one time, a number of authorities argued that an FEV_1 less than 50% of predicted was a contraindication to surgery. This belief was called into question by a 1992 study by Kroenke et al[20] that evaluated 107 general surgical procedures (some high-risk) in 89 patients with severe COPD (ie, FEV_1 < 50% of predicted). Mortality was 6% overall and was clustered in the subset of patients undergoing coronary artery bypass graft (CABG) surgery (5 of 10 patients; 50%); mortality was 1% following the 92 noncardiac operations. Pulmonary complications occurred following 29% of operations; major pulmonary complications occurred after 7%. Although these complication rates are not trivial, they may be acceptable if the need for surgery is sufficiently compelling, even in high-risk patients.

The bottom line

Preoperative PFTs have a limited role in assessing a patient for surgery. PFTs should not be used to deny surgery if the reason for the surgery is compelling. PFTs should be obtained, however, for all patients before lung resection. It is not necessary to routinely obtain PFTs before high-risk noncardiothoracic surgery.

PFTs can be helpful in cases when the history and physical examination leave the degree of risk uncertain—for example, if exercise intolerance or dyspnea remains unexplained after a clinical evaluation. PFTs also may occasionally be helpful if it is unclear whether a patient with COPD or asthma is at his or her best baseline function.

OTHER TESTING OPTIONS: CONSIDER SERUM ALBUMIN AND BUN

The National Veterans Administration Surgical Quality Improvement Program found that levels of serum albumin and blood urea nitrogen (BUN) can be used to identify patients at risk for postoperative pulmonary complications.[10] Both a low serum albumin (< 3 g/dL) and a BUN greater than 30 mg/dL were significant predictors of pulmonary complications.

STRATEGIES FOR REDUCING RISK

Preoperative strategies

Optimize management of chronic lung conditions. The preoperative management of patients with COPD or asthma should be the same as it would be for patients not undergoing surgery. For instance, ipratropium or tiotropium is indicated for all symptomatic patients with COPD. Inhaled beta-agonists can be used as needed for symptoms. Theophylline should be continued if it is used chronically but should not be initiated shortly before surgery is planned. Liberal use of corticosteroids for a short period to "tune up" patients with COPD before surgery is safe and does not increase the risk of pneumonia or wound complications.

Airflow obstruction should be optimized to a goal peak flow that is at least 80% of the patient's personal best. Antibiotics should be used only if a change in the character of sputum suggests infection.

Advise carefully on smoking cessation. Notably, recent cessation of cigarette smoking (≤ 2 months before surgery) may pose a greater risk of postoperative pulmonary complications than smoking continuation. This finding, although not compatible with the notion that the preoperative setting provides a "teachable moment" for effective encouragement of smoking cessation, was suggested by a blinded prospective study of 200 unselected patients undergoing CABG surgery.[21] When the researchers analyzed postoperative pulmonary complication rates by the patients' smoking status, they found the highest rate (57%) to be among those who had stopped smoking 1 to 8 weeks

before surgery. This rate was substantially higher than the 33% complication rate among current smokers. The complication rate among patients who had stopped smoking more than 8 weeks before surgery was the same as among nonsmokers (12%). Two other studies[14,22] have yielded similar findings on high postoperative pulmonary complication rates following recent smoking cessation.

Although this finding may seem counterintuitive, its basis may be that many patients who quit smoking actually feel worse in the first 1 to 2 months and notice increased sputum production and cough.

Postoperative strategies

Lung expansion maneuvers and pain management are the two most important postoperative strategies for reducing the risk of pulmonary complications.

Lung expansion maneuvers work by reducing the expected drop in lung volumes after major surgery, particularly upper abdominal and thoracic surgeries. A meta-analysis of 14 randomized controlled trials of lung expansion maneuvers found that incentive spirometry and deep breathing exercises each reduced the risk of postoperative pulmonary complications by about 50%; no additional benefit was found from combining the two strategies.[23] Continuous positive airway pressure (CPAP) is an equally effective strategy, but it has disadvantages, including cost, its labor-intensive nature, and an association with small risks for barotrauma and aspiration. Nevertheless, CPAP may be preferred for patients who are unable to cooperate adequately with effort-dependent therapies.

Pain control. A meta-analysis of randomized controlled trials of postoperative pain control and pulmonary complications demonstrated that epidural local anesthetics significantly reduce the risk of pneumonia and all postoperative pulmonary complications.[24]

Selective nasogastric decompression in patients undergoing abdominal surgery is a lesser-known strategy for reducing the risk of pulmonary complications. A meta-analysis of 26 studies found that routine, as opposed to selective, use of nasogastric decompression might increase the risk of aspiration and pulmonary complications.[25] The ORs for pneumonia and atelectasis were 0.49 and 0.46, respectively, for patients who had selective nasogastric tube placement based on symptoms (nausea or abdominal distention) compared with routine tube placement.

SUMMARY

Postoperative pulmonary complications are among the most common sources of morbidity in patients undergoing major surgery. For this reason, the preoperative patient evaluation should emphasize risk factors for pulmonary complications as well as for traditional cardiac complications, as the former are comparably frequent and associated with longer hospital stays. Procedure-related risk factors are more important than patient-related risk factors for predicting pulmonary events, but clinicians should assess both types of factors. Pulmonary function testing has a limited role and should not be the basis for denying surgery if the surgical indication is compelling. Strategies to reduce the risk of postoperative pulmonary complications include optimizing management of chronic lung disease before surgery, lung expansion maneuvers, pain control, and selective placement of nasogastric tubes.

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Antibiotic prophylaxis against postoperative wound infections

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Hospital-acquired infections pose a large health burden. Fortunately, much can be done to improve infection control. The value of antibiotic prophylaxis for certain types of surgery is backed by strong evidence, and clear guidelines for its implementation have been issued by surgical societies.

This article reviews the evidence for antibiotic prophylaxis in surgeries with minimal expected contamination of the wound site; discusses the timing, type, and duration of antibiotic administration; and highlights topics of controversy in preventing and managing perioperative infections. Methods of instituting new standards for a hospital team are also discussed.

SURGICAL SITE INFECTIONS CAN BE REDUCED IN THE OPERATING ROOM

Surgical site infections represented the second largest group of nosocomial infections in the United States from 1990 to 1996, according to the National Nosocomial Infections Surveillance System of the Centers for Disease Control and Prevention (urinary tract infections were the largest group, primarily associated with Foley catheters).[1]

The risk of surgical site infection can be reduced by a number of strategies in the operating room, including:

- Optimizing oxygen tension
- Maintaining normal temperature
- Managing fluids
- Controlling blood glucose (especially important for patients undergoing coronary artery bypass graft surgery)
- Not shaving the operative site (or, if shaving is necessary, timing it as soon as possible before surgical incision).

Another factor that is more difficult to control is surgical technique and experience: complication rates tend to be much higher while a surgical team is learning a new procedure compared with after it becomes routine.

ANTIBIOTIC PROPHYLAXIS

Antibiotic prophylaxis is another important method for reducing the incidence of hospital-acquired infections. Because their use in this setting is preventive, antibiotics should be limited to operations in which minimal microbial contamination of the surgical site is expected (ie, clean or clean-contaminated wound classes).

Evidence for the value of antibiotic prophylaxis against infection in surgery is long-standing. In the 1950s, Miles et al[2] injected bacteria intracutaneously in guinea pigs and varied the timing of administration of a single dose of streptomycin and penicillin. Antibiotic administration was effective for infection prevention only in a 2-hour period around the time of bacterial injection, which they termed the "decisive" period.

Burke[3,4] found that the decisive period applied to prophylactic administration of either penicillin, chloramphenicol, erythromycin, or tetracycline from 1 hour before to 2 hours after infection with staphylococci in an animal model.

Hojer and Wetterfors[5] showed that prophylactic administration of doxycycline reduced septic complications following colectomy, with the biggest impact noted in surgeries in which obvious contamination did not occur.

For which procedures is prophylaxis worthwhile?

Since these early studies, antibiotic prophylaxis has proved beneficial for a variety of procedures—gastrointestinal (including appendicitis), oropharyngeal, vascular (abdominal and leg), open heart, obstetric

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and gynecologic, orthopedic hardware placement, and craniotomy, as well as some clean procedures.

Other operations, including many plastic surgery procedures and other less-invasive clean procedures, do not warrant routine antibiotic prophylaxis because the baseline rate of infections is so low. In such situations, the costs of prophylaxis may not justify the benefits.

Choosing an appropriate antibiotic

Antibiotics should be chosen on the basis of their effectiveness against the pathogens most likely to be encountered rather than against every possible pathogen. Skin florae (eg, *Staphylococcus* organisms) are the usual target, so first-generation cephalosporins are most often chosen. Intravenous administration is most common, although a combination of oral and intravenous administration can also be used.

Specific prophylactic antibiotic regimens are becoming standardized through guidelines published by societies such as the Infectious Diseases Society of America, the American Society of Health System Pharmacists, and the Surgical Infection Society, and are available on their Web sites.

TIMING OF PROPHYLACTIC ANTIBIOTICS

Give first dose before incision

Antibiotics should be administered before an incision is made to ensure that antimicrobial levels in the tissue are adequate and maintained for the duration of the procedure.

Stone et al[6] randomly assigned 400 patients undergoing elective gastric, biliary, or colonic operations to one of four regimens: antibiotics administered either 12 hours preoperatively, just before an operation, after an operation, or not at all. The incidence of wound infections was reduced significantly in patients given antibiotics preoperatively. Patients given antibiotics postoperatively had an almost identical infection rate to those not given antibiotics.

Classen et al[7] retrospectively monitored the timing of antibiotic prophylaxis in nearly 3,000 patients undergoing clean or clean-contaminated procedures. Patients who received prophylaxis in the 2-hour period before surgery had the lowest rate of infection, whereas those given prophylaxis more than 2 hours before surgery had a rate comparable to those who received prophylaxis from 3 to 24 hours postoperatively.

Beta-lactam drugs (eg, cefazolin and cefoxitin) have the advantage of an intravenous route of administration with anesthesia induction, leading to high muscle levels at the time of surgery even if given just minutes before the incision.[8]

Continue no longer than 48 hours postoperatively

The consensus of the National Surgical Infection Prevention Project, representing more than a dozen nursing and surgical societies, is that prophylaxis should not extend beyond 24 hours after wound closure.[9] The American Academy of Orthopaedic Surgeons has also issued such a statement, explicitly stating that evidence does not support continuing prophylactic antibiotics until all drains or catheters are removed.[10] The Society of Thoracic Surgeons recommends no more than 48 hours of antibiotic prophylaxis for cardiac surgery[11] (at The Cleveland Clinic, we use prophylaxis for 24 hours).

Most studies have demonstrated efficacy of postoperative antibiotic prophylaxis for only 12 hours or less: whenever short and long courses are compared, the shorter course has proven equally effective.[12–14] A single dose is as effective as multiple doses,[15] and antimicrobial prophylaxis after wound closure is unnecessary.

Prolonged antibiotic prophylaxis beyond 48 hours is not only ineffective in reducing infections but increases antimicrobial resistance[12] and the risk of colitis due to *Clostridium difficile*.

Full therapeutic dose needed

The full therapeutic dose of antibiotic should always be given. The upper range of the dose should be considered for large patients or those undergoing long operations.

Forse et al[16] found that when morbidly obese patients undergoing gastroplasty were given the standard dose (1 g) of intravenous cefazolin, blood and tissue levels of the drug were lower than those found in patients of normal weight. When they increased the dose to 2 g in morbidly obese patients, the wound infection rate dropped from 16.5% to 5.6%.

Redose for long surgeries

Patients undergoing surgery that extends beyond two half-lives of an antibiotic should be redosed intraoperatively.

Scher[17] randomly assigned more than 800 patients undergoing gastrointestinal surgery to one of three regimens: cefazolin (half-life, 2 hours) 1 g preoperatively, cefazolin 1 g preoperatively and a second dose 3 hours later, and cefotetan (half-life, 3 to 4.6 hours) 1 g preoperatively. Patients who underwent surgeries that lasted longer than 3 hours and were given only one dose of cefazolin had a significantly higher infection rate than patients in the other groups.

Zanetti et al[18] similarly found that intraoperative redosing of cefazolin resulted in a lower risk of surgical site infection following cardiac surgery.

Ohge et al,[19] after examining pancreatic tissue con-

centrations of cefazolin at various times in patients undergoing pancreatectomy and determining adequate levels to inhibit bacteria, recommended that a second dose of cefazolin be given 3 hours following initial administration of the drug.

Despite evidence that redosing reduces infection risk, only 12.2% of patients in the National Surgical Infection Prevention Project who underwent surgery for longer than 4 hours received an additional antibiotic dose during the procedure.[9]

VANCOMYCIN IN CARDIAC SURGERY

Vancomycin prophylaxis for cardiac surgery is controversial. Critics of using vancomycin cite that it is increasingly associated with resistance by enterococcal and staphylococcal organisms. It has a narrow spectrum of activity, being effective only against gram-positive bacteria, and no good evidence exists that it actually reduces rates of surgical wound infection. It must be infused over 60 minutes, which can add time to procedures. Furthermore, patients often become allergic to vancomycin. Finally, it has a vasodepressor effect, which can pose problems for patients with cardiac disease.

Supporters of its use argue that cephalosporin-resistant pathogens (methicillin-resistant *Staphylococcus aureus* [MRSA] and *Staphylococcus epidermidis*) are also being observed in incision wounds. Kernodle and Kaiser[20] found that vancomycin is superior to cephalosporins in preventing *S aureus* intermuscular infections in guinea pig models.

The Society for Healthcare Epidemiology of America has issued guidelines[21] recommending routine surveillance cultures of patients at high risk for colonization with MRSA, but no current consensus exists on what constitutes unacceptable levels.

Known carriers of MRSA should probably be treated preoperatively with vancomycin for prophylaxis. At this point, there are no guidelines absolutely contraindicating the use of vancomycin, and the decision on its use is left up to hospitals and doctors.

CLOSING THE ADHERENCE GAP

In some states, legislation has been enacted that requires public disclosure of health care-associated infection rates. Although neither advocating nor opposing such laws, the Healthcare Infection Control Practices Advisory Committee[22] recommends that states in which public reporting has been established should select one or more of the following outcomes measures:

- Central line insertion practices
- Surgical antimicrobial prophylaxis
- Influenza vaccination among patients and health care workers
- Central line-associated bloodstream infections
- Surgical site infections following selected operations.

Evidence is sufficient for many issues in antibiotic prophylaxis that the focus should be on adherence to guidelines.

At The Cleveland Clinic, we have achieved more than 92% compliance with administering prophylactic antibiotics within 60 minutes of cardiothoracic surgeries. For noncardiac procedures, however, the compliance rate was less than 50% over the time studied (January through September 2004).

To implement change, objectives need to be clearly stated and backed by a strong team of stakeholders that includes surgeons. Standards need to be set, and a process established to measure the intervention, provide feedback, and make corrections.

A number of health care organizations are finding the Six Sigma methodology for customer-oriented quality improvement helpful when applied to preventing surgical site infections. By identifying and analyzing all of the component steps of prophylactic antibiotic administration, and then monitoring them for improvement, the Six Sigma approach aims to reduce variation and focus on critical elements to achieve sustainable improvement.

The advent of electronic medical records also offers the opportunity to better measure interventions through the establishment of real-time databases in operating rooms, to allow more extensive and timely accessing and recording of data.

SUMMARY

Prophylactic antibiotics should be given as close to the time of incision as possible to ensure that tissue antimicrobial levels are adequate and maintained for the duration of the procedure. The choice of antibiotic should be based on the organisms most likely to be encountered—usually staphylococcal skin florae. The choice of vancomycin over a cephalosporin may be justified in patients who are known carriers of MRSA. A full therapeutic dose of antibiotic should be used for prophylaxis. Morbidly obese patients should be given twice the standard dose. Redosing during an operation is recommended if the duration of the procedure exceeds two half-lives of the antibiotic administered. Prophylactic antibiotics should not continue to be administered more than 48 hours postoperatively.

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Managing perioperative risk in the hip fracture patient

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Hip fracture is a tremendous physiologic insult—nearly one third of patients die within the first year after sustaining one. For a few types of fractures, repair should be accomplished as soon as possible after the injury. For most, however, medical stabilization to prepare patients for a long and often arduous surgical procedure should be a high priority. The entire medical team, including the surgeon, anesthesiologist, and internist, should work together to optimally manage each patient.

This article provides a case-based overview of the different types of hip fracture and their surgical management and discusses methods to prevent and manage common complications.

CASE: A 78-YEAR-OLD WOMAN WITH HIP FRACTURE

A 78-year-old woman presents to the emergency department after slipping and falling on the ice. She had no loss of consciousness or head trauma but has severe left hip pain and is unable to bear weight. She has type 2 diabetes mellitus, hypertension, and rheumatoid arthritis, as well as a history of depression and hypothyroidism. Her functional capacity is limited and she lives in a single-floor home. She has no drug allergies.

Medications. Atenolol 50 mg/day, levothyroxine 88 µg/day, sertraline 25 mg/day at bedtime, methotrexate 5 mg/week orally, lisinopril 10 mg/day, simvastatin 20 mg/day at bedtime, raloxifene 60 mg/day, hydrochlorothiazide 25 mg/day, and a combined calcium and vitamin D supplement twice daily.

Vital signs. Blood pressure is 154/88 mm Hg, heart rate is 92 beats per minute, temperature is normal, and respiratory rate is normal.

Physical examination. The patient is not in acute distress. Cardiopulmonary and neurologic examinations are normal. She has tenderness in her lateral left hip and has some external rotation but no foreshortening.

Laboratory examination. Complete blood cell count and basic metabolic panel are normal.

Radiography. A radiograph of her left hip is shown in Figure 1.

CLASSIFYING AND MANAGING HIP FRACTURES

Femoral neck fractures and intertrochanteric fractures are typical low-energy fractures in elderly patients after a fall from a chair or a slip on the ice. Subtrochanteric fractures, which involve the proximal shaft of the femur, are less common, and usually occur from higher-energy trauma.

Stress fractures can also occur in the proximal femoral region, and are suspected in a patient with intractable pain that does not respond to weight-bearing with walking aides. This situation should be evaluated with sequential plain radiographs and magnetic resonance imaging to avoid propagation and/or completion. When these fractures are recognized, they can be pinned surgically or followed closely in dependable patients.

Nondisplaced (impacted) femoral neck fractures can be repaired with a limited incision and percutaneous pinning. Prognosis with repair of this type of fracture is good, with a quick return to high-level functioning.

Impacted femoral neck fractures must be fixed surgically, preferably within 6 hours. Not only can delay cause further displacement, but pressure in the sur-

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rounding hip capsule can promote devascularization of the femoral head, leading to avascular necrosis. Even if fixation is successful after this point, the femoral head may die and collapse, requiring a second surgery. For this reason, an impacted fracture that appears unstable 24 to 48 hours after the injury should be treated with a total hip replacement to avert the need for a second surgery.

Displaced femoral neck fractures require a bipolar hemiarthroplasty or total hip replacement, depending on the degree of arthritis present before the fracture occurred. Although performed through small incisions, total hip replacement is invasive, and can result in significant fluid shifts and blood loss. These surgical procedures can be complex and extensive, and patients should be optimized and well managed by a multidisciplinary team both preoperatively and postoperatively. Younger patients (< 50 years of age) with displaced femoral neck fractures who have few or no medical problems should proceed to operative repair as soon as possible. Delay can lead to femoral head necrosis, which may necessitate a second surgery later for a hip arthroplasty.

Intertrochanteric hip fractures, if minimally displaced, can be repaired by a number of fixation methods; the screw and sideplate and short proximal intramedullary nails are currently useful options. The more distal the fracture, the more difficult it is to treat. Based on her radiograph, our patient has an intertrochanteric fracture.

Subtrochanteric hip fractures, which involve the proximal shaft of the femur, can be repaired or replaced with a bipolar or total hip replacement based on the bone quality and complexity. These procedures are usually extensive, can be expected to involve significant intraoperative blood loss, and carry a high risk of complications, cardiac arrest, and death. Medical conditions should be critically evaluated and optimized prior to proceeding with this operation.

ASSESSING THE RISK OF PROCEDURES

In general, perioperative risk depends on the invasiveness of the procedure, the amount of destruction that occurred during the injury, and the patient's medical status at the start of surgery. Specific concerns are as follows:

- Bone marrow instrumentation and the cement applied put the patient at risk for embolization.
- The larger the incision, the greater the risk. Simple pinning can sometimes be performed with only local anesthetics for very sick patients.
- Risk is increased with the duration of the procedure.
- Procedures that require large incisions and considerable muscle dissection, such as those for intertrochanteric fractures, increase risk due to extensive bleeding and fluid shifts.

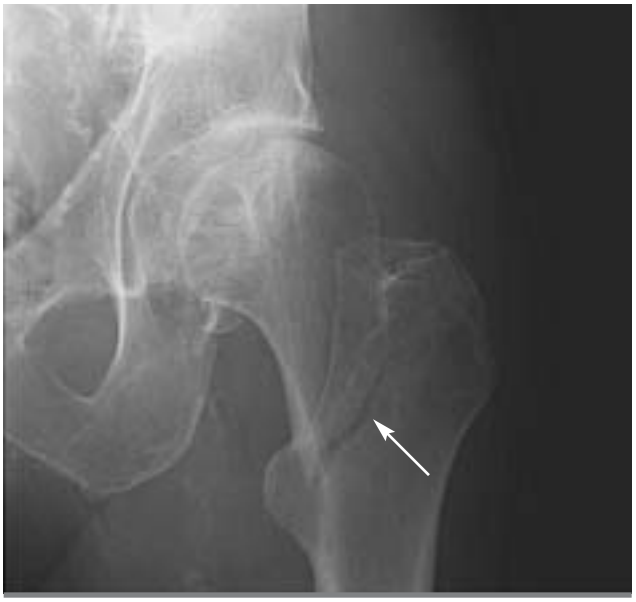

FIGURE 1. Radiograph of the left hip reveals an intertrochanteric fracture without displacement (arrow).

PREOPERATIVE MANAGEMENT

How should our patient, who has diabetes, hypertension, and rheumatoid arthritis, be managed before undergoing surgery for her intertrochanteric fracture?

A. Proceed to surgery as soon as possible regardless of her medical condition

B. Proceed to surgery once her medical condition is optimized

C. Because of her diabetes and limited functional capacity, delay surgery until she has undergone noninvasive stress testing

D. Because of her multiple medical problems, forego operative treatment

The best answer for this patient is B; however, each case must be treated individually as there are no absolute guidelines for treating hip fractures. For example, a patient with unstable angina should be stabilized before entering the operating room, but if the patient has a long history of unstable angina that is refractory to treatment, the best decision may be to proceed despite the risk.

Team management improves outcome

For each case, the surgical team must carefully consider the risks and the best course of action. Each member of a team has a specific role in assessing patients, and good communication between all members is essential to success.

The orthopedic surgeon rapidly assesses the type and extent of surgery required.

The internal medicine consultant evaluates the patient medically and stabilizes him or her before surgery. Postoperatively, the medical consultant manages complications such as malnutrition, delirium, hyponatremia, and diabetes.

The anesthesiologist assesses preoperative risk, plans for advanced intraoperative monitoring needs, and manages hematologic issues.

Vidan et al[1] randomly assigned 319 elderly patients during the acute phase of hip fracture to receive either multidisciplinary geriatric care or usual care (in which orthopedic surgeons completely handled care). Patients who received the multidisciplinary intervention had a significantly lower risk of in-hospital mortality (0.6% vs 5.8% for the usual care group, $P = .03$) and major medical complications (45.2% vs 61.7%, $P = .003$) and a reduction in the median length of stay that did not quite achieve statistical significance (16 vs 18 days, $P = .06$). Functional recovery was better 3 months postoperatively in the multidisciplinary care group but was not statistically different from the usual care group at 6 and 12 months.

Timing of surgical repair

In nine cohort studies (as reviewed by Morrison et al[2]), surgical hip fracture repair within 48 hours of medical evaluation and stabilization was associated with fewer perioperative complications and a reduced risk of death within 1 year. Inadequate control of variables in these studies, however, does not permit the issuance of absolute guidelines. More recent studies[3,4] have found no association between mortality and time to surgery when adjusting for demographic variables and for severity of underlying medical problems. However, these studies did note fewer decubitus ulcers, reduced pain scores, and shorter hospital stays with earlier operation.

In general, delaying surgery hampers the return to weight-bearing and overall functional recovery, but failure to stabilize medical problems increases the risk for perioperative complications.

RISK OF POSTOPERATIVE COMPLICATIONS IS HIGH

Complications associated with hip repair are common, even with the best care. In the study by Vidan et al,[1] postoperative medical complications occurred in 45% of patients receiving multidisciplinary care.

Among studies published from 1990 to 2002 that enrolled at least 100 patients and for which mortality data were cited, the rate of mortality during hospitalization for hip fracture ranged from 7% to 11%, and at 1 year postoperatively it was as high as 43%.[5]

Below we provide an overview of the medical complications most often encountered in patients undergoing surgery for hip fracture, along with a brief overview of strategies for their prevention. Most of these complications and their prevention in general surgical patients are explored in depth in other articles in this supplement, and the prevention and management principles outlined in these articles also apply to the patient undergoing surgery for hip fracture.

Lawrence et al,[5] in a retrospective cohort study of nearly 9,000 patients who underwent hip fracture repair, found that 19% developed postoperative medical complications. The most common complications were cardiac (8%, including myocardial infarction, congestive heart failure, or arrhythmia) and pulmonary (4%, including pneumonia and respiratory failure). Mortality at 30 days was 14% among patients with a complication and 1.7% among those without a complication; at 1 year, the mortality rates were 34% and 12%, respectively.

Wound infections

First- and second-generation cephalosporins are recommended for prophylaxis of wound infections, with vancomycin being the choice for patients with penicillin allergy. The optimal time of initial administration is 0 to 2 hours before surgery,[6] and prophylaxis should be continued for 24 hours. Gillespie and Walenkamp,[7] in a systematic review of more than 8,000 patients in 22 controlled trials for hip fracture repair, found that prophylactic antibiotics at the time of surgery for hip or other closed long bone fracture reduced the risk of deep wound infections by 60% and also reduced the risk of superficial wound infections, urinary tract infections, and respiratory tract infections.

Venous thromboembolism

Multiple prospective studies using contrast venography found rates of total and proximal deep vein thrombosis of approximately 50% and 27%, respectively, in the absence of prophylaxis.[8] A delay in operative repair greater than 48 hours from injury increases the risk of venous thromboembolism.[9,10] In 2004, the Seventh American College of Chest Physicians

Conference on Antithrombotic and Thrombolytic Therapy recommended routine prophylaxis for all patients undergoing hip fracture surgery, continuing until full ambulation is reached.[8]

Patients undergoing hip surgery at The Cleveland Clinic receive a first dose of enoxaparin on admission the evening before morning surgery. Preoperative dosing is essential to minimize the risk of intraoperative pulmonary embolism, an infrequent but devastating complication.

Preoperative anticoagulant dosing has an impact on the choice of anesthesia. According to the 2002 Consensus Conference by the American Society of Regional Anesthesia,[11] patients who receive prophylactic dosing of enoxaparin can have a spinal or epidural anesthetic 12 hours after the last dose. Those who are on therapeutic doses (such as 1 mg/kg enoxaparin every 12 hours) need to wait 24 hours after the last dose before receiving a neuraxial anesthetic. These guidelines are due to be updated, but we urge great caution about performing neuraxial anesthesia in patients on low-molecular-weight heparin and similar medications.

Patients on hormone replacement therapy have an increased risk of thromboembolism. Surgery should not be delayed because a patient is on hormone replacement therapy; rather, appropriate thromboembolic prophylaxis should be provided.

Malnutrition

Malnutrition is associated with increased surgical morbidity and mortality.[12] Malnutrition is common in the elderly: up to 20% of older patients with hip fracture are severely malnourished. Protein supplementation during hospitalization for hip fracture improves nitrogen and caloric balance, reduces length of hospital stay, and leads to better 6-month outcomes, with fewer complications and deaths.[13–15] Bastow et al[16] found that supplemental nocturnal nasogastric tube feeding of patients with hip fracture led to increased weight and, in very thin patients, a shorter time to achieving independent mobility.

Urinary retention and infection

Urinary retention is another common complication of hip surgery and is associated with high mortality.[17] To reduce the risk of infection, indwelling urinary catheters should be removed within 24 hours of surgery whenever possible. Intermittent straight catheterization reduces the incidence of urinary retention and bladder overdistention without increasing the rate of urinary tract infection, and may be used to facilitate the return of spontaneous voiding.[18,19]

TABLE 1
Tranquilizer regimens for treating delirium

Medication	Dosage
Haloperidol	0.25–0.5 mg orally or intravenously every 6 hours
Risperidone	0.25–0.5 mg orally twice daily
Olanzapine	2.5 mg/day orally

Delirium

Delirium (acute confusional state) is associated with a longer hospital stay, more complications, poorer outcomes after discharge, and an increased mortality rate. An estimated 61% of patients undergoing surgery for hip fracture develop delirium, with baseline risk factors that include old age, history of cognitive impairment or alcohol use, severe illness, and poor functional status.[20] Precipitating factors during hospitalization include medications (especially opioids, sedatives, and anticholinergic drugs), electrolyte imbalances, hypotension, infection, and sensory and environmental problems.[2,20,21]

Approaches to prevent delirium and control it when it develops include:[20,21]

- Minimizing sedative-hypnotic and anticholinergic drugs
- Assessing for withdrawal from benzodiazepines and alcohol
- Providing supportive reorientation to the patient and facilitating a calm and quiet environment
- Using adequate pain control (meperidine should be avoided because normeperidine, its active metabolite, can accumulate in the central nervous system and lead to seizures and worsened delirium)
- Providing a low-dose tranquilizer (Table 1).

SUMMARY

Patients with hip fracture benefit from a multidisciplinary team approach for preoperative and postoperative care. Team members, consisting of the orthopedic surgeon, internal medicine consultant, and anesthesiologist, should each have a role in determining a patient's readiness for surgery and communicate with one another about appropriate management.

How urgently a hip fracture needs repair depends on the type of injury. In general, most injuries should be repaired as soon as the patient can be medically optimized (preferably 24 to 48 hours), keeping in mind that procedures are often lengthy and maximally

invasive, and frequently involve complications. Nondisplaced (impacted) femoral neck fractures, however, should be repaired within 6 hours if possible to avert avascular necrosis of the femoral head and the need for total hip replacement.

The following interventions are helpful for preventing complications following hip fracture repair:

- Perioperative prophylaxis against infection and thromboembolism
- Daily protein supplementation for malnourished patients
- Removal of indwelling urinary catheters within 24 hours (intermittent straight catheterization may be used as needed)
- Monitoring for acute onset of delirium, and prompt treatment if it occurs.

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Perioperative management of the bariatric surgery patient:

Focus on cardiac and anesthesia considerations

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The obesity epidemic and the limited efficacy of dietary therapy to treat obesity have resulted in a surge in the volume of bariatric surgery. Obesity-related comorbidities are numerous and present a variety of preoperative, intraoperative, and postoperative challenges in obese patients undergoing any type of surgery and in those specifically referred for bariatric surgery. At the same time, the outcomes of bariatric surgery are increasingly good in terms of excess weight loss, reductions in comorbidities, increased life span, and overall medical costs.

Using a case for illustrative purposes, this article examines clinical considerations in the management of obese surgical patients as well as patients undergoing gastric bypass surgery.

OVERVIEW OF BARIATRIC SURGERIES

A variety of surgical options (Figure 1) have been developed to treat the morbidly obese patient (ie, with a body mass index [BMI] > 35 kg/m^2).

Restrictive procedures

The simplest concept is gastric restriction, which involves the creation of a small gastric pouch to cause early satiety; a small outlet to the pouch is also created to prolong satiety.

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Disclosure: Dr. Chand reported that he is a consultant for the Ethicon Endo-Surgery, Gore, and Sanofi-Aventis corporations. Dr. Schauer reported that he has received grant support from the US Surgical, Stryker, Ethicon, Inamed, Gore, and Baxter corporations. Drs. Gugliotti and Steckner reported that they have no financial relationships that pose a potential conflict of interest with this article.

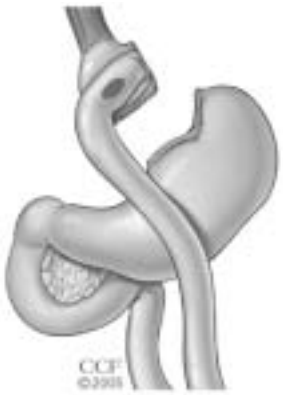
Vertical-banded gastroplasty, the first major restrictive procedure, was the most commonly performed bariatric operation in the United States until about 10 years ago. Initial weight loss can be substantial with vertical-banded gastroplasty, but because of high weight regain caused by maladaptive eating behavior, the popularity of this operation has decreased dramatically. The procedure consists of the creation of a small gastric pouch or reservoir based on a vertical staple line, which is reinforced by a fixed band. The pouch and its outlet must be small enough to sufficiently restrict intake yet not so small as to cause obstruction. Because the fixed band is not adjustable, it often limits the patient's ability to consume solid food, which most often results in reliance on high-calorie "junk" food.

Adjustable laparoscopic gastric banding is an alternative restrictive operation that has for the most part replaced vertical-banded gastroplasty. Adjustable gastric banding was introduced outside the United States in the early 1990s. It offers an improvement over fixed vertical-banded gastroplasty in that the silicone collar employed is adjustable postoperatively, allowing for titration of diet to maximize weight loss and minimize side effects (ie, vomiting, reflux) and potential weight regain.

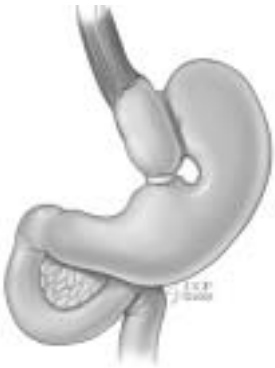
The benefits of restrictive procedures are their technical simplicity and their avoidance of protein-calorie malabsorption or vitamin or mineral deficiencies. Their disadvantages include less weight loss relative to other procedures and a higher rate of late failures owing to pouch or anastomosis dilation or to maladaptive eating behaviors.

Malabsorptive procedures

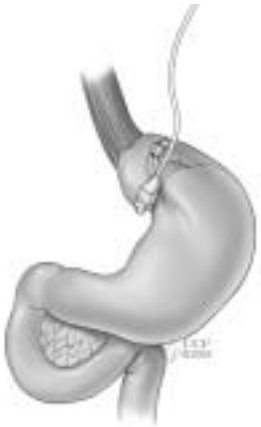
Malabsorptive procedures rely on bypass of a portion of the small intestine to cause malabsorption. Their relative benefits are sustained weight loss that is less reliant on dietary compliance compared with restrictive procedures. Their drawbacks are relative techni-



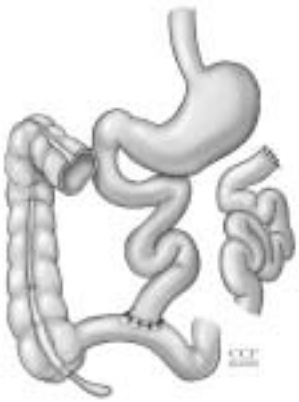
The **gastric bypass** (Roux-en-Y procedure) constitutes the vast majority of US bariatric surgeries today. The small intestine is reconfigured into a Y, consisting of two limbs and a common channel. The pancreo-biliary limb is proximal small bowel, attached to the stomach and the duodenum. The Roux limb (food limb) is attached to the gastric pouch.



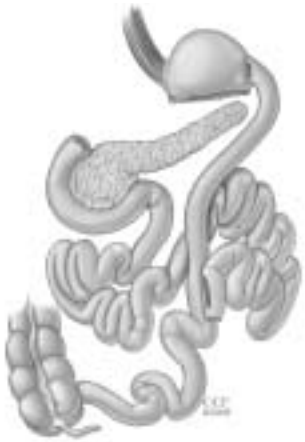
Vertical-banded gastroplasty is an outdated restrictive procedure that decreases the size of the stomach, usually by division or partitioning, to create early satiety. A small reservoir is created based on a vertical staple line reinforced by a fixed band.



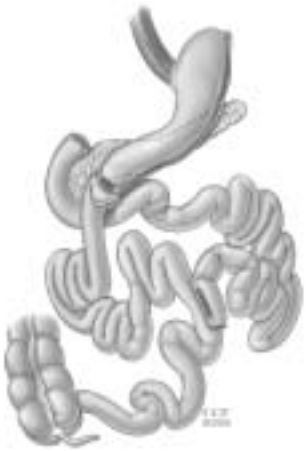
Adjustable laparoscopic banding employs an adjustable silicone collar, allowing for titration of diet and weight loss.



Jejunoileal bypass is a malabsorptive procedure that short-circuits the small intestine. It is no longer performed because of a high rate of metabolic complications such as vitamin and protein deficiency, kidney stones, and liver failure.



Biliopancreatic diversion involves a limited gastrectomy. The remaining pouch is connected directly to the final segment of the small intestine, bypassing the duodenum and the jejunum.



Biliopancreatic diversion with duodenal switch also involves a limited gastrectomy, but the remaining stomach remains attached to the duodenum. Continuity of the gastric lesser curve is maintained, and the duodenal switch maintains continuity of the gastro-duodeno-jejunal axis.

FIGURE 1. Bariatric surgery options include gastric bypass (Roux-en-Y), which constitutes the vast majority of bariatric surgeries performed in the United States; vertical-banded gastroplasty, which has fallen out of favor due to maladaptive eating behavior; adjustable laparoscopic banding, which has replaced vertical-banded gastroplasty; jejunoileal bypass, the initial malabsorptive procedure; and biliopancreatic diversion with or without duodenal switch, which are second-generation malabsorptive procedures.

cal complexity and a heightened risk of malnutrition and vitamin deficiencies, along with a resultant need for close follow-up.

Jejunoileal bypass. The first malabsorptive procedure, the jejunoileal bypass, was introduced in the 1950s but has been abandoned because of unacceptable rates of morbidity, which include gas-bloat syndrome, steatorrhea, metabolic imbalances, hepatic fibrosis and failure, and nephrolithiasis. The procedure did, however, result in substantial weight loss even in the face of high caloric intake.

Biliopancreatic diversion. Jejunoileal bypass has been replaced somewhat by biliopancreatic diversion with or without duodenal switch, which is a less extreme malabsorptive procedure. Biliopancreatic diversion involves some gastric volume reduction as well. In the procedure, a horizontal partial gastrectomy is performed, but with the creation of a reduced intestinal bypass compared with jejunoileal bypass, such that an "alimentary" common channel of approximately 50 cm is constructed. This biliopancreatic diversion/duodenal switch procedure carries a much lower risk of malnutrition sequelae compared with jejunoileal bypass. Protein malabsorption, however, is still a risk, occurring in approximately 7% of patients.

Gastric bypass

One of the most commonly performed bariatric surgeries is the gastric bypass procedure (Roux-en-Y gastric bypass), which represents about 80% of bariatric operations performed by American surgeons. It is principally a restrictive procedure, involving creation of a small pouch and bypass of a small portion of the foregut, although this bypass rarely leads to protein malnutrition.

Effectiveness correlates with invasiveness

The effectiveness of the various bariatric procedures generally correlates with their invasiveness. The percentage of excess weight lost is about 40% with restrictive procedures, 65% to 70% with gastric bypass, and 80% to 85% with malabsorptive procedures.[1]

CASE STUDY: EVALUATION PRIOR TO BARIATRIC SURGERY

A 53-year-old woman with morbid obesity (BMI of 45.97 kg/m^2) is referred for evaluation prior to bariatric surgery (Roux-en-Y gastric bypass). She has classic risk factors for coronary disease, including a 30-pack-year history of smoking, hyperlipidemia, obstructive sleep apnea, uncontrolled hypertension despite pharmacotherapy (losartan 50 mg/day and hydrochlorothiazide 25 mg/day), and borderline type 2 diabetes mellitus (elevated blood glucose levels in the past 2 to 3 years; rarely > 200 mg/dL). She also has hypersomnolence, depression, gastroesophageal reflux disease, and stress incontinence.

At presentation, her laboratory evaluation is normal, her fasting blood glucose is 129 mg/dL, and her blood pressure is 152/88 mm Hg. Her hypersomnolence is being treated with methylphenidate 10 mg twice daily, her sleep apnea with nighttime continuous positive airway pressure, and her dyslipidemia with ezetimibe 10 mg/day. Other than obesity, her physical examination is unremarkable. She has trace lower extremity edema but normal cardiac and pulmonary examinations.

Determining cardiac status

Establishing physical exertional status is valuable. Exercise tolerance is a predictor of surgical outcomes in general. In one study, symptom-limited stair climbing predicted postoperative cardiopulmonary complications after high-risk surgery.[2]

The patient denies having chest pain with exertion. She has no history of cardiac disease, myocardial infarction, stroke, arrhythmias, or heart failure. She reports being able to walk about one or two blocks on level ground but experienced shortness of breath but no chest pain when climbing two flights of stairs (10 steps each) and "panting" after three flights of stairs. She reports having had an episode of chest squeezing while climbing an observation tower, which resolved with rest. Resting electrocardiography (ECG) is normal.

What role for stress testing and imaging studies?

Given that this patient has had some vague symptoms that may or may not have been related to cardiac disease, mounting evidence suggests that proceeding to surgery with appropriate risk stratification and medications (ie, beta-blocker) may be acceptable.

An ECG exercise stress test probably has limited value in the obese patient because of the difficulty in getting adequate tracing, particularly in women, and because the ability to exercise is compromised.

The types of stress echocardiography are exercise stress echocardiography, dobutamine stress echocardiography, transesophageal dobutamine stress echocardiography, and contrast-enhanced stress echocardiography. Exercising to an adequate heart rate is essential to maximize the sensitivity of exercise stress echocardiography. Preliminary investigation suggests that contrast-enhanced stress echocardiography or transesophageal dobutamine stress echocardiography may be superior to the other types of stress echocardiography testing for obese patients. Obtaining appropriate echocardiography windows and high-quality two-dimensional images may be problematic when

performing transthoracic stress echocardiography.

Photon scatter and attenuation artifacts are problems with single-photon emission computed tomography (SPECT) using thallium or technetium 99m. Positron emission tomography (PET) may provide better visualization of the myocardium and less attenuation than SPECT imaging.

Several investigators have studied the accuracy of thallium scanning in obese patients. Hansen et al[3] stratified 567 patients who underwent thallium SPECT into two groups: a low-risk group or patients who had had catheterization within 60 days of stress testing (without an intervening event or procedure). Of the 216 patients with a BMI greater than 30 kg/m^2, 91 had coronary artery disease diagnosed based on the findings from catheterization. The accuracy of thallium 201 scanning was found to be significantly diminished in patients with a BMI greater than 30 kg/m^2.

Freedman et al[4] compared thallium 201 SPECT scanning to PET scanning in 161 patients, 81 of whom were normal weight and 80 who were overweight (BMI > 27 kg/m^2). The results were compared with angiographic findings in 75 patients; concordance and discordance were calculated for territories of three major arteries. They found concordance between the two types of nuclear tests in 75% (367/483) of arterial territories. More defects on thallium scanning were found in all territories except for the left circumflex artery, and there were differences among the incidences of defects between SPECT and PET, which were significant in the left anterior descending artery for women and in the right coronary artery for men and women. A significant difference in the right coronary artery territory was observed between obese patients and nonobese patients, which would be expected since obese patients have larger abdomens. PET had greater specificity (84%) compared with SPECT (64%) for the subset of 75 patients who underwent angiography.

Case continued

Our patient undergoes a stress echocardiogram, and she is able to exercise at 90% of her maximum predicted heart rate and at 5.5 metabolic equivalents with negative findings for ischemia. She is cleared for surgery with the addition of a beta-blocker.

ARRIVAL IN THE OPERATING ROOM: WHAT ARE THE CONCERNS?

Maintaining glycemic control and hemodynamic stability during this patient's operation will require an armamentarium of medications and monitoring equipment. The biggest concern for the anesthesiologist will be managing her airway. It is reassuring to know from preoperative testing that the patient is free of coronary artery disease, but she has a number of other worrisome issues, such as diabetes and sleep apnea, which may increase the risk of a difficult intubation. Obstructive sleep apnea can increase the sensitivity to sedative medications; thus, doses of benzodiazepines are minimized and the patient is offered vocal reassurance just before the anesthetic is started. In patients with sleep apnea, the use of anesthetic agents with a short duration of action is preferred so that their action can be terminated upon completion of surgery. A number of clinical factors can be used to predict ventilation and tracheal intubation difficulty: primarily neck circumference, visualization of oropharyngeal structures (Mallampati score), thyromental distance, and dental configuration. Based on this patient's clinical presentation, ventilation and intubation should not be overly difficult and most anesthesiologists would elect to induce general anesthesia for this patient, and secure the airway with the patient asleep. Another option is to intubate the patient while awake, with the aid of a fiberoptic bronchoscope, and then to induce general anesthesia.

For blood pressure control, the use of short-acting beta-blockers and antihypertensive drugs is preferred rather than deeper levels of anesthesia. Monitors such as the bispectral index can indicate an adequate level of sedation. Anesthesia can be maintained with anesthesia vapors such as sevoflurane, desflurane, and opioid infusions, thereby minimizing postoperative sedation.

Most bariatric surgeries, perhaps more than 90%, can be performed laparoscopically. The preoperative prediction of a successful laparoscopic outcome is based on the patient's BMI, with higher BMIs being more challenging laparoscopically as a result of difficult insufflation of the abdomen. Laparoscopic procedures are more difficult to perform in patients who have truncal obesity or who have had previous abdominal surgery, but they can be successful even in these types of patients.

Issues in airway management

Brodsky et al[5] studied 100 morbidly obese patients and found that only 1 could not be intubated and 12 had "problematic" intubations. Optimal positioning of the patient, and consideration of an algorithm for difficult airway management such as the American Society of Anesthesiologists' Practice Guidelines for Management of the Difficult Airway,[6] will help to achieve safe and rapid airway management. Additional personnel, as well as equipment such as fiberoptic bronchoscopes on a well-stocked airway cart, laryngeal mask airways, and alternatives to conventional laryngoscopy (eg,

Bullard scope, GlideScope), will be key resources for difficult airway management.

The head-up or reverse Trendelenburg position can improve oxygen reservoirs in patients who are given oxygen before the anesthetic is started, and will delay the time to desaturation due to consumption of oxygen in the functional residual capacity. Desaturation is normally much faster in a morbidly obese patient; one who is preoxygenated with 100% oxygen will desaturate within 4 minutes, whereas a normal-weight patient has a 10-minute margin of safety. For example, a morbidly obese patient who is critically ill and returns to the operating room with abdominal sepsis will have increased oxygen consumption and will experience hypoxemia very quickly after induction of general anesthesia.

Hemodynamics of laparoscopic surgery

Even when done laparoscopically, bariatric surgery is a stressful surgery. Cardiac output is usually well preserved but systemic vascular resistance can be increased; tachycardia, bradycardia, and hypertension are common, depending on the levels of surgical stimulation and the adrenergic state of the patient. Five percent to 10% of our patients will become hypotensive for a brief period after institution of the pneumoperitoneum and steep reverse-Trendelenburg (head-up) positioning.[7] This hypotension appears to be related to preoperative hypovolemia (fasting, bowel prep, and antihypertensive medications) and responds quickly to treatment with intravenous fluid boluses of 500 to 1,000 mL.

Postoperative analgesia

Balanced multimodal postoperative analgesia (ie, local anesthetics in the wound, nonsteroidal anti-inflammatory drugs, and modest doses of opioids) will help minimize respiratory depression after surgery. We consider epidural analgesia if the patient is scheduled for an open procedure; however, there is an increased risk for epidural hematoma in patients receiving low-molecular-weight heparins. The risks and benefits of neuraxial pain relief are weighed, using information from guidelines on regional anesthesia in the anticoagulated patient issued by the American Society of Regional Anesthesia and Pain Medicine.[8]

POSTOPERATIVE COMPLICATIONS OF BARIATRIC SURGERY

Because comorbidities are common in obese patients, the risk of postoperative complications is relatively high.

Intestinal leak

The International Bariatric Surgery Registry[9] includes more than 10,000 patients and provides data on complications. The most frequent complication is intestinal leak. Of the staple lines that can result in a leak, the gastrojejunostomy is the most vulnerable. Such a leak can potentially result in severe peritonitis and is the most common cause of surgically related mortality in patients undergoing bariatric surgery.

Early diagnosis of an intestinal leak is challenging because symptoms are often masked in obese patients. This requires the surgeon and team managing the patient to have a high index of suspicion of an underlying leak.

Pulmonary embolism/deep vein thrombosis

The second most common cause of mortality related to bariatric surgery is pulmonary embolism (PE).[9] The combined incidence of deep vein thrombosis (DVT) and PE following bariatric surgery is 2%.[10] In patients with a low risk of bleeding, pharmacologic prophylaxis of DVT may be a useful adjunct to mechanical prophylaxis. The data to support the choice of therapy and appropriate dosing for DVT prophylaxis in bariatric surgery are limited, with no randomized controlled trials completed. Success has been reported using enoxaparin and heparin prophylaxis.

Higher than standard doses of enoxaparin may be required for prophylaxis in obese patients undergoing bariatric surgery. A retrospective analysis of 481 patients who underwent Roux-en-Y gastric bypass[11] indicated that 40 mg of enoxaparin twice daily may be superior to 30 mg of enoxaparin twice daily in reducing the incidence of postoperative symptomatic DVT/PE without an increase in bleeding complications. The trend in practice is toward use of 40 mg of enoxaparin twice daily, but the timing of administration is debatable. Because most patients are at highest risk at the time of induction, preoperative dosing is reasonable.

Weight-based dosing of unfractionated heparin aimed at keeping Factor anti-Xa levels at 0.11 to 0.25 units/mL has been studied in 700 patients after gastric bypass.[12] There were no cases of DVT and three cases of nonfatal PE. Bleeding requiring cessation of unfractionated heparin occurred in 16 cases (2.3%) and bleeding requiring transfusion occurred in 7 (1.0%). The authors concluded that weight-based dosing is an improvement over fixed dosing, although the trial was not randomized and contained no control arm.

Other complications

Other common complications are cardiopulmonary complications (1% to 5% incidence), respiratory compromise (1% to 2%), wound complications (1% to 2%), bowel obstructions (1% to 2%), strictures (3% to 8%), and perioperative bleeding (0.3%).[1]

It behooves not just the surgeon but the entire team

managing the patient to be aware of these complications, anticipate them, and act before they become severe.

OUTCOMES OF BARIATRIC SURGERY

Buchwald et al[13] collected data on outcomes of bariatric surgery in a meta-analysis of 22,094 patients. The average excess weight loss for all types of procedures was 61.2%. When stratified by type of surgery, the average excess weight loss was:

- 47.5% for gastric banding
- 61.6% for gastric bypass
- 68.2% for gastroplasty
- 70.1% for biliopancreatic diversion/duodenal switch.

Overall, each type of surgery was safe, with the more complex surgeries carrying a greater risk of morbidity and mortality. Mortality ranged from a low of 0.1% for restrictive procedures to 1.1% for biliopancreatic diversion/duodenal switch.

Effect on comorbidities

Importantly, the reductions in comorbidities are also quite impressive. In this same meta-analysis, diabetes resolved in 76.8% of cases, lipid profiles improved in 70.0%, hypertension resolved in 61.7%, and obstructive sleep apnea resolved in 85.7%.[13]

Effect on life span

Evidence suggests that bariatric surgery also increases life span. In a study comparing survival between 62,781 morbidly obese patients who had undergone gastric bypass and 3,328 morbidly obese patients who had not, the 15-year survival rate using Cox regression analysis for patients younger than 40 years was 13.8% for those who underwent surgery vs 3.0% for those who did not.[14]

Effect on overall health costs

Studies are beginning to emerge that suggest that bariatric surgery yields savings in overall health care expenditures over time. Typical are the results of a retrospective study by Potteiger et al[15] in 51 consecutive patients with obesity-related hypertension and diabetes who underwent bariatric surgery. The average number of medications taken by these patients fell to from 2.44 preoperatively to 0.56 at 9 months after surgery, and the total monthly cost of their diabetic and antihypertensive medications declined 77% over the same period.

SUMMARY

Obesity is a major public health problem in developed nations worldwide. Currently, the only treatment for severe obesity (BMI ≥ 35 kg/m^2 with comorbidity) that provides long-term weight loss is bariatric surgery. Restrictive, malabsorptive, and combination procedures have been developed. Each type of procedure has its merits and unique set of risks and complications. Weight loss after bariatric surgery is accompanied by predictable improvement or resolution of obesity-related comorbidities and improved quality of life and life expectancy.

Candidates for bariatric surgery are often at high risk for complications because of obesity-related comorbidities. Therefore, careful patient selection for bariatric surgery, together with well-designed strategies for preventing and managing complications, are keys to success. Close monitoring for nutritional deficiencies and short- and long-term complications is required to completely assess outcomes of these procedures.

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Ambulatory anesthesia:

Preventing perioperative and postoperative complications

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The rate of ambulatory surgery has been increasing steadily in the United States over the past 20 years. In the past, patients referred for ambulatory surgery were generally in good health, and the types of surgeries performed were limited to simple procedures of short duration. More recently, patients who have significant medical conditions or who have factors that increase their risk of complications from anesthesia, such as obesity or tobacco use, are being considered for ambulatory surgery. Patients with complicated disease states such as diabetes, heart disease, or poorly controlled hypertension are also being considered. In addition, populations excluded in the past, such as the very old and very young, are being seen on a more routine basis at freestanding ambulatory surgery centers (ASCs).[1]

Not all of the changes are related to the patient's medical condition. More complex surgeries of longer duration, and even dual surgeries, are being performed as well. Some of these longer, more complex surgeries are starting to be performed in settings that may have less technical support and expertise readily available, such as in surgeons' offices rather than in ASCs.[1]

Advances in ambulatory surgery have allowed these changes, but without proper caution, these trends elevate the risk for perioperative and postoperative complications, and consequently an increase in morbidity and mortality. Misperceptions about ambulatory anesthesia may heighten the risk of complications. This article will explore appropriate candidates for ambulatory surgery, the selection of anesthesia, and effective ways to prevent complications.

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GEARED TOWARDS EFFICIENCY

A range of surgeries is now being performed in ASCs. These include urologic, orthopedic, obstetric/gynecologic, colorectal, and otolaryngologic procedures. In addition, the majority of cosmetic plastic surgery cases are performed in ASCs or physicians' offices. Vascular surgery is also increasingly being considered, although there is currently a debate about whether arteriovenous fistulas can be performed safely despite being associated with a low rate of complications when performed in an inpatient setting.

The financial benefit to performing surgery in an ambulatory rather than hospital environment is considerable. Cost consideration is possibly the main driver behind the push to increase the types of surgeries performed in an ambulatory setting, in addition to the type of patients who are considered candidates to undergo these procedures.[2]

The concept of ambulatory surgery is structured around efficiency, which allows the centers to perform many surgeries with rapid turnover. ASCs have a higher volume of patients and shorter times to surgery than do hospitals. The ability to perform surgery is not tied to the availability of hospital beds, as the centers have been designed with adequate recovery rooms so that patients can recover from anesthesia and be discharged home quickly. From an anesthesiologist's perspective, this rapid turnover affords the ability to assist at many more surgeries and to enjoy more control over the progress of the workday.

In operating rooms located within the hospital, turnover time is variable depending on the type of case and instruments required, but usually will be 30 to 45 minutes. In ASCs, the expected turnover time, as determined by the ASC's administration, is frequently 15 minutes or less. Thus with faster turnover and shorter recovery times, a greater number of cases may be performed at an ASC compared with similar cases performed in a hospital setting.

RISKS IN THE CURRENT ENVIRONMENT

When the decision is made to perform surgery in an ambulatory setting, the complexity of surgery and the patient's medical condition must be simultaneously taken into account. Failure to do so may expose the vulnerable patient to serious risks. Even minor surgeries, such as carpal tunnel release or cosmetic procedures, can be risky for patients with multiple medical conditions. When the procedures become more complex and longer, the risk is compounded.

We are in an era in which surgeries as complex as a cholecystectomy or abdominoplasty combined with liposuction may be performed in an ASC and in some cases in surgeons' offices. To ensure that the highest level of quality is maintained, various accrediting organizations, such as the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), define standards by which ASCs are measured. A difference still exists between the support available in a hospital operating room vs that at a freestanding ASC. As an example, the ability to obtain laboratory tests postoperatively, provide blood or blood products, or obtain consultations is frequently available in a hospital operating room. Rarely is it possible to provide this type of care in a freestanding ASC.

Decisions related to the appropriateness of a patient for surgery at an ASC can be complex. Sometimes patients receive an inadequate preoperative evaluation because the primary care physician or general internist performing the evaluation does not understand the complexity of the surgery or the risks inherent in the setting of an ASC. Cases scheduled by the surgeon may only take into account the complexity of surgery and not the associated medical problems. For patients with significant medical conditions, a team approach involving the patient's primary care physician, surgeon, and anesthesiologist is the best system to ensure optimal care for the patient pre-, intra-, and postoperatively.

Despite the considerable benefits and pressures to perform surgery on an outpatient basis, physicians should be mindful that serious complications and deaths do occur. Preventing these outcomes hinges on a careful preoperative screening and evaluation. The elements to consider when deciding whether a case is appropriate for ambulatory surgery and anesthesia are:

- Surgical setting (surgeon's office vs ASC)
- American Society of Anesthesiologists (ASA) physical status (overall health of the patient)
- Surgical complexity and length
- Social support following surgery
- Anesthetic technique and its risk for the patient.

THE PREOPERATIVE EVALUATION

Not only does prescreening allow the ASC to determine which patients are not acceptable candidates for the proposed surgery, it helps the surgical center to operate efficiently by avoiding problems on the day of surgery. Problem avoidance may vary from simple actions such as requiring that a responsible adult accompany the patient home after surgery, to obtaining and reviewing all of the pertinent laboratory and test results or the reports of any required subspecialty medical evaluations.

A telephone call from the surgical center to the patient before surgery or a medical questionnaire completed by the patient and sent to the center before surgery are options for prescreening. When a medical questionnaire is used, patients can be called if further questions about their medical condition arise during its review.

The goals of prescreening are to uncover any morbidity that increases risk and to ensure that any disease state has been optimally controlled. Before coming to the ASC, all patients should have had a careful history taken, a physical examination performed, and any appropriate tests ordered.

Proper evaluation and disease optimization decreases delays and cancellations, identifies the possibility of avoidable complications, and ultimately improves outcomes.

PREVENTING COMPLICATIONS: FACTORS TO CONSIDER

Acceptable patient characteristics

Patients who are healthy (ASA class 1; see Table 1) or who have mild systemic disease (ASA class 2) are the best candidates for ambulatory surgery. However, patients who have systemic disease (ASA class 3) or severe systemic disease that is life threatening (ASA class 4) are now being scheduled for ambulatory surgery. At our ASC, we limit surgery to patients of ASA class 3 status or better. Occasionally, patients with ASA class 4 status are considered if the procedure is superficial and can be performed with minimal anesthesia. Patients with significant disease states must have information or results demonstrating that their disease processes have been adequately controlled for at least the 3 previous months. For instance, a patient with congestive heart failure (CHF) who has had symptoms in the past 3 months would not be an acceptable candidate for surgery at any of our ASCs.

The chronologic age of a patient is not the deciding factor as to whether surgery can be performed at

an ASC. Rather, the status of the comorbid medical states in the elderly is the deciding factor. An 80-year-old patient with significant cardiac or pulmonary disease may be acceptable for surgery at an ASC only if these conditions are adequately controlled and if the surgery is of limited complexity and duration. A similar patient with little or no systemic disease may undergo a more complex and lengthly case with little risk of peri- or postoperative complications.

The invasiveness of a procedure should also be considered when deciding if a surgical procedure is acceptable for an ASC. The complexity and duration of procedures is increased as invasiveness is increased. Laparoscopic cholecystectomies are considered acceptable for ASCs; open cholecystectomies are not. The reason is that the physiologic changes that occur with these two cases will be dramatically different.

Increased complexity of surgery is usually associated with greater fluid shifts intraoperatively and greater blood loss, and in those patients with significant comorbid disease states, a greater risk of complications in the postoperative phase. Greater fluid shifts may be associated with signs of dehydration postoperatively, producing postural hypotension or decreased urinary output. Both of these symptoms would prevent discharge from an ASC.

In addition, for surgery that produces significant blood loss, transfer to a local hospital would be required because freestanding ASCs do not have the ability to store blood or blood products.

For patients who undergo surgery in the prone position, a significant amount of facial and therefore airway edema may be present, which may require prolonged ventilation before extubation can take place safely.

Many ASCs cannot allow for prolonged recovery time, although some are now able to provide extended recovery of up to 23 hours postoperatively. However, as the complexity of surgery is increased, so too is the duration. Together, they can be associated with an increased rate of postoperative complications, which many ASCs are not designed to handle except on an emergency basis.

Existing medical conditions

Existing medical conditions that increase the risk of complications from anesthesia or ambulatory surgery are cardiac disease, pulmonary disease, and morbid obesity. Patients at the extremes of the age spectrum should be considered candidates only after careful deliberation. Patients with cardiac or pulmonary disease should have their disease state well controlled and their cardiac or pulmonary function optimized in order to continue for ambulatory surgery. Patients with chronic pain also require special consideration.

TABLE 1
ASA physical status classification

Class 1	Normal healthy patient
Class 2	Patient with mild systemic disease
Class 3	Patient with severe systemic disease
Class 4	Patient with severe systemic disease that is a constant threat to life
Class 5	Moribund patient who is not expected to survive without the operation

ASA = American Society of Anesthesiologists

Cardiac disease. The patients with the greatest risk of complications from anesthesia are those with cardiac disease, mainly uncontrolled hypertension, CHF, or angina. In a study of existing medical conditions as predictors of perioperative adverse events from ambulatory surgery, Chung et al found that patients with CHF had a 12% longer postoperative stay, which in some instances included admission to hospital.[3] They also found a twofold increase in intraoperative cardiovascular events in patients with hypertension. Interestingly, these researchers found no association between merely having coronary artery disease and any excess morbidity or mortality.[3]

Pulmonary disease. Chronic obstructive pulmonary disease (COPD), asthma, and tobacco abuse often lead to pulmonary complications. In the same study discussed above,[3] Chung et al examined the impact of pulmonary disease on complications from ambulatory surgery. Their results showed that asthma was associated with a fivefold increase in postoperative respiratory adverse events and that smoking was associated with a fourfold increase. In 2001, Arozullah et al found that patients with COPD had twice the standard risk for pulmonary complications from ambulatory surgery as did patients without COPD.[4]

Morbid obesity. The morbidly obese frequently have comorbidities, including coronary artery disease, CHF, hypertension, and obstructive sleep apnea. The study by Chung et al found a fourfold increase in adverse pulmonary events in morbidly obese patients compared with those of normal body weight.[3]

In patients with morbid obesity, the problem is twofold. Intraoperatively, these patients are prone to rapid desaturation. Adequate preoxygenation is

therefore mandatory in these patients. In addition, the morbidly obese patient can experience bronchospasm, making ventilation difficult. Some ASCs are staffed such that limited help is available should an emergency occur. For these reasons, surgery that requires more than mild sedation for anesthesia in patients with a body mass index of greater than 35 kg/m^2 is discouraged at our ASCs.

Obstructive sleep apnea is known to increase the rate of airway events during induction of anesthesia, intubation, or when patients emerge from anesthesia. Currently, the ASA is developing guidelines for the care of patients with diagnosed or suspected sleep apnea. Once formulated, these guidelines will help determine which patients may have surgery at an ambulatory surgery facility and the precautions that should be taken for their care postoperatively.

Extremes of age. Patients older than 85 who are undergoing prolonged surgery and who have certain diseases, including cardiac disease, peripheral vascular disease, cerebrovascular disease, and malignancies, have an increased risk of postoperative complications with general anesthesia.[5] The complications include cardiac, pulmonary, and others.

Chronic pain. Patients with chronic pain are also being managed at ASCs. Because these patients' pain may be particularly difficult to control after surgery, and may require high-dose narcotics, a 23-hour stay may be required, even after minor surgery. In addition, narcotic requirements may be higher for these patients. Some anesthesiologists may be uncomfortable prescribing the doses of narcotics required following some procedures. Therefore, communication with the pain management specialist taking care of the patient is important.

Contraindications for ambulatory surgery and anesthesia

Uncontrolled chronic disease. Ambulatory surgery is not appropriate for patients with chronic disease that is not optimally managed. These include patients with unstable angina, symptomatic asthma, and brittle diabetes. Morbidly obese patients with known cardiac or pulmonary disease should be hospitalized following surgery.

Premature infants who are less than 60 weeks' postconceptual age should also have surgery only in the hospital setting.

Patients without adequate social support. Patients must have a responsible adult at home with them the night of the surgery, an especially important consideration for the elderly. JCAHO rules dictate that surgical providers can be held responsible should serious complications occur at home postoperatively when no one was available to attend to the patient.

Surgical contraindications. Procedures that would cause substantial blood loss or cause severe pain or immobility after the operation should not be performed in an ambulatory setting. All significantly invasive surgeries should be performed in an operating room located within a hospital.

ANESTHETIC TECHNIQUES: CHOICE IS BASED ON TYPE OF SURGERY, CONDITION OF PATIENT

Physicians should be mindful of the risks of ambulatory anesthesia in the vulnerable patient and that these risks can be compounded by other factors. As stated, a careful preoperative evaluation is required to prevent the serious peri- and postoperative complications that can otherwise occur.

The ideal anesthetic technique for ambulatory surgery provides a rapid and smooth onset of action, produces adequate amnesia and sufficient anesthesia intraoperatively, provides optimal conditions for surgery with no adverse effects, and allows for quick recovery. Because this desired result is not always achieved, the anesthesiologist must monitor the patient with the same level of vigilance and be prepared to use the same equipment as in a hospital operating room. The choice of anesthetic is based on the type of surgical procedure and the condition of the patient.

General anesthesia

General anesthesia is probably the most widely used technique in ambulatory surgery. General anesthesia produces changes in blood pressure, heart rate, and respiratory rate (which it can, of course, suppress to the point of stopping respiration).

For inhalational general anesthesia, the inhalational agents sevoflurane or desflurane are often used, as these agents are metabolized quickly, which allows rapid awakening. A drawback of inhalational agents may be a higher incidence of postoperative nausea and vomiting.

In total intravenous anesthesia, the medication propofol is combined with a short-acting narcotic such as alfentanil or remifentanil. Propofol has a short half-life, thus leading to rapid emergence or awakening. Because of this property, propofol is frequently used for the induction and maintenance of anesthesia in the ambulatory surgery setting.

Monitored anesthesia care

Monitored anesthesia care (MAC) is perceived as low risk. Yet patients undergoing MAC require constant

vigilance by an expert to maintain adequate ventilation and oxygenation. With this technique, the patient can progress quickly from being lightly anesthetized to a deep sedation. The line between wakefulness and deep sedation is a fine one; the patient can move from being verbal to apneic in a short time.

MAC is also known as "conscious sedation." The goal of this technique is to cause minimal depression of consciousness, hence allowing rapid recovery, while providing anxiolysis, analgesia, and some sedation. With withdrawal of anesthesia, the patient should be awake and ambulatory. MAC is usually accomplished by a combination of intravenous sedation along with local infiltration of agents.

A perception exists that MAC can keep a patient from moving or talking but that at the same time it causes only light sedation. Such a scenario in reality does not exist. It is a technique that should not be taken lightly, and should not be administered by someone who lacks experience in ventilating a patient and keeping open an airway. Constant monitoring is critical.

Regional anesthesia

Regional anesthesia may be central (neuraxial) or peripheral.

Neuraxial anesthesia may be provided by a spinal or epidural block. Spinal and epidural anesthesia have few side effects but, depending on the local anesthetic agent used, may be associated with long recovery times, thus delaying discharge from the recovery room, which ultimately reduces the efficiency of the ASC. One of the side effects associated with neuraxial anesthesia is the development of a sympathetic block. This may cause profound changes in blood pressure. In addition, spread of the local anesthetic to the cardiac accelerators of the spinal cord can make a patient profoundly bradycardic. This type of block, therefore, should not be used in patients in whom dramatic changes in blood pressure or heart rate would be problematic. Central blocks also can cause urinary retention, which lengthens time in recovery.

Peripheral nerve blocks are best for upper and lower extremity surgery. They provide good analgesia intra- and postoperatively, allow the patient to go home quickly, and produce few hemodynamic changes. They include axillary, interscalene, IV (Bier), popliteal, and ankle blocks. These blocks may also be converted to provide continuous analgesia with a nonelectric infusion pump.

Other options for postoperative pain relief include small multiport catheters inserted in the incision by the surgeon and attached to a small grenade-shaped device filled with local anesthetic. The local anesthetic is continually released, producing localized anesthesia for 2 or 3 days postoperatively.

CONCLUSION

The number and complexity of surgeries performed in the outpatient setting will no doubt continue to rise. Careful evaluation and optimization of patients' medical conditions is critical for continued positive outcomes. Awareness of the patient's medical condition, the type of surgery, and the setting in which the procedure will be performed can minimize inefficiencies and dangerous complications.

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Evaluating postoperative fever:

A focused approach

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Postoperative fever is one of the most common problems seen by both surgeons and medical consultants. Most cases of fever immediately following surgery are self-limiting, but it is critical not to miss more serious etiologies. When evaluating postoperative fever, it is important to recognize when a wait-and-see approach is appropriate, when further work-up is needed, and when immediate action is indicated.

Using case studies, this article discusses typical scenarios involving postoperative fever, and provides a framework for evaluating and managing them.

CASE 1: FEVER IMMEDIATELY AFTER SURGERY

A 58-year-old man is referred to your clinic for a preoperative evaluation before bilateral total knee arthroplasty. He has well-controlled hypertension, hyperlipidemia, and osteoarthritis, and you determine that he is medically optimized for surgery.

The day after surgery, the patient is feeling well except for moderate knee pain controlled by pain medication.

- New medications: cefazolin for prophylaxis of surgical site infection.
- Physical examination: normal except for a small amount of serosanguineous drainage from the right knee.
- Vital signs: temperature 38.7°C (101.6°F), blood pressure 130/72 mm Hg.
- Laboratory results: white blood cell count 11,000/mm^3.

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Which of the following diagnostic studies and treatment options do you recommend?

A. Blood and urine cultures
B. Choice A plus chest radiography
C. Choice B and begin vancomycin
D. Observation only

The correct answer is D. Most early postoperative fevers (within the first 48 hours after surgery) have no clearly defined infectious cause and resolve without therapy.

Is the fever caused by infection?

Postoperative fever is very common. However, published incidence rates range widely (from 14% to 91%)[1] depending on how fever was defined and the patient population of the study. The more important issue is whether infection is the underlying cause. In the vast majority of studies, the incidence of infection in patients with postoperative fever is less than 10%, indicating that fever is not a specific marker of infection in this setting.

Fanning et al,[2] in a retrospective review of 537 patients who underwent gynecologic surgery, found that 211 (39%) developed fever postoperatively, but no infectious etiology was found in 92% of these cases.

Shaw and Chung,[3] in a retrospective review of 200 patients undergoing total hip or knee arthroplasty, reported that "virtually all" had elevated temperatures postoperatively but none had documented infection. Most patients had a maximum temperature on the first postoperative day and had normal temperatures by the fourth postoperative day. Nearly one fifth of the patients had a maximum temperature of 39.0°C (102.2°F) or greater, indicating that the magnitude of fever is also not a reliable marker of infection.

Garibaldi et al,[4] in a prospective study of 81 patients who developed unexplained postoperative fever, found that 80% of those with fever on the first postoperative day had no infection. However, the sit-

uation was quite different for patients who developed a fever on or after the fifth day following surgery, as approximately 90% of these patients had an identifiable infection, in most cases wound infection (42%), urinary tract infection (29%), or pneumonia (12%).

Fever as a response to injury

A variety of conditions—including trauma and infection—lead to the release of pyrogenic cytokines, primarily interleukin 1 (IL-1), IL-6, tumor necrosis factor, and interferon-γ. These cytokines act directly on the anterior hypothalamus and its surrounding structures, causing the release of prostaglandins, which appear to mediate the febrile response.

Wortel et al[5] measured IL-6 levels in 16 patients who developed postoperative fever in the first 24 hours after undergoing a Whipple procedure. Levels of IL-6 directly correlated with the magnitude of fever (average maximum temperature, 38.8°C [101.8°F]).

Other investigators have found that the more traumatic the surgery, the higher the risk of postoperative fever, and that IL-6 is an important driver of this response. Frank et al[6] prospectively studied 271 patients in the first 24 hours following various vascular, abdominal, and thoracic surgeries. Patients who underwent peripheral vascular procedures involving the lower extremities were the most likely to develop a fever, followed by patients who underwent thoracic procedures, abdominal procedures, and carotid endarterectomies. The mean time to maximum temperature elevation was 11 hours after surgery. Blood concentrations of IL-6 correlated with fever elevation.

CASE 2: FEVER 4 DAYS AFTER SURGERY

A 61-year-old woman with rheumatoid arthritis (medications: methotrexate and hydroxychloroquine) who is otherwise in generally good health undergoes a left total hip replacement. A Foley catheter is placed during surgery. Following surgery, she is sent to the regular orthopedic unit, where she begins to ambulate the day following surgery. A fever of 38.1°C (100.6°F) is noted on the first postoperative day. Her Foley catheter is removed on postoperative day 2. Her temperature is normal on postoperative days 2 and 3, but on postoperative day 4, her temperature is 38.5°C (101.3°F).

What is the most likely cause of her fever now?

A. Joint hemarthrosis
B. Urinary tract infection
C. Superficial wound infection
D. Prosthesis infection

B is correct. Although all choices are possible, urinary tract infection is the most common cause of fever appearing 4 days after surgery.

The patient's urine is cultured, and grows *Proteus mirabilis* (>10^5 colonies). Oral ciprofloxacin therapy is started, and the patient's fever subsides.

Evaluating postoperative infection

Infection is much more likely to be present in a patient with a fever that develops after the first 2 days following surgery. The most common causes are:

Urinary tract infection, especially in a patient who has had urinary catheterization.

Surgical site infection, typically seen on postoperative day 4 or 5 or later.

Pneumonia, especially in patients with preexisting chronic obstructive pulmonary disease or who have been mechanically ventilated.

Intravenous catheter–related infections, which can be caused either by peripheral catheters (usually leading to thrombophlebitis or cellulitis) or by central catheters (usually causing bloodstream infection).

Clostridium difficile–associated diarrhea. Appropriate prophylactic antibiotics can help prevent surgical site infections. However, even a few doses of perioperative antibiotics can make a patient susceptible to *C difficile*, the frequency and virulence of which are increasing.

Less common causes of postoperative infection include:

Intra-abdominal infection, especially following abdominal or pelvic surgery.

Sinusitis, typically in patients who undergo nasogastric intubation for long periods.

Acalculous cholecystitis, particularly in very sick and debilitated patients who are not receiving enteral nutrition.

Prosthesis infection, which may manifest within a few days of surgery, especially if it is caused by *Staphylococcus aureus*.

CASE 3: FEVER AND ATELECTASIS

A 48-year-old woman in generally good health undergoes an abdominal hysterectomy. On the first day following surgery, she develops a maximum temperature of 38.7°C (101.7°F), and she remains febrile on postoperative day 2. She has some pain at the incision. She looks comfortable and is hemodynamically stable.

- Physical examination: normal except for mild bibasilar crackles heard in the lung fields.
- Chest radiography: atelectasis in both lung bases.

- Laboratory results: white blood cell count 10,500/mm^3.

What is the most likely cause of her fever?

A. Urinary tract infection
B. Atelectasis
C. Deep venous thrombosis
D. Other

The answer is D. Considering that it is still only 2 days after surgery, and that the patient generally looks and feels well, the fever is more likely to be caused by cytokine release from the surgical trauma than from infection.

Atelectasis does not cause fever, despite widespread misconception to the contrary. Engoren[7] monitored 100 patients for 2 days following cardiac surgery with daily portable chest radiography and continuous bladder thermometry. During this period, the incidence of fever progressively declined while that of atelectasis increased, demonstrating a negative correlation between them. Roberts et al[8] similarly reported poor correlation between fever and atelectasis in a study of 270 patients following abdominal surgery.

How to target the evaluation of postoperative fever

Fever should never be ignored. Appropriate evaluation of early postoperative fever includes a careful history, a targeted physical examination, and additional studies if indicated. Special attention should be paid to the following:

Preoperative course. Details of the period before hospitalization can be critical. For example, a patient with a hip fracture may have fallen because of an occult urinary tract infection, pneumonia, or cardiac arrhythmia.

Details of the procedure. Duration of surgery, blood products administered, and any complications may be important. The operative note can be helpful if present; if questions remain, directly speaking to the surgeon can fill in the gaps.

Nursing information is often important, such as if the patient has diarrhea or is coughing.

Physical examination should target vital signs and the heart and lungs, as well as the surgical and catheter sites for infection, the skin for rash, and the joints for inflammation.

Laboratory and imaging studies should be used sparingly and only as directed by the history and physical examination. Blood cultures for fever within the first 48 hours following surgery are usually unnecessary, as the chance of an abnormal result is very low in most patients.[2,9–11] In general, blood cultures should be reserved for high-risk patients, such as those who appear septic, are immunocompromised, have a central venous catheter, or have an obvious wound infection.

CASE 4: OTHER NONINFECTIOUS ETIOLOGIES OF POSTOPERATIVE FEVER

A 49-year-old man is admitted to the vascular surgery service with dry gangrene of the left foot. He has a history of lower extremity arteriosclerosis obliterans, hyperlipidemia, gout, and hypertension, as well as a 60-pack-year smoking history.

- Medications: hydrochlorothiazide, lisinopril, atorvastatin, aspirin.
- Magnetic resonance imaging: evidence of osteomyelitis in the left foot.

The patient undergoes a left transmetatarsal amputation. He is given combined piperacillin and tazobactam postoperatively, as well as his previous medications and opiates for pain. He does well over the first 2 days. On day 3, however, he develops a temperature of 38.5°C (101.3°F) and right knee pain. The knee is warm and tender.

What is the next step?

A. Aspirate the knee
B. Change his antibiotics to imipenem
C. Begin indomethacin
D. "Pan-culture" and obtain a chest radiograph

There is no good reason to change his antibiotics or to obtain blood, urine, or sputum cultures at this time. Knee aspiration would be a reasonable option for determining whether gout or infection is the cause of this episode. Since the patient is known to have a history of gout, the physician opts to empirically begin indomethacin. One study found a 15% incidence of gouty attacks in the early postoperative period among patients with a history of gout. The knee appears to be the most commonly affected joint in this setting, and this study found that fever accompanied the gout flare in virtually all cases.[12]

The symptoms resolve rapidly and the patient does well. He is moved to a skilled nursing facility, where he develops a fever of 38.8°C (101.8°F) on postoperative day 7. At this time, the physical examination is normal, with no apparent infection at the site of the peripherally inserted central catheter or at the amputation site. Laboratory findings are notable only for a white blood cell count showing 18% eosinophils.

What is the most appropriate next step?

A. Discontinue indomethacin
B. Change the combined piperacillin and tazobactam to another antibiotic

C. Add vancomycin to cover resistant gram-positive organisms in the wound
D. Both A and B

The best answer is D. Both indomethacin and particularly piperacillin/tazobactam are reasonably likely causes of drug fever. Based on available information, there is no reason to implicate a resistant gram-positive organism causing infection at the operative site.

The most common noninfectious causes of postoperative fever include:

Drug fever, which may present with skin rash or eosinophilia, but often provides no clue. It is an especially important diagnosis to consider with phenytoin, beta-lactam antibiotics, and sulfonamide antibiotics.

Hematoma, which can cause both fever and leukocytosis.

Gout (see above).

Transfusion reactions are usually obvious because they occur at the time of transfusion, although the temporal relationship is sometimes less clear.

Venous thromboembolic disease must always be suspected postoperatively. Although fever is not clearly linked with deep venous thromboembolism, low-grade fever is not uncommon in patients with pulmonary embolism, and high fever, though rare, may also occur.[13]

Pancreatitis may complicate intra-abdominal procedures, particularly those involving the upper abdomen, and often manifests with fever.

Alcohol withdrawal is frequently accompanied by low-grade fever, along with mental status changes and adrenergic hyperactivity.

CASE 5: FEVER AND ACUTE ILLNESS 1 DAY AFTER SURGERY

A previously healthy 58-year-old man has a right nephrectomy for asymptomatic renal cell carcinoma. On the first postoperative day, the patient appears ill and is anxious. His temperature is 38.7°C (101.7°F), his blood pressure 88/40 mm Hg, and his heart rate 122 beats per minute. The surgical site is dressed.

Which of the following is *unlikely* to be the cause of the patient's condition?

A. Malignant hyperthermia
B. Clostridial wound infection
C. Pulmonary embolism
D. Acute adrenal insufficiency

The correct answer is A. Malignant hyperthermia generally becomes apparent intraoperatively, although rarely it may present as long as several hours after surgery. Fever beginning on postoperative day 1 may be safely assumed *not* to be due to malignant hyperthermia. The other three answers are all plausible in an individual who develops fever and becomes hemodynamically unstable in the early postoperative period.

The patient's wound is undressed, and the surrounding tissue is pale and tender, with copious foul-smelling, seropurulent drainage from the wound. Gram staining of the drainage shows many gram-positive bacilli and few neutrophils. Antibiotic therapy is initiated, and the patient is taken urgently to the operating room for wound debridement.

Emergent causes of early postoperative fever

Early postoperative fever, while usually self-limiting, can be caused by life-threatening conditions. If these conditions are present, it is critical to recognize them immediately. The following are important possibilities to consider:

Myonecrosis, due to either *Clostridium* species (as in the case above) or group A streptococci, is a surgical emergency. Antibiotics, although important, play an adjunctive role to debridement, which may need to be extensive.

Pulmonary embolism may present with fever, although most commonly it does not. The possibility of pulmonary embolism should always be considered in the postoperative patient with unexplained hemodynamic instability.

Alcohol withdrawal, as already noted, frequently presents with fever. Prompt recognition and treatment will reduce morbidity and even prevent mortality.

Bowel leak should be considered in a patient who has undergone abdominal or pelvic surgery and develops evidence of sepsis in the early postoperative period. Intraperitoneal contamination may occur from an inadvertent bowel enterotomy during surgery or from leakage from a bowel anastomosis.

Adrenal insufficiency may cause fever and refractory hypotension postoperatively, typically in the setting of a patient whose hypothalamic-pituitary-adrenal axis is iatrogenically suppressed due to prolonged corticosteroid administration. Timely steroid supplementation may be lifesaving in this situation.

Malignant hyperthermia may present up to 10 hours after induction of general anesthesia.[14] The disorder is characterized by muscle rigidity, tachycardia, and life-threatening hyperthermia. Prompt administration of dantrolene is critical.

SUMMARY

Postoperative fever should be evaluated with a focused approach rather than in "shotgun" fashion. Most fevers

that develop within the first 48 hours after surgery are benign and self-limiting. However, it is critical that physicians who provide postoperative care be able to recognize the minority of fevers that demand immediate attention, based on the patient's history, a targeted physical examination, and further studies if appropriate.

Fever that develops after the first 2 days following surgery is more likely to have an infectious cause, but noninfectious causes that require further evaluation and treatment must also be considered. When evaluating postoperative fever, a helpful mnemonic is the "four Ws":

- Wind (pulmonary causes: pneumonia, aspiration, and pulmonary embolism, but *not* atelectasis)
- Water (urinary tract infection)
- Wound (surgical site infection)
- "What did we do?" (iatrogenic causes: drug fever, blood product reaction, infections related to intravenous lines).

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Septic shock in the postoperative patient:

Three important management decisions

ALI JAHAN, MD

Septic shock is one of the most mismanaged forms of shock. This is primarily due to the lack of focus on the most important aspects: early diagnosis and early, aggressive volume resuscitation. For example, advances in the management of acute coronary syndromes and cerebral ischemic syndromes have resulted from a focus on early, aggressive identification and intervention.

This article provides guidance on three basic questions in the management of septic shock. In doing so, it underscores the clinical significance of early goal-directed therapy and the role for supranormal oxygen delivery, reviews vasopressor use in septic shock, and discusses new concepts in the clinical management of septic shock.

DEFINING SEPSIS

Clinicians need to have a high suspicion for sepsis because the mortality rate for septic shock remains high (30% to 50%). The rate remains unchanged despite advances in critical care medicine. The annual incidence of severe sepsis in the United States has been estimated at 751,000, with 215,000 deaths annually, more than lung and breast cancer combined.[1]

Sepsis is a systemic inflammatory response syndrome (SIRS) that occurs as a result of an infection. SIRS is characterized by the following:

- Temperature of ≥ 38°C or ≤ 36°C
- Heart rate of ≥ 90 beats per minute
- Respiratory rate of ≥ 20 respirations per minute
- White blood cell count of ≥12,000 cells/μL or ≤4,000 cells/μL.

Severe sepsis is defined as sepsis with acute organ dysfunction caused by the sepsis. Severe sepsis results from not only an inflammatory response but also a procoagulant response, which leads to endovascular injury, microvascular thrombosis, organ ischemia, multiorgan dysfunction, and ultimately death.

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MANAGEMENT ISSUE 1: OXYGEN DELIVERY

Should supranormal oxygen levels be targeted?

Studies in which supranormal oxygen levels have been a target of therapy have been difficult to perform and have yielded mixed results. Three major problems with the design of these studies are patient selection, time of enrollment, and inability to reach targeted endpoints. First, the definition of a *high-risk* patient is unclear in many studies. Next, some studies enrolled pre-insult patients, some enrolled post-insult patients, and others enrolled both. Finally, most studies targeted an oxygen delivery level, a cardiac index, or a mixed venous level, but rarely were they able to attain those targeted goals. Not surprisingly, these problems have led to difficulties in interpreting data.

Clinical evidence for intervention. One of the first studies of supranormal oxygen delivery was conducted by Shoemaker and colleagues.[2] Having previously observed that survivors of shock had higher oxygen delivery levels compared with nonsurvivors, they hypothesized that increasing oxygen delivery to supranormal levels might improve outcome.

Although their findings showed that outcomes did indeed improve, the study had significant flaws. It consisted of a small number of relatively young trauma patients, the comparison groups were poorly matched, and the treatment regimens were unclear. Additionally, treatment goals were achieved with fluids alone in two thirds of the patients, with only a small number of patients requiring inotropic support. This study was later followed by other trials,[3–5] which continued to struggle with similar challenges with design, making it difficult to interpret the clinical applicability of their results.

Interpretation. Being able to generate normal or supranormal oxygen levels may be associated with improved outcomes, but having to augment cardiac output with inotropic support to reach supranormal levels is not necessarily beneficial.

Early goal-directed therapy

Early goal-directed therapy involves the early identification of patients with septic shock followed by immediate, aggressive fluid resuscitative efforts and use of antibiotics along with appropriate vasoactive medications.

In 2001, Rivers et al[6] evaluated early goal-directed therapy in emergency room patients with septic shock. They randomized patients to receive either standard therapy at the clinician's discretion or 6 hours of intensive goal-directed therapy.

Patients assigned to early goal-directed therapy had placement of a central venous catheter that measured central venous oxygen saturation (CVO_2), which was monitored continuously. If central venous pressure was less than 8 mm Hg, crystalloid was administered to achieve a central venous pressure of 8 to 12 mm Hg. If mean arterial pressure (MAP) was less than 65 mm Hg, vasopressors were administered to maintain a MAP of at least 65 mm Hg. If the MAP was greater than 90 mm Hg, vasodilators were given until it was 90 mm Hg or less. Once the targeted MAP was achieved, patients whose CVO_2 was less than 70% received transfusions to achieve a hematocrit of at least 30%. If the CVO_2 remained less than 70%, they were given dobutamine (Figure 1).

In-hospital mortality was significantly lower in the group assigned to goal-directed therapy (30%) than in those assigned to standard therapy (46%). Additionally, the critical endpoint of CVO_2 was achieved in 95% of patients assigned to goal-directed therapy. This is unprecedented since in most studies targeting supranormal oxygen delivery levels, equivalent endpoints have only been achieved in 20% to 25% of patients.

A significant finding in support of early, aggressive therapy is that during the first 6 hours of treatment, patients in the goal-directed therapy group received an average of 5 L of fluid, compared with only 3.5 L in the standard therapy group.

Comments. Early, aggressive intervention is important in order to avoid irreversible systemic damage, as demonstrated by the results of Rivers et al.[6] Early intervention may also explain why the hemodynamic goals were obtainable in 95% of patients. This study also suggests that a simple-to-obtain hemodynamic endpoint may have significant practical implications. While most studies require placement of a pulmonary artery catheter for hemodynamic measurement, this study effectively used the results obtained from a central line to guide therapy during the early phases of septic shock.

MANAGEMENT ISSUE 2: CHOICE OF VASOPRESSOR

Which vasopressor should be used?

Along with fluid resuscitation, vasopressors may be needed to help manage persistent hypotension associated with septic shock. Among norepinephrine, dopamine, phenylephrine, epinephrine and vasopressin, norepinephrine is the most appropriate first choice, for reasons reviewed below.

Norepinephrine, after initially developing a negative reputation (it was colloquially known as "Leave 'Em Dead" in a play on its brand name, Levophed), has evolved into the leading choice for vasopressor support in septic shock. Its initial negative reputation stemmed from a variety of factors, including its *potential* negative effect on splanchnic and renal blood flow, its association with renal failure when infused into the renal artery of dogs, and an association with digital ischemia. Consequently, norepinephrine was used as a last resort in many studies, resulting in predictably poor outcomes.

With additional evidence, however, it is now thought to be the least harmful vasopressor in compromising splanchnic perfusion and to contribute to increases in urine output and creatinine clearance. Furthermore, it contributes to preserving organ blood flow by maintaining if not increasing cardiac output.[7,8]

Dopamine. The Surviving Sepsis Campaign guidelines published in March 2004 state that norepinephrine and dopamine are appropriate first-choice drugs to support MAP.[9] In clinical practice, however, dopamine has fallen out of favor. Several studies suggest improved efficacy with norepinephrine when compared with dopamine.

In a 1993 crossover study by Martin et al,[7] 32 patients were randomized prospectively to receive dopamine or norepinephrine. Although dopamine was successful in reversing hemodynamic abnormalities in 5 of 16 patients, norepinephrine was beneficial in 15 of 16 patients. Also, 10 of the 11 nonresponders in the dopamine group responded to norepinephrine, while the one nonresponder in the norepinephrine group did not respond to dopamine. Survival was 59% in the norepinephrine compared with 17% in the dopamine group.

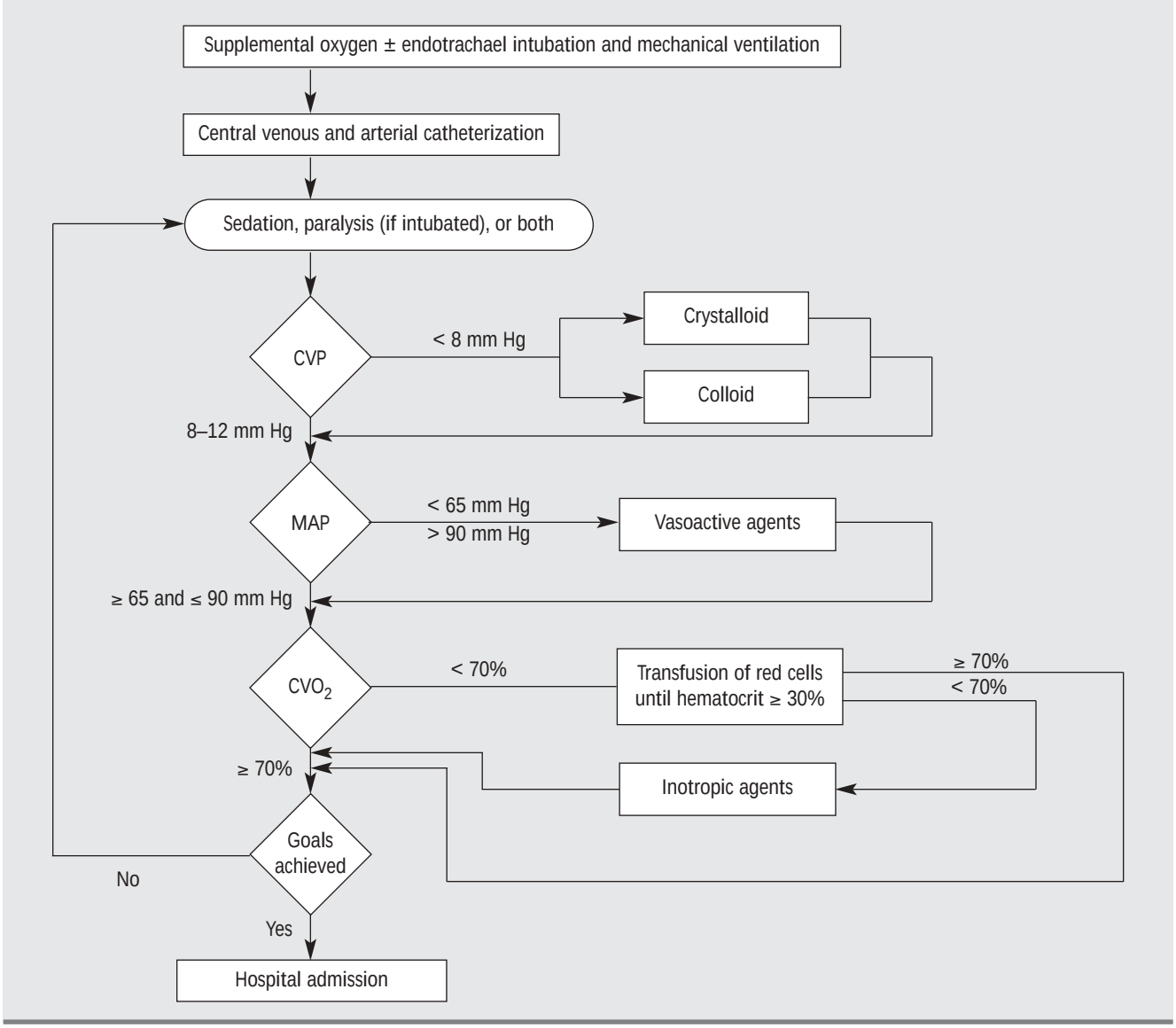

FIGURE 1. Early goal-directed therapy uses a central venous catheter to monitor central venous oxygen saturation (CVO_2) continuously. Interventions are then directed to achieve predefined goals for central venous pressure (CVP), mean arterial pressure (MAP), and CVO_2. Reprinted, with permission, from Rivers E, et al, N Engl J Med 2001; 345:1368–1377. Copyright © 2001 Massachusetts Medical Society. All rights reserved.

The same group of investigators later published an observational study that sought to identify factors associated with outcome among 97 patients with septic shock who were treated with either norepinephrine or high-dose dopamine.[8] Among various factors assessed, the only one that was associated with a favorable outcome was the use of norepinephrine as part of hemodynamic support.

Furthermore, low-dose dopamine is no longer recommended for renal protection. This recommendation is based on the results of a large randomized controlled trial that revealed no clinically significant benefit of dopamine against renal failure[10] and on concerns over potential reductions in secretion of several important hormones, potentiation of immune suppression, and possible splanchnic mucosal ischemia.

Phenylephrine. Few clinical data are available on the use of phenylephrine for hypotension, but its use usually results in an increase in vascular resistance and a subsequent decrease in cardiac output. This decrease in cardiac output leads to reduced splanchnic blood flow and oxygen delivery. Furthermore, a practical concern is that it is frequently ineffective in patients with septic shock.

Epinephrine is not recommended for use as a vasopressor or as an inotropic agent because it compromises splanchnic blood flow, increases lactate production, and potentiates dysrhythmias. Dobutamine is the preferred inotropic agent for use in septic shock if one is needed. For patients with significant hypotension and compromised contractility, the combination of dobutamine and norepinephrine is a reasonable choice.

Vasopressin. The use of vasopressin for management of hypotension associated with septic shock is relatively new. Circulating levels of vasopressin have been found to be inappropriately low in patients with septic shock. Several case reports indicate that when vasopressin is used in patients who remain hypotensive, blood pressure may improve to the point that they can be weaned off norepinephrine. Vasopressin, therefore, should be considered in situations in which escalating doses of norepinephrine are required. However, because vasopressin can have potential adverse effects on splanchnic perfusion and can reduce cardiac output, caution needs to be taken when considering its use. Because of these concerns and a lack of outcomes data, vasopressin is not recommended as a first-line agent for hypotension in septic shock.

MANAGEMENT ISSUE 3: USE OF STEROIDS, ACTIVATED PROTEIN C

Should other interventions be considered?

Consider empiric use of steroids as well as early use of activated protein C, if the clinical condition is appropriate.

Steroids. Preclinical studies conducted in the 1960s suggested that high-dose steroids would improve overall survival for septic shock. However, subsequent human trials have produced inconsistent results, and three meta-analyses conducted in the 1990s suggested no benefit, if not a worsening of outcomes.[11–13]

A renewed interest in steroids was prompted by the realization that severe sepsis may be associated with relative adrenal insufficiency. Also, several studies showed that prolonged treatment with relatively low doses of hydrocortisone improved time to vasopressor therapy withdrawal.

In 2002, Annane et al[14] conducted a study of 300 patients with septic shock who were randomized to a 7-day course of steroids or placebo. Patients were diagnosed with relative adrenal insufficiency if cortisol levels increased by 9 µg/dL or less following stimulation with 250 µg of adrenocorticotropic hormone analog. Steroid treatment reduced the risk of death significantly in the patients with septic shock and relative adrenal insufficiency.

Although these findings are encouraging, long-term outcomes studies are still needed, as well as studies to determine optimal dosing, duration of therapy, and the best means of tapering steroid treatment. An ongoing National Institutes of Health study of 800 patients will address some of these issues.[15]

Activated protein C. Activated protein C (drotrecogin alfa activated) is an endogenous protein that acts as an anti-inflammatory, inhibits thrombosis, and promotes fibrinolysis in sepsis. Evaluating its benefits, the Recombinant Human Activated Protein C Worldwide Evaluation in Severe Sepsis (PROWESS) study[16] found a 6.1% absolute reduction and a 19.1% relative reduction in the risk of death with activated protein C compared with placebo. This difference in risk translates into one additional life saved for every 16 patients with sepsis who are treated with activated protein C.

The Surviving Sepsis Campaign Management Guidelines Committee[9] recommends using activated protein C in patients at high risk of death from sepsis (Acute Physiology and Chronic Health Evaluation [APACHE] score ≥ 25). Its use is contraindicated in patients whose risk of death would further increase if bleeding were to occur. Accordingly, the primary patient group in the PROWESS study was nonsurgical. No breakdown was provided for bleeding events related to surgery; however, a significantly higher incidence of severe bleeding occurred in the group randomized to activated protein C.

The Surviving Sepsis Campaign committee also recommended aggressive glucose control, management of acute respiratory distress syndrome using lower tidal volumes, daily stoppage of sedation for assessment of need, stress ulcer prophylaxis, prevention of deep vein thrombosis, and prevention of ventilator-related pneumonia.

SUMMARY

The medical consultant should have a high index of suspicion for sepsis. Early goal-directed therapy is recommended and includes early, aggressive fluid resuscitation, antibiotics, and vasoactive agents, if needed. CVO_2 may be helpful in guiding therapy, but targeting supranormal levels of oxygen delivery is not necessary. Empiric use of steroids and early use of activated protein C also need to be considered. Vasopressin should be considered if hypotension persists or if the situation requires escalating doses of norepinephrine.

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Optimizing postoperative pain management

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Postoperative pain management is an important but seemingly undervalued component of perioperative care. Over the past decade, medical societies, governmental agencies, and accrediting bodies such as the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) have paid increasing attention to the management of all types of pain, including postoperative pain.

Despite this increased focus, the literature suggests that many patients continue to experience significant postoperative pain. A nationwide survey of 250 patients who had undergone surgery in the previous 5 years revealed that 82% reported postoperative pain, and 86% of those who reported postoperative pain had moderate, severe, or extreme pain.[1] It is clear that we have not yet won the battle against postoperative pain, and it is imperative that we bring every weapon at our disposal to the front.

This review will discuss potential consequences of postoperative pain and briefly outline some management options, including intravenous patient-controlled opioid analgesia (IV PCA).

CONSEQUENCES OF POSTOPERATIVE PAIN

Inadequately controlled pain can cause postoperative morbidity, prolong recovery time, delay return to normal living, and decrease satisfaction with care. Inadequate pain management increases the use of health care resources, thereby increasing total health care costs.[2]

Postoperative pain may be a factor in the development of chronic pain. In a literature review looking at chronic pain as an outcome of surgery, the severity of postoperative pain was positively correlated with the incidence of chronic pain after breast surgery, thoracotomy, and inguinal hernia repair.[3]

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CONVENTIONAL THERAPIES

Acetaminophen: Safe, but watch the total dose

Acetaminophen is considered a weak analgesic compared with other therapies. It has a ceiling effect for analgesia. Although it is considered safer than nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen has an upper-level dose above which patients are at increased risk for liver toxicity. The recommended maximum dosage in adults is 4,000 mg/day.

When acetaminophen is used postoperatively in combination with opioids, approximately 20% less morphine is required to achieve an equivalent level of analgesia; however, there does not appear to be a concomitant reduction in opioid-related side effects, including nausea and vomiting.[4]

NSAIDs: May reduce opioid-related side effects

In appropriate patients, NSAIDs are excellent analgesics for the postoperative period. A recent meta-analysis found that NSAID administration decreased postoperative nausea and vomiting by 30%, most likely because of decreased opioid requirements.[5]

Potential side effects of NSAIDs include increased risks of bleeding (particularly gastrointestinal), gastrointestinal ulceration, and adverse renal effects.

Opioids: The gold standard

Opioids are the gold standard of postoperative analgesia despite their undesirable side effects. They are the mainstay of treatment for moderate to severe pain and can be given by virtually any route. If not for the many adverse effects associated with opioids—some of them potentially serious—the search for other therapies would be much less necessary.

NONTRADITIONAL THERAPIES

Ketamine: Excellent analgesia at very low doses

Ketamine is an *N*-methyl D-aspartate (NMDA) receptor antagonist. This spinal cord receptor facili-

tates the development of pain sensitization and has an influence on the development of opioid tolerance. Subanesthetic doses of ketamine have been shown to decrease opioid requirements, decrease pain scores, and possibly prevent the development of opioid tolerance.[6] Ketamine, however, has significant adverse psychotomimetic effects, which limit its usefulness.

Gabapentin: Analgesic and anxiolytic

Gabapentin is a gamma-aminobutyric acid (GABA) analog, but it does not act through the GABA-ergic system. Its exact mechanism of analgesia is unknown. Gabapentin was originally approved as an anticonvulsant but has been found to be effective in the treatment of chronic neuropathic pain.

Gabapentin also has been shown to be effective as a postoperative analgesic as well as an effective anxiolytic. Premedication with gabapentin was studied in patients undergoing arthroscopic anterior cruciate ligament repair.[7] Twenty-five patients received placebo and an equal number were given a single preoperative dose of 1,200 mg of gabapentin. Patients who received gabapentin had a reduction in preoperative anxiety scores, required less postoperative morphine, had less pain postoperatively, and had greater range of motion during postoperative physical therapy than the control group.

ADVANCED OPTIONS FOR PAIN MANAGEMENT

Epidural analgesia: Efficacious, but more difficult to manage

In an overview of randomized trials, Rodgers et al sought to determine reliable estimates of the effects of spinal or epidural anesthesia on postoperative morbidity and mortality.[8] A correlation was found between the use of these forms of anesthesia and a reduction in the risks of all-cause mortality, deep vein thrombosis, pulmonary embolism, blood loss, respiratory depression, transfusion requirements, and pneumonia.

Continuous epidural analgesia is one of the most effective options for postoperative analgesia. Problems with the technique center around the intense labor requirements to manage it and safety issues associated with thromboprophylaxis therapy.

Peripheral nerve blocks and catheters: Extended-duration analgesia at home?

Peripheral nerve blocks of the upper and lower extremities are useful for postoperative pain relief and, in appropriate situations, as the main anesthetic for surgery.

Extremity surgery is particularly amenable to this type of postoperative pain management. In a study involving patients undergoing rotator cuff surgery, nerve block anesthesia (interscalene brachial plexus blockade) was compared with general anesthesia.[9] One half of the patients received general anesthesia followed by bupivacaine (0.25%) wound infiltration and the other half received interscalene brachial plexus block (0.75% ropivacaine). Compared with the group randomized to general anesthesia, patients assigned to receive the interscalene block had less pain, had less nausea and vomiting, were discharged earlier, were more satisfied with their overall therapy, and were more likely to accept the same therapy if they needed surgery again. Four patients in the group receiving general anesthesia required admission postoperatively because of intractable pain.

The placement of peripheral nerve *catheters* is an option that potentially allows for extended analgesia in an outpatient setting. An appropriate infrastructure must be in place, which includes thorough patient education and around-the-clock availability of staff for questions and issue resolution.[10]

INTRAVENOUS PATIENT-CONTROLLED OPIOID ANALGESIA

IV PCA continues to be a popular choice for postoperative pain control. With IV PCA, after an appropriate loading dose to achieve analgesia, the patient titrates the dosage to his or her comfort level. This method attempts to solve the problem of the wide variability in response to opioids among patients. A systematic review of trials in which opioid-based PCA was compared with the same opioid given intramuscularly, intravenously, or subcutaneously showed that IV PCA improved analgesia and was the preferred route of administration.[11]

Nevertheless, IV PCA is not appropriate for all patients, particularly those who may not have the mental capacity to use it advantageously. Older patients in particular tend to have less success using this mode of analgesia. Patients must be actively managed for IV PCA to be effective; it cannot be a "set and forget" therapy.[12]

Three opioids are typically used for IV PCA: morphine, fentanyl, and hydromorphone. Meperidine has fallen out of favor.

Morphine is the most commonly used opioid, and it is well tolerated at low doses in patients with liver dysfunction. However, it has a renally excreted active metabolite, morphine-6-glucuronide, which can accumulate in patients with renal insufficiency and can increase the risk of sedation and respiratory depression.

TABLE 1
Equianalgesic opioid doses for intravenous patient-controlled analgesia

Morphine 2 mg
Fentanyl 20 µg
Hydromorphone 0.2 mg

Fentanyl is another commonly used opioid in IV PCA. It has a rapid onset and a short duration of action. It has no active metabolites and can be used safely in patients with significant renal or hepatic dysfunction.

Hydromorphone also has no active metabolites. It is five to eight times as potent as morphine and may have fewer side effects.

Opioid dosing for IV PCA. Equianalgesic opioid doses for IV PCA have been established (Table 1), permitting easy interchangeability between opioids.

Meperidine has a renally excreted active metabolite, normeperidine, which has a very long half-life and can accumulate even in patients who have normal renal function. Normeperidine causes neurologic side effects such as shakiness, tremors, myoclonus, jitters, and seizures. A retrospective review of the medical records of 355 patients showed that as the dose and duration of meperidine increased, so did the incidence of side effects and neurologic complications.[13] The authors found a 2% incidence of central nervous system excitation in the patients who were using the highest dosages (600 mg/day) for the longest duration of time. They recommended that if meperidine is used for IV PCA, the dosage should be limited to a maximum of 10 mg/kg/day for no more than 3 days. Meperidine is not used for IV PCA at The Cleveland Clinic.

Example of an IV PCA program for morphine

Table 2 presents a standard PCA program for morphine administration in adults at our facility, with ranges for lower and upper limits. The demand dose (patient-activated dose) of morphine is usually started at 1 mg. The interval between available doses (lockout interval) is 6 minutes. We limit the number of patient-activated doses to a maximum of 10 per hour. For opioid-naïve patients, we do not initiate a continuous infusion, as it has been shown to increase the incidence of respiratory depression.[14] It is important to provide readily available doses that can be administered by the patient's nurse (nurse-activated dose) when breakthrough pain occurs.

TABLE 2
A typical PCA program for morphine

Dose: 1 mg (0.5–2 mg)
Lockout: 6 min (5–12 min)
Hourly limit: 10 doses (5–10)
Basal rate: 0 mg/hr (0–2 mg/hr)
Clinician (nurse-activated) dose

PCA = patient-controlled analgesia

MULTIMODAL ANALGESIA

Multimodal analgesia is a "shotgun" approach to postoperative analgesia. It relies on different classes of analgesics acting at different sites. Using a variety of analgesics at lower doses potentially provides effective analgesia while minimizing adverse effects of the individual therapies.[15] An example of multimodal analgesia would be the treatment of a patient who has had a total knee replacement with a continuous lumbar epidural utilizing a local anesthetic combined with an opioid. In addition, the patient may receive a scheduled dose of an NSAID as well as acetaminophen. Local therapy such as ice might also be applied.

MANAGING INADEQUATE ANALGESIA

As stated earlier, IV PCA is not a "set and forget" therapy. Some patients do not attain effective analgesia and must be evaluated and managed in an expedient manner. Table 3 provides a list of steps to manage a patient who is not responding favorably to your efforts.

Evaluate

First, evaluate the patient to determine the location of the pain and to assess for signs of a possible emerging process (ie, vital signs, physical exam, urine output). Assess the patient's intravenous site for evidence of infiltration or disconnection. Determine whether the patient is using the PCA appropriately, which can be assessed by reviewing the PCA flow sheet and by interrogating the PCA pump. If re-educating the patient does not result in increased use of the pump, an alternative to PCA should be provided, such as around-the-clock opioid administration by the nurse or, in some situations, continuous IV opioid infusion.

All of these therapies rely on frequent assessments of adequacy of analgesia and monitoring for possible sedation and respiratory depression.

Reassess

After making the assessment, attempt to improve the patient's condition by administering additional doses of opioid (such as morphine 2 to 4 mg IV push). If the patient is actually self-administering more than 3 doses per hour and is still uncomfortable, increasing the demand dose by 50% to 100% and/or adding a continuous infusion is appropriate. The easiest way to add an infusion is by starting with a low dosage (morphine 1 mg/hr). If not already prescribed, an adjunctive medication such as an NSAID or acetaminophen is reasonable. Changing to an alternative opioid can be beneficial, as some patients respond better to one opioid than another.

Consult

Finally, if the patient's pain is still uncontrolled, consider obtaining a pain management consult. A pain management consultant is usually more comfortable aggressively dosing opioids as well as adding nontraditional therapies. The consultant may be able to provide advanced pain management options such as peripheral nerve blockade and epidural analgesia. Finally, he or she will be able to help with the transition to oral analgesics.

TRANSITIONING TO ORAL ANALGESICS

The transition from IV PCA to oral analgesics can result in therapeutic failure and decreased patient satisfaction if dosages are inadequate and dosing intervals are improper. These outcomes are particularly a possibility for patients who have been on chronic opioid therapy prior to surgery (see the following section). A recommended approach to handle this transition is the scheduled dosing of an acetaminophen/opioid combination such as 2 tablets of acetaminophen 325 mg/oxycodone 5 mg every 4 hours for 24 to 48 hours, depending on the patient's level of pain. This schedule will help reduce the delays inherent in as-needed dosing strategies.

Early in the transition period, extra medication should be readily available in case the initial therapy is inadequate. A pure oral opioid, such as oxycodone, and/or an NSAID (if not already prescribed as a scheduled medication) is appropriate (eg, oxycodone 5 to 10 mg orally every 4 hours as needed). With more painful procedures, an additional IV opioid as needed is appropriate (eg, morphine 2 to 4 mg IV every 4 hours as needed for breakthrough pain).

TABLE 3
Approach to the patient who has received inadequate analgesia

Evaluate patient
Reassess program
Increase dose
Add basal dose
Change narcotic
Consider adjunct medications
Consider pain management consult

MANAGING OPIOID-DEPENDENT PATIENTS

Mitra and Sinatra have published a useful review of perioperative pain management in the opioid-dependent patient.[16] Many of the concepts presented in this section have been described in their review.

Besides illicit use and use for cancer pain, opioids are being used more frequently for noncancer-related pain. Patients with noncancer ("benign") pain frequently use long-acting opioids, sometimes at alarmingly high doses. As a result, more patients are coming to the operating room with a significant tolerance to opioids, and often suffer excruciating pain postoperatively because they are routinely relatively underdosed. If possible, a pain management consultant should be involved with these patients' care from the beginning.

Very few opioid-dependent patients are truly addicted. They are tolerant to opioid effects, however, and can have a physical dependence to opioids. Tolerance and physical dependence are not equivalent to addiction.

Prevent withdrawal

The first step in managing the opioid-dependent patient is to prevent opioid withdrawal. Patients should be instructed to take their morning dose of opioids on the day of surgery. Consider the patient's preoperative opioid use to be the baseline requirement. If the patient will be NPO after surgery, convert this dose into an equivalent continuous intravenous infusion. It is important to remember (but is often forgotten) that this baseline infusion only covers the patient's *preoperative* requirements. The patient's postsurgical requirements will have to be added to the

baseline. These patients often require doses of analgesics that make any practitioner nervous.

Reduce opioid requirement when possible (but maintain baseline requirements)

Using a multimodal approach is beneficial when managing an opioid-dependent patient. Local anesthetic infiltration by the surgeon, ketamine infusion, clonidine patch, acetaminophen and NSAIDs, muscle relaxants, anxiolytics, peripheral nerve block, and epidural analgesia should be used when appropriate.

Do not rely solely on pain scores when assessing analgesic efficacy

Opioid-dependent patients and patients with chronic pain routinely report high pain scores regardless of their overall condition. They may report a verbal pain rating of 8 out of 10, but then say they are feeling fairly well. Looking at as many objective signs as possible when assessing their overall progress is important. Diet intake, ambulation, ability to cough and breathe deeply, and resumption of "normal" activities (such as smoking) are all important aspects of recovery, and failing to appreciate these aspects may result in unnecessary increases in analgesic doses.

Transition to oral opioids

Opioid-tolerant patients often require an increase in their baseline oral opioid requirements in the several days following surgery. Increases of 30% to 50% are not unusual. Dosages can be tapered back to their baseline requirements over a 1- to 2-week period. If the surgery actually resulted in a decrease of their preoperative pain, further weaning may be possible. Weaning of opioids is a gradual process and should be carried out with the assistance of a physician knowledgeable in this process.

SUMMARY

The quality of postoperative pain management can be improved. Although many safe and effective therapies exist, their utilization varies considerably between and within institutions. Major challenges include the appropriate prescribing of analgesic therapies and the timely response to suboptimal pain control. Patients' satisfaction with their analgesic care may depend less on how well their pain is controlled and more on the attentiveness of their caregivers.

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Nutritional issues in the surgical patient

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In surgical patients, the clinical implications of "malnutrition" (in the broadest sense of the term) include impaired wound healing, immunocompromise, diminished cardiac and respiratory function, and a host of other complications that can lead to longer hospitalizations and higher mortality rates. Studies have shown that the consequences of malnourishment—protein calorie malnutrition (PCM) in particular—might be avoided by the administration of pre-, peri-, and postoperative nutrition support, delivered either parenterally or enterally.

This article reviews evidence on the utility of perioperative nutrition support, provides guidance on patient selection for this support, and outlines calorie and protein requirements.

STUDIES OF PARENTERAL NUTRITION

Preoperative and perioperative TPN: Mixed results

Evidence that pre- and perioperative total parenteral nutrition (TPN) contributes somewhat to better postoperative outcomes has been reported in several studies and meta-analyses. Other reports, however, have indicated that TPN has little effect.

The value of preoperative TPN in preventing serious complications in malnourished patients following major abdominal or thoracic surgery was addressed in a 1991 report by a Veterans Affairs study group.[1] The authors followed 395 patients (99% men) who had undergone nonemergent laparotomy or noncardiac thoracotomy. PCM was assessed by calculating the nutrition-risk index from the following formula, with a score of less than 100 indicating PCM:

$$1.519 \times \text{serum albumin level (g/L)} + 0.417 \times (\text{current weight/usual weight}) \times 100$$

Patients were randomized to receive either TPN for 7 to 15 days preoperatively and 3 days postoperatively (TPN group) or no perioperative TPN (control group). Postoperative follow-up lasted for 90 days, with an interim assessment at 30 days. Patients in both groups were subclassified according to whether or not they had been operated on for cancer (65% of the TPN group and 68% of the controls had cancer). TPN was delivered to a daily caloric goal of 1,000 kcal greater than the resting metabolic expenditure.

The rates of major complications at 30 days were similar: 25.5% in the TPN group and 24.6% in the control group. Likewise, mortality rates at 90 days were comparable: 13.4% and 10.5%, respectively. One of the few statistically significant differences between the two groups was in the incidence of postoperative infection. Infection rates were 14.1% among the treated patients and 6.4% among the controls ($P = .01$; relative risk [RR]: 2.2). The postoperative infections in the TPN group occurred primarily in those patients who had only mild or borderline PCM; overall, TPN provided no demonstrable benefit to these patients.

There was a trend toward a higher incidence of noninfectious complications in the control group as a whole (22.2% vs 16.7%), but the difference was not significant ($P = .20$; RR: 0.75). Again, one significant difference was observed when subgroups were analyzed according to the degree of PCM; TPN recipients with severe PCM had a significantly lower incidence of noninfectious complications than did controls with severe PCM (5% vs 43%; $P = .03$; RR: 0.12).

Hyperglycemia was more common in patients who received nutrition support, but it is possible that the study's designers simply provided too many calories in the TPN doses. If so, this would perhaps explain why so few patients derived any benefit from TPN.

The authors concluded that the use of perioperative TPN should be limited to patients who are

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severely malnourished unless other specific indications are present. Indeed, this is one of the reports that we point to when we argue that perioperative nutrition support is of benefit for a small subgroup of patients.

In 1997, Klein et al combined data from 13 randomized clinical trials involving more than 1,250 patients.[2] They found that 7 to 10 days of preoperative TPN led to a 10% reduction in postoperative complications with no significant effect on postoperative mortality.

In 2001, Koretz et al, under the auspices of the American Gastroenterological Association, published a meta-analysis of 61 randomized clinical trials of perioperative TPN for hospitalized surgical patients.[3] The authors concluded that perioperative TPN failed to improve outcomes in the cohort as a whole, although a few subgroups did receive some benefit. Overall, TPN was associated with a 6% decrease in postoperative complications, but this difference was not statistically significant. They calculated that 17 patients would have to be treated for 7 days in order to achieve a reduction of just one complication. One finding that was not consistent with the previously mentioned VA study[1] was that TPN was more effective in patients who did not have severe PCM. Also, TPN was more beneficial in patients with upper gastrointestinal (GI) malignancies. Finally, Koretz et al concluded that although TPN did not provide any benefit, neither did it cause any harm.

In a meta-analysis published in 2001, Heyland et al combined data on 2,907 patients who had participated in 27 randomized clinical trials.[4] Patients who received TPN preoperatively had a lower rate of postoperative complications than did patients who received standard care with an oral diet and intravenous dextrose. TPN was most effective in patients who had experienced significant (> 10%) weight loss. No difference in postoperative mortality was observed between the two groups.

Postoperative TPN: Often more harmful than helpful

A very limited number of studies of postoperative TPN has shown that administering it without regard to patients' nutritional status does more harm than good. In a meta-analysis of eight studies, Torosian found that postoperative TPN actually increased the incidence of complications by 10%.[5] Similar findings were reported by Klein et al in a meta-analysis of nine trials.[2] Other studies[6] have shown that postoperative TPN improved wound healing and decreased morbidity and mortality.

The take-home message is that postoperative TPN should be reserved for patients who have a prolonged postoperative ileus, which is generally regarded as greater than 7 to 10 days, and for those who are severely malnourished and whose diet cannot be advanced in 3 to 5 days.

STUDIES OF ENTERAL NUTRITION

A literature search uncovered only three comparative studies of enteral nutrition support, and all of them are relatively old.[7–9]

In a randomized study of 24 patients published in 1981, Lim et al found that TPN was superior to gastrostomy feeding—but not significantly so—in terms of achieving a positive nitrogen balance and weight gain during a 4-week period.[7] The authors preferred gastrostomy in view of its lower cost, ease of administration, and safety and because it does not restrict freedom of movement.

The same year, Sako et al reported a randomized study of 69 patients who had undergone radical resection for head and neck cancer.[8] They found no difference between TPN and enteral nutrition administered for at least 14 days postoperatively in terms of immune status, wound healing, complications, and survival.

Finally, Campos and Meguid reported in 1992 that enteral nutrition was equal to both TPN and ad libitum oral nutrition in improving postoperative clinical outcome.[9]

In sum, there were no statistically significant differences in morbidity and mortality between patients who received enteral nutrition or TPN in any of these studies. The take-home message is one that we teach medical students on their first day of rounds: if the gut works, use it.

CLINICAL PRACTICE GUIDELINES

The American Society for Parenteral and Enteral Nutrition (ASPEN) published its practice guidelines in 2002.[6] Several of the ASPEN's main recommendations echo some already cited:

- Preoperative nutrition support should be given for 7 to 14 days to patients with moderate to severe PCM who are undergoing major GI surgery (level A recommendation).
- TPN should not be given during the immediate postoperative period to patients who have undergone major GI surgery (level A recommendation).
- Nutrition support should be given to patients who will be unable to eat for 7 to 10 days postoperatively (level B recommendation).

TABLE 1
Standards for laboratory studies relevant to nutrition status

	Normal	Mildly depleted	Moderately depleted	Severely depleted
Albumin (g/dL)	3.5–5.0	3.0–3.4	2.1–2.9	< 2.1
Transferrin (mg/dL)	176–315	134–175	117–133	< 117
Prealbumin (mg/dL)	18–45	10–17	5–9	< 5
Total lymphocyte count (cells/mm^3)	1,801–3,500	1,501–1,800	900–1,500	< 900

PATIENT SELECTION

Routine investigations

In addition to the medical history, physical examination, and laboratory results, two important factors to consider when deciding whether a patient is a candidate for nutrition support are weight history and anthropometry.

Weight history. More than half the patients who present to our department are overweight, with a body mass index (BMI) of 25 or greater. Evaluating a patient's weight requires care and precision. A patient should not simply be classified as a "well-developed, well-nourished white male" without giving it some thought and inquiry. Likewise, one cannot just look at a patient, pronounce him "overweight," and automatically conclude that he does not need nutrition support. Clinicians must sit down with patients and ask them specific questions, such as, *What is your usual weight? Has there been any change in your weight? If so, what was the pattern of the weight change?* Patients who lose weight rapidly are at greater risk for postoperative complications than patients who lose weight gradually. Patients who lose weight and regain it for whatever reason are at less risk than patients who have simply lost weight.

Taking a brief dietary history can help identify any unusual features of a patient's diet that may have an impact on the postoperative outcome, such as an exclusion of or overindulgence in certain food groups.

Anthropometry. Anthropometry is the act of measuring the body as it relates to its form or shape. The simplest anthropometric measure is height and weight. These data can be used to determine the patient's BMI, a measure of body fatness. Performing upper arm anthropometry is a more sophisticated measure and provides information on both body fat stores and muscle mass. These measures help provide information on the patient's energy and protein stores.

Other investigations. The importance of the medical history is obvious. The physical examination should focus on detecting muscle wasting, skin abnormalities, cheilosis, glossitis, etc. Laboratory studies must evaluate the visceral protein deficiency (see "Laboratory-based classification" below). The chemistry panel can detect deficiency and excess of electrolytes and minerals, and a blood count can identify nutrition-associated anemias.

Classifications of malnutrition

Weight-based classification. One classification system for PCM is based on percentages of ideal and usual body weight:

- Mild PCM: 80% to 90% of ideal body weight or 90% to 95% of usual body weight
- Moderate PCM: 70% to 79% of ideal weight or 80% to 89% of usual weight
- Severe PCM: less than 70% of ideal weight or less than 80% of usual weight.

Laboratory-based classification. Measurement of any of the visceral proteins—albumin, transferrin, or prealbumin—can be used to determine the degree of protein malnutrition (Table 1). However, since these proteins are decreased in the systemic response to injury and sepsis, some practitioners have argued that they should not be used to assess nutrient status in hospitalized patients. While this is true, I would suggest that visceral proteins can still be used in the hospital setting, since when they are depressed, they identify patients with poor outcomes who may benefit from nutrition support. In addition, the total lymphocyte count can be used to assess a patient's immune function, which has been shown to correlate with the degree of visceral protein depletion and clinical outcome.

Albumin. There are several reasons a patient's albumin level might be low. These include protein malnutrition, redistribution from the vascular to the interstitial space as part of the injury response, and

fluid excess following resuscitation. In the hospital, severity of illness and state of hydration affect albumin concentrations more than nutrient status. Because of its long half-life (18 to 21 days), albumin only improves slowly with oral nutrition and nutrition support.

Transferrin has a half-life of 7 or 8 days. Low transferrin levels can occur with the injury response and with overhydration, while it can be elevated in patients who are iron-deficient. Because of its shorter half-life it can be measured once a week to assess the response to nutritional intervention.

Prealbumin has a half-life of 2 days, allowing for a more rapid assessment of a patient's response to nutrition support. Prealbumin concentrations can be increased by renal disease and decreased by fluid status and injury response. Although some physicians find this rapid change useful in performing a nutrition assessment and might be tempted to make frequent changes to a tube feeding of parenteral nutrition formula, I suggest that changes in a nutrient prescription be made no more than once per week because so many other factors can affect these proteins.

NUTRITIONAL REQUIREMENTS

The prescription of energy and protein to the perioperative patient who cannot eat is far different from the amount required to maintain the nutrient status in normal subjects and ambulatory patients. The primary objective in this setting is to improve organ and immune function and to promote wound healing while at the same time avoiding complications of nutrition support, such as hyperglycemia, which has been associated with poor outcome and can undermine the primary objective.

Prior to surgery, total energy needs should be met to promote nitrogen balance, while in the immediate postoperative period, permissive underfeeding is accepted for a brief time, since nitrogen balance can generally never be met during the injury response. In addition, the ability to metabolize carbohydrate and fat is decreased during the injury response, especially when these substrates are provided with TPN. Once patients recover from the stress of surgery and any associated complications, energy requirements can be increased to full goal, assuming glycemic control can be maintained. The suggestions below for energy and protein requirements (see next two sections) are target amounts for most hospitalized patients and should be adjusted depending on substrate tolerance and the response to therapy as measured by visceral proteins, weight gain, wound healing, and functional status.

Calories

Patients who are at or below their ideal weight should be provided with energy based on their current weight. Underweight patients should not be given calories based on their ideal weight, as this generally provides energy above their total requirements and may result in complications of overfeeding. Total energy expenditure in these patients ranges from 25 to 35 kcal/kg. Patients who are overweight may not tolerate full feeding, especially with TPN, since it is provided in the central circulation and first travels to the muscle and other organs for metabolism, rather than being metabolized by the liver first, as occurs with the ingestion of enteral feeding. Choban et al[10] have shown that providing energy in an amount that approximates a low-calorie diet for the treatment of obesity is adequate to allow for recovery of obese patients in the hospital setting.

We have developed an approach that uses BMI, which is calculated by dividing the patient's weight (in kg) by the square of height (in cm) and is an accepted measure of body fatness, to calculate the energy dose for overweight (BMI > 25) and obese (BMI > 30) patients that leads to the desired outcome in most patients. In overweight and obese patients, we do not advance the energy dose as they recover, as the energy deficit is made up by the utilization of the patient's excess energy stores. The method we use to calculate the initial energy dose is listed below and uses the patient's current weight:

- Normal weight/underweight (BMI < 25): 25 to 35 kcal/kg
- Overweight (BMI 25 to 29.9): 20 to 25 kcal/kg
- Obese (BMI 30 to 34.9): 15 to 20 kcal/kg
- Morbidly obese (BMI ≥ 35): 10 to 15 kcal/kg.

Proteins and amino acids

Protein is another matter. The recommended dietary intake of protein in healthy people is approximately 0.8 g/kg/day. In contrast, patients who are sick do not metabolize protein normally, and most of them require approximately 1.5 g/kg/day of protein in enteral solutions and amino acids in parenteral solutions.

Because overweight patients are provided with less energy in their nutrient solution, they must be given plenty of nitrogen to promote wound healing and fight infection. We do not generally give adults more than 2 g/kg unless they experience huge protein losses secondary to fistulas or wounds. In our department, we care for a number of people with graft-versus-host disease, which is a severe protein-losing enteropathy, and occasionally provide up to 2.5 g/kg of amino acids.

Children, however, are given as much as 3 or 4 g/kg of protein or amino acids because growth must also be promoted. Such a high dose in an adult does not lead to an improvement in nutritional status because most of the extra amount is excreted in the urine.

A guide to protein dosing based on BMI follows:

- Normal weight/underweight (BMI < 25): 1.5 g/kg of *current* weight
- Overweight/obese (BMI ≥ 25): 2.0 g/kg of *ideal* weight.

CONCLUSION

The best evidence for pre- or perioperative nutrition support is in patients who are severely malnourished. The use of postoperative TPN should also be reserved for patients with severe malnourishment or patients who are NPO beyond 7 to 10 days; broad use of postoperative TPN is not likely to be helpful and may actually increase the rate of postoperative complications.

Enteral nutrition has been shown to be equivalent to TPN in improving postoperative outcomes and should be used if the patient can eat or a feeding tube can be placed.

Height, weight, weight history, and visceral proteins can be used to assess candidates for preoperative TPN, to determine calorie and protein requirements, and to monitor response to nutrition support.

Finally, it is important to note that preoperative nutrition support should be considered only in patients who are moderately to severely malnourished in whom a major operation is planned, such as thoracoabdominal surgery, and for whom surgery can be delayed for 7 to 10 days to receive an adequate dose of this therapy. In other words, patients who require emergent or urgent surgical intervention should not be given preoperative TPN, even if they are severely malnourished. In addition, we should not expect to see an improvement in visceral proteins in patients with an ongoing injury response; nutrition support is just that—it supports, it does not cure the underlying disease.

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Perioperative medication management:

A case-based review of general principles

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Understanding and applying general principles of perioperative medication management can greatly improve the outcomes of patients undergoing surgery. Although published clinical trial data in this area are limited, the medical consultant can follow a conceptual framework based on case reports, expert consensus, in vitro studies, and pharmaceutical manufacturer recommendations. Other important considerations include pharmacokinetics, the effects of various medications on the primary disease, the impact on perioperative risk, and potential drug interactions with anesthetic agents.

This review uses a series of case studies to illustrate general principles that are the essence of effective perioperative medication management. These principles are helpful in formulating recommendations for the use of medications in this setting, which has been the focus of very few controlled trials. Because discussion of every possible medication is beyond the scope of this article, I will focus on medications known to have perioperative effects and those in common use.

ROLE OF THE MEDICAL CONSULTANT

The primary role of the medical consultant in perioperative medication management is to understand the patient and his or her diseases. A detailed medical history should be taken prior to surgery, including the use of prescribed medications, over-the-counter medications, vitamins, and herbal products.

Medications associated with known morbidity when withdrawn abruptly should be continued during the perioperative period whenever possible; the classic example is clonidine. Medications thought to increase the risk of surgical complications that are not essential for short-term improvement in quality of life should be held through the perioperative period.[1]

Medications not meeting either of these criteria can be discontinued or continued at the managing physician's discretion. If continued, the physician should keep in mind that many other medications are administered perioperatively during a short period and that these may interact with chronic medications. Moreover, the metabolism and elimination of chronic medications and their metabolites may be altered during the perioperative period.

CASE 1: CHRONIC ASPIRIN USE IN A PATIENT UNDERGOING WISDOM-TOOTH EXTRACTION

A 28-year-old woman is scheduled for a wisdom-tooth extraction. She has a history of migraines and uses the combination analgesic product Fiorinal (aspirin, caffeine, and the nonnarcotic barbiturate butalbital) almost daily. What perioperative recommendations should be made regarding this aspirin use?

The decision to continue or discontinue aspirin use preoperatively should balance the consequences of perioperative hemorrhage against the risk of perioperative vascular complications. Aspirin is an irreversible inhibitor of platelet cyclo-oxygenase. This effect leads to increased intraoperative blood loss and transfusion requirements.[2] Nonetheless, in selected patient populations, especially those who are undergoing coronary artery bypass graft surgery, observational studies suggest that withdrawal of aspirin preoperatively is associated with increased in-hospital mortality.[3,4] A similar risk has been observed in patients undergoing surgery for peripheral vascular disease.[5] On the other hand, with cataract surgery, the risk of ocular hemorrhage in patients taking aspirin is extremely low and similar to that in patients not taking aspirin. Aspirin should be withheld before surger-

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ies in which perioperative hemorrhage could be catastrophic (eg, central nervous system surgery).

Remember that the circulating platelet pool is replaced every 7 to 10 days.[6] Since aspirin is an irreversible inhibitor of platelet cyclo-oxygenase, aspirin use should be stopped 7 to 10 days prior to surgery, when applicable.

CASE 2: NSAID USE AND HORMONE REPLACEMENT THERAPY IN A HIP REPLACEMENT CANDIDATE

A 68-year-old woman with severe osteoarthritis is scheduled for a total hip replacement. She takes acetaminophen and ibuprofen for her arthritis, and she is also receiving postmenopausal hormone replacement therapy (HRT). What recommendations should be provided regarding this patient's medications?

Acetaminophen is relatively safe, has few side effects, and does not affect bleeding and therefore can be continued safely in patients undergoing major surgery.

NSAIDs. Ibuprofen is a nonsteroidal anti-inflammatory drug (NSAID), and NSAIDs are reversible inhibitors of platelet cyclo-oxygenase. They can induce renal failure in combination with other drugs, specifically angiotensin-converting enzyme (ACE) inhibitors, particularly in the presence of hypotension and dehydration. Cyclo-oxygenase-2 (COX-2) inhibitors (ie, celecoxib) have much less effect on platelet function, although the potential for nephrotoxicity remains.

In general, because they are reversible inhibitors of platelet cyclo-oxygenase, NSAIDs should be held approximately 3 days before surgery. However, this recommendation is not evidence-based, as illustrated by a recent study by Goldenberg et al,[7] who prospectively examined the duration of platelet dysfunction after a 7-day course of ibuprofen in 11 healthy subjects. They were able to show that platelet function normalized by 24 hours after the last dose. This was a small study, however, and the generalizability of its findings is limited because only healthy subjects were included. We clearly need more studies to answer this question fully.

HRT. In 2000, the large randomized Heart and Estrogen/progestin Replacement Study (HERS) revealed that postmenopausal HRT increased the risk of deep vein thrombosis and pulmonary embolism in women with coronary heart disease (Table 1).[8] This risk increased after patients sustained a lower extremity fracture. After surgery, the risk was magnified and stayed magnified for about 3 months postoperatively. For this reason, many experts recommend stopping HRT for approximately 4 weeks before major surgery.

TABLE 1
Key findings of HERS trial of hormone replacement therapy and venous thromboembolic risk*

- HRT increased risk of VTE 2.7-fold overall
- HRT increased risk of VTE 18-fold in patients with lower extremity fractures
- HRT increased risk of VTE approximately 5-fold in the 90 days following inpatient surgery
- HRT increased risk of VTE 5.7-fold in the 90 days following hospitalization

* In postmenopausal women with coronary heart disease. Data are from reference 8.

HERS = Heart and Estrogen/progestin Replacement Study; HRT = hormone replacement therapy; VTE = venous thromboembolism

The HERS trial included only women with coronary heart disease, however, and routine discontinuation of HRT for major noncardiac surgery is controversial. A recent case-control study with 108 cases and 210 controls found no association between perioperative HRT use and postoperative venous thromboembolism.[9]

At The Cleveland Clinic's IMPACT (Internal Medicine Preoperative Assessment, Consultation, and Treatment) Center and at many other institutions across the country, patients are typically seen 1 to 2 weeks before surgery. In that situation, the prothrombotic state that HRT produces is not going to dissipate if the patient stops the drug 1 week prior to surgery; this prothrombotic state actually takes a few weeks to dissipate. Several experts feel that routine HRT discontinuation may be unnecessary in patients receiving appropriate pharmacologic antithrombotic prophylaxis.[9]

CASE 3: CARDIOVASCULAR AND PULMONARY DRUGS IN THE SETTING OF ABDOMINAL SURGERY

A 64-year-old man with a history of stable angina, congestive heart failure (CHF), ventricular tachycardia, and chronic obstructive pulmonary disease (COPD) is scheduled for inguinal hernia repair. His medications include digoxin, atenolol, atorvastatin, amiodarone, furosemide, clopidogrel, lisinopril, and inhalers for his COPD. How should these cardiovascular and pulmonary medications be managed perioperatively?

Cardiovascular medications

The most commonly prescribed cardiovascular drugs or drug categories include clopidogrel, nitrates, digoxin, beta-blockers, calcium channel blockers, antiarrhythmics, ACE inhibitors, angiotensin II receptor

TABLE 2
Perioperative recommendations for common cardiovascular drugs

Drug/drug category	Recommendations
Clopidogrel	Discontinue 7–10 days before major surgery (due to irreversible antiplatelet effect)
Nitrates Digoxin Clonidine Beta-blockers Calcium channel blockers Antiarrhythmics	Continue up to and including day of surgery, particularly clonidine and beta-blockers. If therapy cannot be interrupted and patient is on parenteral feeding, consider transdermal or intravenous administration.
Diuretics ACE inhibitors Angiotensin II receptor blockers	Hold on morning of surgery, especially if the indication is congestive heart failure[10,11]
Niacin Fibric acid derivatives Cholestyramine Colestipol	Hold at least 1 day before surgery
Statins	Continue in the perioperative period[12–14]

blockers, diuretics, and cholesterol-lowering medications, including statins.

The decision about whether and when to withhold various cardiovascular drugs prior to surgery varies by the type of medication, as detailed in Table 2.[10–14]

Clopidogrel is an irreversible platelet inhibitor: it blocks the adenosine diphosphate receptor, which prevents fibrinogen binding at that site and thereby reduces the possibility of platelet adhesion and aggregation. For this reason, clopidogrel should be stopped 7 to 10 days before surgery.

Nitrates, digoxin, clonidine, beta-blockers, calcium channel blockers, and antiarrhythmic drugs are essentially safe to continue perioperatively. If therapy cannot be interrupted and the patient is being fed parenterally, consider transdermal or intravenous administration as needed.

At our institution, we generally hold diuretics, ACE inhibitors, and angiotensin II receptor blockers the morning of surgery, especially if CHF is the indication for their use.[10,11] If the indication is hypertension and the systolic blood pressure is, for example, 160 mm Hg, the physician may make an informed decision to continue the medication on the day of surgery. However, if the medications are being taken for CHF and the systolic blood pressure is 110 mm Hg or lower, it is typically advisable to hold the drug on the day of surgery. This approach is based on two studies from the 1990s that demonstrated an increased risk of hypotension after induction of anesthesia if patients received ACE inhibitors on the day of surgery.[10,11] It is generally advisable to hold diuretics in light of their associated risk of hypokalemia.

Several cholesterol-lowering medications, including niacin, fibric acid derivatives, cholestyramine, and colestipol, carry a theoretical risk of rhabdomyolysis and myositis, and the literature does not demonstrate that these medications have an impact on short-term cardiovascular outcomes. Hence, patients should be advised to stop these medications 1 day before surgery.

Statins are a different issue, however. Evidence is emerging that statins may prevent vascular events through mechanisms other than cholesterol reduction (ie, plaque stabilization, reduction in inflammation, decreased thrombogenesis). These benefits may be lost if statins are discontinued, and some data from animal models suggest that discontinuation of statins in patients who have been taking them chronically can produce a rebound prothrombotic state. For these reasons, statins should be continued in the perioperative period.[12–14]

Pulmonary medications

Commonly prescribed pulmonary medications include theophylline, inhaled beta-agonists, inhaled ipratropium, inhaled corticosteroids, and leukotriene inhibitors.

Theophylline can be a difficult drug to manage. It has a very narrow therapeutic window and is associated with several drug-drug interactions that can lead to toxicity. We typically ask our patients to discontinue theophylline the evening before surgery. The individual managing physician may decide to continue the drug, however, in which case monitoring for symptoms and signs of theophylline toxicity, including taking a blood level, is important.

Other pulmonary medications, including inhaled beta-agonists, inhaled ipratropium, inhaled corticosteroids, and leukotriene inhibitors, are typically continued up to and including the day of surgery. These medications are essential for reducing postoperative pulmonary complications, especially in patients who have COPD or asthma.

CASE 4: ELECTIVE SURGERY AFTER RECENT DRUG-ELUTING STENT PLACEMENT

A 55-year-old man is referred for medical evaluation. He is scheduled to undergo elective total right-sided

knee replacement in the coming week. His medical history includes known coronary artery disease, and he underwent coronary revascularization with placement of a paclitaxel-coated stent 8 weeks ago. His medications include aspirin (81 mg/d), clopidogrel (75 mg/d), atenolol (50 mg/d), and atorvastatin (40 mg/d). How should these medications be managed in the perioperative period?

Stent placement calls for full course of antiplatelet therapy

The patient's atenolol and atorvastatin could be continued safely (see previous case); the question here centers on the antiplatelet agents. There is significant controversy over the optimal management of patients undergoing noncardiac surgery who have not completed their course of antiplatelet therapy for a recently implanted drug-eluting coronary stent. Mounting evidence suggests that premature discontinuation of antiplatelet therapy is associated with a very high rate of stent thrombosis and may be associated with a high case fatality rate.[15,16]

With a paclitaxel-eluting coronary stent system, current recommendations call for a minimum of 6 months of uninterrupted dual-antiplatelet therapy. With a sirolimus-eluting coronary stent, a minimum of 3 months of uninterrupted antiplatelet therapy is recommended. The reason that aggressive antiplatelet therapy is recommended with the use of drug-eluting stents is because the sirolimus and paclitaxel coatings may retard the endothelialization process, thereby markedly raising the risk of thrombogenesis.

A case like this is further confounded by the following factors:

- Surgery is a prothrombotic state.
- The true incidence of stent thrombosis and postoperative myocardial infarction (MI) in patients undergoing noncardiac surgery is not known.
- Most surgeons will not operate on patients receiving antiplatelet therapy, which can pose a real dilemma.

Further studies needed—and under way

Because this patient's scheduled surgery is an elective one, the prudent course would be to delay it until his full recommended course of post-stenting antiplatelet therapy is completed, after which the antiplatelet agents can be more safely stopped for the surgery.

Cases in which surgery is not elective, however, demand better answers to the questions raised by this case. To help further clarify such questions, we recently initiated a study at our IMPACT Center to examine the incidence and the predictors of postoperative MI, stent thrombosis, and bleeding outcomes in patients with implanted drug-eluting coronary stents undergoing noncardiac surgery (elective and emergent) who had premature cessation of antiplatelet therapy. These results will be available in the next few months.

CASE 5: TOE AMPUTATION IN A PATIENT WITH TYPE 2 DIABETES

A 72-year-old man who has a history of type 2 diabetes mellitus treated with insulin for the past 20 years develops a diabetic foot infection. Despite 6 weeks of intravenous antibiotics, the foot does not heal and it is determined that his toe needs to be amputated. He is receiving neutral protamine Hagedorn (NPH) insulin (20 U in the morning and 10 U in the evening) and 8 U of fast-acting insulin lispro with each meal. How should his diabetes therapy be managed in the perioperative period?

While there are no clear evidence-based recommendations for perioperative management of insulin or other medications for type 2 diabetes, a few general principles can be set forth:

Insulin. Current consensus among clinicians generally supports giving long-acting insulin at half the normal dose and holding short-acting insulin. At our institution, however, we hold all insulin on the morning of surgery and we generally resume the home insulin regimen when the patient resumes taking medication orally postoperatively. Patients with type 2 diabetes are triaged to be the first surgical cases of the day so that the anesthesiologists can assume the diabetes management early on.

Metformin is held for 2 days before surgery because of the risk of lactic acidosis if a patient were to develop a renal problem perioperatively.

Other oral antidiabetic agents. Sulfonylureas, thiazolidinediones, and alpha glucosidase inhibitors are held the morning of surgery.

CASE 6: PSYCHOTROPIC DRUGS IN A MASTECTOMY CANDIDATE WITH SEVERE DEPRESSION

A 38-year-old woman with a history of severe depression is scheduled for a mastectomy for breast cancer. Her medications include fluoxetine, olanzapine, and lorazepam, all taken for many years. How should these agents be managed?

Antidepressants. Selective serotonin reuptake inhibitors such as fluoxetine are very safe in the perioperative setting and may be continued without concern. Tricyclic antidepressants inhibit the uptake of norepinephrine and serotonin and may enhance the action of sympathomimetics. Little evidence is available to guide decisions about their perioperative use,

but our institution typically continues tricyclic antidepressants throughout the perioperative period, especially for patients on high doses.

Monoamine oxidase inhibitors (MAOIs) carry a potential risk for hypertensive crises and a large number of drug-drug interactions. MAOIs are usually taken by patients with more refractory depression. A MAOI-safe anesthetic technique has been described and used in patients requiring emergency procedures. The decision to continue or withhold MAOIs before surgery requires close collaboration with the patient's anesthesiologist and psychiatrist.

Benzodiazepines such as lorazepam are very safe perioperatively. For this reason and because their abrupt withdrawal can lead to an excitatory state (with hypertension, agitation, delirium, and seizures), they should be continued.

Antipsychotics such as olanzapine are also continued perioperatively.

CASE 7: HERBAL PRODUCTS AND PRESCRIPTION DRUGS IN A HIP REPLACEMENT CANDIDATE

A 68-year-old woman with a history of hypertension, osteoarthritis, and osteoporosis is scheduled for total hip replacement and presents for a consult. Her medications include atenolol, hydrochlorothiazide, and alendronate. She also reports taking the herbal supplements ginkgo biloba and echinacea. How should these herbal products be managed?

Herbal use widespread, perioperative risks real

A comprehensive literature review published in JAMA in 2001 documented widespread use of herbal supplements among the presurgical population: approximately one third of patients from the included studies were taking herbal products.[17] The review identified eight common herbal supplements that may pose a safety concern during the perioperative period: ginkgo biloba, echinacea, ephedra, garlic, ginseng, kava, St. John's wort, and valerian. The potential complications identified were serious, including MI, stroke, bleeding, and prolongation of the action of anesthetic drugs, which can cause inadequate anesthesia and interference with other drugs.

In light of these findings, patients should generally be asked to stop all herbal supplements at least 5 to 7 days before surgery. Risks specific to individual herbal preparations are detailed below.

The "three Gs" and bleeding risk. Ginkgo biloba, garlic, and ginseng—sometimes referred to as the "three Gs"—may all increase the risk of bleeding.

- Ginkgo biloba can cause bleeding through inhibition of platelet-activating factor, so patients should be asked to stop this supplement 36 hours before surgery.
- Garlic inhibits platelet aggregation (potentially as an irreversible inhibitor), may increase fibrinolysis, and has equivocal antihypertensive activity. Its use should be discontinued at least 7 days before surgery.
- Ginseng also inhibits platelet aggregation (potentially as an irreversible inhibitor). There is also some suggestion of an increased risk of hypoglycemia in chronic users of ginseng. This product may also reduce the anticoagulant activity of warfarin. It should be stopped at least 7 days before surgery.

Echinacea. The pharmacologic effect of echinacea is activation of cell-mediated immunity. Allergic reactions and immune system dysfunction also may occur. Data on perioperative discontinuation of echinacea are extremely limited, but patients at our institution are typically asked to discontinue it before surgery as a safeguard.

Ephedra. Perioperative concerns include tachycardia and hypertension, MI, stroke, hemodynamic instability, and drug-drug interactions with some psychiatric medications. Patients should be asked to stop ephedra 24 hours before surgery.

Kava causes sedation and potentiation of anesthetic medications, and its use is associated with concerns about withdrawal, tolerance, and addiction. Patients should be asked to stop kava 24 hours before surgery.

St. John's wort is associated with many potential drug-drug interactions through its induction of cytochrome P-450 enzymes. This supplement should be discontinued at least 5 days before surgery.

Valerian has a sedative pharmacologic effect, so it can increase the sedative effect of anesthesia, whereas its withdrawal may raise anesthetic requirements. No data are available on its perioperative discontinuation or use.

What about vitamins?

Many surgical patients are likely to also be taking vitamins. Multivitamins are highly safe perioperatively. Because vitamin E supplements carry a risk of bleeding, patients should be asked to stop their use 10 days before surgery.

CASE 8: RHEUMATOID ARTHRITIS DRUGS IN A PATIENT UNDERGOING CHOLECYSTECTOMY

A 55-year-old woman is scheduled to undergo laparoscopic cholecystectomy in 2 weeks. She has a history of stable rheumatoid arthritis, and her medications include weekly methotrexate and hydroxychloroquine. What medication recommendations are in order?

Hydroxychloroquine is believed to be safe in the perioperative period.

Methotrexate and other DMARDs. Data on the perioperative use of methotrexate are limited. One prospective randomized trial published in 2001 focused on rheumatoid arthritis patients taking methotrexate who underwent elective orthopedic surgery, and it found no increase in infection rate or surgical complications when methotrexate was continued.[18]

There are no published data on the perioperative use of other disease-modifying antirheumatic drugs (DMARDs). Because many DMARDs are renally excreted, impaired kidney function can lead to an accumulation of these drugs or their metabolites, which may lead to bone marrow suppression. Methotrexate should be held for 2 weeks before surgery in patients with renal insufficiency.

TNF-alpha inhibitors. Only one study has been published on the perioperative use of tumor necrosis factor (TNF)-alpha inhibitors in patients with rheumatoid arthritis.[19] This single-center, nonrandomized, prospective cohort trial involved 31 patients with rheumatoid arthritis who underwent elective foot and ankle surgery. Half of the patients were receiving TNF-alpha inhibitors and half were not; all patients continued their antirheumatic drug regimens unaltered in the perioperative period. Postoperative outcomes were similar between the patients who received TNF-alpha inhibitors and those who did not in terms of surgical healing and infection rates. The authors concluded that TNF-alpha inhibitors may be safe in the perioperative period, but further studies are needed.

SUMMARY

Medical consultants need to recommend the safest and the most effective ways to manage chronic medications in the perioperative period. Outcomes data from clinical trials are limited in regard to perioperative medication management, so specific clinical trials are not available to guide decision-making in most circumstances. More studies in this field are needed. Communication and collaboration with anesthesiologists and surgeons as well as with primary care physicians are key to achieving optimal outcomes.

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Preventing venous thromboembolism in surgical patients

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Venous thromboembolism (VTE) is a common cause of postoperative morbidity and mortality that can be prevented effectively with well-established, hospital-based prevention strategies. VTE prophylaxis should be considered for all hospitalized patients, although not all surgical patients will ultimately receive it based on their risk factor profile. This article discusses the extent of VTE and provides guidance for appropriate pharmacologic and nonpharmacologic strategies for prophylaxis in surgical patients.

PREVENTION EFFORTS NEED TO BE INCREASED

Many cases of VTE, which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), could be prevented by increasing efforts at prophylaxis. In a recent study of 2,726 patients with DVT diagnosed from 183 hospitals in the United States, only 42% received prophylaxis within 30 days before their diagnosis.[1]

Prophylaxis appears to be practiced more consistently by surgeons than by other specialists.[2] The incidence of fatal PE is less in surgical patients (< 0.6%) compared with hospitalized medical patients (3.3%).[3] In a series in Sweden, patients admitted for general surgery had a lower incidence of fatal PE than patients admitted for orthopedic surgery, infectious diseases, general medicine, or cancer.[4] The trends may reflect that strategies for prophylaxis were introduced more than 30 years sooner for surgical patients than for medical patients.[5]

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Recommendations abound, requirements coming

Guidelines from the Seventh American College of Chest Physicians (ACCP) Conference on Antithrombotic and Thrombolytic Therapy in 2004 recommend that every hospital develop a formal strategy to prevent the complications of thromboembolism.[6] In addition, the Agency for Healthcare Research and Quality (AHRQ) lists appropriate prophylaxis against VTE for patients at risk as one of its top 10 safety practices,[7] and a similar recommendation has been made by the National Quality Forum.[8] Although recommendations for VTE/DVT prophylaxis have been promulgated by various organizations since 1986, fewer than one in 10 acute care hospitals has such a program.

The Centers for Medicare and Medicaid Services is expected to eventually require an appropriate prophylaxis strategy for VTE as part of public reporting, with federal financing of hospitals dependent on such a strategy being in place.

Asymptomatic thromboemboli are appropriate targets

Traditionally, clinically relevant thromboembolism (ie, likely to cause an acute, and possibly fatal, pulmonary embolism) has been defined as thrombi in the proximal system that cause symptoms. In contrast, asymptomatic distal venous thrombi, which are typically only discovered by ultrasonography or venography in research studies, are generally deemed clinically unimportant. These silent thromboemboli are often used as surrogate markers for clinically relevant thromboemboli, and meta-analyses of orthopedic trials have found that prevention of venographic clots mirrors a reduction in clinical events.[9]

The consequences of VTE are large

Each year, DVT develops in an estimated 2 million people worldwide, of whom about 600,000 develop a PE and 100,000 die.[10] About one third of patients who survive VTE develop venous stasis syndrome within 10 years.[11–13]

SURGICAL PATIENTS AT HIGH RISK

Risk assessment models and scoring systems have been developed for determining who is at risk for venous stasis, endothelial damage, or hypercoagulation (Table 1).[14,15] Most hospitalized patients, whether medical or surgical patients, have at least one risk factor for DVT, with obesity being the most common, and many have multiple risk factors.[16]

In the absence of prophylaxis, rates of postoperative DVT are high and vary with the type of procedure. This risk is greatest in patients undergoing knee surgery (65%), followed by hip surgery (50%), neurosurgery (29%), general surgery (20%), gynecologic surgery (19%), and prostate surgery (11%). Without prophylaxis, surgery for hip fracture has the highest rate of fatal PE (5%).[6]

Such estimates have enabled the categorization of risk for developing DVT or PE in the absence of prophylaxis (Table 2).[17] In practice, however, relying on complicated risk stratification is probably less advisable than considering nearly all hospitalized patients who are sick, old, or having surgery as being at risk for developing thromboembolism. In general, patients who are undergoing minor same-day procedures and are ambulatory have a low risk, and patients who require a hospital stay of more than 1 to 2 days have a greater risk.

TABLE 1
Risk factors for venous stasis and endothelial damage[14,15]

Risk factors for venous stasis
Age > 40 yr
Immobilization
Varicose veins
Myocardial infarction
Congestive heart failure
Stroke
Paralysis
Spinal cord injury
Hyperviscosity syndromes
Polycythemia vera
Severe chronic obstructive pulmonary disease
Anesthesia
Repair or ligation of major venous injury
Risk factors for endothelial damage
Surgery (orthopedic, pelvic, neurologic, abdominal)
Prior deep vein thrombosis
Central venous access
Trauma

NONMEDICATION STRATEGIES FOR PROPHYLAXIS

Ambulation

Many regard ambulation as a preventive strategy, but it has never been tested as such. Studies in which aggressive ambulation has been encouraged have not included a nonambulating control group. Although ambulation is appropriate postoperative care, it should not be regarded as a sufficient strategy for DVT prophylaxis.

Compression stockings

The evidence to recommend the use of elastic or graded compression stockings as a prevention strategy is insufficient. Although stockings have been shown to prevent DVT compared with placebo,[18] the effect is only modest, and most studies have enrolled only low-risk patients. Another unresolved issue is whether thigh-high stockings are superior to calf-high stockings, as most studies combine both types.

Studies that show that compression stockings are helpful when combined with additional measures for prophylaxis are also not applicable to modern practice. They tend to be early studies that compared stockings with treatments such as aspirin or dextran that are no longer deemed sufficient today.

The best evidence for benefit with elastic stockings is as an adjunct to other methods of VTE prophylaxis following gynecologic surgery, especially for cancer.

Mechanical devices

Mechanical devices such as sequential compression devices improve venous flow. Compliance is a barrier to their use as indicated: to be effective, these devices need to be worn nearly 90% of the day.[19] In the surgical setting, mechanical devices should be placed on the patient before inducing anesthesia.

New small, portable devices offer continuous compression therapy, and if they prove successful may bring about a major advance in this strategy.

The 2004 ACCP guidelines recommend that mechanical devices be used primarily for prophylaxis of VTE in patients at high risk for bleeding.[6] This practice is especially applicable to specific surgical situations in which the use of prophylactic drugs has not been studied carefully, such as neurosurgery, complicated orthopedic spine surgery, and plastic surgery.

PHARMACOLOGIC PREVENTION STRATEGIES

Pharmacologic strategies entail the risk of bleeding, and although the drugs used for VTE prophylaxis

TABLE 2
Levels of thromboembolic risk in surgical patients without prophylaxis

Risk level (examples)	Calf DVT, %	Proximal DVT, %	Clinical PE, %	Fatal PE, %
Low risk (minor surgery in patients < 40 yr with no additional risk factors)	2	0.4	0.2	0.002
Moderate risk (minor surgery in patients with additional risk factors; nonmajor surgery in patients aged 40–60 yr with no additional risk factors; major surgery in patients < 40 yr with no additional risk factors)	10–20	2–4	1–2	0.1–0.4
High risk (nonmajor surgery in patients > 60 yr or with additional risk factors; major surgery in patients > 40 yr or with additional risk factors)	20–40	4–8	2–4	0.4–1.0
Highest risk (major surgery in patients > 40 yr plus prior VTE, cancer, or molecular hypercoagulable state; hip or knee arthroplasty, hip fracture surgery; major trauma; spinal cord injury)	40–80	10–20	4–10	0.2–5

DVT = deep vein thrombosis; PE = pulmonary embolism; VTE = venous thromboembolism
Adapted, with permission, from reference 17.

have been well assessed for safety, individual variation must be considered. Doses of drugs that are cleared by the kidneys (ie, low-molecular-weight heparins [LMWHs], fondaparinux, direct thrombin inhibitors, and other antithrombotic agents) should be determined only after taking into account the possibility of renal impairment, especially in elderly patients or those at high risk for bleeding.[6]

Aspirin: Controversies continue

The use of aspirin as prophylaxis against thromboembolism has become controversial. The 2004 ACCP guidelines recommend that aspirin not be used for VTE prophylaxis in any patient group.[6]

Two large studies show that aspirin reduces the risk of VTE. The Antiplatelet Trialists' Collaboration[20] conducted an overview of 53 trials that involved 8,400 patients undergoing general or orthopedic surgery who received an average of 2 weeks of antiplatelet therapy or control. Twenty-five percent of patients assigned to antiplatelet therapy developed DVT compared with 34% of controls (two-sided $P < .00001$), and 1.0% of patients allocated antiplatelet drugs developed PE vs 2.7% of controls (two-sided $P < .00001$).

In the Pulmonary Embolism Prevention (PEP) trial,[21] more than 17,000 patients who were undergoing surgery for hip fracture or elective hip or knee arthroplasty were randomized to at least 160 mg of aspirin for 35 days or no aspirin. Both groups continued to have access to prophylaxis strategies as recommended by their treating physicians. In the overall study population, the relative risk of PE or DVT was reduced by 34% ($P = .0003$) among aspirin recipients.

Among patients with hip fracture in the PEP trial, a subgroup that also received LMWH did not derive significant additional benefit from aspirin, although the hazard ratio for PE and symptomatic DVT was less than 1.0 among aspirin users. No significant benefit to aspirin was observed during the first postoperative week, a period during which the risk of thromboembolism may be greatest.

Patients in the PEP trial who underwent elective hip or knee arthroplasty did not benefit significantly from aspirin, but their absolute risk of thromboembolism was lower compared with the much larger group of patients with hip fracture. In addition, one third of the patients undergoing elective hip or knee arthroplasty received prophylaxis with LMWH, which may have masked a possible favorable effect of aspirin.

Often overlooked in the PEP data is the significant risk of bleeding with aspirin. The risks of gastrointestinal bleeding and wound bleeding in the PEP trial were higher in aspirin recipients. This risk of bleeding outweighed the benefit of a reduction in the risk of DVT events: for every symptomatic DVT

TABLE 3
FDA-approved thromboembolic prophylaxis indications of available anticoagulants

Indication	Low-molecular-weight heparins			Fondaparinux	UFH
	Enoxaparin	Dalteparin	Tinzaparin		
Prevention of DVT in hip replacement	Yes	Yes	No	Yes	No
Extended DVT prophylaxis in hip replacement	Yes	Yes	No	No	No
Prevention of DVT in knee replacement	Yes	No	No	Yes	No
Prevention of DVT in abdominal surgery	Yes	Yes	No	Yes	No

DVT = deep vein thrombosis; UFH = unfractionated heparin

averted, an increase of one wound hemorrhage and 10 gastrointestinal hemorrhages was observed in patients assigned to aspirin.

Although aspirin may have a role for thromboembolic prophylaxis in patients with hip fracture, or as extended prophylaxis (beyond the first week following surgery), it offers no clear benefit for prophylaxis among patients undergoing hip or knee arthroplasty.

Unfractionated heparin and low-molecular-weight heparins

Both low-dose unfractionated heparin (UFH) and, more recently, LMWHs have been standard therapies for VTE prophylaxis in a wide range of surgical settings. As opposed to UFH, which must be given two or three times daily, LMWHs can be given once or twice daily because of their longer plasma half-lives. The anticoagulant response to LMWH is also more predictable than the response to UFH. For prophylactic use, neither UFH nor LMWH requires monitoring.

In a 1994 meta-analysis of 56 trials that compared various therapies (aspirin, dextran, warfarin, UFH, LMWH, and compression stockings) to prevent VTE following total hip replacement, all therapies except aspirin were found to reduce the risks of DVT and proximal venous thrombosis compared with controls, but only LMWH and stockings reduced the risk of PE.[22]

Vitamin K antagonists

In a 2004 meta-analysis, Mismetti et al[23] found that LMWH strategies were superior to vitamin K antagonists (eg, warfarin) for prophylaxis against VTE in patients undergoing major orthopedic surgery. LMWHs performed better than vitamin K antagonists in preventing total and proximal DVT. No significant difference was found between the two strategies in the prevention of clinical PE or death, or in rates of wound hematomas or major bleeding.

Although vitamin K antagonists such as warfarin are convenient to use because they are available in oral form, they are less effective than the newer anticoagulants and require titration to achieve and maintain a therapeutic level, defined as an international normalized ratio (INR) of 2.0 to 3.0. Furthermore, achieving a full therapeutic window takes a minimum of 72 hours, which means patients will not receive the benefit of prophylaxis for the first 3 or 4 days after surgery.

New medications

Fondaparinux is the first drug in a new class of synthetic inhibitors of factor Xa.[24,25] In four large phase 3 trials, fondaparinux was found to be equal or superior to LMWHs in preventing VTE in patients undergoing orthopedic surgery.[26–29]

In the setting of hip arthroplasty, an analysis of the aforementioned phase 3 studies of fondaparinux for thromboembolic prophylaxis demonstrated outcomes comparable to those achieved with LMWH, using efficacy endpoints established by the 2004 ACCP guidelines.[30] Using these same endpoints, fondaparinux was found to be superior as prophylaxis in hip fracture surgery and knee arthroplasty.

Bauer et al[29] randomized more than 1,000 patients undergoing knee arthroplasty to fondaparinux (2.5 mg/day) or LMWH (enoxaparin 30 mg twice daily) and found significantly more bleeding events in patients randomized to fondaparinux.

Table 3 profiles the prophylaxis indications approved by the US Food and Drug Administration for the various available heparin products and fondaparinux.

Appropriate timing and dosing is critical

There is often a gap in the rates of safety and efficacy when drugs are used in clinical trials as opposed to clinical practice. One cannot expect to achieve the same results unless the same protocols are followed,

TABLE 4
Guidelines for thromboembolic prophylaxis in surgical patients[6]

Risk category	Prophylaxis strategy
Very low (for minor, same-day surgery)	Aggressive ambulation
Moderate (for gynecologic surgery in patients aged < 60 yr and laparoscopic procedures)	Elastic stockings, intermittent pneumatic compression boots, low-dose UFH (twice daily), or LMWH
High (for general surgery, colorectal surgery, gynecologic surgery in patients aged > 60 yr, urologic surgery)	Low-dose UFH (every 8 hours) or LMWH, with or without intermittent pneumatic compression boots
Very high (for orthopedic surgery, trauma, spinal cord injury, cancer surgery)	LMWH or warfarin or fondaparinux

UFH = unfractionated heparin; LMWH = low-molecular-weight heparin

both for dosing and for timing of administration.

For example, in clinical trials fondaparinux was given 6 to 8 hours after major joint replacement, but in practice in the United States it is usually initiated only on postoperative day 1. Similarly, LMWHs are usually initiated in general surgery patients (in the absence of neuraxial anesthesia) on postoperative day 1 even though their package inserts recommend initiation 2 hours before surgery.

OUTPATIENT EXTENDED PROPHYLAXIS

The evidence is now clear to support extended prophylaxis for patients following hip replacement, and programs should be established to ensure that extended prophylaxis in this setting becomes standard care.

Bergqvist et al[31] randomized 262 patients following total hip replacement to receive either LMWH for 30 days following surgery or LMWH inpatient prophylaxis followed by placebo. The incidences of both VTE and DVT were significantly reduced in patients who received extended prophylaxis compared with those who received hospital prophylaxis only.

Planes et al[32] studied 179 consecutive patients who had undergone total hip replacement, randomizing them to the LMWH enoxaparin (40 mg once daily) or placebo at hospital discharge 13 to 15 days after surgery. At day 21 after discharge, the rate of DVT was significantly lower in the enoxaparin group than in the placebo group (7.1% vs 19.3%; $P = .018$). The reduction in the risk of proximal DVT with extended prophylaxis was not statistically significant, although the study population may not have been large enough to detect a significant difference.

In a meta-analysis of nine studies that included nearly 4,000 patients, Eikelboom et al[33] found that extended prophylaxis after total hip or knee replacement significantly reduced the risk of symptomatic VTE. The incidence of minor bleeding events but not major bleeding events was increased with extended prophylaxis.

Hull et al[34] conducted a review of six double-blind randomized trials in which extended out-of-hospital LMWH prophylaxis was compared with placebo in patients who had undergone elective hip arthroplasty. The frequencies of DVT, proximal venous thrombosis, and symptomatic VTE were all reduced significantly with extended out-of-hospital prophylaxis.

Comp et al[35] randomized 873 patients following elective total hip or knee replacement to receive 4 weeks of enoxaparin (40 mg/day) or placebo and found that extended therapy reduced the risk of VTE in patients following hip replacement but produced no significant benefit for patients following knee replacement.

GUIDELINES FOR PROPHYLAXIS

Table 4 presents prophylaxis recommendations for surgical patients from the 2004 ACCP guidelines.[6] The higher the risk, the more reliance is placed upon pharmacologic methods for prophylaxis.

Because patients undergoing orthopedic surgery constitute a high-risk subgroup of surgical patients, guidelines for prophylaxis have been developed specifically for them (Table 5).[6] The guidelines recommend LMWH therapy of various durations depending on the type of orthopedic surgery.

SPECIAL ISSUES IN PROPHYLAXIS

Heparin-induced thrombocytopenia (HIT). Patients exposed to any heparin product may develop HIT antibodies if a second exposure occurs within 100 days. Although LMWH is less likely to stimulate antibody production than UFH, cross-reaction does occur. The section of the 2004 ACCP guidelines on HIT recommends establishing a baseline platelet count and monitoring levels during therapy.[36]

Neuraxial anesthesia, when used with anticoagulation, increases the risk of epidural hematoma.

Epidural hematoma had been a particular concern with fondaparinux, but a study by Eriksson et al[27]

TABLE 5
Options for prophylaxis in orthopedic patients[6]

Hip replacement (prophylaxis for 30 days)
- Enoxaparin 30 mg every 12 hours
- Dalteparin 5,000 IU every 12 hours
- Warfarin (St. Francis method: target INR 2.0–3.0)
- Fondaparinux 2.5 mg daily

Knee replacement (prophylaxis for 7–14 days)
- Enoxaparin 30 mg every 12 hours
- Warfarin (St. Francis method: target INR 2.0–3.0)
- Fondaparinux 2.5 mg daily

Hip fracture
- Enoxaparin 40 mg daily
- Fondaparinux 2.5 mg daily

INR = international normalized ratio

TABLE 6
Recommendations on anticoagulant administration in patients undergoing neuraxial anesthesia[39]

Preoperative

Needle can be placed:
- 12 hours after a prophylactic dose of LMWH
- 24 hours after a treatment dose of LMWH

Other anticoagulants and platelet inhibitors contraindicated

Postoperative

Once-daily LMWH dosing
- First dose can be given 6–8 hours postoperatively
- Second dose given at least 24 hours after first dose
- Epidural catheter can be removed 12 hours after LMWH dose

Twice-daily LMWH dosing
- First dose should be given at least 24 hours postoperatively and 2 hours after removal of epidural catheter

LMWH = low-molecular-weight heparin

indicated that this risk is no greater than with LMWH. In this study, fondaparinux (2.5 mg/day) was compared with enoxaparin (40 mg/day) in more than 17,000 patients undergoing surgery for hip fracture, almost 70% of whom received neuraxial anesthesia; overall, no significant difference in clinically relevant bleeding was found between the fondaparinux and enoxaparin groups.

Some studies have specifically addressed risk factors for spinal hematoma following neuraxial anesthesia.[37,38] One of the biggest factors is poor communication between the anesthesia team, surgeons, medical consultants, and nurses. Ensuring that orders for timing medications are carried out properly can reduce the risk of spinal hematoma.

Guidelines issued in 2003 by the American Society of Regional Anesthesia specifically addressed timing of anticoagulant administration for neuraxial anesthesia (Table 6).[39] Some of the specific recommendations are avoiding needle placement for 24 hours after a full dose of LMWH and for 12 hours following the final prophylactic dose, waiting at least 2 hours to give LMWH after epidural catheter removal, and avoiding anticoagulants in patients who have had traumatic needle or catheter insertion.

Patients with a preexisting coagulopathy, such as from liver disease or another cause, are at a much greater risk of bleeding from anticoagulant prophylaxis. In some studies, patients with alcoholic cirrhosis were found to have a lower risk of developing DVT than patients with normal liver function.

When considering a drug-based strategy for a patient with a coagulopathy, first consider whether the patient would be a candidate for pharmacologic therapy or a filter should a clinical DVT develop. If a drug would be chosen to treat a clinical DVT, then a medication is appropriate for prophylaxis. If instead a filter would be the treatment of choice for a clinical DVT, then a mechanical device is probably best for prophylaxis.

Patients with mild to moderate thrombocytopenia are generally good candidates for pharmacologic prophylaxis, as they are at very high risk of DVT. If the cause of thrombocytopenia is unknown or if the platelet count drops suddenly, I recommend a mechanical device for prophylaxis.

SUMMARY

Hospital strategies to prevent VTE are important to reduce acute morbidity and mortality as well as the long-term consequences caused by venous stasis syndrome. Patients at low risk (eg, those who are ambulatory or undergoing a same-day procedure) or who are at high risk for bleeding (including those with severe renal impairment) are candidates for nonpharmacologic strategies for thromboembolic prophylaxis. Mechanical devices are effective if used appropriately, but compliance is a challenge. Patients who require a hospital stay of more than a day or two should receive a medication-based strategy, preferably using LMWH or fondaparinux. Patients undergoing hip replacement should receive extended prophylaxis with LMWH.

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Perioperative management of diabetes mellitus:

How should we act on the limited evidence?

BYRON J. HOOGWERF, MD

The proportion of US surgical patients who have diabetes is 15% to 20%,[1] and the percentage may be even greater among those undergoing cardiothoracic surgery. Unfortunately, little evidence-based medicine and no prospective randomized controlled trials exist to guide clinicians in effectively reducing perioperative risk in patients with diabetes.

This article discusses preoperative and postoperative considerations in the management of surgical patients with diabetes and uses case studies to explore practical issues in the management of such patients, including the importance of glucose control in preventing postoperative complications, the role of intensive insulin therapy, and insulin dosing strategies. Because good evidence on the perioperative management of diabetes is lacking, much of this discussion is based on our experience at The Cleveland Clinic.

PREOPERATIVE CONSIDERATIONS

Preoperative considerations for the patient with diabetes include the patient's diet, the medications he or she is taking, and the associated complications of diabetes.

Diet

There is no such thing as the "usual diabetic diet." Nutrient status is obviously adequate if patients are freestanding and eating in the preoperative state. Perioperative management of the diet is straightforward and consists of putting patients on a "nothing by mouth" (NPO) order for most procedures. For some this means missing a single meal during the day and for others it means missing several meals, depending on the surgical procedure. Gut procedures, for example, require patients to be NPO for more than 1 day.

Diabetes medications

Insulin. The appropriate strategy for insulin management in a patient with diabetes who is taking insulin should mimic physiologic insulin secretion—ie, a basal plus a calorie-stimulated bolus of insulin. Even if the patient is NPO, basal insulin replacement should be continued. Removing the basal insulin will make diabetes control more difficult from the start.

An appropriate strategy is to use one half to two thirds of the patient's usual insulin dose in the form of an intermediate-acting insulin the evening before and the morning of surgery, with the option to give a full dose. Basal insulin with insulin glargine is fairly stable and generally can be given as a full dose.

Preoperatively, blood glucose levels should be less than 200 mg/dL; higher levels can cause neutrophil dysfunction, compromising bacterial killing. Elevated blood glucose levels can be brought down to 150 mg/dL safely with neutral protamine Hagedorn (NPH) insulin.

Oral diabetes medications should be held on the day of surgery. How to manage metformin administration is somewhat controversial. Based on recommendations in the package insert that metformin should be stopped 48 hours before administration of radiocontrast materials, many physicians stop metformin 48 hours before a surgical procedure. No evidence exists to support this recommendation in patients with normal renal function. If metformin is to be restarted after the procedure, be certain that renal function is normal before doing so. Sulfonylureas and thiazolidinediones can typically be stopped on the morning of surgery.

Diabetes complications

The complications of diabetes must be considered in the preoperative assessment.

Coronary heart disease. The risk of coronary heart disease (CHD) is increased twofold to fivefold in dia-

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betic as opposed to nondiabetic patients, and the risk of CHD conferred by diabetes is greater in women than in men.[2–6] Be aware that diffuse CHD may be present in the absence of symptoms (ie, "silent" CHD). Women with CHD are less likely to present with classic symptoms and have less chest pain, so the threshold for suspicion of CHD needs to be lower in women.

As opposed to the risk factor–based approach that the American Diabetes Association recommends when screening for CHD,[7] which is based on traditional risk factors such as dyslipidemia and hypertension, one of the best predictors of silent myocardial disease is autonomic neuropathy, even in the absence of other cardiovascular risk factors. Therefore, the patient with neuropathy, gastroparesis, and orthostatic hypotension is at increased risk for CHD and should undergo additional screening for CHD. Albuminuria increases the risk of not only renal disease but CHD as well.

Diabetic nephropathy increases substantially the risk of CHD, volume overload, and hyperkalemia, and affects glucose-lowering agents but usually not anesthetic agents.

Peripheral neuropathy is a major contributor to lower extremity infection; in the insensate foot, infection often goes unrecognized. When managing a hospitalized patient with diabetes, remove the patient's bedsheet and look at the heels. It is simple to do but not done as consistently as it should be.

Beta-blocker use

Caution should be exercised in the use of beta-blockers, as the beneficial effects of preoperative beta-blocker use have not been firmly established in patients with diabetes mellitus.

In the Diabetic Postoperative Mortality and Morbidity (DIPOM) trial, a randomized controlled study of 921 patients reported in abstract form,[8] metoprolol started the evening before surgery and continued until discharge was not associated with a reduction in all-cause mortality or adverse cardiac outcomes compared with placebo in patients with diabetes, and there was a nonsignificant trend toward more adverse events in the metoprolol recipients. Heart failure accounted for most of the excess adverse events in the metoprolol group. The message from the DIPOM trial is not to withhold beta-blockers in patients with diabetes but to be attentive that insidious heart failure may be more common with beta-blockade in diabetic patients.

Preoperative instructions

Preoperative written instructions may need to be different for diabetic patients. For instance, many patients with diabetic retinopathy have difficulty with color vision and contrast vision. Preoperative instructions should therefore be printed in black on a white or yellow background, and in at least 14-point type.

POSTOPERATIVE CONSIDERATIONS

Diet/nutritional intake, medications, and complications also need to be considered in the postoperative phase.

Diet

Most patients are NPO at the start of the postoperative period, at least temporarily. Clear liquids that contain no nutrients, even if caloric, probably do not reverse the catabolic state. In general, the diet in the hospital does not have to be very restrictive. The goal is adequate wound healing and nutrition. A diet that does not conform entirely to the recommended outpatient diet is better than not eating at all upon discharge.

Some patients may need nutritional support as total parenteral nutrition (TPN) or enteral nutrition (tube feedings). Tube feedings are usually given continuously over 24 hours at a fixed rate. However, if the tube feeding is likely to be needed after discharge, then feedings may be given intermittently. Often such feedings are given overnight (eg, from 6:00 PM to 6:00 AM); patients are encouraged to eat during the day. The transition from continuous to intermittent (nighttime) feeding is difficult. For a patient who will be recommended for a switch from continuous to nighttime enteral feeding, making that change a couple of days before discharge will provide time to make adjustments in the insulin administration schedule.

Insulin

Postoperative insulin needs can be estimated by preoperative insulin requirements. As a general rule, half the preoperative insulin requirement can be given as a basal dose. For example, if the patient had been taking 100 U/day, he or she can be moved up to 50 U of basal insulin very quickly, even if he or she is NPO.

The postoperative insulin requirement is also dependent on nutrient intake. When making rounds in the morning, I ask patients, "What did you eat yesterday and how well do you think you will be able to eat today?" I do not want hyperglycemia to be the factor that extends hospital stay, so if the patient did not eat much the day before and was on clear liquids the previous night but now is ready to eat breakfast, I must start increasing the insulin, especially meal-related (prandial) insulin.

For patients on intravenous continuous nutrients, use of "coverage" insulin or a "sliding scale" alone is too late because the glucose level is already elevated. When managing patients on intravenous or (espe-

cially) oral nutrients, a preprandial dose of insulin along with sliding scale–based administration is effective when some basal insulin is already on board. For instance, if the patient normally takes 4 to 8 U of short-acting insulin before meals, and anticipates eating about half of his or her usual meal, administration of 2 U plus a correction bolus would be appropriate.

Compared with TPN, enteral feeding is associated with substantially lower insulin requirements. During enteral feeding, a compound called glucagon-like peptide-1 stimulates the pancreas to produce more insulin. Therefore, transitioning patients from TPN to enteral feeding may require reducing insulin doses by half if the pancreatic reserve is adequate.

When tube feeding is given at a continuous rate over 24 hours, frequent administration of intermediate- and short-acting insulin simulates "continuous" insulin administration. A regimen that works well consists of 70/30 insulin (70% NPH insulin and 30% regular insulin) given every 8 hours with "coverage" regular insulin given every 4 hours. Once during every 24-hour period, the total dose of coverage insulin is added into the total daily dose of 70/30 insulin (eg, if a patient is receiving 15 U of 70/30 insulin every 8 hours and requires a total of 15 U of regular insulin through the previous 24-hour period, the 70/30 insulin dose is increased to 20 U every 8 hours). This insulin regimen must be adjusted if the patient is going to receive nighttime feeding. If the patient receives continuous nutrients from 6:00 PM to 6:00 AM and will be fed during the day, we often will give NPH plus regular insulin at 6:00 PM and additional regular insulin at 10:00 PM and 2:00 AM, followed by a small amount of basal/bolus insulin during the day when he or she is eating. This is a circumstance in which we may use NPH insulin at night and insulin glargine during the day.

Complications

The presence of adrenergic symptoms, especially sweating, in diabetic patients does not always imply hypoglycemia. Such symptoms may also be a reflection of autonomic neuropathy or a sign of myocardial infarction or an infection. In patients with renal disease a drop in blood sugar levels may also be associated with acute renal failure.

In a patient with reasonably controlled blood glucose levels in the hospital, an unexpected increase in blood glucose values requires evaluation for a wound infection. Hyperglycemia may antedate fever. Glucose levels are a sensitive marker of counterregulatory hormones, which often are activated before patients become febrile.

Diabetic patients may be more susceptible to nerve palsies because they already are at risk for compressive neuropathies, which may be aggravated in the perioperative state.

Consider heel protectors if the patient's foot is insensate and at risk for ulceration, especially if there are preexisting calluses or foot deformities. Heel protectors are relatively inexpensive and reduce the risk for foot breakdown.

CASE 1: INSULIN MANAGEMENT AFTER CABG

A 65-year-old man with a 20-year history of diabetes has blood glucose values of 100 to 180 mg/dL on an insulin infusion of 2 U/hr intravenously in the ICU after coronary artery bypass graft (CABG) surgery. He had been treated preoperatively with a total daily insulin dose of 70 U (eg, 40 U of NPH insulin and 10 U of regular insulin before each meal). Which of the following insulin regimens should be used in transitioning to subcutaneous insulin?

A. Discontinue insulin drip and start regular insulin given on a sliding scale

B. Discontinue insulin drip and start a short-acting insulin analog (eg, insulin lispro or aspart) on a sliding scale

C. Discontinue insulin drip and start NPH insulin 5 U plus regular insulin on a sliding scale

D. Continue insulin drip for 2 hours and start NPH insulin 20 U plus regular insulin on a sliding scale

E. Continue insulin drip for 2 hours and start insulin glargine 20 U plus an insulin analog on a sliding scale

The best response is D, but E would also be acceptable. In general, when patients have been on NPH insulin, we tend to continue it. NPH insulin acts faster than insulin glargine, which has a slower onset and whose maximal effect may not be seen for a few days. Even though use of insulin glargine is increasing, data are more abundant on insulins that exert their effect hours instead of days after administration. The main message is to get adequate basal insulin on board.

Basal insulin needs are predicted by the patient's insulin needs prior to hospitalization and the insulin infusion rate. Starting the basal insulin at half the preoperative dose is generally safe. "Sliding scale" or coverage insulin alone is usually inadequate. The sliding scale is usually every 4 hours until the patient starts to eat, at which time he or she can be switched to premeal prandial insulin plus a correction dose for hyperglycemia.

Glucose level related to in-hospital mortality

Several retrospective analyses have shown an association between blood glucose level and hospital mortality in the post-CABG setting, with a flattening of the mor-

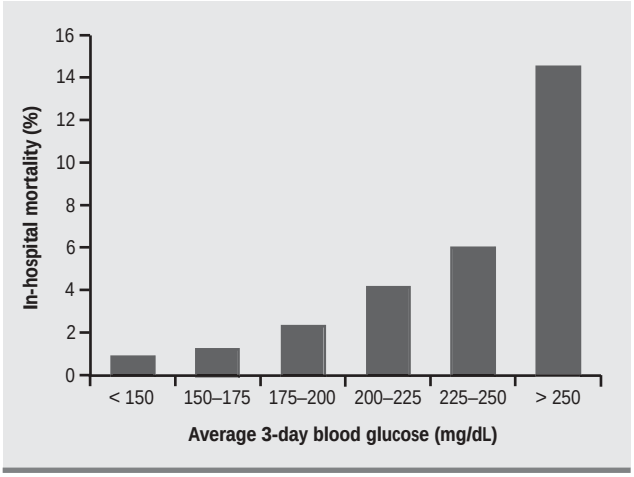

FIGURE 1. In-hospital mortality, by blood glucose level, among 3,554 patients with diabetes undergoing coronary artery bypass graft surgery from a retrospective analysis. The glucose-related increase in mortality ($P < .001$) was due overwhelmingly to increased cardiac-related mortality. Reprinted from reference 11, copyright 2003, with permission from American Association for Thoracic Surgery.

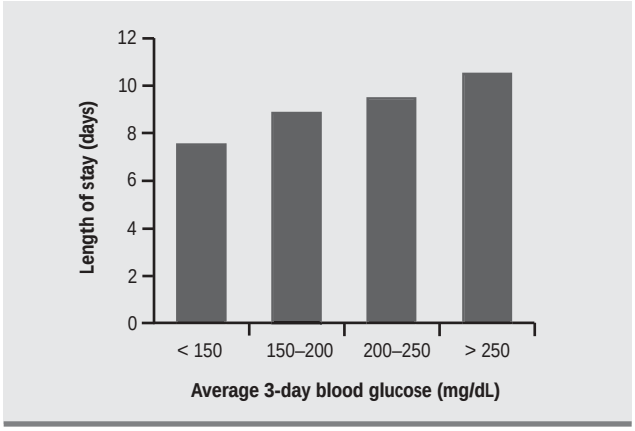

FIGURE 2. Length of hospital stay, by blood glucose level, among 2,105 patients with diabetes following coronary artery bypass graft surgery. Data from reference 12.

tality curve once the average 3-day blood glucose value falls below 150 mg/dL.[9–11] Figure 1 illustrates the findings from one of these studies.[11] The lowest threshold for blood glucose is not known, but the evidence is compelling in support of reducing levels to less than 200 mg/dL to reduce the risk of in-hospital mortality. A similar association has been observed between blood glucose and length of hospital stay (Figure 2).[12] It should be noted that these data were unadjusted for Acute Physiology and Chronic Health Evaluation (APACHE) scores, but they suggest a role for glucose control in reducing in-hospital mortality and length of stay.

Intensive insulin therapy for the critically ill

A large prospective study by Van den Berghe et al[13] showed that, among critically ill patients, intensive insulin therapy (to a target blood glucose of 110 mg/dL or lower) was superior to a conventional insulin infusion strategy (target blood glucose of 180 to 200 mg/dL) on several outcome measures. The intensive strategy was associated with a reduction in ICU mortality, from 8.0% to 4.6% (43% relative reduction), as well as substantial reductions in hospital mortality, ICU days, time on a ventilator, the incidence of renal failure, and the incidence of systemic infection (Table 1). Whether the insulin therapy itself or the blood glucose levels achieved were responsible for the risk reductions is uncertain, since insulin is an anabolic compound that may have effects other than lowering blood glucose.

CASE 2: GLUCOSE CONTROL AFTER POSTOPERATIVE STROKE

A 70-year-old white man has a postoperative stroke requiring continuous feeding via a feeding tube. His prehospital glucose regimen was a sulfonylurea plus metformin. His blood glucose values are greater than 180 mg/dL with a caloric intake of 20 kcal/hr, and his projected need is 70 kcal/hr. Which of the following regimens should be recommended?

A. Sulfonylurea and metformin (at preoperative doses)
B. Sulfonylurea, metformin, and a thiazolidinedione
C. Sulfonylurea, metformin, and regular insulin given on a sliding scale
D. NPH insulin 20 U every morning and 10 U every evening with regular insulin four times daily
E. 70/30 insulin 10 U every 8 hours plus regular insulin on a sliding scale every 4 hours

My philosophy is that perioperative glucose management in the hospital consists of insulin administration. Insulin is safe for patients of any age; can be given to patients with heart, liver, or kidney failure; has a rapid onset and clearance; has few drug interactions; and has been used for more than 8 decades. Many diabetic patients will require insulin later in their disease course, and the perioperative setting provides an excellent opportunity for teaching them how to administer it.

Regular insulin at low doses has a peak effect at 3 to 4 hours and a duration of 6 to 8 hours, whereas NPH insulin has a peak effect at 6 to 10 hours and a duration of 18 to 24 hours. The pharmacokinetic principle behind 70/30 insulin is that the overlapping half-lives of an intermediate-acting insulin and regular insulin (which has a more rapid onset) will produce near steady-state plasma insulin concentrations.

The regimen I would recommend, consistent with Cleveland Clinic practice, is to start with 70/30 insulin and then add regular insulin given subcutaneously on a sliding scale every 4 hours. As noted above, if the sliding scale coverage during the previous 24 hours totals 15 U, then 5 U should be added to each of the three doses of 70/30 insulin. In addition, as the tube feeding rate increases, a corresponding increase in the 70/30 dose should be implemented at the same time. For example,

TABLE 1
Outcomes with conventional vs intensive insulin therapy in critically ill patients

	Conventional therapy (n = 783)	Intensive therapy (n = 765)	Relative risk reduction	*P*
Death in intensive care unit	8.0%	4.6%	43%	< .04*
Death in hospital	10.9%	7.2%	34%	.01
> 14 days in intensive care unit	15.7%	11.4%	28%	.01
Ventilator required > 14 days	11.9%	7.5%	37%	.003
Renal failure	8.2%	4.8%	41%	.007
Septicemia in intensive care unit	7.8%	4.2%	46%	.003

* *P* value adjusted for repeated interim analyses.
Adapted from reference 13.

if a patient needs 10 U every 8 hours for a tube feeding rate of 30 mL/hr, one can estimate that at least twice this dose will be needed for a rate of 60 mL/hr, and this change can be incorporated into insulin orders.

With this regimen and a continuous nutrient intake, the blood glucose can be stabilized within 24 hours and maintained safely in the range of 100 to 120 mg/dL—and possibly lower. The risk of hypoglycemia with such a regimen is low in patients receiving continuous nutrients.

Other options include frequent doses of NPH or 50/50 insulin, or insulin glargine twice daily, although the onset of action of insulin glargine would be slower than the alternatives mentioned.

What about oral antidiabetic agents?

There is little role for oral agents in the immediate postoperative phase. Oral agents can be started postoperatively when the patient starts eating again; at this point in the postoperative period there is little need to worry about the ischemic preconditioning associated with some of the first- and second-generation sulfonylureas. Metformin can be restarted if the renal function is stable and nausea is not a concern. Carbohydrase inhibitors (eg, acarbose, miglitol) have a rapid onset, whereas thiazolidinediones (eg, pioglitzone, rosiglitazone) have a slower onset. Short-acting insulin secretagogues (eg, meglitinide, nateglinide) can also be considered.

SUMMARY

Patients with diabetes mellitus are at higher risk for complications from surgery than their nondiabetic counterparts. Evidence-based guidance on the perioperative management of diabetic patients is still very limited. Management is best guided by careful preoperative and postoperative consideration of diet, antidiabetic medication regimens, and the likelihood of specific complications of diabetes. Good postoperative glucose control reduces the risk of in-hospital death and shortens length of stay. Insulin is the mainstay of perioperative glucose management, and intensive insulin therapy (to a target blood glucose of 110 mg/dL or lower) improves a range of clinical outcomes in critically ill patients relative to less aggressive insulin strategies. There is little role for oral antidiabetic medications in the early postoperative phase.

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Anticoagulation management strategies for patients on warfarin who need surgery

AMIR K. JAFFER, MD

Surgical candidates who are receiving chronic warfarin therapy pose a management dilemma to the perioperative consultant. Continuing warfarin up to the time of surgery increases the risk of bleeding, so these patients' warfarin traditionally was stopped 5 days before surgery. Yet during this time and afterward, these patients are believed to be at increased risk of thromboembolism.

In light of this dilemma, 250,000 surgical patients in North America on warfarin therapy are assessed annually for perioperative anticoagulation with a heparin product to bridge the gap in thromboembolic protection if warfarin is stopped.[1] This review explores key issues and questions surrounding "bridging" anticoagulation and describes the bridge therapy protocol in use at The Cleveland Clinic.

PERIOPERATIVE THROMBOEMBOLISM IN WARFARIN RECIPIENTS: RISK IS LOW BUT RESULTS CAN BE DEVASTATING

A systematic review published in 2003[2] reveals that the risk of perioperative thromboembolism among patients receiving long-term anticoagulation therapy is low. The limitations of this review are that no randomized controlled trials could be identified for inclusion and the overall quality of the reports was deemed poor. The overall thromboembolic event rate was 1.6%. The rates of major bleeding were approximately 2% to 4% in patients undergoing major surgery and 0% to 2% in those undergoing invasive procedures, but interpretation of the bleeding rates is difficult because the studies identified included surgical procedures with varying risks of bleeding and, as stated, none was randomized.

The consequences of interrupting warfarin therapy must be understood for effective decision making. In patients with a previous episode of venous thromboembolism (VTE), 5% to 10% of recurrent VTEs are fatal.[3] Twenty percent of arterial thromboembolic events are fatal, and more than 50% result in permanent disability.[4] Bridge therapy with heparin can reduce this risk of thromboembolism by nearly 70% but may lead to an increased risk of bleeding. Nine percent to 13% of patients with a major bleed will die, but major bleeding events rarely result in permanent disability because resuscitation with fresh frozen plasma or other blood products is possible.[5]

WHAT DO THE GUIDELINES SAY?

In its recent consensus guidelines, the American College of Chest Physicians (ACCP) suggests various management options for oral anticoagulation during invasive procedures.[6]

For patients at low risk of thromboembolism, it recommends stopping warfarin 4 days preoperatively and considering unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH) postoperatively, and perhaps preoperatively as well, although preoperative use is not well explained.

For patients at intermediate risk of thromboembolism, it suggests stopping warfarin 4 days preoperatively, starting a prophylactic dose of UFH or LMWH pre- and postoperatively, and restarting warfarin postoperatively.

For patients at high risk of thromboembolism, its guidelines recommend stopping warfarin 4 days preoperatively, starting full-dose UFH or LMWH preoperatively and then full-dose UFH or LMWH postoperatively, and restarting warfarin postoperatively.

The 1998 American College of Cardiology/

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American Heart Association (ACC/AHA) guidelines[7] for the management of valvular heart disease state that LMWH is not recommended for perioperative bridge therapy. Bridging with UFH is recommended for patients with Bjork-Shiley valves, atrial fibrillation and two or more risk factors for thromboembolism, or a mechanical mitral valve plus one risk factor.

New data that contradict the ACCP and ACC/AHA guidelines suggest that LMWH is both safe and efficacious for perioperative bridge therapy and are reviewed later in this article.

CASE 1: MINOR SURGERY IN A PATIENT WITH AF

An 85-year-old man with a history of atrial fibrillation, stroke, and congestive heart failure is scheduled for cataract surgery. He is on warfarin with a target INR of 2.0 to 3.0. How should this patient be managed?

A. Stop warfarin 5 days before surgery (ie, hold for four doses before surgery)
B. Use UFH or LMWH as bridge therapy
C. No reason to discontinue warfarin therapy

The aforementioned systematic review[2] demonstrated that major bleeding while receiving oral anticoagulation was rare for cataract surgery and other minor procedures, and therefore can be continued without alteration. Because these data are not well known, educating patients and ophthalmologists that cataract surgery can be performed safely with anticoagulation on board is wise.

In addition to cataract surgery, procedures that can be performed on full-dose anticoagulation include various dental, dermatologic, and gastrointestinal procedures. The decision to continue anticoagulation in patients undergoing gastrointestinal procedures is especially controversial. Guidelines from the American Society of Gastrointestinal Endoscopy[8] state that low-risk procedures such as diagnostic endoscopies and colonoscopies (even with biopsies) can be performed without adjusting warfarin. Despite this recommendation, many gastroenterologists don't agree. A classic example is the patient on long-term warfarin therapy who needs a surveillance colonoscopy following polyp removal in the past; in such a patient, warfarin need not be stopped unless another polypectomy is anticipated. On the other hand, if another polypectomy is anticipated, then withholding anticoagulation is reasonable.

INR nomogram

A nomogram has been developed to decrease the international normalized ratio (INR) in patients undergoing dental surgery, another low-risk procedure.[9] The daily warfarin dose is decreased by 50% on days 4, 3, and 2 before surgery; the original warfarin dose is resumed 1 day before surgery; and the dose of warfarin is doubled on the day of surgery followed by the usual maintenance dose on the day after. This nomogram would be appropriate for other minor surgeries as well. It was tested in 80 consecutive anticoagulated patients who were scheduled for minor surgery, and resulted in no thromboembolic events up to 1 month after surgery, with the caveat that the study contained no control group. In addition to being safe, this strategy is inexpensive.

Timing of warfarin discontinuation

The timing of warfarin discontinuation in patients undergoing elective surgery has been studied by White et al.[10] Among 22 patients on a fixed evening dose of warfarin who had warfarin temporarily discontinued, interpatient variation in the rate of INR decrease was wide, especially among the elderly, but some general rules for interrupting therapy could be established from this small study. To ensure that the INR is less than 1.2 at the time of surgery, warfarin should be withheld for four doses if the steady-state INR is 2.0 to 3.0 and for five doses if the INR is 3.0 to 4.0.

CASE 2: URGENT SURGERY IN A PATIENT WITH AF

An 82-year-old woman with a history of atrial fibrillation, hypertension, and coronary disease is admitted to the hospital with hip fracture. She had a stress test in the past year which was negative. Her INR is 5.5 on admission, and the surgery is scheduled in approximately 18 hours. How should the INR be reduced to less than 1.5 so that the surgeon can operate on this patient?

A. Use fresh frozen plasma
B. Use 10 mg vitamin K subcutaneously
C. Use 2.5 mg vitamin K orally
D. Use 2.5 mg vitamin K intravenously (IV)

Although subcutaneous vitamin K is widely used to reduce the INR prior to surgery, absorption through the subcutaneous route is not predictable.[11] The route of administration of vitamin K that acts most rapidly to reduce the INR is IV, followed by oral and subcutaneous.[11–13] Fresh frozen plasma is probably necessary for surgeries within 12 hours. For surgeries more than 24 hours away, oral vitamin K is usually an effective option.

The proper way to manage this patient is to administer IV vitamin K and recheck the INR in the early morning. In this patient, administering IV vitamin K immediately will most likely result in an INR of 1.5 to 2.0 in 24 hours. If the INR is still close to 2.0, order 2

TABLE 1
Estimated rates of thromboembolism and risk reduction with anticoagulation

Indication	Rate without therapy (%)	Risk reduction with therapy (%)
Acute VTE*		
Month 1	40	80
Months 2 and 3	10	80
Recurrent VTE*†	15‡	80
Nonvalvular AF	4.5‡	66
Nonvalvular AF and previous embolism	12‡	66
Mechanical heart valve	8‡	75
Acute arterial embolism		
Month 1	15	66

VTE = venous thromboembolism; AF = atrial fibrillation

* Surgery-associated increase in risk of VTE (estimated to be 100-fold) is not included in these rates.

† Refers to patients whose last episode of VTE occurred more than 3 months before evaluation but who require long-term anticoagulation because of high risk of recurrence.

‡ Annual rate.

U of fresh frozen plasma to be given to the patient on call to the operating room.

Hypotension and allergic reactions are a small risk in patients who receive IV vitamin K, occurring in about 1% to 2% of these patients.

IDENTIFY THE WARFARIN INDICATION, ASSESS PATIENT RISK

Identify the indication for anticoagulation

When managing the patient on warfarin who is undergoing an elective procedure, identifying the indication for anticoagulation is most important. The risk of thrombosis needs to be quantified, which involves understanding the patient's risk factors for thromboembolism, considering the type of surgery/procedure to be performed, and determining how long the patient needs to be off anticoagulation. For example, the primary risk in a patient with AF in whom anticoagulation must be interrupted prior to surgery is arterial thromboembolism from removal of the anticoagulation plus the risk of VTE related to the surgery. The risk of bleeding from the procedure also needs to be quantified, and the consequences of thromboembolism and bleeding need to be weighed.

Risk determines bridge strategy

The risk of thromboembolism will determine the need for anticoagulation bridging, the risks and benefits of which must also be weighed. Use of a perioperative anticoagulant will decrease the risk of a perioperative thromboembolic event but carries the potential risks of postoperative bleeding and development of heparin-induced thrombocytopenia.

For bridge therapy, outpatient UFH is not practical given the need for partial thromboplastin time measurements, leaving LMWH as the best option for out-

TABLE 2
Which patients on warfarin should receive heparin bridging before surgery?

High risk for thromboembolism: bridging advised

Known hypercoagulable state as documented by a thromboembolic event and one of the following:
- Protein C deficiency
- Protein S deficiency
- Antithrombin III deficiency
- Homozygous factor V Leiden mutation
- Antiphospholipid-antibody syndrome

Hypercoagulable state suggested by recurrent (two or more) arterial or idiopathic venous thromboembolic events*

Venous or arterial thromboembolism in prior 1–3 months

Rheumatic atrial fibrillation

Acute intracardiac thrombus visualized by echocardiogram

Atrial fibrillation plus mechanical heart valve in any position

Older mechanical valve model (single-disk or ball-in-cage) in mitral position

Recently placed mechanical valve (< 3 months)

Atrial fibrillation with history of cardioembolism

Intermediate risk for thromboembolism: bridging on a case-by-case basis

Cerebrovascular disease with multiple (two or more) strokes or transient ischemic attacks without risk factors for cardiac embolism

Newer mechanical valve model (eg, St. Jude) in mitral position

Older mechanical valve model in aortic position

Atrial fibrillation without a history of cardiac embolism but with multiple risks for cardiac embolism†

Venous thromboembolism > 3–6 months ago‡

Low risk for thromboembolism: bridging not advised

One remote venous thromboembolism (> 6 months ago)‡

Intrinsic cerebrovascular disease (eg, carotid atherosclerosis) without recurrent strokes or transient ischemic attacks

Atrial fibrillation without multiple risks for cardiac embolism

Newer-model prosthetic valve in aortic position

* Not including primary atherosclerotic events, such as stroke or myocardial infarction due to cerebrovascular or coronary disease.

† For example, ejection fraction < 40%, diabetes, hypertension, nonrheumatic valvular heart disease, transmural myocardial infarction within preceding month.

‡ For patients with a history of venous thromboembolism undergoing major surgery, consideration can be given to postoperative bridging therapy only (without preoperative bridging).

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TABLE 3
Published bridging studies of low-molecular-weight heparin

Author	No. patients (no. valves)	Low-molecular-weight heparin	Rate of bleeding	Rate of thromboembolism
Spandorfer[20]	20	Enoxaparin	5% major, 10% minor	0%
Tinmouth[21]	24 (12)	Dalteparin	0% major, 8.3% minor	4.2%
Dotan[22]	20 (3)	Enoxaparin	0% major, 10% minor	0%
Ferreira[23]	74 (74)	Enoxaparin	1.35% major, 10.8% minor	0%
Jaffer[24]	69 (21)	Enoxaparin or tinzaparin	2.8% major, 1.3% minor	0%
Spyropoulos[25]	84 (27)	Enoxaparin	3.5% major, 3.5% minor	0%
Douketis[26]	650 (215)	Dalteparin	1.85%*, 0.74%†	1.85%*, 0.74%†
Kovacs[27]	224 (112)	Dalteparin	6.7% major	3.6%

* Procedures with high bleeding risk (received only preprocedural bridging therapy).
† Procedures with high bleeding risk plus nonsurgical procedures without high bleeding risk.

patient therapy. Inpatient IV UFH is another option.

The rates of thromboembolism and the reductions in risk with bridge therapy have been quantified by Kearon and Hirsh (Table 1).[14] They state that patients who have had VTE or arterial thromboembolic events in the past month are at extremely high risk for thromboembolism, as are patients with AF who have had a prior stroke. They also believe that bridge therapy decreases the risk of a perioperative thromboembolic event by 70% to 80%, on average.

Thromboembolism risk stratification

An extensive literature review has helped define the risk of perioperative thromboembolism in patients on chronic anticoagulation.[15] Patients were classified as low risk, intermediate risk, and high risk based on their annual risk of an arterial thromboembolic event or their monthly risk of VTE (Table 2).

Low-risk patients in this classification are those with a less than 5% per year risk of an arterial thromboembolic event or a less than 2% per month risk of VTE.

Intermediate-risk patients are those with a 5% to 10% per year risk of an arterial thromboembolic event or a 2% to 10% per month risk of VTE.

High-risk patients are those with a greater than 10% per year risk of an arterial thromboembolic event or a greater than 10% per month risk of VTE.

The CHADS 2 risk classification scheme can be used to estimate the annual (not perioperative) risk of stroke in atrial fibrillation patients by assigning point values to stroke risk factors. It assigns 1 point each for the presence of Congestive heart failure, Hypertension, Age 75 years or older, and Diabetes mellitus; and 2 points for a history of Stroke or transient ischemic attack. Anticoagulation as a bridge to surgery may be reasonable in patients with a CHADS 2 score of 3 or greater, which indicates a 6% annual risk of stroke.[16]

CASE 3: COLECTOMY IN A PATIENT WITH A MECHANICAL VALVE: UFH OR LMWH FOR BRIDGE THERAPY?

A 65-year-old man with an older-generation valve, a Starr-Edwards, is diagnosed with colon cancer and needs a colectomy. The patient's personal physician recommends stopping warfarin 5 days before surgery and admitting the patient for IV UFH therapy because LMWH is not shown to be safe and effective for patients with mechanical heart valves. How should you, the medical consultant, advise the patient's physician?

A. Tell him he is right—there is little evidence to support the use of LMWHs in mechanical valve patients.

B. Tell him there is in fact more evidence in the literature to support the use of LMWHs than UFH for bridging with mechanical valves.

The better answer is B. Bridge studies using IV UFH are few and poorly done.[17–19] In these studies, the rate of bleeding was 2.6% and the overall rate of thromboembolism was 3.4% in patients bridged with UFH.

Published bridge studies of LMWH have demonstrated very acceptable rates of major bleeding (Table 3) and a rate of thromboembolism of 0% to 4%.[20–27] In a large unpublished registry[28] in which enoxaparin 1.5 mg/kg once daily was used for bridging, the rate of major bleeding was 22% with major surgery and 0% with minor surgery, although the overall rate of major bleeding was only 3.6%. The rate of thromboembolic events in this registry was 2.6% and the rate of VTE was 1%. In another large unpublished registry (REGIMEN),[29] the rates of major bleeding were 3.3% with major surgery and 10% with minor surgery, and the rate of thromboembolism was 0.9%.

Perioperative anticoagulation strategies and adverse events were examined in a preliminary analy-

TABLE 4
Exclusion criteria for bridge therapy with low-molecular-weight heparin

- Weight > 150 kg
- Pregnancy or childbearing potential without adequate contraception
- History of heparin-induced thrombocytopenia
- End-stage renal disease
- Allergy to low-molecular-weight heparin or unfractionated heparin
- History of noncompliance, language barriers, or unsuitable home environment
- Gastrointestinal bleeding in last 10 days
- Major trauma or stroke in past 2 weeks

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sis of 425 of 500 planned patients from nine anticoagulation clinics.[30] Patients were stratified a priori according to bridge strategy, procedure/surgery using the Johns Hopkins bleeding classification scheme, and their risk of thromboembolism and VTE. Of the patients in this registry, 46% did not receive bridge therapy, 30% received bridge therapy, and 3.8% had warfarin continued. The others received various combinations of no anticoagulation, intermediate-intensity anticoagulation, and high-intensity anticoagulation pre- and postoperatively.

Overall, mortality was 0.5%, the thromboembolic event rate was 0.9%, and the rate of major bleeding was 2.1%. Eight of the nine major bleeding events and 12 of the 15 bleeding events overall occurred in the 40% of patients who received full-dose bridge therapy.

Interpretation of bridge studies

Bridge therapy must be tailored to the individual patient. Careful selection of patients for bridge therapy is required, with resumption of the anticoagulant postoperatively when hemostasis has been achieved.

Cost considerations. Admitting patients for anticoagulation is costly and therefore discouraged. In a managed care setting, Spyropoulos et al[31] determined that use of LMWH as opposed to UFH for bridge therapy, starting 10 days before an elective surgical procedure and continued for 30 days after the procedure, can achieve a cost saving of approximately $13,000, taking into account expected differences in the rates of adverse events and the costs associated with inpatient/outpatient care, outpatient surgery, and laboratory, pharmacy, and professional fees.

CLEVELAND CLINIC ANTICOAGULATION CLINIC BRIDGE THERAPY PROTOCOL

The Cleveland Clinic Anticoagulation Clinic has a bridge therapy protocol in which the timing of warfarin interruption is based on the preoperative INR.[15] If the preoperative INR is 2.0 to 3.0, warfarin is stopped 5 days before surgery (four doses); if the preoperative INR is 3.0 to 4.5, warfarin is stopped 6 days before surgery (five doses). Enoxaparin 1 mg/kg or dalteparin 100 IU/kg, delivered subcutaneously every 12 hours, is started 36 hours after the last warfarin dose. The final dose of LMWH is administered 24 hours before surgery. The plan is discussed with the surgeon, the anesthesiologist, and the patient, during which time the risks and benefits of LMWH are outlined. Patients receive instruction on self-administration, the signs and symptoms of bleeding, and the course of action in the event of an emergency.

The postoperative protocol calls for restarting LMWH at full doses approximately 24 hours after the procedure only if hemostasis has been achieved. Prophylactic doses on postoperative days 1 and 2 should be considered if patients are at high risk for bleeding. Warfarin is restarted at preoperative doses on postoperative day 1. The INR should be monitored daily until the patient is discharged and periodically thereafter until it is in the therapeutic range. Patients should be screened for heparin-induced thrombocytopenia with platelet counts at days 3 and 7. LMWH should be discontinued when the INR is 2.0 to 3.0 for 2 consecutive days.

Exclusions to bridge therapy

Table 4 provides a list of exclusion criteria for bridge therapy with LMWH. Body weight greater than 150 kg is an exclusion for practical reasons; two syringes of enoxaparin would be required in such a patient. Also, the risk of overdosing increases with increasing weight because the relationship between volume of distribution of LMWH and weight is not linear. Patients who are heavier than 150 kg are admitted to the hospital and treated with UFH, after which their partial thromboplastin time is monitored every 6 hours and the UFH is discontinued 5 hours before surgery.

REGIONAL ANESTHESIA CONSIDERATIONS

Recommendations to minimize risk in anticoagulated patients undergoing regional anesthesia have been published by the American Society of Regional Anesthesia and Pain Medicine.[32] Preoperative recommendations include needle placement 12 hours after prophylactic LMWH (24

hours if the dose is ≥ 1 mg/kg). Postoperatively, an indwelling catheter must be removed prior to starting twice-daily LMWH, with the first dose of LMWH to be given 2 hours after catheter removal; once-daily LMWH is acceptable, but the first dose should be given 6 to 8 hours postoperatively and the second dose 24 hours later. Concurrent use of an indwelling catheter and once-daily LMWH is acceptable, but not twice-daily LMWH. The catheter should be removed 12 to 24 hours after the last dose.

CONCLUSION

The risk of thromboembolism is small but real in patients undergoing procedures or surgeries off their chronic warfarin therapy. This risk ranges from 1% to 2%, and is possibly even greater. If the patient is not comfortable with this level of risk, bridge therapy should be offered, with the knowledge that it will slightly raise the risk of minor or major bleeding. Until a randomized controlled trial is published, the risk of bleeding and thromboembolism should be balanced in every patient, which requires an individualized, tailored approach.

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Perioperative care of the elderly patient

ROBERT M. PALMER, MD

Patients age 65 and older account for 38% of discharges from acute nonfederal US hospitals and for 46% of all hospital days of care, even though they represent only 13% of the US population. Older patients typically have longer hospital stays, greater costs of care, and greater risks of adverse health outcomes related to surgical or medical problems than younger patients.[1–3]

Older patients admitted to the hospital for hip fractures or other conditions that require surgery may have additional complicated medical problems that are not present in younger patients, making perioperative management more complicated.

This article reviews factors that put older patients at particular risk of perioperative complications and uses a case study to explore many of the complications that can arise during the postoperative management of an older patient. In doing so, it will illustrate the importance of a vigilant preoperative assessment, anticipating potential complications, and working to prevent them.

WHAT PUTS THE ELDERLY AT GREATER PERIOPERATIVE RISK?

Cognitive impairment. Older patients are more likely than younger patients to have cognitive impairment, either dementia prior to surgery or delirium related to the illness or following surgery.

Frailty, in which there is impaired homeostasis, also is common in older adults. Physiologic function in the organ systems of older adults is impaired as a result of the aging process, not just as a result of an acute or chronic illness. Frailty may predispose older patients to severe and multiorgan system failure even from a relatively minor perturbation of surgery that would not affect the average younger patient.

Immobility and functional dependency are common in the older age group. Before surgery, older adults might be struggling to walk or perform independently their basic activities of daily living (ADLs). If the patient is already functionally impaired, anticipate significant postoperative problems related to weight-bearing, transfers, and independent ambulation.

Poor nutrition. Older patients also might present with poor nutrition from the presence of chronic diseases, from the illness they have near the time of surgery, or both. Poor nutrition complicates the postoperative management of these patients by impairing wound healing or by producing generalized sarcopenia, muscle loss, and weakness, thereby prohibiting successful rehabilitation.

Complicated transitions. Older patients may have complicated transitions from the hospital to home. Unlike a younger patient with a more straightforward medical case, the older patient may have chronic illnesses, cognitive impairment, and functional needs. These factors, together with the poor social support systems available to many older patients, may make a direct return home unlikely or make even a post-rehabilitation return home unsafe.

CASE PRESENTATION

An 82-year-old woman is admitted for hip fracture and undergoes successful open reduction and internal fixation. She has a history of osteoarthritis, systolic hypertension, and mild visual and hearing impairment. She is taking a beta-blocker, a thiazide diuretic, analgesics as needed, and a multivitamin.

Prior to the hip fracture she was independent in all of her basic ADLs and had no significant mobility problems despite her arthritis. She is a social drinker with no history of cigarette smoking. Review of systems reveals no significant cardiovascular, lung, or renal disease. Baseline laboratory studies are all normal, including complete blood count, basic metabolic panel, thyroid-stimulating hormone, and vitamin B_{12}.

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Assess the risk of delirium

Which of the following statements about this patient is most correct?

A. She is at high (> 50%) risk of postoperative delirium
B. She is at low risk of postoperative delirium
C. Postoperative delirium can be prevented
D. Surgery is not warranted because of a risk of delirium

This patient is at low risk of postoperative delirium based on the postoperative delirium prediction rule (Table 1) developed by Marcantonio et al,[4] in which points are assigned to each preoperative risk factor for postoperative delirium and totaled to calculate the risk of delirium. This patient would receive 1 point for age, which would put her in the low-risk category, based on this scale. Although one can argue that every 82-year-old patient is at risk for postoperative delirium, this patient is at relatively low risk.

TABLE 1

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Please see original source table (table 6) in:
Marcantonio ER, Goldman L, Mangione CM, et al. A clinical prediction rule for delirium after elective noncardiac surgery. JAMA 1994; 271:134–139.

REDUCING THE RISK OF DELIRIUM

Once a patient's risk factors are identified, is it possible to reduce the risk of postoperative delirium? An attempt was made to answer this question by evaluating postoperative care among 126 consenting patients age 65 and older who were admitted to an orthopedic surgery service for emergency hip fracture repair.[5] Subjects received a baseline assessment and were randomized to receive one of two types of postoperative care: usual care or proactive geriatric consultation, which began preoperatively or within 24 hours of surgery. For patients assigned to proactive geriatric consultation, a geriatrician made daily visits and targeted recommendations based on a structured protocol. Among the interventions recommended by the geriatrician were:

- Supplemental oxygen
- Restoring serum sodium, potassium, and glucose to normal limits
- Stopping high-risk medications
- Assuring adequate nutritional intake
- Getting the patient out of bed on postoperative day 1
- Treating severe pain.

The consultation-based intervention reduced the incidence of postoperative delirium: the delirium rate was 50% in those receiving usual care vs 32% in those receiving the proactive geriatric consultation.[5] Most studies in which postoperative delirium was evaluated in older patients demonstrate a risk of delirium of approximately 50%. Some of these patients have severe delirium, in which they are agitated, uncooperative, and threaten to walk out of the hospital, so preventing delirium is key to successful postoperative care and rehabilitation.

High-risk medications

The list of potentially inappropriate medications[6] for patients at risk for delirium is a long one, but a few classes of drugs carry particular risk of postoperative acute confusion or delirium.

Anticholinergic drugs encompass a wide range of agents used to treat a variety of diseases, and include bladder relaxants, drugs for Parkinson disease, and other agents not traditionally thought of as having anticholinergic properties (eg, antihistamines, especially first-generation agents such as diphenhydramine and hydroxyzine), all of which can increase the risk of postoperative delirium. These medications should be avoided in older patients, even low-risk ones, to try to prevent postoperative delirium.

Benzodiazepines (eg, alprazolam, clonazepam) can cause an agitated, confused state and increase the risk of falls and are therefore contraindicated in hospitalized older patients.

Meperidine is a high-risk medication because it has a long-acting metabolite that is neurotoxic. This toxin accumulates with repeated doses, so it should be avoided. Other opioids, such as morphine sulfate, are better suited for use in older patients.

H_2-receptor antagonists. At high doses, H_2-receptor antagonists—most notoriously cimetidine—can cause delirium.

Functional status affects prognosis

In frail older patients, use of functional status measures (eg, ADLs) is essential in the perioperative period to assess clinical progress.

ADLs indicate how well a patient can transfer from a bed to a chair and how well the patient bathes, dresses, and ambulates.

Depressive symptoms. Older patients with depressive symptoms, including patients who have undergone hip surgery, have prolonged hospitalizations, have worse in-hospital outcomes, and are less likely to have good long-term outcomes.

Cognitive dysfunction is a common functional status measure that confounds the outcomes of hospitalization. Cognitive abilities should be assessed, and most importantly, delirium or acute confusion must be detected so that offending medications can be stopped or fluid and electrolyte problems aggressively treated. A brief test of attention (eg, a digit span of five numbers) can be helpful to detect patients with cognitive impairment.

Nutrition. Although the data are sparse, some evidence suggests that nutritional supplements given to patients following hip surgery may improve outcomes and reduce mortality.[7]

POSTOPERATIVE DAY 2: PATIENT IS WEAK AND IN PAIN

On postoperative day 2, the patient appears weak, slightly confused, and is not eating. The neurologic examination is normal, but she is crying in pain.

The most important next step is to:

A. Order increased physical therapy
B. Begin an antidepressant
C. Insert a nasogastric feeding tube
D. Increase doses of analgesics

The best answer is to increase doses of analgesics because the patient's pain must be managed before rehabilitation can continue. Ordering physical therapy might be appropriate, but this patient is not likely to benefit from physical therapy until she has adequate pain control. Because the patient was healthy at baseline, considering an antidepressant or a feeding tube would be premature. Those treatments might be indicated, however, if she had symptoms of depression or became malnourished.

POSTOPERATIVE DAY 3: WHAT IS CAUSING ELECTROLYTE IMBALANCE?

On postoperative day 3, the patient is still weak. Laboratory evaluations show a creatinine level of 0.5 mg/dL, a sodium level of 128 mmol/L, and a potassium level of 3.4 mmol/L.

The most likely reason for these low levels of electrolytes is:

A. Frailty (impaired homeostasis)
B. Excessive intravenous (IV) saline
C. Polydipsia

The major issue in this patient is frailty and impaired homeostasis. Acute illness causes a sudden decline in physical functioning, and if measures aren't taken to prevent further decline or return patients to their baseline strength level, then the resultant loss of strength is identified clinically as frailty.

Physiologic frailty results from failure of multiple organ systems: brain failure, which includes acute confusion or delirium; heart failure, when diastolic dysfunction pushes the patient over the edge (producing symptoms or signs of heart failure); and renal failure, whether it is the inability to excrete the free water load or the occurrence of prerenal azotemia in the postoperative period.[8]

Preventing frailty in older patients requires identifying those at risk and aggressively managing them after the acute illness, in this case major surgery, to successfully restore them to their baseline level of strength.

In considering the other two possible answers to the question above, polydipsia would be reasonable to assume if this patient had psychogenic polydipsia, for example, and wasn't able to effectively excrete a free water load. Excessive IV saline would be more likely to cause hypernatremia rather than the hyponatremia that we see in this patient.

POSTOPERATIVE DAY 4: PAIN IS CONTROLLED, COGNITION IS IMPROVED

By postoperative day 4, the patient's pain is controlled and her cognition has improved. Her diet is poor. She now takes short, shuffling steps and is unsteady.

The most important next step is to:

A. Begin treatment for Parkinson disease
B. Increase physical therapy
C. Begin nasogastric tube feedings
D. Reduce the level of analgesic therapy

Increasing physical therapy is the appropriate next step. The medical staff should try to transfer the patient, have her bear weight, increase her range-of-motion exercises, and have her perform low-impact aerobic exercise, such as walking to the physical therapy department or walking up and down the hallway. As the patient progresses, more aggressive measures can be implemented, such as low-intensity resistive exercises

using bands, tubes, and weights. Following hospital discharge, rehabilitation can be increased to include high-intensity exercises using machines or pulleys.

The other options should be considered and might be appropriate in other circumstances. For example, reducing analgesic therapy might be considered if this patient's cognitive function were impaired, if she were having hallucinations, or if she had received meperidine and was experiencing psychosis, nausea, or seizures. However, her cognition has improved and she does not have constipation, fecal impaction, or vomiting, and her bowels are moving, indicators that her analgesic profile is reasonably good.

Nasogastric tube feeding would be reasonable to consider at this point—it's postoperative day 4 and she is still not eating well—but this patient clinically seems to be turning the corner. With help from dietitians, nutrition support, and supplements, improving her nutritional status should be possible. This patient is a good candidate for oral feeding with or without nutritional supplements because she is alert, has normal swallowing mechanics, and is normally nourished or only mildly malnourished. The markedly malnourished patient would require more aggressive intervention with IV fluids or nasogastric tube feeding, nutritional support, and dietetic counseling.

In this patient, beginning treatment for Parkinson disease would be inappropriate because her parkinsonian symptoms are probably caused by deconditioning and generalized weakness. In addition, this patient's baseline neurologic examination was normal, and she has no history of Parkinson disease.

POSTOPERATIVE DAY 5: CAN THE PATIENT GO HOME?

On postoperative day 5, the patient appears well and is eating and walking with the assistance of a walker. She refuses to be admitted to a skilled nursing facility and asks if she can go home.

The best next step is:

A. Psychiatry consult to judge competence
B. Family conference
C. Call the patient's power of attorney designate for health care
D. Discharge patient to home

In this case a family conference would be a helpful first step. When the diagnosis isn't clear or the patient has concurrent illnesses or psychosocial issues, a family conference will help do the following:

- Clarify the goals of therapy, the patient's wishes and values, and likely hospital outcomes
- Review advance directives
- Resolve conflicts in care management.

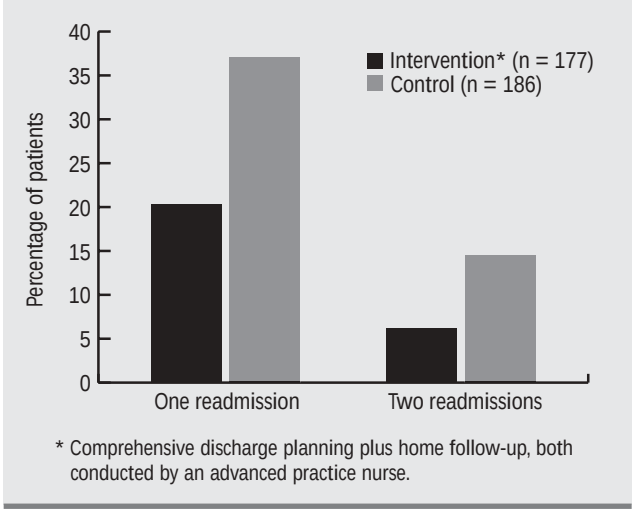

FIGURE 1. Comprehensive discharge planning reduced the number of hospital readmissions (within 24 weeks of index discharge) compared with usual care ($P \leq .01$) in a randomized trial of patients age 65 and older. Data from reference 9.

Family conferences that take place early in complicated cases and then periodically as needed are a worthwhile investment of time.

Regarding the other possible next steps, psychiatric consultation to judge competence might be indicated because the patient is refusing what appears to be appropriate therapy (in this case transitional care in a skilled nursing facility following major surgery and a complicated postoperative hospital stay). Nevertheless, this patient is cognitively normal, does not have a history or findings of dementia, and would be deemed to have intact medical decision-making capacity, so psychiatric consultation would not be appropriate at this time.

Calling the patient's power of attorney designate would be reasonable if she were unable to make an informed judgment for herself—for example, if she were delirious, in a coma, or severely demented. Again, this patient is not in that situation.

Discharging the patient to home is a reasonable option to consider with arrangements for home care intervention. The issue in this case is that the patient has had a complicated postoperative hospital stay, she is weak, and she has not been eating well, so she is likely to have an unplanned readmission to the hospital because she will probably not do well at home.

Sending her home may have been possible if comprehensive discharge planning had been instituted on day 1 of her hospitalization and a case manager or spe-

cially trained advanced practice nurse helped manage her in the hospital and then made home care visits once she was sent home. Comprehensive discharge planning conducted by an advanced practice nurse was shown to be effective in a randomized trial of high-risk patients age 65 and older (including those who had undergone hip fracture treatment).[9] The study found that comprehensive discharge planning, which in this case also included home follow-up and telephone calls to the patient, reduced single readmissions and multiple readmissions (Figure 1), lengthened the time between discharge and readmission, and reduced length of stay on readmission compared with a control group that did not receive the intervention.

SUMMARY

Perioperative management is typically more complicated in older patients than in younger patients and requires more assessment and evaluation before surgery as well as precautionary steps after surgery to manage these high-risk patients.

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Optimizing the preoperative evaluation of patients with aortic stenosis or congestive heart failure prior to noncardiac surgery

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Aortic stenosis poses a preoperative management dilemma for patients who are scheduled to undergo noncardiac surgery. Likewise, congestive heart failure (CHF) is a significant surgical risk factor, and it merits careful patient selection and perioperative management.

Unfortunately, we have few data on the preoperative evaluation of patients with either of these two conditions. The guidelines for perioperative cardiovascular evaluation for noncardiac surgery that were developed jointly by the American College of Cardiology and the American Heart Association (ACC/AHA) devote minimal discussion to aortic stenosis and CHF.[1,2] Although the guidelines raise numerous red flags, they do not provide much guidance. In the absence of hard evidence-based data, I have structured this review around my own clinical impressions and clinical experience.

AORTIC STENOSIS AS A SURGICAL RISK FACTOR

Goldman et al determined that "important valvular aortic stenosis" is a major cardiac risk factor in patients who undergo noncardiac surgery.[3] They studied 1,001 consecutive patients aged 40 years and older and found that 23 of them had severe aortic stenosis. Of these 23 patients, 3 died during or shortly after noncardiac surgery (mortality rate, 13%). Admittedly, these numbers are not very robust.

Torsher et al conducted a retrospective study of risk in 19 patients with severe aortic stenosis who underwent a total of 28 noncardiac operations.[4] They found only 2 complications (7%) and concluded that selected patients with severe aortic stenosis who are managed appropriately may proceed to noncardiac surgery with an acceptable risk. They postulated that aggressive intraoperative and postoperative monitoring and therapy yields positive results and that prompt recognition and treatment of intraoperative hypotension is necessary to avoid peripheral hypoperfusion.

According to the ACC/AHA guidelines, "Severe aortic stenosis poses the greatest risk for noncardiac surgery. If the aortic stenosis is severe and symptomatic, elective noncardiac surgery should generally be postponed or canceled. Such patients require aortic valve replacement before elective but necessary noncardiac surgery."[5]

Although the risk imposed by aortic stenosis can be managed, optimal management of aortic stenosis in a patient who is undergoing noncardiac surgery has not been fully defined, and much depends on individual physician experience, patient comorbidities, and the absolute necessity of the intended surgery. In light of the need for a somewhat individualized approach, I will walk through an actual case study.

CASE STUDY

A 55-year-old man presented to his primary care physician with symptomatic lower extremity claudication upon walking 50 feet. His activity level had been severely reduced by the leg pain as well as by dyspnea. The patient was referred to a vascular surgeon, who recommended aorto-bifemoral bypass surgery. The patient was then referred for preoperative evaluation.

History. The patient's comorbidities included ongoing smoking (40 pack-years), type 2 diabetes

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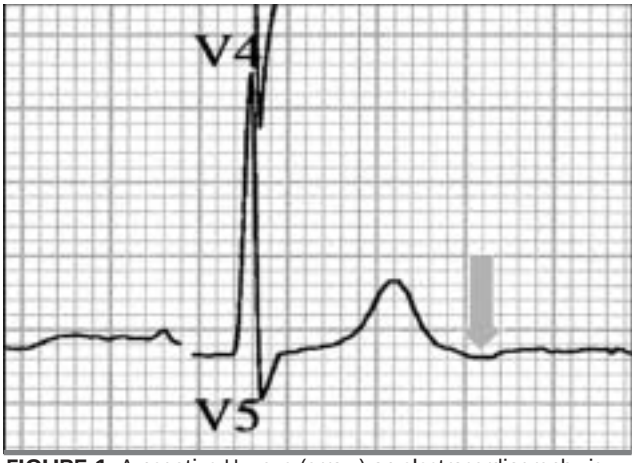

FIGURE 1. A negative U wave (arrow) on electrocardiography is usually a sign of left ventricular hypertrophy and/or obstructive coronary disease.

mellitus, hypertension, and a longstanding poorly characterized heart murmur. He was taking only three medications: baby aspirin, amlodipine, and metformin.

Physical exam. The patient was 5′ 8″ tall and 247 lb with a waist size of 46 in. His blood pressure was elevated and equal in both arms (178/104 mm Hg), and his jugular venous pressure was elevated (~8 cm H_2O at 45°). His lungs were characterized by a diffuse decrease in breath sounds without clear focality, there was a harsh systolic murmur best heard at the left upper sternal border, and S_2 was indistinct. His carotid pulses were reduced and delayed, and the results of a lower extremity and femoral exam confirmed severe lower extremity arterial vascular disease including a marked reduction of pedal pulse intensity and loud bifemoral bruits. Findings on a limited abdominal exam secondary to increased girth were normal.

Laboratory tests. The patient's basic metabolic profile was normal, but his fasting glucose level was not ideal (142 mg/dL), his hemoglobin A_{1c} level was elevated (7.7%), and his B-type natriuretic peptide level was 380 pg/mL. He had mild proteinuria (1+ protein) and his lipid profile was as follows: total cholesterol, 276 mg/dL; high-density lipoprotein cholesterol, 42 mg/dL; low-density lipoprotein cholesterol, 194 mg/dL; and triglycerides, 264 mg/dL.

Other investigations. Chest radiograph demonstrated an enlarged cardiac silhouette, but no abnormal lung fields. Electrocardiography (ECG) detected a prominent "negative U wave," which is a terminally negative deflection after the T wave (Figure 1). This underappreciated ECG abnormality is present in two circumstances—left ventricular hypertrophy (LVH) and/or obstructive coronary disease—making it a potentially useful marker for underlying pathology, especially in patients with multiple coronary artery disease (CAD) risk factors. Two-dimensional echocardiography identified significant LVH and severe aortic stenosis. The aortic valve peak gradient was 96 mm Hg and the mean gradient was 64 mm Hg (a mean gradient ≥ 40 mm Hg in a patient with normal LV systolic function reflects severe aortic stenosis).

Establishing a risk profile

Risk factors. Before making a decision, a review of the ACC/AHA's broad categories of cardiac risk considerations and how they apply to this patient is in order:

- *The type of operation and its risk*. An aortobifemoral bypass is a major operation with the potential to cause significant hemodynamic stress.
- *The presence and severity of CAD*. We do not know if our patient has CAD, but our suspicion is high as he has large-vessel lower extremity arterial vascular disease.
- *LV function*. Our patient's LV function is almost normal; it is at most slightly depressed.
- *Age*. Age is not a mitigating factor in this case.
- *The presence and severity of valvular heart disease*. Present and severe.
- *Serious cardiac arrhythmias*. No historical evidence of arrhythmias was found, but the substrate for arrhythmias (LVH, severe valvular heart disease) is present.
- *Comorbidities*. Several.
- *Overall functional status*. Suboptimal.

When the risk factors are added, the patient is considered to be at high cardiac risk—that is, he has a greater than 5% chance of perioperative mortality or significant morbidity because of the high potential for hemodynamic shift.

Clinical predictors. In addition to cardiac risk factors, the ACC/AHA guidelines also take into account "clinical predictors" of an adverse perioperative cardiac event (Table 1). These predictors are classified as major, intermediate, and minor. Major predictors include:

- *A recent unstable coronary syndrome, such as an acute myocardial infarction (MI) within the previous 7 days, an acute MI with residual ischemia within the previous 1 month, or unstable angina*. When any of these circumstances is present, it is best to postpone any elective or semi-elective surgery for as long as possi-

ble, optimally for at least 1 month and preferably for 3 to 6 months. Our patient does not have an unstable coronary syndrome.

• *Decompensated CHF.* Do not perform surgery on such a patient until the CHF symptoms can be stabilized and reversed. The presence of CHF is usually a greater risk to the patient than the indication for surgery.

• *Significant arrhythmias*. Again, we do not suspect arrhythmia in our patient.

• *Severe valvular disease*. We have established that our patient has severe valvular disease.

In the future, levels of B-type natriuretic peptide may be incorporated into preoperative risk assessment indices. In patients undergoing cardiac surgery, preliminary evidence suggests that preoperative B-type natriuretic peptide levels may predict length of stay, morbidity, and mortality.[6]

Functional capacity. Functional capacity can be determined by asking patients if they are independent and if they can exercise, go to the grocery store, climb a flight of stairs, etc. As established previously, our patient's functional capacity is limited.

TABLE 1
Major clinical predictors of an adverse perioperative cardiac event

Unstable coronary syndromes
• Acute myocardial infarction (< 7 days previously)
• Recent myocardial infarction with residual ischemia (< 1 month)
• Unstable angina
Decompensated congestive heart failure
Significant arrhythmias
• High-grade atrioventricular block
• Symptomatic ventricular
• Supraventricular with poor ventricular rate control
Severe valvular heart disease

Indications for coronary angiography

Is coronary angiography best performed in this patient? Let us review the class I and class II indications.

Class I indications are those for which the data strongly support performing angiography. They apply to patients with known or suspected CAD. These indications include:

• *Evidence of a high potential for an adverse outcome based on noninvasive testing results*. The resting echocardiogram in our patient detected the valvular abnormalities, but no other noninvasive tests that would detect CAD were performed.

• *Unstable angina or angina pectoris that is unresponsive to medical therapy*. Our patient does not have angina.

• *Equivocal results on a noninvasive stress test in a high-risk patient undergoing high-risk surgery*. Although CAD is almost a certainty in this patient, we need to know whether or not it is functionally significant and therefore flow-limiting. In a patient with severe aortic stenosis, prominent CAD risk factors, and upcoming noncardiac surgery with significant hemodynamic risk, invasively assessing the coronary artery circulation is indicated.

Class II indications are not as fully supported by the data, and indicate a divergence of opinion about the usefulness of performing the procedure. These indications are:

• *The presence of multiple markers of intermediate clinical risk in a patient scheduled for vascular surgery*. As addressed in the prior section, these criteria certainly apply to our patient. The general recommendation is to consider a noninvasive test first, although some physicians proceed directly to cardiac catheterization. In the absence of valvular heart disease and LV systolic dysfunction, we should proceed with noninvasive imaging—typically, a dobutamine echocardiogram. If those results are satisfactory, then we can proceed with surgery. If the patient does have concomitant LV dysfunction or significant valvular disease in the absence of LV dysfunction, we would perform a cardiac catheterization first.

• *A moderate to large ischemic burden on a noninvasive stress test in a patient without high-risk features and a preserved LV ejection fraction*. Most physicians would consider this a class I indication. Almost all patients with a large ischemic burden undergo cardiac catheterization.

• *Nondiagnostic noninvasive test results in an intermediate-risk patient who is undergoing high-risk surgery*. The decision rests on individual clinical judgment, but most physicians would favor cardiac catheterization.

• *Urgent noncardiac surgery for a patient convalescing from a recent MI*. This decision rests on which circumstance takes precedence—the urgency of the planned operation or the risk of catheterization. This is a complex situation. It might be best to per-

form a simple balloon angioplasty without stenting in the setting of residual myocardial ischemia in order to avoid the need for anticoagulation. If stenting becomes necessary to treat residual CAD, it could be performed later after the patient has healed, but this practice is controversial and recommendations are in flux.

How is our patient best managed?

To review, an aorto-bifemoral bypass has been proposed for this patient. The patient has multiple cardiac risk factors, near-normal LV function, no known arrhythmias, and severe aortic stenosis. He has a reduced exercise tolerance, although ascribing the patient's reduced exercise tolerance solely to cardiac disease is problematic because he has exercise-limiting claudication and a longstanding history of tobacco use.

What is our next step?

- Optimize medical therapy, then proceed with noncardiac surgery
- Cancel the aorto-bifemoral bypass, prescribe cilostazol and a walking program, and reassess in 1 month
- Perform dobutamine echocardiography and reassess surgical candidacy
- Cancel the bypass and perform cardiac catheterization, aortic valve replacement, and possibly coronary artery bypass graft surgery.

It is fairly clear that the next step is to cancel the aorto-bifemoral bypass and perform cardiac catheterization and aortic valve replacement—that is, to treat this man like any other patient who presents to our office with severe aortic stenosis. The two circumstances that will guide our course of action are that (1) our patient has severe aortic stenosis and suspected CAD and (2) he has serious quality-of-life–limiting symptoms related to his peripheral vascular disease.

The outcome

The cardiac catheterization in our patient confirmed that his LV systolic function was normal (LV ejection fraction, ~55%). He had significant CAD, primarily in the proximal right coronary artery (80% to 90% stenosis) and to a much lesser degree in the left anterior descending artery (30%). An aortogram confirmed that both the peripheral vascular disease and the aortic stenosis were severe, and it identified a mild poststenotic dilation of the ascending aorta. The patient was referred to a cardiac surgeon so that his heart problems could be addressed prior to treatment of his lower extremities.

ADDITIONAL CONSIDERATIONS WITH AORTIC STENOSIS

Aortic stenosis and coexisting conditions

Angina and CHF. Patients with aortic stenosis who also have angina and CHF have a poor short-term prognosis, so it is best to proceed with a diagnostic work-up with the intent to perform an aortic valve replacement. Again, echocardiography is an invaluable tool that has supplanted cardiac catheterization for the hemodynamic evaluation of aortic stenosis in the vast majority of cases.

Severe LV dysfunction. Patients with suspected advanced aortic stenosis and severe LV dysfunction may actually have "pseudoaortic stenosis," which is a low-gradient aortic stenosis in the presence of severe LV dysfunction. We must determine if severe valvular aortic stenosis is present vs severely reduced cardiac output and forward perfusion pressure preventing adequate aortic valve excursion. We can differentiate the two by performing dobutamine echocardiography; if leaflet excursion is increased or if the calculated aortic valve area increases, the patient likely has pseudostenosis. In contrast, if the calculated valve area remains constant and the leaflets do not demonstrate increased excursion, we can confidently proceed to aortic valve replacement as this represents a true case of valvular stenosis.

Correcting stenosis prior to noncardiac surgery

When noncardiac surgery is absolutely necessary in a patient whose aortic valve surgical risk would otherwise be deemed prohibitive, one option is to perform a valvuloplasty. However, it is fraught with risks, particularly embolism. Also, rates of recurrent aortic stenosis are extremely high, so valvuloplasty might turn out to be only a temporary palliative procedure.

CHF AS A SURGICAL RISK FACTOR

Growing number of surgical candidates with CHF

In addition to the paucity of published data on the preoperative evaluation of patients with CHF, our assessment is complicated by the changing epidemiology of patients who are undergoing noncardiac surgery. First, increasing life spans mean that a greater number of older patients are undergoing noncardiac surgery. Second, surgeons are developing less invasive surgical options. Both of these factors have broadened the base of older patients who are eligible for surgery, and these patients often possess more comorbidities and more complex medical problems. CHF is one of the most serious of these comorbidities, and it is becoming more common.

Systolic vs diastolic: Better differentiation needed

An important aspect of CHF is that systolic and diastolic heart failure have not yet been preoperatively differentiated. Of the two, more attention has been given to systolic heart failure, but older patients with noncompliant hypertrophied ventricles can experience significant intraoperative and postoperative difficulties as well—particularly with fluid shifts, excessive fluid administration, and perhaps some concomitant myocardial ischemia. There may be important differences between systolic and diastolic heart failure with respect to risk stratification and management, but we just do not know at present.

A more important risk than CAD?

It seems as if the focus on preoperative risk has generally been CAD, but some studies have shown that CHF is actually more serious. For example, Hernandez et al retrospectively reviewed the records of 1,532 patients with CHF who had undergone major cardiac surgery.[7] These patients were among thousands in a national Medicare database, and they represented a broad spectrum of older patients who underwent major noncardiac surgery. The researchers found that among patients aged 65 years or older, those with CHF experienced significantly greater morbidity and mortality than did patients without CHF, including those with CAD. In fact, the complication rate in CHF patients (11.7%) was nearly double the rate in patients with CAD (6.6%) and in controls who had neither CHF nor CAD (6.2%). Overall, the mere presence of CAD was not necessarily significant. The trend was observed throughout for various endpoints, including operative mortality, 30-day mortality, postdischarge mortality, length of hospitalization, the need for intensive care, and readmission rates. The trend was maintained regardless of the type of procedure or the urgency of the operation.

Certainly, this study had some inherent weaknesses. For example, it would be interesting to see how outcomes would have differed if the patients with CHF had been compared to patients with *functionally significant* CAD instead of being compared to all patients with CAD regardless of severity. Another concern is that many of the patients with CHF may not have been on beta-blockers—or if they were, the dosages may not have been titrated to the level of maximum therapeutic benefit. The myth persists that beta-blockers can be deleterious in patients with CHF, yet the risk of beta-blockade is typically small in patients who are either compensated or nearly compensated, while the benefit in these patients is clearly elucidated. Despite the study's limitations, it did bring to the fore the importance of CHF as a significant perioperative risk factor. Therefore, careful preoperative patient selection and perioperative management is mandatory.

DIFFICULT DECISIONS

Suppose we determine that cardiac surgery is necessary just to prepare a high-risk patient for subsequent noncardiac surgery. We must ask ourselves if two operations are worth the expected outcome. What will all this surgery do to the patient's quality of life? Is it better to do nothing?

These are hard questions, and we will not always find the answers in published guidelines or in a textbook. This is when we are truly "doctors." This is when we call on our judgment, experience, and instincts as well as our commitment that whatever we do will be dictated by what is best for the patient.

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Minimizing perioperative complications in patients with renal insufficiency

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Development of acute renal failure perioperatively is associated with considerable mortality and often with incomplete recovery regardless of baseline renal function. A thorough evaluation of perioperative risk in patients with renal insufficiency should therefore include an additional assessment of the risk for renal injury that might require dialysis and add to the operative mortality.

This article will describe the risk for renal injury, elucidate the mechanisms of injury, review the impact of serum creatinine elevations and changes on operative outcomes, and suggest specific measures to reduce perioperative risk.

KIDNEYS ARE SUSCEPTIBLE TO VASCULAR INSULT

Kidneys are highly vascular and therefore at risk for problems that affect the renal vascular bed. The older and sicker a patient is, the likelier that his or her body will be unable to autoregulate renal perfusion and preserve the glomerular filtration rate (GFR). The resultant kidney injury in turn increases susceptibility to complications in a variety of common surgical settings.

Acute renal injury causes tubular damage, resulting in backleak or tubular obstruction, which reduces glomerular filtration and the kidney's ability to concentrate the urine and reabsorb sodium. Any vascular insult may reduce renal blood flow and the filtration fraction, thereby reducing overall GFR.

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ACUTE RENAL FAILURE: A SERIOUS PERIOPERATIVE COMPLICATION

Acute renal failure is a serious complication: only about 15% of patients who develop acute renal failure perioperatively fully recover. About half of patients who develop acute renal failure postoperatively die, approximately 5% survive but remain in renal failure, and approximately 5% recover incompletely and have continually declining renal function. Another 15% recover incompletely and remain stable for a time but are at increased risk of developing chronic kidney disease. Patients who are older, are sicker, or sustain a more severe insult are especially at risk of a poor outcome.

Monitoring acute changes in renal function

Of the approaches to monitor acute changes in renal function perioperatively, monitoring serum creatinine is currently the most commonly employed and clinically practical method. The serum creatinine measurement, while not as precise as iothalamate or inulin clearance techniques, can be used to estimate GFR accurately in a stable patient in the outpatient setting.

Serum creatinine. The serum creatinine varies inversely with GFR. An elevated serum creatinine level is a late indicator of renal injury: even a relatively minor increase is clinically significant, indicating that damage is already established and a patient has lost his or her renal reserve.

Thakar et al,[1] in a study of more than 31,000 patients who underwent cardiac surgery, found that a greater than 30% decline in postoperative GFR increases the risk of mortality, regardless of the baseline creatinine level. Even renal dysfunction not requiring dialysis is an independent risk factor for mortality after cardiac surgery. Lassnigg et al[2] studied more than 4,000 patients after cardiac or thoracic aortic surgery and found that compared with a mild fall in serum creatinine, an increase in serum creatinine of more than 0.5 mg/dL within 48 hours postoperatively is associated with more than an 18-fold

greater risk of mortality over the next 30 days.

Estimating GFR based on the Modification of Diet in Renal Disease (MDRD) equation, while helpful in the outpatient setting for estimating residual renal function, is less accurate in the hospitalized patient with a "new" increase in serum creatinine. It correlates poorly with the more accurate method of measuring GFR using iodine 125-iothalamate.[3]

Biomarkers in the urine (eg, kidney injury molecule-1, cystatin C, neutrophil gelatinase-associated lipocalin) or in the blood (cystatin C) will likely be used increasingly in the future to screen patients for renal failure postoperatively, prior to an actual increase in serum creatinine. Markers are being sought to promptly identify "early" injury in a patient with apparent renal insult (whether due to nephrotoxic injury, a perioperative ischemic event, trauma, or radiocontrast agents).

ASSESSING RISK OF RENAL FAILURE PREOPERATIVELY

Case: A woman with diabetes and congestive heart failure facing cardiac surgery

A 60-year-old woman is scheduled to undergo mitral valve replacement and two-vessel coronary artery bypass graft (CABG) surgery. She has diabetes, peripheral vascular disease, a history of myocardial infarction, and congestive heart failure (ejection fraction, 40%). Her serum creatinine is 2.3 mg/dL.

What is her risk of postoperative acute renal failure?

Traditionally, a serum creatinine of less than 3.0 mg/dL has justified a "watchful waiting" approach, provided the patient has no protein in the urine and the GFR is greater than 30 mL/min. The projected risk of acute renal failure in this setting was more often based on anecdotal experience rather than well-designed databases.

More recently, Thakar et al[4] assessed the risk of acute renal failure in 22,589 patients who underwent open heart surgery at The Cleveland Clinic between 1993 and 2000. Acute renal failure was defined in three ways: (1) acute renal failure requiring dialysis during the postoperative period, (2) a 50% or greater decline in creatinine clearance but not requiring dialysis, and (3) a 50% or greater decline in GFR or requirement of dialysis. Important risk factors for developing acute renal failure after open heart surgery were identified, as detailed below.

Combined procedure. The frequency of acute renal failure requiring dialysis or a 50% or greater decline in GFR was 3.8% among patients undergoing CABG, 4.5% among those undergoing a valve procedure, and 7.9% among those who underwent both CABG and valve replacement.

Female gender. Nearly 29% of women with a baseline serum creatinine level of more than 4.0 mg/dL developed acute renal failure, and women had a higher risk of developing acute renal failure than men at every level of baseline serum creatinine, with increasing risk observed at higher levels.

Other risk factors. Other variables associated with an elevated risk of acute renal failure requiring dialysis included a greater cardiopulmonary bypass time, having emergency surgery, the presence of peripheral vascular disease, and having preoperative intra-aortic balloon pumping. Black race was found to be a risk factor for acute renal failure by univariate analysis, but not by multivariate logistic regression analysis.

Consequences beyond kidney function

Consequences of postoperative acute renal failure extend beyond kidney function: acute renal failure requiring dialysis is associated with a 60% frequency of serious infection and a 26% risk of sepsis; patients with acute renal failure not requiring dialysis have nearly a 25% chance of serious infection and a 13% chance of sepsis.[5] Both infections and sepsis are important determinants of mortality. Other factors associated with acute renal failure and higher mortality rates include proinflammatory and anti-inflammatory cytokines, levels of the insulin-like growth factor binding proteins IGFBP-1 and IGFBP-3, and hyperglycemia.

Predicting risk based on preoperative factors

Predicting the risk of acute renal failure after open heart surgery can be approached with an algorithm based on preoperative factors (Figure 1).[6] If we implement this algorithm for the patient in our case study (see bold arrows in Figure 1), her risk of acute renal failure requiring dialysis is 5.6%, and her risk for a 50% or greater decline in GFR is 8.7%.

An alternative approach to predicting risk is with a system that awards points based on risk factors (Table 1).[7] In this system, our patient would earn 1 point for being a woman, 2 points for use of an intra-aortic balloon pump preoperatively, 1 point for having congestive heart failure, 2 points for her scheduled CABG and valve procedure, and 5 points for having a preoperative serum creatinine level of 2.1 mg/dL or greater. With 11 points, her corresponding risk of acute renal failure is approximately 20% under the scoring model developed (21.5% of patients in the model with risk scores of 9 to 13 developed acute renal failure).

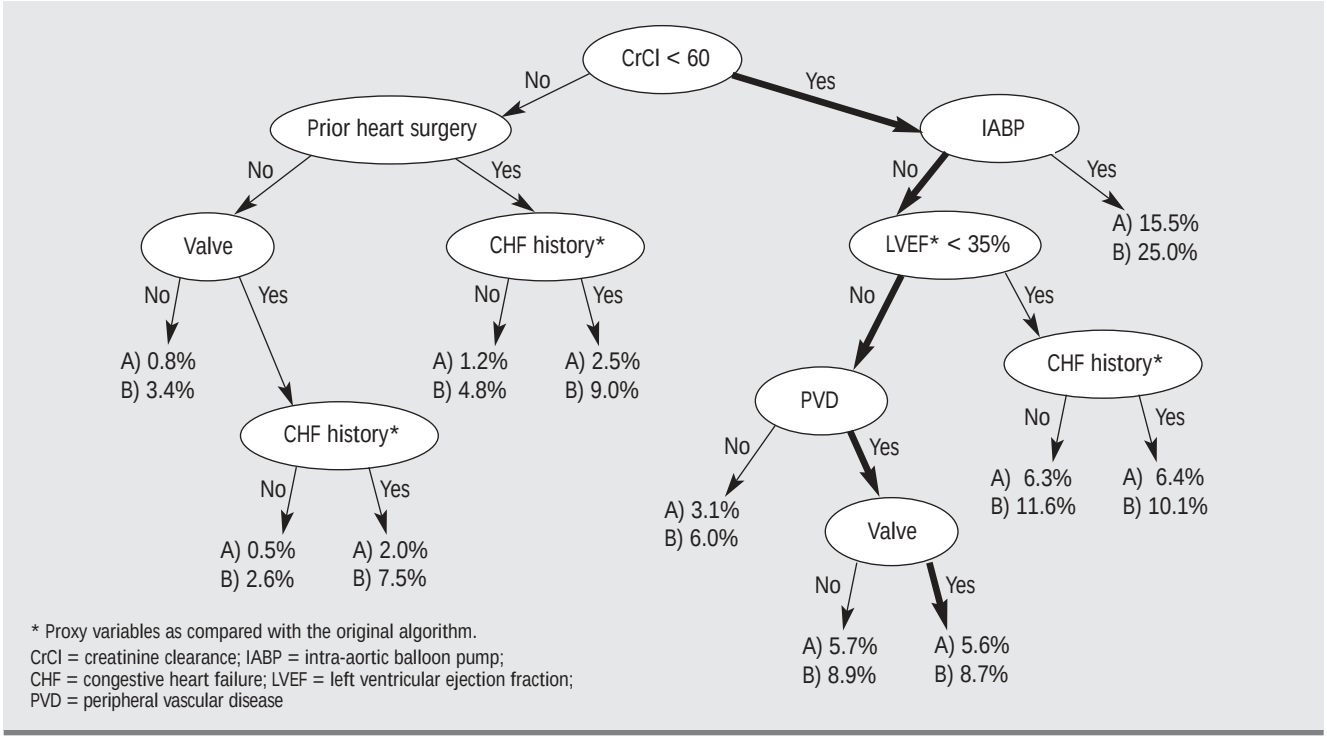

FIGURE 1. An algorithm that incorporates preoperative risk factors can be used to estimate the risk of acute renal failure after open heart surgery. Based on the clinical scenario, the algorithm estimates the risk of acute renal failure, defined as either requiring dialysis (values designated as "A") or a 50% or greater decline in glomerular filtration rate or requiring dialysis (values designated as "B"). The arrows in boldface indicate the risk factors present in the patient in the case study (see text). Adapted, with permission, from reference 6.

It is important that a patient at high risk be informed and that the medical team also is made aware of the risk, since prevention is a more powerful approach than attempted treatment after an established insult.

PREOPERATIVE MEASURES TO PREVENT RENAL FAILURE

After assessing the degree of risk, based on a patient's individual risk and the characteristics of the procedure, several preoperative measures to prevent renal injury should be considered.

Adjust medications

Calculate the estimated GFR preoperatively and determine which medications warrant adjustment based on residual renal function. Avoid medications such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and nonsteroidal anti-inflammatory drugs as well as overzealous diuresis, each of which may compromise maintenance of effective filtration pressure.

Optimize volume and solute status

Volume status must be optimized perioperatively to decrease the risk of renal ischemia from renal hypoperfusion in the setting of either dehydration or congestive heart failure with hypotension. Patients with diabetes also present more of a challenge both preoperatively and postoperatively because the alveolar-arterial gradient for the same central venous pressure is broader compared with nondiabetic patients, highlighting an increased risk for respiratory failure with hypervolemia in diabetes.

Ensure adequate urine flow, but avoid high-dose loop diuretics

Achieving an adequate urine flow rate (> 100 to 150 mL/hour) is critical to avoiding tubular obstruction with acute renal failure.

A danger in patients with high volume overload is overly aggressive use of loop diuretics in an attempt to remove fluids. High-dose loop diuretics may decrease GFR, activate neurohormones (sympathetic nervous system, renin-angiotensin-aldosterone system), cause sodium reaccumulation, and adversely affect clinical outcomes (eg, length of hospital stay, mortality).

Mehta et al[8] categorized 552 patients with acute renal failure in intensive care units by their use of diuretics immediately before nephrology consultation. Diuretic use was associated with a significant increase in the risk of death and nonrecovery of renal function. Even in light of the significant comorbidities in this population, these findings raise concerns regarding the link between high-dose diuretics and poor outcome.

A patient at risk of developing acute renal failure who does not respond to reasonable doses of diuretics

TABLE 1

This table adapted from reference 7. Permission not granted to reprint this table online.

Please see original source table (table 5) in: *Thakar CV, Arrigain S, Worley S, Yared J-P, Paganini EP. A clinical score to predict acute renal failure after cardiac surgery. J Am Soc Nephrol 2005; 16:162–168.*

TABLE 2
Regimens for continuous intravenous infusion of diuretics

For patients in stable chronic renal failure (creatinine clearance rate about 18 mL/min), use the following:

- Furosemide: 20 to 40 mg/hr
  or
- Bumetanide: 1 to 2 mg/hr
  or
- Torsemide: 10 to 20 mg/hr

If ineffective, add a thiazide diuretic or use hemofiltration

(Table 2) should undergo volume removal by an extracorporeal therapy to allow the kidney to reset itself. A number of therapies can be used perioperatively, including standard hemodialysis, hemofiltration and ultrafiltration.

Consider options to enhance diuretic administration and effect

Clinical trials have failed to prove that perioperative administration of dopamine infusions with furosemide improves urine flow rate or is protective against renal dysfunction.[9,10]

Patients who are hypoalbuminemic are often resistant to diuresis, however, and it is theoretically possible that administering albumin may improve delivery of furosemide to the endothelium. Infusing furosemide and salt-poor albumin has not proven effective in clinical studies.[11,12]

Whether diuretics should be administered intravenously or as a bolus is another controversial issue. Diuresis is enhanced by continuous infusion rather than boluses in certain clinical settings with low colloid osmotic pressure and increased extracellular volume. A bolus results initially in high rates of diuretic excretion, but rates soon taper off. With high boluses, renal function may deteriorate because of vasoconstriction from neurohormonal activation. Furosemide delivered by bolus also has the disadvantage that it may cause ototoxicity, especially in elderly patients. Patients who do not respond to a bolus are less likely to respond to continuous infusion. Extracorporeal support should be considered earlier, especially in patients with relative hypotension, hypervolemia, congestive heart failure, and minor increases in serum creatinine on standard diuretic therapy.

Optimize hematocrit levels

The true impact of hematocrit levels and erythropoietin on perioperative acute renal failure and outcomes is not well defined. Comparisons of risk factors for hospital mortality among dialysis patients have identified hematocrit in the intensive care unit as the most dominant risk factor in this population. Moreover, cardiopulmonary bypass hemodilution (< 24%) is associated with a systematically increased likelihood of renal injury. Experimental data suggest that erythropoietin has unexpected cytokine actions that may be important for recovery from acute renal failure. Further study of erythropoietin therapy in this setting is warranted.

Limit use of intravenous contrast agents

Contrast agents increase vasoconstriction and cause tubular ischemia, sloughing of tubules, and obstruction.

Patients who already have renal insufficiency or develop it acutely are at risk for contrast-induced nephropathy after coronary angiography or other procedures requiring contrast. Patients with any elevation in serum creatinine should be viewed as high risk for acute renal failure.

If contrast is needed, a nonionic agent is preferable, delivered with intravenous fluids before and after procedures to increase urine flow to protect against obstruction. Sodium bicarbonate infusion may also reduce the risk of contrast-induced nephropathy and should be used, especially in high-

risk patients. Measures to possibly ameliorate risk, including giving the antioxidant acetylcysteine or fenoldopam, a dopamine-1 receptor agonist, are currently under investigation, and conclusions are still uncertain.[13–15]

SUMMARY

Patients with an elevated serum creatinine or whose serum creatinine levels increase postoperatively, regardless of baseline levels, are at increased risk for elevated mortality. Women have a higher risk from acute renal failure than men at every level of serum creatinine. Acute renal failure confers an increased risk of mortality, chronic renal insufficiency, and postoperative infection independent of other postoperative complications. Preoperative measures to reduce risk of acute renal failure include optimizing volume and solute status, ensuring adequate urine flow, avoiding high doses of diuretics, optimizing hematocrit levels, and avoiding contrast agents.

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