PREOPERATIVE AND POSTOPERATIVE MANAGEMENT

Zara Cooper • Edward Kelly

Surgeons of every specialty face increasingly complex surgical challenges. In addition, modern surgical treatment can be offered to more fragile patients, with successful outcomes. Mastery of the scientific fundamentals of perioperative management is required to achieve satisfactory results. The organ system–based approach presented here allows the surgeon to address the patient's pre- and postoperative needs with a comprehensive surgical plan. This chapter will serve as a summary guide to best practices integral to conducting surgical procedures in the modern era.

MANAGEMENT OF PAIN AND DELIRIUM

The most common neuropsychiatric complications following abdominal surgery are pain and delirium. Moreover, uncontrolled pain and delirium prevent the patient from contributing to vital aspects of his or her care, such as ambulation and respiratory toilet, and promote an unsafe environment that may lead to the unwanted dislodgment of drains and other supportive

devices, with potentially life-threatening consequences. Pain and delirium usually coexist in the postoperative setting, and each can contribute to the development of the other. Despite high reported rates of overall patient satisfaction, pain control is frequently inadequate in the perioperative setting,[1] with high rates of complications such as drowsiness from overtreatment and unacceptable levels of pain from undertreatment. Therefore, it is mandatory that the surgical plan for every patient include close monitoring of postoperative pain and delirium and regular assessment of the efficacy of pain control.

Pain management, like all surgical planning, begins in the preoperative assessment. In the modern era, a large proportion of surgical patients will require special attention with respect to pain control. Patients with preexisting pain syndromes, such as sciatica or interspinal disc disease, or patients with a history of opioid use may have a high tolerance for opioid analgesics. Every patient's history should include a thorough investigation for chronic pain syndrome, addiction (active or in recovery), and adverse reactions to opioid, nonsteroidal, or epidural analgesia. The pain control strategy may include consultation with a pain control anesthesiology specialist, but it is the responsibility of the operating surgeon to identify complicated patients and construct an effective pain control plan.

Opioid Analgesia

Postoperative pain control using opioid medication has been in use for thousands of years. Hippocrates advocated the use of opium for pain control. The benefits of postoperative pain control are salutary and include improved mobility and respiratory function and earlier return to normal activities. The most effective strategy for pain control using opioid analgesia is patient-controlled analgesia (PCA), wherein the patient is instructed in the use of a preprogrammed intravenous pump that delivers measured doses of opioid (usually morphine or meperidine). In randomized trials, PCA has been shown to provide superior pain control and patient satisfaction compared to interval dosing,[2] but PCA has not been shown to improve rates of pulmonary and cardiac complications[3] or length of hospital stay,[4] and there is evidence that PCA may contribute to postoperative ileus.[5] In addition, PCA may be unsuitable for patients with a history of substance abuse, high opioid

tolerance, or those with atypical reactions to opioids.

Regional Analgesia

Due to the limitations of PCA, pain control clinicians have turned to regional analgesia as an effective strategy for the management of postoperative pain. Postoperative epidural analgesia involves the insertion of a catheter into the epidural space of the lumbar or thoracic spine, enabling the delivery of local anesthetics or opioids directly to the nerve roots. The insertion procedure is generally safe, with complication rates of motor block and numbness between 0.5% and 7%,[6] and an epidural abscess rate of 0.5 per thousand.[7] Potential advantages of epidural analgesia include elimination of systemic opioids, and thus less respiratory depression, and improvement in pulmonary complications and perioperative ileus. There have been several large trials,[8-10] a meta-analysis,[6] and a systematic review[11] comparing PCA with epidural analgesia in the setting of abdominal surgery. These studies indicate that epidural analgesia provides more complete analgesia than PCA throughout the postoperative course. Furthermore, in randomized prospective series of abdominal procedures, epidural analgesia has been associated with decreased rates of pulmonary complications[12,13] and postoperative ileus.[14,15] Epidural analgesia requires a skilled anesthesia clinician to insert and monitor the catheter and adjust the dosage of neuraxial medication. Some clinicians may prefer correction of coagulopathy before inserting or removing the catheter, although the American Society of Anesthesiologists (ASA) has not issued official guidelines on this issue.

Peripheral nerve blocks are also effective in perioperative pain control and do not carry the same potential morbidities as the epidural approach. Using ultrasound guidance, a skilled practitioner can deliver a long-acting local anesthetic into the transversus abdominis plane (TAP) or in the rectus sheath to establish analgesia both intraoperatively and postoperatively. Randomized clinical data have confirmed the efficacy of regional blocks in controlling pain and reducing use of opioid analgesia.[16,17]

Analgesia with Nonsteroidal Anti-Inflammatory Drugs

Oral nonsteroidal anti-inflammatory drugs (NSAIDs) have long been used for postoperative analgesia in the outpatient setting and, with the development of parenteral preparations, have come into use in the inpatient population. This class of medication has no respiratory side effects and is not associated with addiction potential, altered mental status, or ileus. In addition, these medications provide effective pain relief in the surgical population. However, use of NSAIDs has not been universally adopted in abdominal surgery due to concerns regarding the platelet dysfunction and erosive gastritis associated with heavy NSAID use. In prospective trials, NSAIDs were found to provide effective pain control without bleeding or gastritis symptoms following laparoscopic cholecystectomy,[18] abdominal hysterectomy,[19] and inguinal hernia repair.[20,21] NSAIDs have also been shown to improve pain control and decrease morphine dosage when used in combination following appendectomy.[22]

The sensation of pain is very subjective and personal. Accordingly, the surgeon must individualize the pain control plan to fit the needs of each patient. The pain control modalities discussed above can be used in any combination, and the surgeon should not hesitate to use all resources at his or her command to provide adequate relief of postoperative pain.

Postoperative Delirium

Delirium, defined as acute cognitive dysfunction marked by fluctuating disorientation, sensory disturbance, and decreased attention, is an all too common complication of surgical procedures, with reported rates of 11% to 25%, with the highest rates reported in the elderly population.[23,24] The postoperative phase of abdominal surgery exposes patients, some of whom may be quite vulnerable to delirium, to a large number of factors that may precipitate or exacerbate delirium (Table 2-1). These factors can augment one another: postoperative pain can lead to decreased mobility, causing respiratory compromise, atelectasis, and hypoxemia. Escalating doses of narcotics to treat pain can cause respiratory depression and respiratory acidosis. Hypoxemia and delirium can cause agitation, prompting treatment with benzodiazepines, further worsening respiratory function and delirium. This vicious cycle can result in serious complications or death. Preoperative recognition of high-risk patients and meticulous monitoring of every patient's

mental status are the most effective ways to prevent postoperative delirium; treatment can be remarkably difficult once the cycle has begun.

TABLE 2-1: CAUSES OF PERIOPERATIVE DELIRIUM

Pain
Narcotic analgesics
Sleep deprivation
Hypoxemia
Hyperglycemia
Acidosis
Withdrawal (alcohol, narcotics, benzodiazepines)
Anemia
Dehydration
Electrolyte imbalance (sodium, potassium, magnesium, calcium, phosphate)
Fever
Hypotension
Infection (pneumonia, incision site infection, urinary tract infection)
Medication (antiemetics, antihistamines, sedatives, anesthetics)
Postoperative myocardial infarction

Patient factors that are associated with high risk of perioperative delirium include age greater than 70 years, preexisting cognitive impairment or prior episode of delirium, history of alcohol or narcotic abuse, and malnutrition.[22,25] Procedural factors associated with high delirium risk include operative time greater than 2 hours, prolonged use of restraints, presence of a urinary catheter, addition of more than 3 new medications, and reoperation.[26]

Once the patient's risk for postoperative delirium is identified, perioperative care should be planned carefully to decrease other controllable factors. Epidural analgesia has been associated with less delirium than PCA after abdominal surgery.[26] Sedation or "sleepers" should be used judiciously, if at all, with high-risk patients. If the patient requires sedation, neuroleptics such as haloperidol and the atypical neuroleptics such as olanzapine are

tolerated much better than benzodiazepines.[27] The patient's mental status, including orientation and attention, should be assessed with every visit and care should be taken to avoid anemia, electrolyte imbalances, dehydration, and other contributing factors.

Once the diagnosis of postoperative delirium is established, it is important to recognize that some of the causes of delirium are potentially life-threatening, and immediate action is necessary. Evaluation begins with a thorough history and physical examination at the bedside by the surgeon. The history should focus on precipitating events such as falls (possible traumatic brain injury), recent procedures, use of opioids and sedatives, changes in existing medications (eg, withholding of thyroid replacement or antidepressants), and consideration of alcohol withdrawal. The vital signs and fluid balance may suggest sepsis, hypovolemia, anemia, or dehydration. The exam should include brief but complete sensory and motor neurologic examinations to differentiate delirium from stroke. Pay attention to common sites of infection such as the surgical wound, the lungs, and intravenous catheters. Urinary retention may be present as a result of medication or infection. Deep venous thrombosis may be clinically evident as limb swelling. Postoperative myocardial infarction (MI) may often present as acute cardiogenic shock.

The history and physical examination should then direct the use of lab tests. Most useful are the electrolytes, blood glucose, and complete blood cell count. Pulse oximetry and arterial blood gases may disclose hypercapnia or hypoxemia. Chest x-ray may disclose atelectasis, pneumonia, acute pulmonary edema, or pneumothorax. Cultures may be indicated in the setting of fever or leukocytosis, but will not help immediately. Electrocardiogram (ECG) and cardiac troponin may be used to diagnose postoperative MI.

Resuscitative measures may be required if life-threatening causes of delirium are suspected. Airway control, supplemental oxygen, and fluid volume expansion should be considered in patients with unstable vital signs. The patient should not be sent out of the monitored environment for further tests, such as head computed tomography (CT), until the vital signs are stable and the agitation is controlled. Treatment of postoperative delirium depends on treatment of the underlying causes. Once the underlying cause has been treated, delirium may persist, especially in elderly or critically ill patients, who regain orientation and sleep cycles slowly. In these patients, it is important to provide orienting communication and mental stimulation during

the day and to promote sleep during the night. The simplest ways are the most effective: contact with family members and friends, use of hearing aids, engagement in activities of daily living, and regular mealtimes. Sleep can be promoted by keeping the room dark and quiet throughout the evening and preventing unnecessary interruptions. If nighttime sedation is required, atypical neuroleptics or low-dose serotonin reuptake inhibitors such as trazodone are better tolerated than benzodiazepines. If agitation persists, escalating doses of neuroleptics (or benzodiazepines in the setting of alcohol withdrawal) can be used to control behavior, but underlying organic causes of delirium must be investigated.

CARDIAC EVALUATION

Risk Assessment

It has been estimated that 1 million patients have a perioperative MI each year, and the contribution to medical costs is $20 billion annually.[28] Thoracic, upper abdominal, neurologic, and major orthopedic procedures are associated with increased cardiac risk. Diabetes, prior MI, unstable angina, and decompensated congestive heart failure (CHF) are most predictive of perioperative cardiac morbidity and mortality, and patients with these conditions undergoing major surgery warrant further evaluation[29] (Table 2-2). Patient factors conferring intermediate risk include mild angina and chronic renal insufficiency with baseline creatinine ≥2 mg/dL.[30] It is worth noting that women were underrepresented in the studies on which the American College of Cardiology and the American Heart Association (ACC/AHA) guidelines are based.[31] A retrospective study in gynecologic patients found that hypertension and previous MI were major predictors of postoperative cardiac events, as opposed to the ACC/AHA guidelines, which indicate that they are minor and intermediate criteria, respectively.[32] Vascular surgical patients are at highest risk because of the prevalence of underlying coronary disease in this population.[29,33] Other high-risk procedural factors include emergency surgery, long operative time, and high fluid replacement volume. Intraperitoneal procedures, carotid endarterectomy, thoracic surgery, head and neck procedures, and orthopedic procedures carry an intermediate

risk and are associated with a 1% to 5% risk of a perioperative cardiac event.[30]

TABLE 2-2: CLINICAL PREDICTORS OF INCREASED RISK FOR PERIOPERATIVE CARDIAC COMPLICATIONS

Major

Recent myocardial infarction (within 30 days)
Unstable or severe angina
Decompensated congestive heart failure
Significant arrhythmias (high-grade atrioventricular block, symptomatic ventricular arrhythmias with underlying heart disease, supraventricular arrhythmias with uncontrolled rate)
Severe valvular disease

Intermediate

Mild angina
Any prior myocardial infarction by history or electrocardiogram
Compensated or prior congestive heart failure
Diabetes mellitus
Renal insufficiency

Minor

Advanced age
Abnormal electrocardiogram
Rhythm other than sinus (eg, atrial fibrillation)
Poor functional capacity
History of stroke
Uncontrolled hypertension (eg, diastolic blood pressure >10 mm Hg)

Perioperative evaluation to identify patients at risk for cardiac complications is essential in minimizing morbidity and mortality. Workup should start with history, physical exam, and ECG to determine the existence of cardiac pathology. Screening with chest radiographs and ECG is required for men over 40 and women over 55. According to the ACC/AHA guidelines, initial preoperative cardiac risk can be assessed using a clinical calculator, the

Revised Cardiac Risk Index (RCRI).[34] This index includes history of ischemic heart disease, CHF, cerebrovascular disease, diabetes, chronic kidney disease, and planned high-risk procedure. Advanced or invasive testing is reserved for patients with 2 or more of these risk factors. Overall functional ability is the best clinical measure of cardiac fitness. Patients who can exercise without limitations can generally tolerate the stress of major surgery.[35] Limited exercise capacity may indicate poor cardiopulmonary reserve and the inability to withstand the stress of surgery. Poor functional status is the inability to perform activities such as driving, cooking, or walking less than 5 km/h.

Intraoperative risk factors include operative site, inappropriate use of vasopressors, and unintended hypotension. Intra-abdominal pressure exceeding 20 mm Hg during laparoscopy can decrease venous return from the lower extremities and thus contribute to decreased cardiac output,[36] and Trendelenburg positioning can result in increased pressure on the diaphragm from the abdominal viscera, subsequently reducing vital capacity. Intraoperative hypertension has not been isolated as a risk factor for cardiac morbidity, but it is often associated with wide fluctuations in pressure and has been more closely associated with cardiac morbidity than intraoperative hypotension. Preoperative anxiety can contribute to hypertension even in normotensive patients. Patients with a history of hypertension, even medically controlled hypertension, are more likely to be hypertensive preoperatively. Those with poorly controlled hypertension are at greater risk of developing intraoperative ischemia, arrhythmias, and blood pressure derangements, particularly at induction and intubation. Twenty-five percent of patients will exhibit hypertension during laryngoscopy. Patients with chronic hypertension may not necessarily benefit from lower blood pressure during the preoperative period because they may depend on higher pressures for cerebral perfusion. Those receiving antihypertensive medications should continue them up until the time of surgery. Patients taking β-blockers are at risk of withdrawal and rebound ischemia. Key findings on physical examination include retinal vascular changes and an S_4 gallop consistent with left ventricular hypertrophy. Chest radiography may show an enlarged heart, also suggesting left ventricular hypertrophy.

ECG should be obtained in patients with chest pain, diabetes, prior revascularization, prior hospitalization for cardiac causes, all men age 45 or

older, and all women age 55 or older with 2 or more risk factors. High- or intermediate-risk patients should also have a screening ECG. A lower-than-normal ejection fraction demonstrated on echocardiography is associated with the greatest perioperative cardiac risk and should be obtained in all patients with symptoms suggesting heart failure or valvular disease. Tricuspid regurgitation indicates pulmonary hypertension and is often associated with sleep apnea. The chest x-ray is used to screen for cardiomegaly and pulmonary congestion, which may signify ventricular impairment.

Exercise testing demonstrates a propensity for ischemia and arrhythmias under conditions that increase myocardial oxygen consumption. Numerous studies have shown that performance during exercise testing is predictive of perioperative mortality in noncardiac surgery. ST-segment changes during exercise including horizontal depression greater than 2 mm, changes with low workload, and persistent changes after 5 minutes of exercise are seen in severe multivessel disease. Other findings include dysrhythmias at a low heart rate, an inability to raise the heart rate to 70% of predicted, and sustained decrease in systolic pressure during exercise.

Unfortunately, many patients are unable to achieve adequate workload in standard exercise testing because of osteoarthritis, low back pain, and pulmonary disease. In this case, pharmacologic testing is indicated with a dobutamine echocardiogram. Dobutamine is a β-agonist that increases myocardial oxygen demand and reveals impaired oxygen delivery in those with coronary disease. Echocardiography concurrently visualizes wall motion abnormalities due to ischemia. Transesophageal echocardiography may be preferable to transthoracic echocardiography in obese patients because of their body habitus and has been shown to have high negative predictive value in this group.[37] Nuclear perfusion imaging with vasodilators such as adenosine or dipyridamole can identify coronary artery disease and demand ischemia. Heterogeneous perfusion after vasodilator administration demonstrates an inadequate response to stress. Wall motion abnormalities indicate ischemia, and an ejection fraction lower than 50% increases the risk of perioperative mortality. Angiography should only be performed if the patient may be a candidate for revascularization.

Coronary Disease

Most perioperative MIs are caused by plaque rupture in lesions that do not

produce ischemia during preoperative testing.[38] This presents an obvious challenge for detecting patients at risk. Stress testing has a low positive predictive value in patients with no cardiac risk factors and has been associated with an unacceptably high rate of false-positive results.[39]

Preoperative optimization may include medical management, percutaneous coronary interventions (PCIs), or coronary artery bypass grafting (CABG).[40] The ACC/AHA guidelines[29] recommend revascularization for patients whose preoperative testing reveals severe disease that warrants intervention according to practice guidelines for coronary artery disease, independent of their perioperative status.

Patients warranting emergent CABG will be at greatest risk for that procedure. A recent study from the Veterans Administration hospitals recommends against revascularization in patients with stable cardiac symptoms.[41] Preoperative PCI does not decrease the risk of future MI or mortality in patients with stable coronary disease, and only targets stenotic lesions, rather than those most likely to rupture. One retrospective study found no reduction in morbidity or perioperative MI after percutaneous transluminal coronary angioplasty, and the authors proposed that surgery within 90 days of balloon angioplasty increased the risk of thrombosis.[42] However, PCI done more than 90 days before surgery did provide benefit when compared to those who had no intervention at all. Another retrospective study found that patients who have surgery within 2 weeks of stenting had a high incidence of perioperative MI, major bleeding, or death.[43] Although a retrospective review from the Coronary Artery Surgery Study registry showed a lower mortality rate in patients with coronary artery disease who were post-CABG than those without CABG (0.09% vs 2.4%), this benefit did not include the morbidity associated with CABG itself. Unfortunately, the benefit was overwhelmed by the 2.3% morbidity rate seen with CABG in this cohort.[44] Survival benefit of CABG over medical management is realized at 2 years or more after surgery,[45] so preoperative mortality may decrease overall short-term survival. Revascularization and bypass grafting should be restricted to patients who would benefit from the procedure independent of their need for noncardiac surgery. One of the disadvantages of PCI in the preoperative setting is the need for anticoagulation to prevent early stent occlusion. The use of platelet inhibitors to prevent stent occlusion must be included in the overall risk assessment, especially for surgery of the central

nervous system.

Catecholamine surges can cause tachycardia, which may alter the tensile strength of coronary plaques and incite plaque rupture.[46,47] Catecholamine surges can also increase blood pressure and contractility, contributing to platelet aggregation and thrombosis after plaque rupture and increasing the possibility of complete occlusion of the arterial lumen.[48] Perioperative β-blockade mitigates these effects and has been shown to reduce MI and mortality from MI by over 30% in vascular surgical patients with reversible ischemia.[46] Patients at highest risk still have a cardiac event rate of 10%, even with adequate perioperative β-blockade.[29]

In 1998, a landmark study[49] demonstrated a 55% reduction in mortality in noncardiac surgical patients with known coronary disease who were given atenolol perioperatively. This was followed by the DECREASE trial,[50] which showed a 10-fold reduction in perioperative MI and death compared to placebo. Thereafter, perioperative β-blockade was widely adopted as a quality measure. However, additional later investigations have shown that although perioperative β-blockers benefit patients with known ischemia, low-risk patients may in fact be harmed.[51] Tight rate control has been associated with increased risk of hypotension and bradycardia requiring intervention and stroke without any significant decrease in mortality.[52-55] Furthermore, critical analysis of the literature shows that studies have been inconsistent in the type of medication administered, the duration and timing of administration, and the target for heart rate control.[56] Consequently, results are difficult to interpret. Thus, prophylactic perioperative β-blockade should be restricted to patients with cardiac ischemia and has a limited role in patients with low or moderate risk of postoperative cardiac events.[29]

Congestive Heart Failure and Arrhythmia

CHF is associated with coronary disease, valvular disease, ventricular dysfunction, and all types of cardiomyopathy. These are all independent risk factors that should be identified prior to surgery. Even compensated heart failure may be aggravated by fluid shifts associated with anesthesia and abdominal surgery and deserves serious consideration. Perioperative mortality increases with higher New York Heart Association class and preoperative pulmonary congestion. CHF should be treated to lower filling

pressures and improve cardiac output before elective surgery. β-Blockers, angiotensin-converting enzyme inhibitors, and diuretics can be employed to this end. The patient should be stable for 1 week before surgery.[57]

Arrhythmias and conduction abnormalities elicited in the history, on exam, or on ECG should prompt investigation into metabolic derangements, drug toxicities, or coronary disease. In the presence of symptoms or hemodynamic changes, the underlying condition should be reversed and then medication given to treat the arrhythmia. Indications for antiarrhythmic medication and cardiac pacemakers are the same as in the nonoperative setting. Nonsustained ventricular tachycardia and premature ventricular contractions have not been associated with increased perioperative risk and do not require further intervention.[58,59]

Valvular Disease

Valvular disease should be considered in patients with symptoms of CHF, syncope, and a history of rheumatic heart disease. Aortic stenosis (AS) is a fixed obstruction to the left ventricular outflow tract, limiting cardiac reserve and an appropriate response to stress. History should elicit symptoms of dyspnea, angina, and syncope; examination may reveal a soft S_2, a late-peaking murmur, or a right-sided crescendo–decrescendo murmur radiating to the carotids. AS is usually caused by progressive calcification or congenital bicuspid valve. Critical stenosis exists when the valve area is less than 0.7 cm^2 or transvalvular gradients are greater than 50 mm Hg and is associated with an inability to increase cardiac output with demand. If uncorrected, AS is associated with a 13% risk of perioperative death. Valve replacement is indicated prior to elective surgery in patients with symptomatic stenosis.[29] Myocardial ischemia may occur in the absence of significant coronary artery occlusion in the presence of aortic valve disease. Perioperative management should include optimizing the heart rate to between 60 and 90 beats per minute and avoiding atrial fibrillation if possible. Because of the outflow obstruction, stroke volume may be fixed and bradycardia will lower cardiac output. Similarly, hypotension is also poorly tolerated.

Aortic regurgitation (AR) is associated with backward flow into the left ventricle during diastole and reduced forward stroke volume. Bradycardia

facilitates regurgitation by increased diastolic time. Chronic AR causes massive left ventricular dilatation (cor bovinum) and hypertrophy, which is associated with decreased left ventricular function at later stages. AR is most often caused by rheumatic disease or congenital bicuspid valve. Medical treatment includes rate control and afterload reduction. Without valve replacement, survival is approximately 5 years once patients become symptomatic. This is an obvious consideration when planning any other surgical procedures.

Tricuspid regurgitation is usually caused by pulmonary hypertension secondary to severe left-sided failure. Other causes include endocarditis, carcinoid syndrome, and primary pulmonary hypertension. Hypovolemia, hypoxia, and acidosis can increase right ventricular afterload and should be avoided in the perioperative period.

Mitral stenosis is an inflow obstruction that prevents adequate left ventricular filling. The transvalvular pressure gradient depends on atrial kick, heart rate, and diastolic filling time. Tachycardia decreases filling time and contributes to pulmonary congestion. Mitral regurgitation is also associated with pulmonary hypertension with congestion, as the pathologic valve prevents forward flow, causing left atrial dilatation and subsequent atrial arrhythmias. History and physical exam should focus on signs of CHF such as orthopnea, pedal edema, dyspnea, reduced exercise tolerance, and auscultatory findings such as murmurs and an S_3 gallop. Neurologic deficits may signify embolic sequelae of valve disease. Perioperative rate control is essential for maintaining adequate cardiac output. ECG findings will reflect related arrhythmias and medications but will not be specific for valve disease. Laboratory studies should identify secondary hepatic dysfunction or pulmonary compromise. Left ventricular hypertrophy is an adaptive response, which may cause subsequent pulmonary hypertension and diastolic dysfunction.

Prosthetics in the mitral position pose the greatest risk for thromboembolism, and the risk increases with valve area and low flow. Mechanical valves pose a higher risk than tissue valves in patients with a history of valve replacement. Diuretics and afterload-reducing agents will enhance forward flow and minimize cardiopulmonary congestion. Patients with mitral valve prolapse (MVP) should receive antibiotics.

Mitral regurgitation may also impair left ventricular function and lead to pulmonary hypertension. Stroke volume is reduced by backward flow into the

atrium during systole. The left ventricle dilates to handle increasing end-systolic volume, eventually causing concentric hypertrophy and decreased contractility. The end result may be decreased ejection fraction and CHF. A decrease in systemic vascular resistance and increase in atrial contribution to the ejection fraction can both improve forward flow and reduce the amount of regurgitation. Echocardiography can clarify the degree of valvular impairment. Medical treatment centers on afterload reduction with vasodilators and diuretics. MVP is present in up to 15% of women and is usually associated with a midsystolic click and late systolic murmur on physical exam. Murmur is indicative of prolapse. Although MVP is associated with connective tissue disorders, it usually occurs in otherwise healthy, asymptomatic patients. Echocardiography is used to confirm the diagnosis and evaluate the degree of prolapse. Chronically, MVP may be associated with mitral regurgitation, emboli, and increased risk of endocarditis. Prolapse may be aggravated by decreased preload, which should be minimized in the perioperative period. Patients with MVP are at risk of ventricular arrhythmias with sympathetic stimulation and endocarditis, which can be addressed with pain control and antibiotic prophylaxis, respectively.

Individuals with underlying structural cardiac defects are at increased risk for developing endocarditis after invasive procedures. Surgical procedures involving mucosal surfaces or infected tissues may cause transient bacteremia that is usually short-lived. Certain procedures are associated with a greater risk of endocarditis and warrant prophylaxis (Table 2-3). Abnormal valves, endocardium, or endothelium can harbor the bloodborne bacteria for a longer period of time, and infection and inflammation can ensue. Although there are no randomized trials regarding endocarditis prophylaxis, the AHA recommends prophylaxis for those[60] at high and moderate risk for developing the condition. The highest-risk patients have prosthetic heart valves, cyanotic congenital heart disease, or a history of endocarditis (even without structural abnormality).[61] Conditions associated with moderate risk include congenital septal defects, patent ductus arteriosus, coarctation of the aorta, and bicuspid aortic valve. Hypertrophic cardiomyopathy and acquired valvular disease also fall into this category. MVP is a prevalent and often situational condition. Normal valves may prolapse in the event of tachycardia or hypovolemia and may reflect normal growth patterns in young people. Prolapse without leak or regurgitation seen on Doppler studies is not associated with risk greater than that of the general population, and no antibiotic prophylaxis is necessary.[62,63]

However, the jet caused by the prolapsed valve increases the risk of bacterial adherence and subsequent endocarditis. Leaky valves detected by physical exam or Doppler warrant consideration for prophylactic antibiotics.[64] Patients with significant regurgitation are more likely to be older and men, and other studies have shown that older men are more likely to develop endocarditis.[64-66] Some advocate prophylaxis for men older than 45 years with MVP even in the absence of audible regurgitation.[66] Prolapse secondary to myxomatous valve degeneration also warrants prophylactic antibiotics.[67,68]

TABLE 2-3: AHA ENDOCARDITIS PROPHYLAXIS RECOMMENDATIONS

Antibiotic Coverage Recommended

Respiratory: tonsillectomy/adenoidectomy; bronchoscopy with biopsy; procedures involving respiratory mucosa

Gastrointestinal tract: any procedure in the setting of infected tissue in the gastrointestinal tract

Genitourinary tract: any procedure in the setting of established infection

Antibiotic Coverage Not Recommended

Respiratory: endotracheal intubation; bronchoscopy without biopsy; tympanostomy

Gastrointestinal tract: transesophageal echocardiography; endoscopy without biopsy

In uninfected tissue: urethral catheterization; uterine dilation and curettage; therapeutic abortion; manipulation of intrauterine devices

Other: cardiac catheterization; pacemaker placement; circumcision; incision or biopsy on prepped skin

For patients at risk, the goal should be administration of antibiotics in time to attain adequate serum levels during and after the procedure. For most operations, a single intravenous dose given 1 hour prior to incision will achieve this goal. Antibiotics should generally not be continued for more than 6 to 8 hours after the procedure to minimize the chance of bacterial resistance. In the case of oral, upper respiratory, and esophageal procedures, α-hemolytic *Streptococcus* is the most common cause of endocarditis, and

antibiotics should be targeted accordingly. Oral amoxicillin, parenteral ampicillin, and clindamycin for penicillin-allergic patients are suitable medications. Erythromycin is no longer recommended for penicillin-allergic patients because of gastrointestinal side effects and variable absorption.[69] Antibiotics given to those having genitourinary and nonesophageal gastrointestinal procedures should target enterococci.[69] While gram-negative bacteremia can occur, it rarely causes endocarditis. Parenteral ampicillin and gentamicin are recommended for highest-risk patients. Moderate-risk patients may receive amoxicillin or ampicillin. Vancomycin may be substituted in patients allergic to penicillin.

PERIOPERATIVE MANAGEMENT OF ANTITHROMBOTIC MEDICATION

Estimates suggest that 250,000 patients receiving chronic anticoagulation require surgery in the United States each year. Operative bleeding risk must be balanced against thromboembolic risk for the patient off of anticoagulation and requires careful judgment. Factors that influence the risk of thromboembolism include the condition requiring chronic anticoagulation, the duration of the procedure, time expected off of anticoagulation, and the duration of perioperative immobility. Thromboembolic risk increases with the amount of time that the patient's anticoagulation is subtherapeutic.

Primary indications for chronic anticoagulation include arterial embolism associated with mechanical valves and atrial fibrillation and venous thromboembolism (VTE). Arterial events precipitate stroke, and valvular and atrial clot and systemic emboli are higher risk for morbidity and mortality than venous events. Patients at highest risk for perioperative embolism include those with mechanical prosthetic mitral valves, aortic caged-ball and tilted valves, rheumatic heart disease, or history of stroke or transient ischemic attacks (TIAs) in the past 3 months. The risk of thromboembolism without anticoagulation is higher than 10% per year in these high-risk patients.

Patients at moderate risk of thromboembolism without anticoagulation (4%-10% per year) have atrial fibrillation, a bileaflet valve, or history of stroke or TIA. The $CHADS_2$ score (CHF, hypertension, age, diabetes, and stroke) further stratifies embolic risk for patients with atrial fibrillation based

on comorbidities. One point is assigned for hypertension, diabetes, CHF, and age >75 years; 2 points are assigned for history of stroke or TIA. Patients with a cumulative score of 5 to 6 are highest risk; those with a score of 3 to 4 are moderate risk; and those with a score of 0 to 2 without history of stroke or TIA are low risk.

Chronic anticoagulation is indicated for VTE. Patients with VTE within 3 months of surgery and severe thrombophilia are at highest risk for perioperative events and should receive bridging anticoagulation with therapeutic doses of low-molecular-weight heparin (LMWH) or intravenous unfractionated heparin (UFH). Patients at moderate risk include those with a thromboembolic event 3 to 12 months before surgery and less severe thrombophilias. They can receive therapeutic or subtherapeutic doses of anticoagulation depending on the risk of bleeding associated with the procedure. Patients with a remote event are at lowest risk and do not require bridging anticoagulation. It is generally recommended to stop warfarin 5 days prior to surgery if a normal international normalized ratio (INR) is desired. Vitamin K may be administered in the days leading up to the event if the INR is not correcting quickly enough.

LMWH should be held 24 hours before surgery, and intravenous UFH should be held 4 hours before surgery. Oral anticoagulants may be started 12 to 24 hours postoperatively because they take at least 48 hours to affect coagulation. The timing of resuming intravenous and subcutaneous anticoagulants should be determined on a case-by-case basis.

Low-risk patients receiving clopidogrel or aspirin should have it held 5 to 10 days before surgery. Patients with coronary stents are chronically treated with clopidogrel and aspirin to mitigate the risk of stent thrombosis. Interruptions in therapy are associated with high risk of thrombosis and infarct. Patients with bare metal stents placed within 6 weeks of surgery or drug-eluting stents placed within 12 months of surgery should continue clopidogrel and aspirin in the perioperative period.

The perioperative antithrombotic guidelines[70] from the American College of Chest Physicians are summarized in Table 2-4.

TABLE 2-4: GUIDELINES FOR PERIOPERATIVE MANAGEMENT OF ANTITHROMBOTIC MEDICATIONS

	Standard Anticoagulation	Antiplatelet Therapy	Should Warfarin or Antiplatelet Therapy Be Stopped Preoperatively?	Is Bridging Anticoagulation Indicated?	When Should Anticoagulant or Antithrombotic Be Restarted Postoperatively?
Low-risk atrial fibrillation	Warfarin goal INR 2.0	None	Yes, 5 days	No	When taking orals
Moderate-/high-risk atrial fibrillation	Warfarin goal INR 2.0	None	Yes, 5 days	No	When taking orals
Mechanical mitral valve	Warfarin goal INR 2.5-3.0	None	Yes, 5 days	Yes	Low bleeding risk: 24 hours High bleeding risk: 48-72 hours
Mechanical aortic valve	Warfarin goal INR 2.0	None	Yes, 5 days	Yes	Low bleeding risk: 24 hours High bleeding risk: 48-72 hours
Coronary stent	None	Clopidogrel Aspirin	Yes, 5-10 days No	No	Low bleeding risk: 24 hours High bleeding risk: 48-72 hours
Bare metal coronary stent within 6 weeks	None	Aspirin and clopidogrel	No	No	Low bleeding risk: 24 hours High bleeding risk: 48-72 hours
Drug-eluting stent within 12 months	None	Aspirin and clopidogrel	No	No	Low bleeding risk: 24 hours High bleeding risk: 48-72 hours
History of venous thromboembolism	Warfarin goal INR 2.0 for at least 3 months	No	Yes, 5-7 days	Low risk- no Moderate/ high risk- yes	

Low risk: venous thromboembolism (VTE) >12 months ago; $CHADS_2$ score 0-2 without prior stroke or transient ischemic attack (TIA).
Moderate risk: VTE in past 3-12 months, moderate thrombophilia, recurrent VTE, cancer; $CHADS_2$ score 3-4.
High risk: VTE in past 3 months, prior postoperative VTE, severe thrombophilia; $CHADS_2$ score 5-6, rheumatic heart disease, or stroke or TIA within 3 months.
Abbreviation: INR, international normalized ratio.
Data from Douketis JD, Spyropoulos AC, Spencer FA, et al: Perioperative management of antithrombotic therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines, *Chest* 2012 Feb;141(2 Suppl):e326S-e350S.

PULMONARY EVALUATION

Pulmonary complications are common after surgery and can prolong hospital stays for 1 to 2 weeks.[71] Complications include atelectasis, pneumonia, exacerbations of chronic pulmonary disorders, and respiratory failure requiring mechanical ventilation. Smoking, underlying chronic obstructive pulmonary disease (COPD), and poor exercise tolerance are the greatest risk factors for postoperative pulmonary complications. Physicians should ask about a history of smoking, decreased exercise capacity, dyspnea, and chronic cough. Examination should note pursed lip breathing, clubbing, and chest wall anatomy that could impair pulmonary function. Pulmonary testing is unnecessary in patients without a clear history of smoking or pulmonary disease. The predictive value of screening spirometry is unclear, and no threshold value has been identified to guide surgical decision-making. Forced expiratory volume in 1 second less than 50% of predicted is indicative of exertional dyspnea and may herald the need for further testing. Preoperative chest x-ray abnormalities are associated with postoperative pulmonary complications,[71] but to this point, there are no recommendations for screening radiographs in patients without pulmonary disease. Any

preoperative chest x-ray must be examined for signs of hyperinflation consistent with COPD. While compensated hypercapnia has not been shown to be an independent predictor for postoperative ventilatory insufficiency in patients undergoing lung resection, preoperative arterial blood gas analysis provides useful baseline information for perioperative management of patients with chronic carbon dioxide retention. Transverse and upper abdominal incisions are associated with a higher rate of postoperative pulmonary complications than longitudinal midline incisions and lower abdominal incisions.[72] Surgery longer than 3 hours is also associated with higher risk.[73] General anesthesia is also associated with a higher risk of pulmonary complications than spinal, epidural, or regional anesthesia.[74]

Physiologic changes can be seen in the postoperative period, especially after thoracic and upper abdominal procedures. Vital capacity may decrease by 50% to 60%, and is accompanied by an increased respiratory rate to maintain tidal volumes. Normally, functional residual capacity usually exceeds the closing capacity of the alveoli so they remain open throughout the respiratory cycle. Prolonged effects of anesthetics and narcotics reduce functional reserve capacity postoperatively, causing alveolar collapse. These changes can last for weeks to months. A distended abdomen can impair diaphragmatic excursion; painful incisions around the diaphragm and other respiratory muscles contribute to splinting and inadequate pulmonary toilet. Narcotics can inhibit sighing and coughing reflexes, which normally prevent alveolar collapse during periods of sleep and recumbency. Analgesics must be titrated carefully to permit deep breathing and avoid impairing respiratory effort.

Inspired nonhumidified oxygen and halogenated anesthetics are cytotoxic and interfere with surfactant production and mucociliary clearance. Depressed respiratory reflexes, diaphragm dysfunction, and decreased functional reserve capacity all contribute to alveolar collapse and pooling of secretions. Aspiration risk is also increased. Excess secretions cause further alveolar collapse and create a milieu ripe for bacterial infection and pneumonia. Intubated patients should receive antacid prophylaxis and gastric drainage to minimize the risk of aspiration.

Multiple analyses have found that poor exercise tolerance is the greatest predictor of postoperative pulmonary impairment. The ASA risk classification is a gauge of general status and is highly predictive of both

cardiac and pulmonary complications.[75,76] Although advanced age is associated with increased incidence of chronic pulmonary disease and underlying impairment, it is not an independent risk factor for pulmonary complications.

Clearly, all smokers should be urged to stop before surgery. Even in the absence of coexisting pulmonary disease, smoking increases the risk of perioperative complications. Smoking confers a relative risk of 1.4 to 4.3, but a reduced risk of pulmonary complications has been shown in patients who stop smoking at least 8 weeks before cardiac surgery.[77] Even 48 hours of abstinence can improve mucociliary clearance, decrease carboxyhemoglobin levels to those of nonsmokers, and reduce the cardiovascular effects of nicotine. A nicotine patch may help some patients with postoperative nicotine withdrawal but may not be advisable in patients at risk for poor wound healing.

COPD confers a relative risk of 2.7 to 4.7 in various studies. Symptoms of bronchospasm and obstruction should be addressed before surgery, and elective procedures should be deferred in patients having an acute exacerbation. Preoperative treatment may include bronchodilators, antibiotics, steroids, and physical therapy to increase exercise capacity. Patients with active pulmonary infections should have surgery delayed if possible. Asthmatics should have peak flow equivalent to their personal best or 80% of predicted and should be medically optimized to achieve this goal. Pulse corticosteroids may be used without an increased risk of postoperative infection or other complication.[78,79]

Malnourished patients may not be able to meet the demands of the increased work of breathing, increasing their risk for respiratory failure. Obese patients have higher rates of oxygen consumption and carbon dioxide production, which increases their work of breathing. They may also exhibit restrictive physiology due to a large, stiff chest wall. A complete history should inquire about sleeping difficulty and snoring. Obesity increases the amount of soft tissue in the oropharynx, which can cause upper airway obstruction during sleep. Fifty-five percent of morbidly obese patients may have sleep-related breathing disorders such as obstructive sleep apnea and obesity-hypoventilation syndrome.[80] Symptoms include snoring and daytime sleepiness, and formal sleep studies are employed for definitive diagnosis. Sleep-disordered breathing is associated with hypoxia, hypercapnia, changes

in blood pressure, nocturnal angina, and increased cardiac morbidity and mortality including stroke and sudden death.[81] Arterial blood gas with partial arterial oxygen pressure less than 55 mm Hg or partial arterial carbon dioxide pressure greater than 47 mm Hg confirms the diagnosis. An increased incidence of pulmonary hypertension and right-sided heart failure is seen in patients with obesity hypoventilation syndrome, and these patients should have an echocardiogram before surgery. In severe cases, intraoperative monitoring with a pulmonary artery catheter may be prudent.

In the patient who is awake, postoperative care should include coughing and deep breathing exercises, and in nonambulatory patients, early mobilization should include turning every 2 hours. Early ambulation prevents atelectasis and pooling of secretions and increases the ventilatory drive. Upright position distributes blood flow and minimizes shunting. Preoperative medications should be resumed expeditiously. Incentive spirometry and pulmonary toilet are pulmonary expansion maneuvers, which reduce the relative risk of pulmonary complications by 50%.[81] Patients should receive preoperative education about these techniques. Inhaled ipratropium and β-agonists, used together, may prevent postoperative wheezing and bronchospasm and should be prescribed in patients at risk. Intermittent positive-pressure ventilation and nasal bilevel positive airway pressure may be enlisted for secondary prevention. Epidural analgesia is superior to parenteral narcotics in abdominal and thoracic procedures for preventing pulmonary complications.

GASTROINTESTINAL EVALUATION

Stress ulceration has been a well-recognized complication of surgery and trauma since 1932, when Cushing reported gastric bleeding accompanying head injury. With later research in gastric physiology and shock, it has been recognized that the appearance of gastric erosion results from failure of the protective function of gastric mucosa and back diffusion of hydrogen ion, enabling gastric acid to injure the mucosa. Once the mucosa is injured, the defenses are further weakened, leading to further injury in a vicious cycle. The protective functions of the mucosa rely on the stomach’s rich blood flow to maintain high oxygen saturation. The most critical factor in the development of erosive ulceration now appears to be mucosal ischemia. Once

the rich blood supply of the mucosa is compromised, the protective mechanisms are impaired, and gastric acid causes erosion, bleeding, and perforation.

In the late 1970s,[82] the incidence of gastric bleeding in critically ill patients was 15%. Recognition of the importance of organ perfusion has resulted in decreased rates of erosive stress gastritis. Factors often cited for this observation are improvement in resuscitation and monitoring technology, nutritional support, and effective agents for medical prophylaxis. The prophylactic medicines are targeted to reduce gastric acid secretion. Antacids have been shown to provide effective protection against erosive ulceration; however, there is increased risk of aspiration pneumonia. Antagonists of the histamine-2 (H_2) receptors of the parietal cells impair gastric acid secretion and are effective prophylaxis for erosive ulceration.

With the emergence of proton pump inhibitor (PPI) medications, more effective control of gastric acid secretion was available, leading to widespread use of PPIs for stress ulcer prophylaxis. In high-risk, critically ill patients, PPIs have been shown to decrease the incidence of gastrointestinal bleeding as compared to H_2 blockers, but both carry increased risk of ventilator-associated pneumonia and pseudomembranous colitis.[83]

In the setting of elective operations when the patients are not critically ill, the incidence of stress ulceration is now very low, and routine use of ulcer prophylaxis medication has been questioned. In addition, the routine use of antisecretory medication, in particular in the elective setting, may lead to increased risk of pneumonia and pseudomembranous colitis.

Postoperative Ileus

Ileus is a condition of generalized bowel dysmotility that frequently impairs feeding in the postoperative setting. Ileus typically occurs after abdominal surgery, even if the bowel itself is not altered. It has been shown that laparotomy alone, without intestinal manipulation, leads to impaired gastrointestinal motility. The small bowel is typically affected the least and can maintain organized peristaltic contractions throughout the perioperative period. The stomach usually regains a normal pattern of emptying in 24 hours, and the colon is last to regain motility, usually in 48 to 72 hours.

The exact mechanism that causes postoperative ileus is not known;

however, physiologic studies have demonstrated the significant contribution of both inhibitory neural reflexes and local mediators within the intestinal wall. Inhibitory neural reflexes have been shown to be present within the neural plexuses of the intestinal wall itself and in the reflex arcs traveling back and forth from the intestine to the spinal cord. These neural pathways may account for the development of ileus during laparotomy without bowel manipulation. In addition, inflammatory mediators such as nitric oxide are present in manipulated bowel and in peritonitis and may play a role in development of ileus.

Ileus can be recognized from clinical signs, such as abdominal distension, nausea, and the absence of bowel sounds and flatus, which should prompt the diagnosis. Abdominal x-ray imaging typically shows dilated loops of small bowel and colon. Bowel obstruction must also be considered with these clinical findings, however, and CT or other contrast imaging may be required to rule out obstruction.

Ileus can also appear following nonabdominal surgery and can result from effects of medications (most often narcotics), electrolyte abnormalities (especially hypokalemia), and a wide variety of other factors.

Occasionally, the patient sustains a prolonged period of postoperative ileus. This can be due to a large number of contributing factors, such as intra-abdominal infection, hematoma, effects of narcotics and other medications, electrolyte abnormalities, and pain. In addition, there can be prolonged dysmotility from certain bowel operations, such as intestinal bypass.

The role of laparoscopic surgery in prevention of ileus is controversial. In theory, with less handling of the bowel laparoscopically and with smaller incisions, there should be less stimulation of the local mediators and neural reflexes. Animal studies comparing open and laparoscopic colon surgery indicate earlier resumption of normal motility studies and bowel movements with the laparoscopic approach. Human trials have not been conclusive. Several series demonstrate earlier tolerance of postoperative feeding with the laparoscopic approach to colon resection; however, these have been criticized for selection bias, and such studies are impossible to conduct in a blinded fashion.

Early mobilization has long been held to be useful in prevention of postoperative ileus. While standing and walking in the early postoperative period have been proven to have major benefits in pulmonary function and prevention of pneumonia, mobilization has no demonstrable effect on

postoperative ileus.

In the expected course of uncomplicated abdominal surgery, the stomach is frequently drained by a nasogastric tube for the first 24 hours after surgery, and the patient is not allowed oral intake until there is evidence that colonic motility has returned, usually best evidenced by the passage of flatus. Earlier feeding and no gastric drainage after bowel surgery can be attempted for healthy patients undergoing elective abdominal surgery and has a high rate of success provided clinical symptoms of ileus are not present. In such patients, the use of effective preventive strategies is highly effective. These include maintenance of normal serum electrolytes, use of epidural analgesia, and avoidance of complications such as infection and bleeding. The routine use of nasogastric tubes for drainage in the postoperative period after abdominal surgery has come into question since the mid-1990s.

The most effective strategy for management of postoperative ileus following abdominal surgery has been the development of epidural analgesia. Randomized trials have shown that the use of nonnarcotic (local anesthetic–based) epidural analgesia at the thoracic level in the postoperative period results in a decreased period of postoperative ileus in elective abdominal surgery. Ileus reduction is not seen in lumbar-level epidural analgesia, suggesting that inhibitory reflex arcs involving the thoracic spinal cord may play a major role in postoperative ileus.

Narcotic analgesia, while effective for postoperative pain, has been shown to lengthen the duration of postoperative ileus, especially when used as a continuous infusion or as PCA. Patients report better control of postoperative pain with continuous infusion or PCA as compared to intermittent parenteral dosing. Many studies have been done comparing various types of opioid analgesics, in attempts to find a type that does not prolong ileus. There has been no clearly superior drug identified; all currently available opioids cause ileus. Opioid antagonists such as naloxone have been used in trials to decrease ileus in chronic narcotic use, and there is evidence that antagonists are effective in that setting; however, in postoperative ileus, the antagonists have not been shown to be clinically useful, again suggesting that other mechanisms are contributing to postoperative ileus.

Early Postoperative Bowel Obstruction

Early postoperative bowel obstruction refers to mechanical bowel

obstruction, primarily involving the small bowel, which occurs in the first 30 days following abdominal surgery. The clinical picture may frequently be mistaken for ileus, and these conditions can overlap. The clinical presentation of early postoperative bowel obstruction is similar to that of bowel obstruction arising de novo: crampy abdominal pain, vomiting, abdominal distention, and obstipation. The incidence of early postoperative bowel obstruction has been variable in published series, due to difficulty in differentiating ileus from early postoperative bowel obstruction, but the reported range is from 0.7% to 9.5% of abdominal operations.

Retrospective large series show that about 90% of early postoperative bowel obstruction is caused by inflammatory adhesions. These occur as a result of injury to the surfaces of the bowel and peritoneum during surgical manipulation. The injury prompts the release of inflammatory mediators that lead to formation of fibrinous adhesions between the serosal and peritoneal surfaces. As the inflammatory mediators are cleared and the injury subsides, these adhesions eventually mature into fibrous, firm, bandlike structures. In the early postoperative period, the adhesions are in their inflammatory, fibrinous form and, as such, do not usually cause complete mechanical obstruction.

Internal hernia is the next most common cause of early postoperative bowel obstruction and can be diagnosed with a CT scan but may not be recognized until laparotomy. Internal hernia occurs when gaps or defects are left in the mesentery or omentum or blind gutters or sacs are left in place during abdominal surgery. The typical scenario is colon resection involving extensive resection of the mesentery for lymph node clearance. If the resulting gap in the mesentery is not securely closed, small bowel loops may go through the opening and not be able to slide back out. A blind gutter may be constructed inadvertently during the creation of a colostomy. When the colostomy is brought up to the anterior abdominal wall, there is a space between the colon and the lateral abdominal wall, which may also trap the mobile loops of small bowel. Defects in the closure of the fascia during open or laparoscopic surgery can cause obstruction from incarcerated early postoperative abdominal wall hernia. Fortunately, internal hernia is a rare occurrence in the early postoperative period; however, it must be suspected in cases in which bowel anastomoses or colostomies have been constructed. Unlike adhesive obstruction, internal hernia requires operative intervention due to the high potential for complete obstruction and strangulation of the

bowel.

Intussusception is a rare cause of early postoperative bowel obstruction in adults but occurs more frequently in children. Intussusception occurs when peristalsis carries a segment of the bowel (called the lead point) up inside the distal bowel like a rolled up stocking. The lead point is usually abnormal in some way and typically has some intraluminal mass, such as a tumor or the stump of an appendix after appendectomy. Other rare causes for early postoperative bowel obstruction include missed causes of primary obstruction at the index laparotomy, peritoneal carcinomatosis, obstructing hematoma, and ischemic stricture.

Management of early postoperative bowel obstruction depends on differentiation of adhesive bowel obstruction (the majority) from internal hernia and the other causes and from ileus. Clinicians generally rely on radiographic imaging to discern ileus from obstruction. For many years, plain x-ray of the abdomen was used: if the abdominal plain film showed air-distended loops of bowel and air-fluid levels on upright views, the diagnosis of obstruction was favored. However, plain radiographs can be misleading in the postoperative setting, and the overlap of ileus and obstruction can be confusing. Upper gastrointestinal contrast studies using a water-soluble agent have better accuracy, and abdominal CT using oral contrast has been shown to have 100% sensitivity and specificity in differentiating early postoperative bowel obstruction from postoperative ileus. However, unlike late adhesive bowel obstruction, contrast passage into the colon has not been shown to predict success for nonoperative management.

Once the diagnosis is made, management is tailored to the specific needs of the patient. Decompression via nasogastric tube is usually indicated, and ileus can be treated as discussed. Adhesive bowel obstruction warrants a period of expectant management and supportive care, as the majority of these problems will resolve spontaneously. Most surgical texts recommend that the waiting period can be extended to 14 days. If the early bowel obstruction lasts longer than 14 days, less than 10% resolve spontaneously, and exploratory laparotomy is indicated. The uncommon causes of early postoperative bowel obstruction, such as internal hernia, require more early surgical correction and should be suspected in the setting of complete obstipation, or when abdominal CT suggests internal hernia or complete bowel obstruction.

Renal Evaluation

Patients without a clinical history suggesting renal disease have a low incidence of significant electrolyte disturbances on routine preoperative screening.[84] However, patients with renal or cardiac disease who are taking digitalis or diuretics or those with ongoing fluid losses (ie, diarrhea, vomiting, fistula, and bleeding) do have an increased risk of significant abnormalities and should have electrolytes measured and replaced preoperatively.

Preoperative urinalysis can be a useful screen for renal disease. Proteinuria marks intrinsic renal disease or CHF. Urinary glucose and ketones are suggestive of diabetes and starvation in the ketotic state, respectively. In the absence of recent genitourinary instrumentation, microscopic hematuria suggests calculi, vascular disease, or infection. A few leukocytes may be normal in female patients, but an increased number signifies infection. Epithelial cells are present in poorly collected specimens.

Patients with renal insufficiency or end-stage renal disease often have comorbidities that increase their overall risk in the perioperative period. Hypertension and diabetes correlate with increased risk of coronary artery disease and postoperative MI, impaired wound healing, wound infection, platelet dysfunction, and bleeding. Preoperative history should note the etiology of renal impairment, preoperative weight as a marker of volume status, and timing of last dialysis and the amount of fluid removed routinely. Evaluation should include a cardiac risk assessment. Physical exam should focus on signs of volume overload such as jugular venous distention and pulmonary crackles. In patients with clinically evident renal insufficiency, a full electrolyte panel (calcium, phosphorus, magnesium, sodium, and potassium) should be checked preoperatively, along with blood urea nitrogen and creatinine levels. Progressive renal failure is associated with catabolism and anorexia. Such patients need aggressive nutritional support during the perioperative periods to minimize the risk of infection and poor healing.

Dialysis-dependent patients should have dialysis within 24 hours before surgery and may benefit from monitoring of intravascular volume status during surgery. Blood samples obtained immediately after dialysis, before equilibration occurs, should only be used in comparison to predialysis values to determine the efficacy of dialysis.[85]

Postoperatively, patients with chronic renal insufficiency or end-stage renal disease will need to have surgical volume losses replaced, but care should be taken to avoid excess. Replacement fluids should not contain potassium, and early dialysis should be employed to address volume overload and electrolyte derangements. Patients with impaired creatinine clearance should have their medications adjusted accordingly. For example, meperidine should be avoided because its metabolites accumulate in renal impairment and can lead to seizures.

The choice of postoperative fluid therapy depends on the patient's comorbidities, the type of surgery, and conditions that affect the patient's fluid balance. There is no evidence that colloid is better than crystalloid in the postoperative period, and it is considerably more expensive.[86] Sepsis and bowel obstruction will require ongoing volume replacement rather than maintenance. Ringer's solution provides 6 times the intravascular volume as an equivalent amount of hypotonic solution. In patients with normal renal function, clinical signs such as urine output, heart rate, and blood pressure should guide fluid management. Once the stress response subsides, fluid retention subsides and fluid is mobilized from the periphery, and fluid supplementation is unnecessary. This fluid mobilization is evident by decreased peripheral edema and increased urine output. Diuretics given in the period of fluid sequestration may cause intravascular volume depletion and symptomatic hypovolemia.

Postoperative management includes close monitoring of urine output and electrolytes, daily weight, elimination of nephrotoxic medications, and adjustment of all medications that are cleared by the kidney. Hyperkalemia, hyperphosphatemia, and metabolic acidosis may be seen and should be addressed accordingly. Indications for renal replacement therapy include severe intravascular overload, symptomatic hyperkalemia, metabolic acidosis, and complicated uremia (pericarditis and encephalopathy) (Table 2-5).

TABLE 2-5: OLIGURIA IN THE PERIOPERATIVE PATIENT

	Prerenal	Intrarenal	Postrenal
Causes	Bleeding	Drugs	Obstruction
	Hypovolemia	Contrast medium	
	Cardiac failure	Sepsis	
	Dehydration	Myoglobinuria	
UOsm	>500 mOsm/L	Equal to plasma	Variable
U_{Na}	<20 mOsm/L	>50 mOsm/L	>50 mOsm/L
Fe_{Na}	<1%	>3%	Indeterminate

Abbreviations: Fe_{Na}, fractional excretion of sodium; U_{Na}, urinary sodium concentration; UOsm, urinary osmolality.

Postoperative renal failure increases perioperative mortality. Risk factors for postoperative renal failure include intraoperative hypotension, advanced age, CHF, aortic cross-clamping, administration of nephrotoxic drugs or radiocontrast, and preoperative elevation in renal insufficiency. Up to 10% of patients may experience acute renal failure after aortic cross-clamping. Postoperative renal failure rates are higher in hypovolemic patients, so preoperative dehydration should be avoided. Contrast nephropathy is a common cause of hospital-acquired renal failure and manifests as a 25% increase in serum creatinine within 48 hours of contrast administration.

Nephropathy is caused by ischemia and direct toxicity to the renal tubules. Diabetes and chronic renal insufficiency are the greatest risk factors for dye nephropathy. Early trials[87] indicated that patients receiving contrast have a lower incidence of contrast-induced nephropathy when treated with a sodium bicarbonate infusion or *N*-acetylcysteine. However, recent evidence from multicenter trials and meta-analyses shows no benefit in any pharmacologic intervention in reducing the incidence of radiocontrast nephropathy.[88]

Rising blood urea nitrogen and creatinine and postoperative oliguria (<500 mL/d) herald the onset of postoperative renal failure. Management is determined by the cause of renal insufficiency. Acute renal failure is classified into 3 categories: prerenal, intrarenal, and postrenal. Prerenal azotemia is common in the postoperative period. It is caused by decreased renal perfusion seen with hypotension and intravascular volume contraction. Intrarenal causes of oliguric renal failure include acute tubular necrosis (from aortic cross-clamping, shock, or renal ischemia), and less commonly, acute interstitial nephritis from nephrotoxic medication. Postrenal causes include

obstruction in the collecting system (from bilateral ureteral injury, Foley catheter occlusion, or urethral obstruction). Workup should include urinalysis, serum chemistries, and measurement of the fractional excretion of sodium. Rarely, invasive monitoring and cardiac echocardiogram may be employed to evaluate volume status. Renal and bladder ultrasound is indicated if obstruction is suspected.

Initial management of oliguria in adults includes placement of a bladder catheter and a challenge with isotonic fluids (500 mL of normal saline or Ringer's lactate). If a bladder catheter is already present, it should be checked to ensure that it is draining properly. A urinalysis should be obtained with special attention to specific gravity, casts, and evidence of infection. Hematocrit should be evaluated to exclude bleeding and blood pressure measured to rule out hypotension as causes. The fractional excretion of sodium can help determine the etiology of the renal failure (Table 2-5). Serum creatinine is used to follow the course of acute renal failure. Patients who have been adequately resuscitated or who are in CHF require evaluation to rule out cardiogenic shock. Urinary retention can be treated with a Foley catheter, and ureteral obstruction can be addressed with percutaneous nephrostomy.

Intravascular volume depletion adversely affects cardiac output, tissue perfusion, and oxygen delivery. Monitoring includes total body weight, urine output, vital signs, and mental status. However, body weight should not be used alone because total volume overload can be seen in the setting of intravascular volume depletion. Most cases of postoperative renal failure are associated with an episode of hemodynamic instability,[47] and perioperative hemodynamic optimization has been shown to decrease acute kidney injury and mortality.[89] Invasive monitoring to measure cardiac filling pressures may be utilized when clinical assessment is unreliable.

Fluid overload may be seen in patients with renal, hepatic, and cardiac disease and is associated with increased morbidity.[90] Critically ill patients may develop anasarca. It is difficult to determine volume status by observation alone, and invasive monitoring may be required.

Electrolyte abnormalities are common in the perioperative period. Serum sodium reflects intravascular volume status. Hyponatremia signifies excess free water in the intravascular space and is caused by excess antidiuretic hormone in the postoperative period. It occurs in the setting of normo-, hypo-

, or hypervolemia. It may be avoided by judicious use of isotonic fluids. Conversely, hypernatremia suggests a relative deficit of intravascular free water. Patients who are unable to drink or those with large insensible losses are most at risk. Treatment includes free water replacement.

Diuretics, malnutrition, and gastrointestinal losses may cause postoperative hypokalemia. Metabolic alkalosis shifts potassium into the intracellular compartment. Serum potassium levels less than 3 mEq/L warrant ECG monitoring and replacement in patients who are not anuric. Replacement in patients with renal insufficiency may be complex. Hyperkalemia is more commonly seen in renal patients. It may also be seen in myonecrosis, hemolysis, and acidosis. Cardiac arrhythmias are seen at levels above 6.5 mEq/L, and death is associated with levels greater than 8 mEq/L. These patients should have cardiac monitoring until their levels normalize. ECG will show widened QRS interval, peaked T waves, and absent P waves. Hyperkalemia should be treated with sodium bicarbonate to stimulate acidosis, as well as intravenous calcium and insulin with glucose to drive potassium into the intracellular compartment. Cation exchange resins can be administered orally or per rectum to bind ions in the gastrointestinal tract, but care should be taken for the patient who is post–gastrointestinal surgery or has underlying gastrointestinal problems. Dialysis can by employed if other measures fail.

GLYCEMIC CONTROL

Hyperglycemia is a risk factor for postoperative infection and perioperative mortality. Intensive insulin therapy (IIT) has been associated with improved outcomes for intensive care unit (ICU) patients, and after cardiac surgery, in brain injury, and after acute MI. However, early enthusiasm for IIT has waned as more recent studies have shown that it is not as beneficial in medical patients as it is in surgical patients and has been associated with severe hypoglycemia.[91] More recently, a meta-analysis of 29 randomized trials of IIT in adult ICU patients showed no difference in mortality in patients receiving IIT versus conventional insulin therapy with goal blood sugar <200 mg/dL.[92] Although there does appear to be consensus that controlling glucose is a worthwhile therapeutic goal in surgical patients in particular, appropriate targets for control remain controversial. While

hyperglycemia is associated with increased infection and mortality,[93] IIT is associated with hypoglycemia and increased mortality. Results from an international, randomized controlled trial in ICU patients demonstrated a 2.6% increase in absolute risk of death in ICU patients with a blood glucose target of 81 to 108 mg/dL versus 180 mg/dL.[94] Others suggest that the variability in glucose level may affect morbidity and mortality more than blood glucose levels alone.[95] More investigation is needed to determine the optimal way to manage blood glucose levels in the postoperative patient.

Our current recommendation for glucose control in noncardiac surgery patients is to maintain blood glucose less than 180 mg/dL.

HEMATOLOGIC EVALUATION

A complete preoperative evaluation should include assessment of hematologic disorders, which can increase the risk for postoperative bleeding or thromboembolism. Patients should be asked about a family history of bleeding disorders and personal history of bleeding problems, especially after procedures. Excessive bleeding after dental procedures and menorrhagia in women can alert the physician to undiagnosed hematologic disease. Risk factors for postoperative hemorrhage include known coagulopathy, trauma, hemorrhage, or potential factor deficiency.[96] Factor deficiencies can be seen with a history of liver disease, malabsorption, malnutrition, or chronic antibiotic use. Even high-risk patients have only a 1.7% risk of postoperative hemorrhage and a 0.21% risk of death related to postoperative hemorrhage.[96,97]

Routine tests may include a complete blood count, prothrombin time (PT), activated partial thromboplastin time (PTT), and INR, but are not required in the asymptomatic patient with no associated history. The complete blood count will reveal leukocytosis, anemia, and thrombocytopenia or thrombocytosis. A baseline hematocrit is useful for postoperative management when anemia is suspected. Platelet count also provides a useful baseline but does not provide information about platelet function. A bleeding time may be required to provide more information in select patients. However, bleeding time results are operator-dependent and highly variable, making it a poor screening tool for identifying high-risk patients.[98,99] An abnormal bleeding time is not associated with increased postoperative

bleeding,[100] nor has it proven useful in identifying patients taking NSAIDs or aspirin.[98] None of the aforementioned tests can be used to diagnose hereditary bleeding disorders. However, an elevated PTT may be seen in factor XI deficiency and should be obtained in patients at risk for this deficiency. Low-risk patients are very unlikely to have bleeding complications even if the PTT is abnormal[99] and have an increased risk of false-positive results that can lead to unnecessary testing. PTT is not a reliable predictor of postoperative bleeding[101] and should not be used to screen for bleeding abnormalities in patients without symptoms or risk factors.[102,103]

A platelet count of 20,000 or greater is usually adequate for normal clotting. Aspirin causes irreversible impairment of platelet aggregation and is commonly prescribed in patients at risk of cardiovascular and cerebrovascular disease. The clinical effect of aspirin lasts 10 days, and it is for this reason that patients are asked to stop taking aspirin 1 week before elective surgery. Desmopressin can be used to partially reverse platelet dysfunction caused by aspirin and uremia. Other NSAIDs cause reversible platelet dysfunction and should also be held before surgery. Glycoprotein IIb/IIIa inhibitors prevent platelet-fibrin binding and platelet aggregation and are used for 2 to 4 weeks after coronary angioplasty. Elective surgery should be avoided during these 2 to 4 weeks, as stopping treatment increases the risk of thrombosis. Patients who do not receive 4 weeks of antiplatelet therapy are at risk of stent thrombosis.[104]

Indications for red blood cell transfusion remain somewhat controversial and are often empirical in practice. Transfusing 1 unit of red blood cells or whole blood can increase the hematocrit by approximately 3% or hemoglobin by 1 g/dL. Multiple studies have demonstrated that overusing transfusion may adversely affect patient outcome and increase risk of infection. ASA guidelines[105] suggest that transfusion should be based on risks of inadequate oxygenation, rather than a threshold hemoglobin level. Generally, transfusion is rarely indicated when the hemoglobin level exceeds 10 g/dL but is almost always indicated when it is less than 6 g/dL, especially in the setting of acute anemia. Healthy individuals can usually tolerate up to 40% of blood loss without requiring blood cell transfusion, and blood products should not be used solely to expand volume or to improve wound healing. The decision to transfuse red cells or whole blood should be based on the patient's risk of

complications associated with impaired oxygen delivery, including hemodynamic indices, history of cardiopulmonary disease, rate of blood loss, and preexisting anemia.

Conditions associated with abnormal platelets and low platelet counts can be treated with platelet transfusions. The usual dose, 1 unit of platelet concentrate/10 kg body weight, can be expected to increase the platelet count by approximately 5000 to 10,000 in an average adult. In patients without increased risk of bleeding, prophylactic platelet administration is not indicated until counts fall below 20,000. Higher thresholds may be indicated for patients at increased risk of bleeding or with known platelet dysfunction or microvascular bleeding. Desmopressin can augment platelet function in uremia and incite release of von Willebrand factor (vWF) from the endothelium, which can improve platelet function. The decision to transfuse platelets should be based on the amount of bleeding expected, the ability to control bleeding, and the presence of platelet dysfunction or destruction.

Transfusion of fresh frozen plasma (FFP) is indicated to reverse warfarin before procedures or in the presence of active bleeding, for inherited or acquired coagulopathy that can be treated with FFP, and for massive transfusion of more than 1 whole blood volume. Microvascular bleeding can be seen if the PT/PTT is greater than 1.5 times normal, and FFP can be used to reverse bleeding in this setting. Warfarin reversal can be achieved with doses of 5 to 8 mL/kg, and 30% factor concentration can be achieved with 10 to 15 mL/kg. FFP should not be used to address volume depletion alone. Cryoprecipitate contains factors VIII, vWF, XIII, fibrinogen, and fibronectin, and can be used preventively in patients with these factor deficiencies and uremia.

Endothelial injury and venous stasis are the greatest risk factors for VTE. The patient with hereditary thrombophilia or a personal history of VTE, cancer, or recent surgery (within 4 weeks) has an increased risk of VTE.[106] Preventive measures include external pneumatic leg compression, early mobilization after surgery, and anticoagulation. Compression devices are contraindicated in patients with severe peripheral vascular disease, venous stasis, or risk of tissue necrosis. Inferior vena cava (IVC) filters are indicated in patients who cannot take anticoagulation or who have failed anticoagulation therapy. Patients with a history of VTE benefit from IVC filter placement in the short term, but IVC filter placement is accompanied by an increased incidence of deep venous thrombosis over the long term.[107]

Systemic anticoagulation is the preferred long-term option. LMWH and UFH are equally effective for prevention of pulmonary embolism in patients with deep venous thrombosis.[107] Recent VTE, atrial fibrillation, and mechanical heart valves are common indications for warfarin treatment.

Clinically, UFH activity is measured by PTT, and the therapeutic goal is usually 2.0 to 2.5 times normal. LMWH is a relatively stronger inhibitor of factor Xa and does not have the same effect on the PTT. The anticoagulant effect of LMWH is measured by factor Xa activity. Protamine can reverse the effects of heparin but may cause allergic reactions and induce hypercoagulability and should be used cautiously. FFP will not reverse heparin and can actually increase heparin activity because it contains antithrombin III. Direct thrombin inhibitors can also prolong the PTT. Direct thrombin inhibitors are not reversible with protamine and may require large amounts of FFP for reversal.

Heparin can be used for the prevention and treatment of VTE. Surgical patients over age 40 or those at increased risk for VTE should receive 5000 U subcutaneously every 8 to 12 hours, depending on their weight. High-risk patients with a history of VTE, cancer, or morbid obesity or those having orthopedic procedures should either receive subcutaneous heparin with a goal of high range of normal or LMWH. In the event of acute VTE, intravenous heparin should be started promptly with a therapeutic PTT goal of 1.5 to 2.0 times normal. Oral anticoagulation should be started within 24 hours and continued for 3 to 6 months.[106]

Heparin-induced thrombocytopenia (HIT) is a potentially lethal complication of heparin therapy. HIT is caused by an immunoglobulin G–mediated hypersensitivity reaction between the heparin moiety and platelet factor 4 (PF4). Patients with previous heparin exposure, such as orthopedic and cardiac surgical patients, are at greatest risk. The incidence of HIT is 0.5% to 5.0% in patients receiving UFH. HIT occurs with UFH or LMWH; the risk is highest with UFH.

Platelet counts usually drop 40% to 50% from baseline. Thrombosis can be venous or arterial, leading to deep vein thrombosis, extremity ischemia, and mesenteric ischemia of stroke. Digital ischemia and skin necrosis can also be seen. HIT remains a clinical syndrome that can be diagnosed by a decrease in platelet count <40% of baseline in 4 to 14 days of heparin administration once other causes of thrombocytopenia have been ruled out. The diagnosis can be supported by the enzyme-linked immunosorbent assay

for antiplatelet antibodies.

Because HIT can be life-threatening, heparin should be stopped as soon as HIT is suspected, and treatment with an alternative anticoagulant, such as the thrombin inhibitor bivalirudin, should be started immediately. Platelets should return to baseline after therapy is initiated. If thrombosis is present, patients should be anticoagulated for 6 months with warfarin. Warfarin should not be started until platelet counts have recovered.

Warfarin inhibits synthesis of vitamin K–dependent clotting factors (II, VII, IX, X, and proteins C and S). Poor diet, prolonged antibiotic use, and fat malabsorption can also cause vitamin K deficiency and cause abnormal coagulation. Liver disease can lead to multiple coagulation abnormalities including factor deficiencies, vitamin K deficiency, fibrinolysis, and elevated levels of fibrin degradation products. All patients with known or suspected liver disease should be tested for coagulopathy. Vitamin K can be administered subcutaneously or intravenously in deficient patients. The initiation of warfarin therapy is associated with a transient thrombotic state because plasma concentrations of protein C fall approximately 24 hours before concentrations of other clotting factors.

Heparin is the drug of choice for VTE during pregnancy because it does not cross the placenta. Adverse effects of heparin therapy may include hemorrhage, thrombocytopenia, and osteoporosis. HIT is an immune disorder seen in patients with prior exposure to heparin, which may cause thrombosis. Treatment includes cessation of heparin and utilization of alternative anticoagulants such as lepirudin, danaparoid, or argatroban. These should be given until platelet counts recover.

For patients on long-term anticoagulation therapy, the INR should be 1.5 or lower before elective surgery. After warfarin is discontinued, it takes about 4 days for an INR in the range of 2.0 to 3.0 to spontaneously reach 1.5, and about 3 days for the INR to reach 2.0 after it is restarted. If therapy is withheld preoperatively, most patients will have a window of 2 to 4 days when they are not anticoagulated and at risk for venous thrombosis. This risk is compounded by the increased risk of thromboembolism associated with surgery.[108,109] It has been estimated that surgery increases the risk of VTE by 100-fold in patients with recurrent disease.[110] Without anticoagulation, there is a 50% chance of recurrence within the 3 months after the first episode of venous thrombosis. Warfarin therapy reduces the risk to 10% after 1 month and 5% after 3 months. It is not advisable to interrupt anticoagulation within

1 month after an event of VTE, and if possible, surgery should be deferred until the patient has completed 3 months of therapy.[110] Chronic anticoagulation lowers the risk of thromboembolism in patients with atrial fibrillation and mechanical heart valves by 66% and 75%, respectively.[110]

Patients with prior embolic episodes are at increased risk for recurrence. Six percent of episodes of VTE and 20% of arterial thromboembolisms may be fatal,[110] and a significant percentage cause disability. Alternatively, the risk of death after postoperative hemorrhage is less than 1%,[111] so the judicious use of postoperative anticoagulation can be relatively protective. Preoperative heparinization is not required during the second and third months of warfarin treatment for deep vein thrombosis because the risk is sufficiently low. Such patients have increased VTE risk after surgery and should receive postoperative anticoagulation. Patients who are at risk for recurrent deep vein thrombosis and are within 2 weeks of the first episode or who cannot tolerate anticoagulation are candidates for an IVC filter.[107]

Elective surgery should be deferred for the first month after arterial embolism because of the high risk of recurrence during this period. If necessary, patients should receive perioperative heparin while oral anticoagulation is held. Patients on long-term anticoagulation to prevent arterial thromboembolism do not need perioperative heparin because the risk of bleeding outweighs the risk of arterial embolism during this period.

Heparin should be titrated to a goal PTT of 1.5 to 2.0 times normal and given as a continuous intravenous infusion. It should be stopped 6 hours prior to a procedure and can be restarted 12 hours after surgery if there was no evidence of bleeding at the end of the case. Heparin can be restarted without a bolus at the anticipated maintenance infusion rate.[110,111]

INFECTIOUS COMPLICATIONS

Infectious complications can be most unwelcome and difficult to control after major abdominal surgery, yet they are surprisingly frequent despite all modern prophylactic measures. Reported surgical wound infection rates in elective operations vary from 2% for inguinal hernia repair,[112] to 26% for colectomy,[113] and is even higher for emergency surgery.[114] Surgical site infections (SSIs) increase overall mortality and morbidity and increase hospital length of stay and overall costs. Therefore, prevention and treatment

of infectious complications should be included in surgical decision-making for all abdominal procedures.

Prevention of SSIs begins with preoperative evaluation and identification of patients at high risk for SSI. Patient factors implicated in risk of SSI include age, diabetes mellitus, smoking, steroid use, malnutrition, obesity, active distant infection, prolonged hospital stay, and nasal colonization with *Staphylococcus aureus*.[115-118]

Standard basic surgical rules should be followed with every patient. These were codified as formal guidelines by the Centers for Disease Control and Prevention (CDC) and updated in 2017[119] and include recommendations for skin preparation with alcohol-based skin antiseptics, surgical barriers such as drapes and gowns, careful hand scrubbing, and appropriate selection of prophylactic antibiotics. Preoperative hair removal and antiseptic shower have not been shown to decrease SSI rates, and shaving and clipping of hair can increase SSIs. The CDC recommendations are summarized in Table 2-6.

TABLE 2-6: CDC CATEGORY 1 RECOMMENDATIONS FOR REDUCTION OF SURGICAL SITE INFECTIONS

These are strongly recommended based on best clinical evidence:

Identify and treat distant infections prior to surgery

Do not remove hair routinely; if hair must be removed, use electric clippers immediately prior to surgery

Control hyperglycemia in the perioperative period

Cease tobacco smoking 30 days prior to surgery

Antiseptic shower the night prior to surgery

Antiseptic skin preparation

Surgery team should practice hand scrubs

Administer appropriate antimicrobial prophylaxis

Surgical barriers (gown, gloves, hat, mask)

Do not close contaminated skin incisions

Antibiotic prophylaxis may be indicated for patients at high risk or in contaminated surgical procedures, but antibiotics should not be used indiscriminately. Overuse of antibiotics is associated with emergence of

multidrug-resistant bacteria and increased rates of hospital-acquired infections. Selection of patients for antimicrobial prophylaxis requires stratification of patient risk factors, as discussed above, and procedure-specific risk factors. The degree of contamination in the surgical site has long been recognized as an independent risk factor for SSI,[120] leading to the wound classification system (Table 2-7) in use since 1983.

TABLE 2-7: SURGICAL WOUND CLASSIFICATION

Class I. Clean
Uninfected wounds without contamination

Class II. Clean/Contaminated
Uninfected wounds in procedures where the respiratory, gastrointestinal, or genitourinary tracts are entered in a controlled fashion without gross spillage

Class III. Contaminated
An operation with major breaks in sterile technique, gross spillage, or incisions into inflamed but not suppurating infections; fresh accidental wounds

Class IV. Dirty/Infected
Wounds with necrotic or devitalized infected tissue

Patients undergoing class I (clean) procedures have a very low infection rate and generally do not benefit from prophylactic antibiotics, unless there is some suspicion at the start of the procedure that some contamination may occur, such as unplanned enterotomy in a patient with many previous abdominal procedures. In addition, many surgeons prefer to use antibiotic prophylaxis in class I procedures when a prosthesis is implanted; examples include hernia repair and vascular bypass. In this setting, the risk of SSI is low, but the morbidity and mortality of an infected prosthesis are great, and prophylaxis may decrease the risk. To date, large prospective trials have not shown benefit of antibiotic prophylaxis in preventing prosthetic infections,[121,122] but smaller trials have suggested a decrease in site infection without change in implant infection rate.[123,124] Therefore, there is no strict

guideline for the use of systemic antibiotics for implant surgery, and the surgeon must tailor the use of antibiotics to the individual patient's risk.

Patients with class II (clean/contaminated) surgical wounds do benefit from systemic antibiotic prophylaxis. The most studied example of this class of wound is elective colon resection. Most current guidelines recommend systemic broad-spectrum antibiotic coverage using a second-generation cephalosporin plus metronidazole, if the parenteral route is used, and neomycin plus metronidazole or erythromycin base (both as nonabsorbable antibiotics), if the oral route is used.[125] Published evidence supports administration of antibiotics preoperatively in order to achieve maximum therapeutic levels at the time of incision and continuation of the antibiotic dosing schedule to maintain therapeutic levels during a long procedure. There is no documented study showing benefit to additional doses of antibiotics after the procedure is over and the skin is closed, and prolonged use of prophylactic antibiotics contributes to emergence of resistant bacteria.[126,127]

Patients with class III (contaminated) wounds are a mixed population. Some of these wounds are the result of inadvertent entry into a contaminated field, some result from traumatic injury, and some are planned operations for débridement of infected tissue. In the latter case, antibiotic therapy is indicated for specific therapy rather than prophylaxis. In the case of penetrating traumatic injury to the colon, there is strong evidence to support single-dose antibiotic prophylaxis at the time of laparotomy, similar to elective colon resection.[128,129] Surgical judgment must be individualized in these cases as to whether the risk of skin closure can be justified due to the high rate of wound infection despite antibiotic prophylaxis.

Patients with class IV (dirty) wounds are generally undergoing débridement of already infected and necrotic tissue and should be receiving antibiotic therapy targeted to the relevant organisms. Skin wound closure is generally not advised in these patients.

The wound classification system does not take into account patient risk factors or site-specific risk factors. Various physiologic scoring systems including the Acute Physiology Score and the Acute Physiology, Age, and Chronic Health Evaluation index have been used to predict perioperative infection risk with some success. In an effort to provide more accurate risk stratification, the CDC's National Nosocomial Infection Surveillance project has developed a risk index that accounts for patient risk factors, such as

malnutrition and chronic medical conditions, and operative factors, including duration and site of procedure.[130] Enlightened risk assessment of perioperative infections should be included in the discussion for informed surgical consent.

NUTRITIONAL EVALUATION

The importance of proper nutritional assessment and management cannot be overstressed. In surgical patients, malnutrition increases risk for major morbidity,[131,132] including wound infection, sepsis, pneumonia, delayed wound healing, and anastomotic complications. Careful preoperative clinical assessment can identify patients at increased nutritional risk. The assessment should include a thorough history and physical exam with attention paid to usual weight, recent weight loss, changes in eating and bowel habits, changes in abdominal girth, loss of muscle bulk, and the presence of diseases that carry a risk of malnutrition such as COPD, diabetes mellitus, inflammatory bowel disease, and psychiatric conditions such as bulimia and anorexia nervosa. The history and physical exam should identify patients with nutritional risk; that risk can be stratified by calculation of the Nutritional Risk Index (NRI). The NRI is a simple calculation (15.19 × serum albumin [g/dL] + 41.7 × present weight/usual weight) that has been shown in prospective studies to correlate with increased rates of mortality and complications from major abdominal surgery.[133,134] NRI less than 83 indicates a significantly increased rate of mortality and complications, especially wound dehiscence and infection. Severely malnourished patients have been shown to benefit from preoperative nutritional support.[135,136]

Malnutrition can be classified into protein deficiency (kwashiorkor), calorie deficiency (marasmus), or mixed protein-calorie deficiency. To complete the nutritional assessment and to guide nutritional support, it is useful to classify the patient's specific nutritional state (Table 2-8). Malnutrition states are much more common than is generally acknowledged, with 30% to 55% of hospital inpatients meeting criteria for one of these diagnoses.[137]

TABLE 2-8: ASSESSMENT OF NUTRITIONAL STATUS

Protein Deficiency Criteria

Albumin <2.2 g/dL
Total lymphocyte count 800/μL or less
Weight maintained
Peripheral edema
Inadequate protein intake (<50% of goal for 3 days or <75% for 7 days)
Four criteria out of these five establish the diagnosis of protein deficiency

Calorie Deficiency Criteria

Weight loss: 5% over 1 month or 7.5% over 3 months or 10% over 6 months
Underweight: <94% ideal body weight
Clinically measurable muscle wasting
Serum protein maintained
Inadequate calorie intake (50% for 3 days or <75% for 7 days)
Three criteria out of these five establish diagnosis of calorie deficiency

Mixed Protein-Calorie Malnutrition Criteria

	Mild	Moderate	Severe
Weight loss	5%-9%	10%-15%	10%-15% over 6 months
Underweight	94%-85%	84%-70%	<70% ideal weight
Albumin	2.8-3.4 g/dL	2.1-2.7 g/dL	<2.1 g/dL
Total lymphocytes	1499-1200/μL	1199-800/μL	<800/μL
Transferrin	199-150 mg/dL	149-100 mg/dL	<100 mg/dL
			Muscle wasting
			Deficient intake (at least 3 days)

To establish the diagnoses of mild or moderate protein-calorie malnutrition, 2 of the 5 criteria shown must be met; to establish the diagnosis of severe protein-calorie malnutrition, 3 of the 7 criteria must be met.

Some interval of deficient nutritional intake is expected after an abdominal operation. In uncomplicated cases, this is usually the result of postoperative adynamic ileus and resolves promptly, in less than 7 days. Traditional surgical management includes provision of dextrose-containing intravenous fluids. The goal of this therapy is not to provide sufficient calories for complete nutritional support, but simply to provide enough carbohydrate to prevent breakdown of lean body mass. Certain organs, including the heart and brain, have an obligate requirement for carbohydrate as a primary energy source and do not store energy in the form of fat or glycogen. If intake is insufficient to meet this requirement, the body breaks down hepatic glycogen to provide glucose to the circulation, and ultimately the brain and heart. Once hepatic glycogen stores have been depleted (after about 1 day of no intake), lean muscle mass is converted to glucose via gluconeogenesis to produce carbohydrate. Provision of only 100 g of exogenous glucose per day is sufficient to prevent breakdown of lean muscle mass in otherwise healthy subjects.

In already malnourished patients or in patients who do not return to normal bowel function promptly, nutritional support is indicated. As in the preoperative setting, a thorough evaluation of the patient's nutritional status is necessary, as is the identification of the cause of bowel dysfunction. In the

postoperative setting, there are many potential causes of bowel dysfunction (Table 2-9), and nutritional support should be individualized for each patient's needs. Some patients may respond to enteral support, and some may require parenteral support. Whenever available, the enteral route is the preferred route of support, as it has been shown to cause less morbidity and mortality.[138]

TABLE 2-9: POSTOPERATIVE CAUSES OF DEFICIENT NUTRITIONAL INTAKE

Ileus
Bowel obstruction
Colitis (ischemic, infectious)
Fistula
Dysphagia
Gastric dysmotility
Intestinal insufficiency (short-gut syndrome)

Enteral nutritional support is effective in patients who have functional small bowel; examples include esophageal or gastric resection, patients with postoperative delirium or dysphagia, and patients who have gastroparesis. In the short term, if the dysfunction is expected to respond to treatment, nasogastric tubes can be used effectively to deliver full support. Patients who need long-term enteral support are best served with gastrostomy or jejunostomy tubes, which may be placed operatively or percutaneously. With good preoperative nutritional assessment and sound surgical judgment, these patients' needs for long-term postoperative support can often be anticipated, and long-term feeding access can be included in the operative plan. Enteral support may not be suitable for some patients; examples include early postoperative bowel obstruction, fistula, or intestinal insufficiency (short-gut syndrome). In such patients, parenteral support is indicated and should be initiated without delay, and futile attempts to use the enteral route should be avoided.

Irrespective of the route of support, every patient on nutritional support should have his or her nutritional needs assessed and provided. The

assessment begins with the calorie requirement. There are several formulas and nomograms that estimate basal energy expenditure, accounting for height, weight, age, sex, stress factors, and activity factors.[139] All of these methods are estimations and may underfeed or overfeed certain subgroups, especially the obese. The method in most common clinical use bases basal energy expenditure on adjusted body weight (ABW). Using this method, ABW is defined as the patient's ideal body weight plus the difference between actual body weight (BW) and the ideal body weight (IBW) divided by 2:

$$ABW = IBW + 0.5(BW - IBW)$$

The baseline caloric requirement for weight maintenance based on ABW is 25 kcal/kg/d. This target may be adjusted upward in patients with extreme metabolic demands, as is the case in burns or head injury.[126] Furthermore, the ABW can be used to establish the protein requirement. In unstressed normal subjects, the minimum daily protein requirement is 0.8 g protein/kg/d. In postoperative patients with healing wounds, this target is adjusted to 1.0-1.5 g/kg/d, and in severely ill patients to 2.0 g/kg/d. The highest requirements are seen in severe burn and bone marrow transplant patients.

Essential nutritional components must be provided, again irrespective of the route of support. These include water- and lipid-soluble vitamins, trace elements such as zinc and selenium, essential fatty acids such as linoleic and linolenic acids, and the 8 essential amino acids. These trace elements are provided in abundance in all enteral feeds and are part of the standard additives in parenteral formula.

Once nutritional support has been initiated, the patient's response to support must be followed closely, especially in parenteral support and in patients with preexisting metabolic conditions such as diabetes. Blood glucose should be monitored regularly during the first few days of support. Recent evidence has linked hyperglycemia in the postoperative setting, especially in critically ill patients, with increased risk of death and infection.[140,141] In addition, electrolyte abnormalities (especially those of potassium, magnesium, and phosphate) are often seen in the early period of nutritional support and should be corrected.

It is also important to follow the markers of nutrition repletion to ensure that the calories and protein provided (based on the initial estimate) are

sufficient and the patient is not mobilizing lean body mass due to inadequate support. Serum markers such as prealbumin, retinol-binding protein, and transferrin can be useful in this regard. They are serum proteins with short (2-7 days) turnover times that reflect the body's ability to synthesize new protein.[139] Unfortunately, the serum concentrations of these proteins are also affected by acute disease states and renal and hepatic failure and can be difficult to interpret in postoperative patients. Nitrogen balance can also be used to monitor nutritional support and reflects the ability to synthesize new protein. Nitrogen balance is calculated by subtracting nitrogen excretion from nitrogen intake. Nitrogen intake is calculated from the protein intake, where each gram of protein/6.25 = the number of grams of nitrogen. Nitrogen excretion has 2 components: urinary urea nitrogen (UUN) and insensible loss. UUN can be measured in a 24-hour urine collection; insensible loss is generally accepted to be 4 g/d, unless there is another source of loss, such as abdominal drainage of proteinaceous ascites, enterocutaneous fistula, or nephrotic syndrome. Thus, in most cases, nitrogen balance can be simplified to:

Nitrogen balance = protein intake/6.25 – 24-hour UUN – 4 g (insensible loss)

A patient who takes in more nitrogen than he or she excretes in the urine and feces is in positive nitrogen balance and is synthesizing new protein. On the other hand, a patient who is excreting more nitrogen than he or she is receiving in nutritional support is in negative nitrogen balance and is therefore losing lean body mass, becoming more malnourished. These patients should be reevaluated for nutritional needs and for sources of nutritional depletion, such as uncontrolled diabetes mellitus, sepsis, and organ failure.

By itself, uncontrolled diabetes mellitus can be viewed as a perioperative nutritional complication, as it results in nutritional depletion, interferes with delivery of parenteral and enteral nutrition, and is associated with increased infectious morbidity.[140]

COMPREHENSIVE PERIOPERATIVE MANAGEMENT PATHWAYS

Enhanced recovery after surgery (ERAS) pathways have been proposed[141-143] for the purpose of cost containment, standardization of care, and improvement of surgical outcomes. Initially advanced for elective procedures, especially partial colectomy, these pathways are increasingly being applied to diverse procedures in the elective and emergent setting.[144] The pathways are not universally standardized, but several international societies have published guidelines for the composition of ERAS pathways for elective colon resection based on best evidence-based practices.

For elective colon resection, the ERAS Society has developed a comprehensive, evidence-based bundle of guidelines that include specific recommendations for smoking cessation, preoperative carbohydrate loading (for nondiabetics), intravenous antibiotic prophylaxis, postoperative nausea and vomiting management, core body temperature management, fluid restriction, VTE prophylaxis, and others.[145] Adoption of an ERAS pathway has been associated with shortened length of hospital stay and improved outcomes in colorectal surgery in randomized prospective trials,[146,147] which has led to implementation of the ERAS approach in other procedures.[148-150] It should be noted that the concept of the pathway is that each pathway is specific to a given procedure and no universal ERAS pathway has been investigated.

REFERENCES

1. Bauer M, Bohrer H, Aichele G, et al. Measuring patient satisfaction with anesthesia: perioperative questionnaire versus standardised face-to-face interview. *Acta Anaesthesiol Scand*. 2001;45:65-72.
2. Ballantyne JC, Carr DB, Chalmers TC, et al. Postoperative patient-controlled analgesia: meta-analyses of initial randomized control trials. *J Clin Anesth*. 1993;5:182-193.
3. Nitschke LF, Schlosser CT, Berg RL, et al. Does patient-controlled analgesia achieve better control of pain and fewer adverse effects than intramuscular analgesia? A prospective randomized trial. *Arch Surg*. 1996;131:417-423.
4. Kenady DE, Wilson JF, Schwartz RW, et al. A randomized comparison of patient-controlled versus standard analgesic requirements in patients undergoing cholecystectomy. *Surg Gynecol Obstet*. 1992;174:216-220.
5. de Leon-Casasola OA, Karabella D, Lema MJ. Bowel function recovery after radical hysterectomies: thoracic epidural bupivacaine-morphine versus intravenous patient-controlled analgesia with morphine: a pilot study. *J Clin Anesth*. 1996;8:87-92.
6. Block BM, Liu SS, Rowlingson AJ, et al. Efficacy of postoperative epidural analgesia: a meta-analysis. *JAMA*. 2003;290:2455-2463.
7. Wang LP, Hauerberg J, Schmidt JF. Incidence of spinal epidural abscess after epidural analgesia: a national 1-year survey. *Anesthesiology*. 1999;91:1928-1936.

8. Boylan JF, Katz J, Kavanagh BP, et al. Epidural bupivacaine-morphine analgesia versus patient-controlled analgesia following abdominal aortic surgery: analgesic, respiratory, and myocardial effects. *Anesthesiology*. 1998;89:585-593.
9. Bois S, Couture P, Boudreault D, et al. Epidural analgesia and intravenous patient-controlled analgesia result in similar rates of postoperative myocardial ischemia after aortic surgery. *Anesth Analg*. 1997;85:1233-1239.
10. Wu CL, Naqibuddin M, Fleisher LA. Measurement of patient satisfaction as an outcome of regional anesthesia and analgesia: a systematic review. *Reg Anesth Pain Med*. 2001;26:196-208.
11. Werawatganon T, Charuluxanun S. Patient controlled intravenous opioid analgesia versus continuous epidural analgesia for pain after intra-abdominal surgery. *Cochrane Database Syst Rev*. 2005;1:CD004088.
12. Hendolin H, Lahtinen J, Lansimies E, et al. The effect of thoracic epidural analgesia on respiratory function after cholecystectomy. *Acta Anaesthesiol Scand*. 1987;31:645-651.
13. Cuschieri RJ, Morran CG, Howie JC, McArdle CS. Postoperative pain and pulmonary complications: comparison of three analgesic regimens. *Br J Surg*. 1985;72:495-498.
14. Scheinin B, Asantila R, Orko R. The effect of bupivacaine and morphine on pain and bowel function after colonic surgery. *Acta Anaesthesiol Scand*. 1987;31:161-164.
15. Bredtmann RD, Herden HN, Teichmann W, et al. Epidural analgesia in colonic surgery: results of a randomized prospective study. *Br J Surg*. 1990;77:638-642.
16. De Oliveira GS, Castro-Alves LJ, Nader A, et al. transversus abdominis plane block to ameliorate postoperative pain outcomes after laparoscopic surgery: a meta-analysis of randomized controlled trials. *Anesth Analg*. 2014;118:454-463.
17. Walter CJ, Maxwell-Armstrong C, Pinkney TD, et al. A randomised controlled trial of the efficacy of ultrasound-guided transversus abdominis plane (TAP) block in laparoscopic colorectal surgery. *Surg Endosc*. 2013;27:2366-2372.
18. Horattas MC, Evans S, Sloan-Stakleff KD, et al. Does pre-operative rofecoxib (Vioxx) decrease postoperative pain with laparoscopic cholecystectomy? *Am J Surg*. 2004;188:271-276.
19. Bikhazi GB, Snabes MC, Bajwa ZH, et al. A clinical trial demonstrates the analgesic activity of intravenous parecoxib sodium compared with ketorolac or morphine after gynecologic surgery with laparotomy. *Am J Obstet Gynecol*. 2004;191:1183-1191.
20. Lau H, Wong C, Goh LC, et al. Prospective randomized trial of pre-emptive analgesics following ambulatory inguinal hernia repair: intravenous ketorolac versus diclofenac suppository. *ANZ J Surg*. 2002;72:704-707.
21. Mixter CG 3rd, Meeker LD, Gavin TJ. Preemptive pain control in patients having laparoscopic hernia repair: a comparison of ketorolac and ibuprofen. *Arch Surg*. 1998;133:432-437.
22. Morton NS, O'Brien K. Analgesic efficacy of paracetamol and diclofenac in children receiving PCA morphine. *Br J Anaesth*. 1999;82:715-717.
23. Litaker D, Locala J, Franco K, et al. Preoperative risk factors for postoperative delirium. *Gen Hosp Psychiatry*. 2001;23:84-89.
24. Moller JT, Cluitmans P, Rasmussen LS, et al. Long-term postoperative cognitive dysfunction in the elderly ISPOCD1 study. ISPOCD investigators. International Study of Post-Operative Cognitive Dysfunction. *Lancet*. 1998;351:857-861.
25. Inouye SK, Charpentier PA. Precipitating factors for delirium in hospitalized elderly persons. Predictive model and interrelationship with baseline vulnerability. *JAMA*. 1996;275:852-857.
26. Mann C, Pouzeratte Y, Boccara G, et al. Comparison of intravenous or epidural patient-controlled analgesia in the elderly after major abdominal surgery. *Anesthesiology*. 2000;92:433-441.
27. Skrobik YK, Bergeron N, Dumont M, Gottfried SB. Olanzapine vs haloperidol: treating delirium in a critical care setting. *Intensive Care Med*. 2004;30:444-449.
28. Mangano DT, Goldman L. Preoperative assessment of patients with known or suspected coronary

disease. *N Engl J Med*. 1995;333:1750-1756.
29. Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130:e278-e333.
30. Park KW. Perioperative cardiology consultation. *Anesthesiology*. 2003;98: 754-762.
31. Liu LI, Wiener-Kronish JP. Preoperative cardiac evaluation of women for noncardiac surgery. *Cardiol Clin*. 1998;16:59-66.
32. Shackleford DP, Hoffman MK, Kramer PR Jr, et al. Evaluation of preoperative cardiac risk index values in patients undergoing vaginal surgery. *Am J Obstet Gynecol*. 1995;173:80-84.
33. Mangano DT, Hollenberg M, Fegert G, et al. Perioperative myocardial ischemia in patients undergoing non-cardiac surgery—I: incidence and severity during the 4 day perioperative period. The Study of Perioperative Ischemia (SPI) Research Group. *J Am Coll Cardiol*. 1991;4:843-850.
34. Lee TH, Marcantonio ER, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation*. 1999;100:1043-1049.
35. Mukherjee D, Eagle KA. Perioperative cardiac assessment for non cardiac surgery, eight steps to the best possible outcome. *Circulation*. 2003;107: 2771-2774.
36. Chui PT, Gin T, Oh TE. Anesthesia for laparoscopic surgery. *Anaesth Intensive Care*. 1993;21:163-171.
37. Madu EC. Transesophageal dobutamine stress echocardiography in the evaluation of myocardial ischemia in morbidly obese subjects. *Chest*. 2000;117:657-661.
38. Dawood MM, Gupta DK, Southern J, et al. Pathology of fatal perioperative myocardial infarction: implications regarding pathophysiology and prevention. *Int J Cardiol*. 1996;57:37-44.
39. Boersma E, Poldermans D, Bax JJ, et al. Predictors of cardiac events after major vascular surgery: role of clinical characteristics, dobutamine echocardiography, and beta-blocker therapy. *JAMA*. 2001;285:1865-1873.
40. Gersh BJ, Braunwald E, Bonow RO. Chronic coronary artery disease. In: Braunwald E, Zipes DP, Libby P (eds). *Heart Disease*. Philadelphia, PA: WB Saunders; 2001:1272-1363.
41. McFalls EO, Ward HB, Moritz TE, et al. Coronary artery revascularization before elective major vascular surgery. *N Engl J Med*. 2004;352: 2795-2804.
42. Posner KL, Van Norman GA, Chan V. Adverse cardiac outcomes after noncardiac surgery in patients with prior percutaneous transluminal coronary angioplasty. *Anesth Analg*. 1999;89:553-560.
43. Kaluza GL, Joseph J, Lee JR, et al. Catastrophic outcomes of noncardiac surgery soon after coronary stenting. *J Am Coll Cardiol*. 2000;35:1288-1294.
44. Foster ED, Davis KB, Carpenter JA, et al. Risk of noncardiac operation in patients with defined coronary disease: The Coronary Artery Surgery Study (CASS) registry experience. *Ann Thorac Surg*. 1986;14:42-50.
45. Yusuf S, Zucker D, Peduzzi P, et al. Effect of coronary artery bypass graft surgery on survival: overview of 10-year results from randomized trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. *Lancet*. 1994;344:563-570.
46. Selzman CH, Miller SA, Zimmerman MA, Harkin AH. The case for beta-adrenergic blockade as prophylaxis against perioperative cardiovascular morbidity and mortality. *Arch Surg*. 2001;136:286-290.
47. Lee RT, Grodinsky AJ, Frank EH, et al. Structure dependent dynamic mechanical behavior of fibrous caps from human atherosclerotic plaques. *Circulation*. 1991;83:1764-1770.
48. Rabbani R, Topol EJ. Strategies to achieve coronary arterial plaque stabilization. *Cardiovasc Res*. 1999;4:402-417.