23 Anesthesia and Noncardiac Surgery in Patients with Heart Disease

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Cardiovascular morbidity and mortality represent a special concern in patients with known (or with risk factors for) cardiovascular disease who undergo noncardiac surgery. The cost of perioperative myocardial injury adds substantially to the total health care expenditure, with an average increased length of stay (LOS) of 6.8 days for patients with perioperative myocardial ischemic injury. Perioperative cardiovascular complications not only affect the immediate period but may also influence the outcome over subsequent years with an increased risk of readmission and death. The evidence base for managing patients with cardiovascular disease in the context of noncardiac surgery has grown in recent decades, beginning with identification of those at greatest risk and progressing to randomized trials to identify strategies for reducing perioperative cardiovascular complications. Guidelines provide information for the management of high-risk patients and disseminate best practices published by three major groups. Indeed, over the last decade, mortality rates for all major surgeries have decreased in parallel with implementation of these practices. This chapter distills this information by incorporating guidelines available from the American College of Cardiology and American Heart Association (ACC/AHA),[1] the European Society of Cardiology (ESC),[2] and the Canadian Cardiovascular Society (CCS).[3] The ACC/AHA Guideline was updated in 2014 with a focused update on dual antiplatelet therapy in 2016.[4]

ASSESSMENT OF RISK

Numerous points of entry lead to evaluation of patients before they undergo noncardiac surgery. Primary physicians or cardiologists may encounter such patients. History and physical examination represent the cornerstone of surgical risk evaluation, but risk assessment testing is rarely performed unless changes in management will result. Many patients undergo evaluation just before surgery by the surgeon or anesthesiologist. Importantly, several cardiovascular conditions require assessment independent of the time before surgery.

Ischemic Heart Disease

The stress related to noncardiac surgery increases metabolic requirements and activates the sympathetic nervous system and may raise the heart rate (HR) preoperatively, which is associated with a high incidence of symptomatic and asymptomatic myocardial ischemia. Preoperative clinical evaluation of patients may therefore identify stable or unstable coronary artery disease (CAD). Patients with acute manifestations of CAD such as unstable angina or other cardiac disease like decompensated heart failure (HF) have a high risk for the development of further decompensation, myocardial infarction (MI), and death during the perioperative period. Such patients clearly warrant further evaluation and medical stabilization prior to surgery. If the noncardiac surgery is truly an emergency, several small older case series have shown that intra-aortic balloon pump counterpulsation can provide short-term myocardial protection beyond that afforded by maximal medical therapy, although this measure is seldom used today.

If the patient is clinically stable, identification of known asymptomatic or symptomatic stable CAD or risk factors for CAD can foster the implementation of guideline-based risk reduction therapies. There is currently no significant adjunctive therapy that ameliorates cardiovascular surgical risk. In determining the extent of preoperative evaluation, it is important not to perform testing unless the results will affect perioperative management. In addition, the use of medications or interventions should mirror those that would be implemented in the absence of surgery. Infrequently, these changes in management may include cancellation of surgery (if the risk-benefit ratio is prohibitive) and consideration of palliative therapy, delay of surgery for further medical management, coronary investigation and interventions before surgery, use of an intensive care unit (ICU), and changes in monitoring. As discussed later, few evidence-based therapies are available independent of treating the underlying atherosclerotic risk, and except in the case of left main coronary artery stenosis, current data challenge the benefit of preoperative coronary revascularization. Thus, the primary reason to perform risk assessment is to determine clinical cardiovascular instability and suitability for surgery.

Over the last two decades, there has been a secular decrease in the rates of perioperative type 1 MI and mortality. Finks and colleagues reported a 36% decrease in death after open abdominal aortic aneurysm repair from 2000 to 2008, to a risk-adjusted mortality of 2.8%.[1] More recent data substantiate a decreasing frequency of type 1 MI and increasing rate of type 2 MI, indicating a predominance of subendocardial ischemic events resulting from hemodynamic challenge and more sensitive biomarker testing.[1] Although these events are characterized by increases in troponin and are strongly associated with death, the interval between troponin elevation and adverse events and the higher rate of nonvascular than cardiovascular mortality suggest that this is a marker of illness rather than a mechanism of mortality.

Traditionally, assessment of the coronary risk associated with noncardiac surgery in patients with previous MI was based on the time between the MI and surgery. Multiple older studies have demonstrated an increased incidence of reinfarction after noncardiac surgery if the previous MI had occurred within 6 months of the operation. Improvements in MI management and perioperative care have shortened this

interval. Although in some patients after a recent MI the myocardium may still be at risk for subsequent ischemia and infarction, most patients in the United States will have had critical coronary stenoses identified and revascularized when appropriate and should already be receiving maximal medical therapy. The AHA/ACC Task Force on Perioperative Evaluation of the Cardiac Patient Undergoing Noncardiac Surgery has suggested that the highest-risk patients are those within 30 days of MI, during which time plaque and myocardial healing occur. After this period, risk stratification is based on the features of the disease (i.e., those with active ischemia are at highest risk). It should be noted that a study using administrative data from California demonstrated that the rate of perioperative cardiac morbidity and mortality remained elevated for at least 60 days after an MI, and the current iteration of the guidelines supports such a time frame.[1]

Hypertension

In the 1970s a series of case studies changed the prevailing thought that the use of antihypertensive agents should be discontinued before surgery. The reports suggested that poorly controlled hypertension was associated with untoward hemodynamic responses and that antihypertensives should be continued perioperatively. However, several large prospective studies were unable to establish mild to moderate hypertension as an independent predictor of postoperative cardiac complications including cardiac death, postoperative MI, HF, or arrhythmias. The approach to patients with hypertension therefore relies mostly on management strategies from the nonsurgical literature.

Blood pressure (BP) excursions in the operative and postoperative period portend worsening outcome. A hypertensive crisis in the postoperative period—defined as diastolic BP higher than 120 mm Hg and clinical evidence of impending or actual end-organ damage—poses a definite risk for MI and cerebrovascular accident (CVA, stroke). Iatrogenic precipitants of hypertensive crises include abrupt withdrawal of clonidine or beta blocker therapy before surgery, chronic use of monoamine oxidase inhibitors with or without sympathomimetic drugs, and inadvertent discontinuation of antihypertensive therapy. Similarly, intraoperative hypotension is associated with both type 2 MI and increases in postoperative mortality.[5]

Although postulated to predict an increased rate of myocardial ischemia, none of the recent large clinical trials has shown that chronic hypertension predisposes patients to perioperative cardiovascular events.[1] This finding likely reflects, in part, the excellent perioperative management of hypertension in the current era. The pharmacologic management of patients with hypertension should be continued perioperatively, and BP should be maintained near preoperative levels to reduce the risk for myocardial ischemia. In patients with more severe hypertension, such as a diastolic BP higher than 110 mm Hg, little evidence suggests a benefit of delaying surgery to optimize antihypertensive medications in the absence of a hypertensive urgency or emergency. Currently, debate surrounds the optimal decision on withholding angiotensin-converting enzyme inhibitors and angiotensin receptor blockers on the day of surgery to avoid intraoperative hypotension. Studies support both continuation and withholding, although continuation may require treatment with vasopressin for intractable hypotension. It is important to restart these agents as soon as possible postoperatively.

The importance of perioperative BP management was studied in the Intraoperative Norepinephrine to Control Arterial Pressure (INPRESS) study, a multicenter, randomized, clinical trial of an individualized management strategy aimed at achieving a systolic BP within 10% of the reference value (i.e., patient's resting systolic BP) or standard management strategy of treating systolic BP less than 80 mm Hg or lower than 40% from the reference value during and for 4 hours following surgery. Among 292 patients who completed the trial, management targeting an individualized systolic BP, compared with standard management, reduced the risk of postoperative organ dysfunction.[6]

Heart Failure

HF is associated with perioperative cardiac morbidity after noncardiac surgery in virtually all studies. Since the early work of Goldman and colleagues, who identified signs of HF as a significant risk of adverse perioperative events, HF has become more common with more varied presentations, including the presence or absence of ischemia and of reduced left ventricular ejection fraction. The underlying causes in patients with signs or symptoms of HF who are scheduled for noncardiac surgery require characterization. HF may eclipse CAD as a cause of postoperative adverse events. The 30-day postoperative mortality rate was significantly higher in patients with both nonischemic (9.3%) and ischemic (9.2%) HF compared to those with CAD (2.9%) in a population-based data analysis of 38,047 consecutive patients.[1]

The preoperative evaluation should aim to identify the underlying coronary, myocardial, and valvular heart disease and assess the severity of the systolic and diastolic dysfunction. Hammill and associates used Medicare claims data to evaluate short-term outcomes in patients with HF, CAD, or neither who underwent major noncardiac surgery. Elderly patients with HF who underwent major surgical procedures had substantially higher risk for operative mortality and hospital readmission than other patients, including those with CAD, admitted for the same procedures. A study using the American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) database demonstrated that worsening preoperative HF is associated with a significant increase in postoperative morbidity and mortality when controlling for other comorbidities.[7] In the absence of a surgical emergency, patients with decompensated HF should be treated to achieve a euvolemic, stable state before operation. Ischemic cardiomyopathy is of greatest concern because the patient has the additional substantial risk for the development of further ischemia, which can lead to myocardial necrosis and potentially induce a downward spiral.

Hypertrophic Cardiomyopathy

Treatment of decompensated hypertrophic cardiomyopathy differs from that of dilated cardiomyopathy, and thus the preoperative evaluation can influence perioperative management in this setting (see Chapter 54). In particular, this assessment may influence perioperative fluid and vasopressor management. Obstructive hypertrophic cardiomyopathy was formerly regarded as a high-risk condition associated with high perioperative morbidity. A retrospective review of perioperative care in 35 patients, however, suggested low risk related to general anesthesia and major noncardiac surgery in such patients. This study also suggested that spinal anesthesia was a relative contraindication in view of the sensitivity of cardiac output to preload in this condition. Haering and colleagues studied 77 patients with asymmetric septal hypertrophy identified retrospectively from a large database; 40% had one or more adverse perioperative cardiac events, including one patient with MI and ventricular tachycardia who required emergency cardioversion. Most of the events consisted of perioperative congestive HF, and no perioperative deaths occurred. Unlike the finding in the original cohort of patients, the type of anesthesia was not an independent risk factor. Important independent risk factors for an adverse outcome (as seen generally) included major surgery and increasing duration of surgery.

VALVULAR HEART DISEASE

Aortic stenosis places patients at increased risk. Critical stenosis is associated with the highest risk for cardiac decompensation in patients undergoing elective noncardiac surgery (see Chapter 72). Thus, the presence of any of the classic triad of angina, syncope, and HF in a patient with aortic stenosis should prompt further evaluation and potential interventions (usually valve replacement). Preoperative patients with aortic systolic murmurs warrant a careful history and physical examination—and often further evaluation. Several recent case series of patients with critical aortic stenosis have demonstrated that when necessary, noncardiac surgery can be performed with acceptable risk. In a matched-sample study using the Danish Health Care System, Andersson and colleagues demonstrated that patients with asymptomatic aortic stenosis did not experience a higher rate of major adverse cardiovascular events (MACE) or mortality in elective surgery.[8] Emergency surgery type and symptomatic aortic stenosis increased both MACE and mortality. Aortic valvuloplasty is a bridging option for selected patients who cannot undergo valve replacement or percutaneous intervention in the short term. The substantial risk for procedure-related morbidity and mortality and little evidence to demonstrate a perioperative risk reduction mandate careful consideration before recommending this strategy.[1,9]

Mitral valve disease is associated with a lower risk for perioperative complications than aortic stenosis, although occult rheumatic mitral stenosis can sometimes lead to severe left-sided HF in patients with tachycardia (e.g., uncontrolled atrial fibrillation [AF]) and volume loading (see Chapter 75). In contrast to aortic valvuloplasty, mitral valve balloon valvuloplasty often yields both short- and long-term benefit, especially in younger patients with predominant mitral stenosis but without severe mitral valve leaflet thickening or significant subvalvular fibrosis and calcification.

In perioperative patients with a functioning prosthetic heart valve, antibiotic prophylaxis and anticoagulation require management (see Chapter 79). All patients with prosthetic valves who undergo procedures that can cause transient bacteremia should receive prophylaxis. In patients with prosthetic valves, the risk for increased bleeding during a procedure while receiving antithrombotic therapy must be weighed against the increased risk for thromboembolism caused by stopping the therapy. Common practice in patients undergoing noncardiac surgery with a mechanical prosthetic valve in place is cessation of warfarin 3 days before surgery. This allows the international normalized ratio (INR) to fall to less than 1.5 times normal; oral anticoagulants can then be resumed on postoperative day 1. A multicenter, single-arm cohort study of 224 high-risk patients (prosthetic valves, AF, and a major risk factor) investigated the use of low-molecular-weight heparin (LMWH) as a preoperative bridge to warfarin anticoagulation in which warfarin was withheld for 5 days and LMWH was given 3 days preoperatively and at least 4 days postoperatively. The overall rate of thromboembolism was 3.6% and of cardioembolism 0.9%. Major bleeding was seen in 6.7% of patients, although only 8 of 15 episodes occurred during the administration of LMWH. LMWH is cost-effective because it helps reduce the duration of the hospital stay, but two studies have shown a residual anticoagulation effect in as many as two thirds of patients.[10]

Many current prosthetic valves have a lower risk for valve thrombosis than the older designs, so the risk associated with heparin may outweigh its benefit in the perioperative setting. According to the 2020 AHA/ACC guidelines on management of valvular heart disease,[9] heparin can usually be reserved for high-risk patients. *High risk* is defined by the presence of a mechanical mitral or tricuspid valve or a mechanical aortic valve in the presence of certain risk factors, including AF, previous thromboembolism, hypercoagulable condition, older-generation mechanical valves, an ejection fraction lower than 30%, or more than one mechanical valve. Bridging anticoagulation therapy with heparin during the preoperative time interval when the INR is subtherapeutic should be made on an individualized basis, with the risks of bleeding weighed against the benefits of thromboembolism prevention. Subcutaneous LMWH or unfractionated heparin offers an alternative outpatient approach but has received only a tentative recommendation. Discussion between the surgeon and cardiologist regarding optimal perioperative management is critical. The 2020 ACC/AHA guidelines also note that it is reasonable to consider the need for bridging anticoagulant therapy around the time of invasive procedures in patients with bioprosthetic heart valves or annuloplasty rings who are receiving anticoagulation for AF on the basis of the CHA2DS2-VASc score weighed against the risk of bleeding.[9]

CONGENITAL HEART DISEASE IN ADULTS (SEE ALSO CHAPTER 82)

Congenital heart disease afflicts 500,000 to 1 million adults in the United States. The nature of both the underlying anatomy and any anatomic correction affects the perioperative plan and incidence of complications, which include infection, bleeding, hypoxemia, hypotension, and paradoxical embolization. In a study using the NSQIP database, prior cardiac surgery in a population age 19 to 39 years significantly increased the risk of death, MI, stroke, reoperation, and LOS.[11] Pulmonary hypertension and Eisenmenger syndrome present a major concern in patients with congenital heart disease. Regional anesthesia has traditionally been avoided in these patients because of the potential for sympathetic blockade and worsening of the right-to-left shunt. However, a review of 103 cases found that overall perioperative mortality was 14%; patients receiving regional anesthesia had a mortality of 5%, whereas those receiving general anesthesia had a mortality of 18%. The authors concluded that most deaths probably resulted from the surgical procedure and the disease rather than from anesthesia. Although perioperative and peripartum mortality was high, many anesthetic agents and techniques have been used with success. Patients with congenital heart disease are at risk for infective endocarditis and should receive antibiotic prophylaxis (see Chapter 82).

ARRHYTHMIAS

Cardiac arrhythmias frequently occur in the perioperative period, particularly in older adults or patients undergoing thoracic surgery.[12] Predisposing factors include previous arrhythmias, underlying heart disease, hypertension, perioperative pain (e.g., hip fractures), severe anxiety, and other situations that heighten adrenergic tone. In a prospective study of 4181 patients 50 years or older, supraventricular arrhythmia occurred in 2% during surgery and in 6.1% after surgery. Perioperative AF raises several concerns, including the incidence of stroke (see Chapters 45 and 66). In a study of 317 patients without AF undergoing major vascular surgery reported by Winkle et al. (see "Classic References"), the incidence of new-onset AF was 4.7% and was associated with more than a sixfold increase in cardiovascular death, MI, unstable angina, and stroke in the first 30 days and a fourfold increase over the next 12 months. Early treatment to restore sinus rhythm or control the ventricular response and initiate anticoagulation may be indicated. Prophylactic use of intravenous (IV) diltiazem and esmolol in randomized, placebo-controlled trials of patients undergoing high-risk thoracic surgery reduced the incidence of clinically significant atrial arrhythmias.[12]

Although older studies identified ventricular arrhythmias as a risk factor for perioperative morbidity, recent studies have not confirmed this finding. Current guidelines cite studies of patients undergoing major noncardiac surgical procedures reporting that preoperative arrhythmias are associated with intraoperative and postoperative arrhythmias, but not with nonfatal MI and cardiac death. However, this remains controversial as a population-based study by van Diepen et al. reported that the risk of mortality at 30 days was 6.4% in patients with preoperative AF compared with 2.9% for patients with CAD (see "Classic References").[1] These findings suggest that a preoperative arrhythmia should provoke a search for underlying cardiopulmonary disease, ongoing myocardial ischemia or infarction, drug toxicity, or electrolyte or metabolic derangements as suggested by other clinical circumstances.

Conduction abnormalities can increase perioperative risk and may require placement of a temporary or permanent pacemaker. On the other hand, patients with intraventricular conduction delays, even in the presence of a left or right bundle branch block but without a history of advanced heart block or symptoms, rarely progress to complete heart block perioperatively. The availability of transthoracic pacing units has decreased the need for temporary transvenous pacemakers.

THE DECISION TO UNDERGO DIAGNOSTIC TESTING

The ACC/AHA and ESC proposed algorithms for CAD evaluation based on the available evidence and incorporated the class of recommendations and level of evidence into each step (Figs. 23.1 and 23.2). Current algorithms use a stepwise Bayesian strategy that relies on assessment of clinical markers, previous coronary evaluation and treatment, functional capacity, and surgery-specific risk. Successful use of the ACC/AHA algorithm requires an appreciation of the different levels of risk attributable to the combination of clinical circumstances and type of surgery, levels of functional capacity, and how the information from any diagnostic testing will influence perioperative management.

Multiple studies have attempted to identify clinical risk markers for perioperative cardiovascular morbidity and mortality. As described earlier, patients with unstable coronary syndromes and severe valvular disease have active cardiac conditions. Risk can be divided into low (<1%) and elevated clinical risk. The 2014 ACC/AHA guidelines advocate using a risk index.[1] This includes either the ACS NSQIP risk calculator or myocardial infarction and cardiac arrest (MICA) risk calculator, which incorporates both surgical and clinical risk. Alternatively, the clinician can incorporate the revised cardiac risk index (RCRI) with the estimated surgical risk to differentiate low from elevated risk (Table 23.1). Cardiovascular disease also has clinical risk markers classified as "low-risk factors," each of which is associated with variable levels of perioperative risk. Recent investigation of more than 3 million patients using the United States National Surgical Quality Improvement Program shows patients without hypertension, diabetes mellitus, or current smoking have a postoperative MI and death rate of 0.1% and 0.47%, respectively.[13] The previous classification of perioperative, active clinical risk markers to assess the need for further testing includes issues beyond ischemic heart disease (Table 23.2).

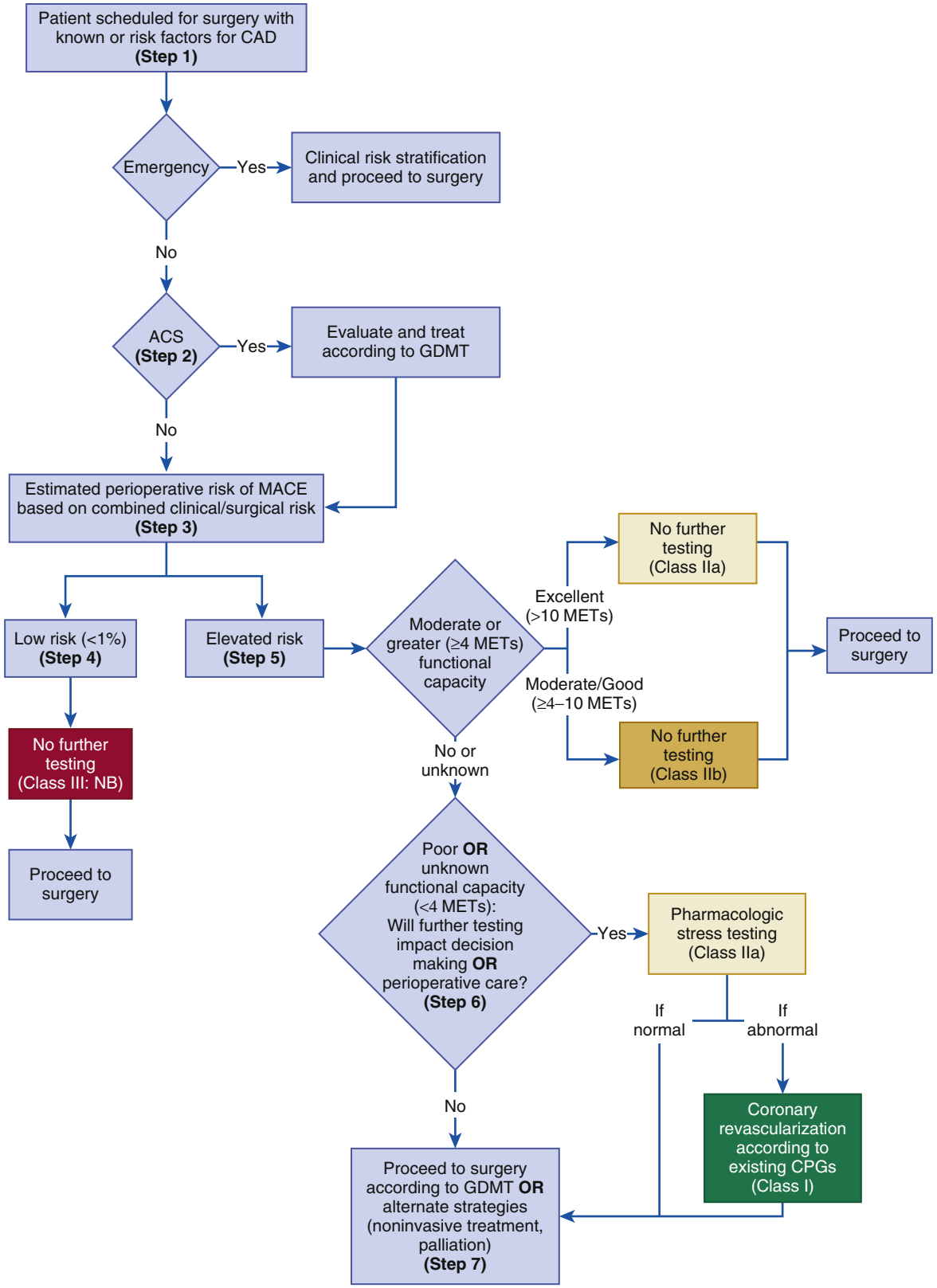


FIGURE 23.1 The 2014 ACC/AHA guideline algorithm depicting the stepwise approach to perioperative cardiac assessment for CAD. *ACS,* Acute coronary syndrome; *CAD,* coronary artery disease; *CPG,* clinical practice guideline; *GDMT,* guideline-directed medical therapy; *MACE,* major adverse cardiac event; *MET,* metabolic equivalent; *NB,* no benefit; *PCI,* percutaneous coronary intervention. (From 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. *J Am Coll Cardiol*. 2014;64:e77–e137.)

Exercise tolerance is one of the strongest determinants of perioperative risk and the need for invasive monitoring. Several scales based on activities of daily living have been proposed to assess exercise tolerance; current guidelines advocate the Duke Activity Scale Index (Table 23.3).

The type of surgical procedure significantly impacts perioperative risk and the amount of preparation required to perform anesthesia safely. For surgical procedures not associated with significant stress or a high incidence of perioperative myocardial ischemia or morbidity, the cost and procedural delay of the evaluation often exceed any

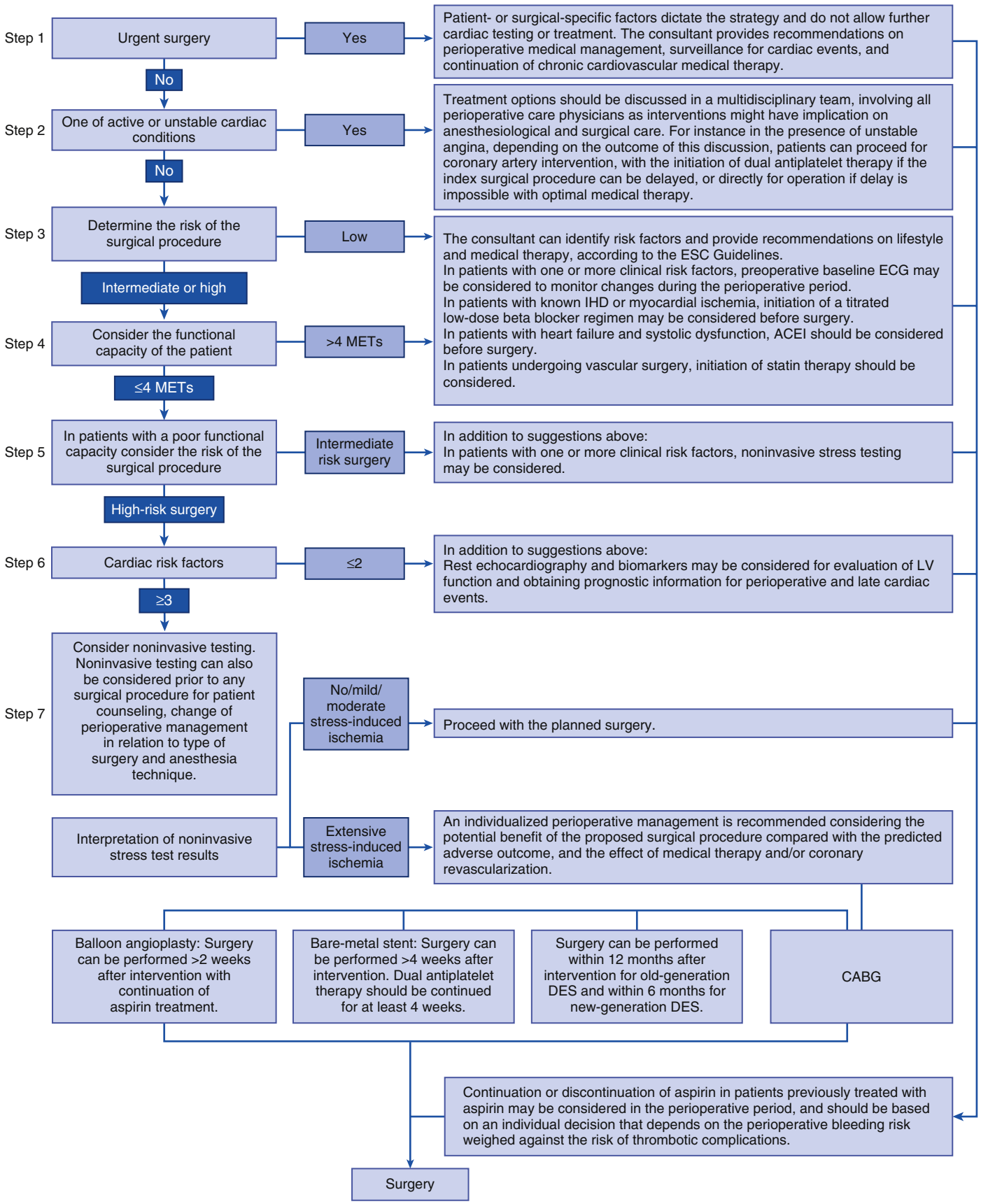


FIGURE 23.2 Summary of preoperative cardiac risk evaluation and perioperative management. *ACEI,* Angiotensin-converting enzyme inhibitors; *CABG,* coronary artery bypass graft; *DES,* drug-eluting stents; *IHD,* ischemic heart disease; *LV,* left ventricular; *METs,* metabolic equivalents. (From Kristensen SD, Knuuti J, Saraste A, et al. 2014 ESC/ESA guidelines on non-cardiac surgery: cardiovascular assessment and management: The Joint Task Force on Non-Cardiac Surgery: Cardiovascular Assessment and Management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). *Eur Heart J.* 2014;35:2383–2431.)

TABLE 23.1 Cardiac Risk* Stratification for Noncardiac Surgical Procedures

RISK STRATIFICATION	EXAMPLES OF PROCEDURES
High (reported cardiac risk often >5%)	Aortic and other major vascular surgery
	Peripheral vascular surgery
Intermediate (reported cardiac risk generally 1%–5%)	Intraperitoneal and intrathoracic surgery
	Carotid endarterectomy
	Head and neck surgery
	Orthopedic surgery
	Prostate surgery
Low† (reported cardiac risk generally <1%)	Endoscopic procedures
	Superficial procedure
	Cataract surgery
	Breast surgery
	Ambulatory surgery

*Combined incidence of cardiac death and nonfatal myocardial infarction.
†These procedures do not generally require further preoperative cardiac testing.
From Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2009;54:e77–e137.

TABLE 23.2 Active Cardiac Conditions for Which Patients Should Undergo Evaluation and Treatment Before Noncardiac Surgery (Class I; Level of Evidence: B)

CONDITION	EXAMPLES
Unstable coronary syndromes	Unstable or severe angina* (CCS class III or IV)†
	Recent myocardial infarction (MI)‡
Decompensated HF (NYHA functional class IV; worsening or new-onset HF)	
Significant arrhythmias	High-grade atrioventricular block
	Mobitz II atrioventricular block
	Third-degree atrioventricular heart block
	Symptomatic ventricular arrhythmias
	Supraventricular arrhythmias (including atrial fibrillation) with an uncontrolled ventricular rate (heart rate >100 beats/min at rest)
	Symptomatic bradycardia
	Newly recognized ventricular tachycardia
Severe valvular disease	Severe aortic stenosis (mean pressure gradient >40 mm Hg, aortic valve area <1.0 cm^2, or symptomatic)
	Symptomatic mitral stenosis (progressive dyspnea on exertion, exertional presyncope, or HF)

*According to Campeau L, Enjalbert M, Lespérance J, et al. Atherosclerosis and late closure of aortocoronary saphenous vein grafts: sequential angiographic studies at 2 weeks, 1 year, 5 to 7 years, and 10 to 12 years after surgery. *Circulation*. 1983;68(Suppl II):1–7.
†May include "stable" angina in patients who are unusually sedentary.
‡The American College of Cardiology National Database Library defines "recent" MI as more than 7 days but 1 month or less (within 30 days) although the 2014 guidelines suggest 60 days.
CCS, Canadian Cardiovascular Society; *HF,* heart failure; *NYHA,* New York Heart Association.
From Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2009;54(22):e77–e137.

TABLE 23.3 Estimated Energy Requirements for Various Activities

	CAN YOU …
1 MET	Take care of yourself?
	Eat, dress, or use the toilet?
	Walk indoors around the house?
	Walk a block or two on level ground at 2–3 mph (3.2–4.8 kph)?
4 METs	Do light work around the house such as dusting or washing dishes?
	Climb a flight of stairs or walk up a hill?
	Walk on level ground at 4 mph (6.4 kph)?
	Run a short distance?
	Do heavy work around the house such as scrubbing floors or lifting or moving heavy furniture?
	Participate in moderate recreational activities such as golf, bowling, dancing, doubles tennis, or throwing a baseball or football?
>10 METs	Participate in strenuous sports such as swimming, singles tennis, football, basketball, or skiing?

MET, Metabolic equivalent; *mph,* miles per hour; *kph,* kilometers per hour.
Modified from Hlatky MA, Boineau RE, Higginbotham MB, et al. A brief self-administered questionnaire to determine functional capacity (the Duke Activity Status Index). *Am J Cardiol*. 1989;64:651–654; and Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2009;54:e77–e137.

benefit from the information gained by preoperative assessment. Outpatient procedures, for example, cause minimal morbidity and mortality; in such patients, cardiovascular status rarely changes perioperative management unless the patient has unstable angina or overt HF. In fact, 30-day mortality after outpatient surgery may actually be lower than that expected if the patient did not undergo surgery. In contrast, open surgery for vascular disease entails a high risk for morbidity and the potential for ischemia. Intra-abdominal, thoracic, and orthopedic procedures are associated with elevated risk, which, when combined with clinical risk factors, determine overall perioperative risk. Endovascular procedures fall into this intermediate-risk category because of their associated perioperative morbidity and mortality, although long-term survival appears to be similar to that in patients who undergo open procedures.

In addition to the risk related to the surgical procedure itself, risk is also correlated with the surgical volume in a given center. Several studies have demonstrated differential mortality rates in both cancer and vascular surgery, with higher mortality occurring in low-volume centers, although recent studies have demonstrated that low-volume centers may also have low mortality rates if proper care systems are in place. Surgical mortality rates may therefore be institution specific, which may influence the decision to perform further perioperative evaluations and interventions.

Risk Calculators

Much of the contemporary study of perioperative cardiac risk has focused on the development of clinical risk indices. The most widely used index was developed in a study of 4315 patients age 50 or older undergoing elective major noncardiac procedures in a tertiary care teaching hospital. The index includes six independent predictors of complications in a *revised cardiac risk index*: high-risk type of surgery, history of ischemic heart disease, history of congestive HF, history of cerebrovascular disease, preoperative treatment with insulin, and preoperative serum creatinine concentration greater than 2.0 mg/dL. Cardiac complication rates rise with an increasing number of these risk factors. Patients are stratified into low, intermediate, or high

cardiovascular risk on the basis of having 0, 1 or 2, or 3 or more factors included in the RCRI, respectively. The RCRI has become a standard tool for assessing the probability of perioperative cardiac risk in a given individual and serves to direct the decision to perform cardiovascular testing and implement perioperative management protocols. The RCRI has undergone validation in vascular surgery populations and serves to predict long-term outcome and quality of life, although one group has advocated inclusion of age as a risk factor and its outcomes are derived from data a quarter century old.

Additional risk indices were developed from the ACS-NSQIP database. Gupta and colleagues developed a risk calculator for predicting perioperative *myocardial infarction and cardiac arrest* (see "Classic References") in a study of 211,410 patients, of whom perioperative MI or cardiac arrest developed in 1371 (0.65%).[1] Multivariate logistic regression analysis identified five predictors of perioperative MI or cardiac arrest: type of surgery, dependent functional status, abnormal creatinine level, American Society of Anesthesiologists class, and increasing age.

A universal risk calculator developed to predict multiple outcomes was based on 1,414,006 patients encompassing 1557 unique surgical procedure codes, which had excellent performance for mortality (C-statistic = 0.944) and morbidity (C-statistic = 0.816). Morbidity is defined as any of the following intraoperative or postoperative events: surgical site infection, wound disruption, pneumonia, unplanned intubation, pulmonary embolism, on ventilator greater than 48 hours, progressive renal insufficiency, acute renal failure, urinary tract infection, stroke/CVA, cardiac arrest, MI, deep venous thrombosis, (systemic sepsis), pneumonia, cardiac event (cardiac arrest or MI), SSI, UTI, VTE, and renal failure (progressive renal insufficiency or acute renal failure) (http://riskcalculator.facs.org).[1] The risk calculator incorporates 21 preoperative risk factors and therefore has more discriminative ability than the MICA-specific risk calculator. Glance and colleagues demonstrated variability in the predicted risk of cardiac complications using different risk-prediction tools, also suggesting that the ACS-NSQIP risk calculator is the best option.[14]

In 2019 American University of Beirut-Pre-Operative Cardiovascular Evaluation Study (AUB-POCES) prospectively derived and validated a new preoperative cardiovascular risk index (CVRI).[15] It was subsequently renamed the AUB-HAS2 based on the six predictors of risk identified by multivariate logistic regression analysis in the derivation cohort: history of **H**eart disease, **H**eart symptoms of angina or dyspnea, **A**ge ≥75 years, **A**nemia with hemoglobin less than 12 mg/dL, vascular **S**urgery, and emergency **S**urgery. Patients were assigned a score of 0, 1, 2, 3, and greater than 3 based on the number of predictors. The incidence of the primary outcome of death, MI, or stroke at 30 days increased steadily across the increasing scores. A subsequent analysis of the performance of AUB-HAS2 in 9 surgical specialty groups and 8 site-specific surgeries using 1,167,278 noncardiac surgeries from the NSQIP database demonstrated superior discriminatory power compared with the RCRI. The performance of the AUB-HAS2 index was superior to that of the RCRI in all surgical subgroups ($P < 0.001$) but needs further evaluation.[15]

THE GUIDELINES APPROACH

The ACC/AHA Task Force for Guidelines for Perioperative Cardiovascular Evaluation and Management for Noncardiac Surgery presented their recommendations in algorithmic form as a framework for determining which patients are candidates for cardiac testing (see Fig. 23.1). Given the availability of the evidence, the writing committee included the level of the recommendations and strength of evidence for each of the pathways. The current algorithm focuses exclusively on the evaluation for CAD. Valvular or other forms of heart disease are not included in the current algorithm.

Step 1: The consultant should determine the urgency of performing noncardiac surgery. In many cases, patient- or surgery-specific factors dictate an obvious strategy (e.g., emergency surgery) that may not allow further cardiac assessment or treatment.

Step 2: Does the patient have an acute coronary syndrome? Acute coronary syndromes include previous MI with evidence of substantial ischemic risk as determined by clinical symptoms or noninvasive study, unstable or severe angina, and new or poorly controlled ischemia-mediated HF. Depending on the results of tests or interventions and the risk inherent in delaying surgery, it may be appropriate to proceed to the planned surgery with maximal medical therapy.

Step 3: What is the estimated perioperative risk of a MACE based on the combined clinical and surgical risk? The use of a validated risk index is advocated, either of the ACS-NSQIP risk indices or combining the RCRI with the estimated surgical risk.

Step 4: Does the patient have low perioperative risk (<1%)? In such cases, no further testing is required.

Step 5: Does the patient have elevated risk? Such circumstances merit assessment of functional capacity. If the patient has at least moderate exercise capacity (≥4 metabolic equivalents), management rarely changes on the basis of the results of any further cardiovascular testing, and it is therefore appropriate to proceed with the planned surgery. The strength of the evidence and the recommendation depends on the degree of exercise capacity, with excellent capacity having stronger evidence and recommendation. In the recently published METS study, subjectively assessed functional capacity should not be used for preoperative risk evaluation. The authors suggested that clinicians could instead consider a standardized measure such as Duke Activity Status Index (DASI) for cardiac risk assessment.

Step 6: In patients with poor (<4 METs) or unknown functional capacity, the physicians and patient should jointly determine if further testing will impact decision making or perioperative care. If not, proceeding to surgery with goal-directed medical therapy is appropriate. In the current guidelines, the identification of elevated risk with poor functional capacity may also lead to the decision to proceed with alternative strategies, such as noninvasive treatment or palliation.

The CCS Guidelines use an entirely different approach and include the RCRI combined with the Brain Natriuretic Peptide (BNP) or NT-proBNP for risk assessment for more extensive postoperative monitoring as opposed to advocating preoperative cardiovascular testing.[3] There is no management strategy to mitigate risk discussed after testing.

TESTS TO IMPROVE IDENTIFICATION AND DEFINITION OF CARDIOVASCULAR DISEASE

The use of testing to identify patients at high cardiovascular risk requires the acknowledgement of several secular outcome changes over time. First, overall results from surgery are excellent, with mortality rates for all patients hovering around 1% in all comers and continual improvement in higher-risk surgery.[1] Second, type 1 MI requiring postoperative revascularization is uncommon. In a recent large, randomized trial of patients at high risk on the basis of an elevated troponin postoperatively requirement for study entry, fewer than 4% of this group underwent coronary revascularization.[16] Indeed, mortality in recent trials is driven more by non-vascular events than vascular ones.[17] From these data, we recommend the focus of testing remain actionable management changes, either providing a target for risk remediation or cancelling of surgery.

Several noninvasive diagnostic methods can diagnose and indicate the extent of CAD before noncardiac surgery. The exercise electrocardiogram (ECG) has traditionally served as an initial evaluation for the presence of CAD. As noted earlier, patients with excellent exercise tolerance in daily life will rarely benefit from further testing. Patients with poor exercise capacity, in contrast, may not achieve an adequate HR and BP for diagnostic purposes on electrocardiographic stress tests. Such patients often require concomitant imaging. Recent work demonstrates the common inappropriate use and lack of predictive value of stress testing in patients undergoing low risk surgery. Among more than 800,000 patients undergoing total hip or knee arthroplasty, half had a low-risk RCRI score of 0 and stress test acquisition resulted in no difference in the primary outcome of MI or cardiac arrest among patients with an RCRI score of ≥1.[18]

Many high-risk patients either cannot exercise or have limitations to exercise (e.g., patients with intermittent claudication or knee arthritis). Pharmacologic stress testing, therefore, has become popular, particularly as a preoperative test in patients undergoing vascular surgery. Several studies have shown that the presence of a redistribution defect on dipyridamole or adenosine thallium or sestamibi imaging in patients undergoing peripheral vascular surgery predicts an increased risk for postoperative cardiac events (see Chapter 18). Pharmacologic stress imaging is best used in patients at moderate clinical risk. Several strategies may increase the predictive value of such tests. The redistribution defect can be quantitated, with larger areas of defect associated with

increased risk. Additionally, either increased lung uptake or dilation of the left ventricular cavity indicate ventricular dysfunction with ischemia. Several investigative groups have demonstrated that delineation of low-risk and high-risk myocardial perfusion scans (larger area of defect, increased lung uptake, and dilation of the left ventricular cavity) greatly improves the test's predictive value. Patients with high-risk scans have a particularly increased risk for perioperative morbidity and long-term mortality.

Stress echocardiography has also been used widely as a preoperative test (see Chapter 16). One advantage of this test is that it dynamically assesses myocardial ischemia in response to increased inotropy and HR, stimuli relevant to the perioperative period. The presence of new wall motion abnormalities occurring at a low HR is the best predictor of increased perioperative risk, with large areas of contractile dysfunction having secondary importance. As part of the DECREASE studies, Boersma and colleagues (as cited in the guidelines) assessed the value of dobutamine stress echocardiography with respect to the extent of wall motion abnormalities and the ability of preoperative treatment with beta blockers to attenuate risk in patients undergoing major aortic surgery. They assigned 1 point for each of the following characteristics: age older than 70 years, current angina, MI, congestive HF, previous cerebrovascular disease, diabetes mellitus, and renal failure. As the total number of clinical risk factors increases, perioperative cardiac event rates also increase. Furthermore, with a high-risk score, abnormal findings on an echocardiogram predict higher risk.

Several groups have published meta-analyses examining various preoperative diagnostic tests. Such studies report good predictive values for ambulatory electrocardiographic monitoring, radionuclide angiography, dipyridamole-thallium imaging, and dobutamine stress echocardiography. Shaw and colleagues also demonstrated excellent predictive values for dipyridamole thallium imaging and dobutamine stress echocardiography.[2] Beattie and colleagues performed a meta-analysis of 25 stress echocardiography studies and 50 thallium imaging studies.[1] The likelihood ratio for stress echocardiography was more indicative of a postoperative cardiac event than that for thallium imaging (likelihood ratio), 4.09; (95% confidence interval (CI), 3.21 to 6.56; versus LR, 1.83; 95% CI, 1.59 to 2.10; $P < 0.001$). The difference was attributable to fewer false-negative stress echocardiograms. A moderate to large abnormality found by either test predicted a greater risk of postoperative MI and death.

Institutional expertise should guide the choice of preoperative testing. The relevant clinical questions also influence the choice of test. For example, if valve function or ventricular wall thickness is of interest, echocardiography has advantages over perfusion imaging. Stress nuclear imaging may have slightly higher sensitivity, but stress echocardiography may have fewer false-positive results. The role of newer imaging modalities such as magnetic resonance imaging, multislice computed tomography, coronary calcium scores, and positron emission tomography in preoperative risk assessment is rapidly evolving.

Over the past decade, cardiopulmonary exercise testing (CPET) has been used as a preoperative test (see Chapter 15), particularly in Great Britain. A consistent finding of the studies was that a low anaerobic threshold was predictive of perioperative cardiovascular complications, postoperative death, or midterm and late death after surgery. An anaerobic threshold of approximately 10 mL O_2/kg/min was proposed as the optimal discrimination point, with a range in these studies of 9.9 to 11 mL O_2/kg/min. The METS study was designed to address the value of subjective assessment of exercise capacity, the objective Duke Activity Specific Index (DASI) questionnaire and a biomarker N-terminal pro-B-type natriuretic peptide (NT-pro-BNP) to predict death or complications after major elective non-cardiac surgery.[19] The investigators documented the poor discriminative ability of anesthesiologists to subjectively predict functional capacity; however, the DASI was predictive of myocardial injury and death. Although CPET did not have increased predictive ability for cardiac events, some of the measured variables were predictive of complications after surgery. CPET is therefore currently under evaluation as a means of determining both the need for and value of "prehabilitation," in which a strategy of exercise is initiated to increase aerobic capacity before surgery.[20] Several groups are studying the value of CPET to inform shared decision making in determining the appropriateness of surgery given the intermediate- and long-term outcomes in high-risk patients.

The use of biomarkers in risk stratification before surgery has also been investigated. A meta-analysis of 18 studies demonstrated that preoperative BNP measurement independently predicted perioperative cardiovascular events in studies that considered only the outcomes of death, or nonfatal MI (odds ratio [OR], 1.9; 95% CI, 1.38 to 2.58).[1] In a large substudy of the Vascular Events in Noncardiac Surgery Cohort Evaluation (VISION) trial of more than 10,400 patients, higher preoperative levels of NT-proBNP associated directly with higher levels of cardiovascular events.[21] In a stepwise pattern, the 30-day risk of vascular mortality increased from 0.2% in subjects with a NT-proBNP of less than 100 g/mL and increased directly with increasing NT-proBNP to 2.1% in patients with NT-proBNP ≥ 1500 pg/mL (HR 6.8 compared to referent). Thirty-day all-cause mortality increased with the previous thresholds from 0.3% to 3.4% (HR 8.4 compared to referent).[21] Similar to exercise and imaging testing above, the lack of a management algorithm after abnormal measurement limits the ability of the clinician to modify surgical risk based on this test. Maile and coworkers reviewed 6030 patients with troponin measured in the 30 days before nonemergent noncardiac surgery and found a 30-day mortality of 4.7% in the group without detectable troponin levels, but a 12.7% mortality in the group with the highest tercile of troponin elevation.[22] The closer in time that an elevated troponin was drawn to the date of surgery, the higher the risk.

OVERVIEW OF ANESTHESIA FOR CARDIAC PATIENTS UNDERGOING NONCARDIAC SURGERY

Three classes of anesthetics exist: general, regional, and local/sedation or monitored anesthesia care (MAC). General anesthesia can be defined best as a state that includes unconsciousness, amnesia, analgesia, immobility, and attenuation of autonomic responses to noxious stimulation, and it can be achieved with inhalational agents, IV agents, or a combination of these (frequently called a "balanced technique"). Contemporary general anesthesia does not always require an endotracheal tube. Laryngoscopy and intubation were traditionally considered the time of greatest stress and risk for myocardial ischemia, but extubation may actually engender even greater risk. Alternative methods for delivering general anesthesia include the use of a mask or a laryngeal mask airway—a device that fits above the epiglottis and does not require laryngoscopy or intubation.

Five inhalational anesthetic agents (in addition to nitrous oxide) are currently approved in the United States, although enflurane and halothane are rarely used today. All inhalational agents have reversible myocardial depressant effects and lead to decreases in myocardial oxygen demand. The degree to which they depress cardiac output depends on their concentration, their effects on systemic vascular resistance, and their effects on baroreceptor responsiveness; agents therefore differ in their specific effects on HR and BP. Isoflurane causes negative inotropic effects and potent vascular smooth muscle relaxation and has minimal effects on baroreceptor function. Desflurane has the fastest onset and is commonly used in the outpatient setting. The onset and offset of action of sevoflurane are intermediate to those of isoflurane and desflurane; the major advantage of sevoflurane is an extremely pleasant smell, which makes it the agent of choice in children.

Issues have arisen regarding the safety of inhalational agents in patients with CAD. Several large-scale, randomized and nonrandomized studies of patients undergoing coronary artery bypass grafting (CABG), however, demonstrated no increased incidence of myocardial ischemia or infarction in patients receiving inhalational agents versus narcotic-based techniques. The use of inhalational anesthetics in patients with CAD also has theoretical advantages. Several investigative groups demonstrated in vitro and in animals that inhalational agents have protective effects on myocardium similar to ischemic preconditioning, although the clinical relevance of this remains unclear.[23]

High-dose narcotic techniques offer the advantages of hemodynamic stability and lack of myocardial depression. Narcotic-based anesthetics were frequently considered the "cardiac anesthesia" and were

advocated for use in all high-risk patients, including those undergoing noncardiac surgery. The disadvantage of these traditional high-dose narcotic techniques is the requirement for postoperative ventilation. The ultrashort-acting narcotic remifentanil obviates the need for prolonged ventilation but provides hemodynamic stability. This agent can assist in early extubation of patients undergoing cardiac surgery and may aid in managing short periods of intense intraoperative stress in high-risk patients.

Despite the theoretical advantages of a high-dose narcotic technique, large-scale trials in patients undergoing CABG showed no difference in survival or major morbidity compared to the inhalation-based technique. This observation has contributed to the abandonment of high-dose narcotics in much of cardiac surgery and to an emphasis on early extubation. Most anesthesiologists use a balanced technique involving the administration of lower doses of narcotics with an inhalational agent. This approach allows the anesthesiologist to derive the benefits of each of these agents while minimizing side effects.

The IV agent propofol is an alternative mode of delivering general anesthesia. An alkyl phenol that can be used for both induction and maintenance of general anesthesia, propofol can cause profound hypotension because of reduced arterial tone with no change in HR. Its major advantage is rapid clearance with few residual effects on awakening, but because it is expensive, its current use tends to be limited to operations of brief duration. Despite its hemodynamic effects, propofol has been used extensively to assist in early extubation after CABG.

Current evidence indicates that there is no single "best" general anesthetic technique for patients with CAD who are undergoing noncardiac surgery, which has led to abandonment of the concept of a cardiac anesthetic.

Regional Anesthesia

Regional anesthesia includes spinal, epidural, and peripheral nerve blocks, and each technique has advantages and risks. Peripheral techniques, such as brachial plexus, femoral nerve, or Bier blocks, offer the advantage of causing minimal or no hemodynamic effects. These techniques are frequently used for orthopedic surgery. In contrast to peripheral nerve blocks, spinal or epidural techniques can produce sympathetic blockade, which can reduce BP and slow the HR. Spinal anesthesia and lumbar or low thoracic epidural anesthesia can also evoke reflex sympathetic activation mediated above the level of blockade, which might lead to myocardial ischemia.

The primary clinical difference between epidural and spinal anesthesia is the ability to provide continuous anesthesia or analgesia with placement of an epidural catheter, as opposed to a single dose with spinal anesthesia, although some clinicians will place a catheter in the intrathecal space. Even though the speed of onset depends on the local anesthetic agent used, spinal anesthesia and its associated autonomic effects occur sooner than when the same agent is administered epidurally. A catheter, usually left in place for epidural anesthesia, permits titration of the agent. Epidural catheters can also be used postoperatively to provide analgesia.

Extensive research has compared regional with general anesthesia for patients with CAD, particularly in those undergoing infrainguinal bypass surgery. In one meta-analysis, overall mortality was reduced by approximately one third in patients allocated to neuraxial blockade, although the findings were controversial because most of the benefit was observed in older studies. Reductions in MI and renal failure also occurred. A large-scale study of regional versus general anesthesia in noncardiac surgery patients did not demonstrate a difference in outcome.

Regional anesthesia has become very common with recent advances in ultrasound-guided administration and development of *enhanced recovery after surgery* (ERAS) protocols. Regional anesthesia offers the opportunity to provide excellent pain relief after surgery, which has proved advantageous and reduces perioperative cardiac stress.[24]

Monitored Anesthesia Care

MAC encompasses local anesthesia administered by the surgeon, with or without sedation. In a large-scale cohort study, MAC was associated with increased 30-day mortality compared with general anesthesia in a univariate analysis, although it did not remain significant in multivariate analysis once patient comorbidity was taken into account. The major issue with MAC is the ability to block the stress response adequately because the tachycardia associated with inadequate analgesia may be worse than the potential hemodynamic effects of general or regional anesthesia. Since the introduction of newer, short-acting IV agents, general anesthesia can now be administered essentially without an endotracheal tube. This approach allows the anesthesiologist to provide intense anesthesia for short or peripheral procedures without the potential effects of endotracheal intubation and extubation and therefore blurs the distinction between general anesthesia and MAC. An analysis of closed insurance claims demonstrated a high incidence of respiratory complications with MAC.

Intraoperative Hemodynamics and Myocardial Ischemia

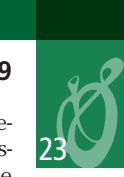
Over the last two decades, numerous studies have explored the relationship between hemodynamics and perioperative ischemia and MI. Tachycardia is the strongest predictor of perioperative ischemia. Although traditionally an HR greater than 100 beats/min defines tachycardia, slower HRs may result in myocardial ischemia. As described later, control of HR with beta blockers decreases the incidence of myocardial ischemia and infarction. In the DECREASE studies, HR control reduced the incidence of perioperative MI, with the greatest benefit achieved if HR was controlled to less than 70 beats/min. Although some are concerned about beta blockers causing intraoperative hypotension in patients with CAD, no evidence supports this contention. However, the Perioperative Ischemic Evaluation (POISE) trial demonstrated that an acute high-dose beta blockade protocol in patients naïve to beta adrenergic blockade therapy was associated with hypotension and a higher rate of stroke in the metoprolol arm.[25] During CABG, the vast majority of episodes of intraoperative ischemia are not correlated with hemodynamic changes. In the absence of tachycardia, hypotension is not associated with myocardial ischemia.

POSTOPERATIVE MANAGEMENT

Postoperative Response to Surgery

Understanding the pathophysiology of perioperative cardiac events helps in determining the best approach to preoperative testing. A full discussion of the pathophysiology of perioperative MI has been published.[26] All surgical procedures cause a stress response, although the extent of the response depends on the extent of the surgery and the use of anesthetics and analgesics to reduce the response. The stress response can increase HR and BP, which can precipitate episodes of myocardial ischemia in areas distal to coronary artery stenoses. Prolonged myocardial ischemia (either prolonged individual episodes or prolonged cumulative duration of shorter episodes) can cause myocardial necrosis and perioperative MI and death. Identification of patients at high risk for coronary artery stenosis, through either the history or cardiovascular testing, can lead to the implementation of strategies to reduce morbidity as a result of supply-demand mismatches. Recent work with highly sensitive markers of myocardial damage has shown a high rate of cardiac injury even in the absence of frank infarction. In the POISE trial, 8.3% of the patients had an elevated cardiac biomarker without other evidence of infarction, whereas 5% also had a second confirmatory marker of MI.[25]

A major mechanism of MI in the nonoperative setting is plaque rupture with subsequent coronary thrombosis (see Chapters 24 and 37). Inasmuch as the perioperative period is marked by tachycardia and a hypercoagulable state, plaque disruption and thrombosis may occur more often than appreciated. Several observations support this contention. Because noncritical stenosis can furnish the nidus for coronary artery thrombosis, preoperative cardiac evaluation may fail to identify patients at risk before surgery. The areas distal to the noncritical stenosis might not have developed collateral coronary flow, and therefore any acute thrombosis may have a greater detrimental effect than it would in a previously severely



narrowed vessel. If a prolonged increase in myocardial oxygen demand in a patient with one or more critical fixed stenoses provoked postoperative MI, preoperative testing would probably identify such a patient.

Evidence from several autopsy and postinfarction angiography studies after surgery supports both mechanisms. Ellis and colleagues demonstrated that one third of all patients sustained events in areas distal to noncritical stenoses. Dawood and associates, as cited in the guidelines, demonstrated that fatal perioperative MI occurs predominantly in patients with multivessel coronary disease, especially left main and three-vessel disease, but the severity of preexisting stenosis did not predict the infarct territory. This analysis suggested that fatal events occurred primarily in patients with advanced fixed stenoses, but that the infarct may result from plaque rupture in a mild or only moderately stenotic segment of the diseased vessel. Duvall and colleagues reviewed hospital records and coronary angiograms from patients who underwent noncardiac surgery complicated by perioperative MI from 1998 to 2006. The distribution of demand, thrombotic, and nonobstructive MI was 55%, 26%, and 19%, respectively. In contrast, Gualandro and colleagues found that almost 50% of patients with perioperative acute coronary syndromes have evidence of ruptured coronary plaque. The evidence therefore shows that several mechanisms may cause perioperative MI. That said, the incidence of type-1, plaque-rupture MI is likely much lower than feared. Wilcox and colleagues reported an all-comers risk of MI of 0.36% in more than 3 million surgeries.[13] Similarly, in the POISE trial of higher cardiovascular risk patients, only 0.04% of patients underwent coronary revascularization in the postoperative period.[25]

POSTOPERATIVE INTENSIVE CARE

Provision of intensive care by intensivists has now become a patient safety goal. Pronovost and coworkers performed a systematic review of the literature on physician staffing patterns and clinical outcomes in critically ill patients (see "Classic References"). They grouped ICU physician staffing into low-intensity (no intensivist or elective intensivist consultation) and high-intensity (mandatory intensivist consultation or closed ICU [all care directed by an intensivist]) groups. High-intensity staffing was associated with lower hospital mortality in 16 of 17 studies (94%) and with a pooled estimate of the relative risk for hospital mortality of 0.71 (95% CI, 0.62 to 0.82). High-intensity staffing was associated with lower ICU mortality in 14 of 15 studies (93%) and with a pooled estimate of the relative risk for ICU mortality of 0.61 (95% CI, 0.50 to 0.75). High-intensity staffing reduced hospital LOS in 10 of 13 studies and reduced ICU LOS in 14 of 18 studies without case-mix adjustment. High-intensity staffing was associated with reduced hospital LOS in two of four studies and lowered ICU LOS in both studies that adjusted for case mix. No study found increased LOS with high-intensity staffing after case-mix adjustment. High-intensity versus low-intensity ICU physician staffing was associated with reduced hospital and ICU mortality and LOS.

POSTOPERATIVE PAIN MANAGEMENT

Postoperative analgesia may reduce perioperative cardiac morbidity. Because postoperative tachycardia and catecholamine surges probably promote myocardial ischemia and/or rupture of coronary plaque, and because postoperative pain can produce tachycardia and increase catecholamines, effective postoperative analgesia may reduce cardiac complications. Postoperative analgesia may also reduce the hypercoagulable state. Epidural anesthesia may decrease platelet aggregability compared with general anesthesia. Whether this decrease relates to intraoperative or postoperative management is unclear. In an analysis of Medicare claims data, the use of epidural analgesia (as determined by billing codes for postoperative epidural pain management) was associated with decreased risk for death at 7 days. As previously noted, regional anesthesia may be advantageous for postoperative pain relief. Future research will focus on how best to deliver postoperative analgesia to maximize the potential benefits and reduce complications.[14]

SURVEILLANCE AND IMPLICATIONS OF PERIOPERATIVE CARDIAC COMPLICATIONS

The optimal and most cost-effective strategy for monitoring high-risk patients for major morbidity after noncardiac surgery is unknown. Myocardial ischemia and infarctions that occur postoperatively are usually silent, most likely because of the confounding effects of analgesics, postoperative surgical pain, and their hemodynamic demand mismatch origin. Intraoperative hypotension confers a fourfold increase in the risk of troponin elevation.[6] Most perioperative MIs do not cause ST-segment elevation, and less specific ST-T wave changes are common after surgery with or without MI. These considerations therefore render the diagnosis of perioperative MI particularly difficult to make.

A marked elevation in mortality associated with postoperative MI provides continuing impetus for improved methods of detection and management. Biomarkers may help identify myocardial necrosis. Lee and colleagues found that troponin T had similar efficacy as creatine kinase (CK) MB in diagnosing perioperative MI but significantly better correlation with major cardiac complications developing after acute MI. Mohler and colleagues evaluated troponin I (cTnI) and CK-MB in 784 high-risk vascular surgery patients on the day of surgery and at 24, 72, and 120 hours postoperatively. They reported a sensitivity of 51% and a specificity of 91% for the defined cardiovascular event by using a receiver operating characteristic (ROC)–defined cutoff point for CK-MB of 3.1 ng/mL.[1]

In the VISION study, 15,133 participants undergoing noncardiac surgery had troponin T measurements performed between 6 and 12 hours postoperatively and on postoperative days 1, 2, and 3.[17] Troponin T levels above the baseline level of 0.01 ng/mL or lower were associated with increased rates of 30-day mortality. Indeed, a troponin T level of 0.02 ng/mL was associated with more than a twofold risk for death. With a troponin T level of 0.3 ng/mL or higher, the hazard ratio (HR) for death increased to more than 10-fold above that in patients without any elevation in troponin. Mortality was 16.9% with a troponin T level of 0.3 ng/mL or higher, versus 1% in the group without troponin elevation. Although troponin T levels stratified the rate of mortality across a low spectrum of positive levels, it could not predict the cause of death. Both vascular and nonvascular death increased similarly with increasing troponin T levels, and more than half of all deaths were from nonvascular causes. An elevated troponin T level thus provides adverse prognostication without direction for appropriate therapy.

Three important points can be made from these data. First, noncardiovascular causes of mortality now outnumber cardiovascular causes, indicating important new areas for research. Second, even if there is evidence of troponin elevation, death is remote from the event, suggesting that troponin elevation is not causally related to an immediate event but is a marker of illness and clinical instability. Third, true type 1 MI is rare. In the POISE trial, 7521 participants were screened to find 697 (9.2%) with troponin elevations, but only two individuals of the total cohort were referred for coronary revascularization.[1] In our opinion, troponin measurement should be avoided in the asymptomatic patient without hemodynamic embarrassment or ischemic ECG change. Troponin elevations in this setting provide neither diagnostic direction nor specific management to implement. Should future trials identify management strategies for troponin elevations, we would reconsider routine troponin measurement in high-risk patients.

Evidence for the first step toward a management plan for elevations in troponin after operation is provided by the MANAGE trial[27] which randomly assigned 1754 postoperative noncardiac surgery patients with an elevated troponin level to dabigatran 110 mg BID or placebo. The dabigatran-treated patients had fewer of the primary composite outcome events (vascular mortality and non-fatal MI, non-hemorrhagic stroke, peripheral arterial thrombosis, amputation, and symptomatic venous thromboembolism). The study enrolled slowly, so the investigators reduced the sample size by 45% and expanded the primary outcome. Nearly half the patients discontinued the study drug. Moreover, there was a significant increase in important bleeding, even if criteria for major bleeding (>4 g/dL decline in hemoglobin or ≥3 units of red blood cell transfusion) weren't met. The study raises the possibility of benefit for treatment of patients identified by postoperative troponin elevations, but additional investigation is required before a recommendation can be made.[27]

Several studies have evaluated BNP in the postoperative period showing the impact of markers of increased volume. A meta-analysis showed that the addition of postoperative BNP measurements to a risk prediction model of 30-day death and MI had a net reclassification

index of 20%.[28] Moreover, elevated postoperative BNP increased the rate of death and MI by 3.7-fold.

Traditionally, perioperative MI has been associated with 30% to 50% short-term mortality, but recent series have reported a fatality rate of less than 20% for perioperative MI. Studies from the 1980s suggested a peak incidence on the second and third postoperative days. Puelacher and colleagues, using troponin T as a marker for MI in high-cardiac-risk patients, suggested that the highest incidence occurred during the immediate postoperative days,[29] as confirmed in other studies. The finding that tachycardia, hypotension, and hypertension in the operative suite predicted release of troponin suggests a hemodynamic consequence rather than plaque rupture event (type 2 vs. type 1 MI).[16] Further, acute surgical anemia, expressed as a greater than 35% drop on preoperative hemoglobin, increases major acute coronary morbidity.[1] Thus the change is probably related to more robust surveillance methods, not to a fundamental shift in how or when myocardial ischemia or infarction occurs.

Increasing evidence has associated perioperative MI or biomarker elevation with worse long-term outcome. Oberweis and colleagues[30] studied 3050 patients who underwent orthopedic surgery. Of the 179 in whom myocardial necrosis occurred, mortality was 16.8% in patients with biomarker elevation at a mean follow-up of 3 years compared to 5.8% in patients without elevation. Landesberg and coworkers, as cited in the guidelines, demonstrated that postoperative CK-MB and troponin, even at low cutoff levels, are independent and complementary predictors of long-term mortality after major vascular surgery. Mahla and colleagues have also shown that elevations in BNP are associated with a fivefold increased long-term risk for cardiac events. The appropriate use of screening biomarkers in current preoperative risk assessment algorithms remains unstudied because there is no evidence-based intervention to apply in response to a biomarker elevation.

STRATEGIES TO REDUCE THE RISK ASSOCIATED WITH NONCARDIAC SURGERY

Coronary Artery Revascularization

The treatment of patients before noncardiac surgery should follow the same trajectory as in the absence of impending surgery. As such, it should be noted that the recently completed International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) trial showed that coronary revascularization in patients with moderate or severe stable CAD neither reduces MI nor death in patients with or without advanced kidney disease.[31] Indeed, over optimum medical treatment, coronary revascularization in stable patients has limited value.[1] Despite this evidence and recent data that the postoperative incidence of type 1 MI requiring revascularization is 0.3% to 0.5%, some have suggested coronary revascularization as a means of reducing the perioperative risk related to noncardiac surgery.[32] This view is derived from retrospective evidence of patients who survived initial surgery in the Coronary Artery Surgery Study (CASS) registry, which enrolled patients from 1978 to 1981, an era that antedates almost all the current therapies shown to be effective for reducing coronary events. This observational analysis did not randomly assign patients, however, and reflects a different era in preventive strategies and higher rates of adverse outcomes after noncardiac surgery.

Several cohort studies have examined the benefit of percutaneous coronary intervention (PCI) before noncardiac surgery. Posner and colleagues, as cited in the guidelines, used an administrative dataset of patients who underwent PCI and noncardiac surgery.[1] They matched patients with coronary disease undergoing noncardiac surgery with and without previous PCI and examined cardiac complications. In this nonrandomized analysis, they noted a significantly lower rate of 30-day cardiac complications in patients who underwent PCI at least 90 days before the noncardiac surgery. PCI within 90 days of noncardiac surgery did not improve outcomes. The advent of drug-eluting stents requiring prolonged antiplatelet therapy may promote operative bleeding complications or increase subacute stent thrombosis if antiplatelet treatment is stopped perioperatively.

Several randomized trials have now addressed the value of both CABG and PCI in a subset of patients. McFalls and coauthors reported the results of a multicenter randomized trial in the Veterans Affairs Health System in which patients with documented CAD on coronary angiography, excluding those with left main CAD or a severely depressed ejection fraction (≤20%), were randomly assigned before elective major vascular surgery to CABG (59%) or PCI (41%) versus routine medical therapy.[1] At 2.7 years after randomization, mortality in the revascularization group did not differ significantly (22%) from that in the no-revascularization group (23%). Within 30 days after the vascular operation, postoperative MI, defined as elevated troponin levels, occurred in 12% of the revascularization group and in 14% of the no-revascularization group ($P = 0.37$). The authors suggested that coronary revascularization is not indicated in patients with stable CAD and that PCI or CABG for one- or two-vessel disease before noncardiac surgery does not prevent perioperative MI. A reanalysis of the data found that the completeness of revascularization affects the rate of perioperative MI, with CABG being more effective than PCI. Similarly, Garcia and colleagues analyzed both randomly and nonrandomly assigned patients who underwent coronary angiography before vascular surgery in the CARP trial registry; 4.6% of these patients had unprotected left main CAD. Only this subset of patients showed a benefit of preoperative coronary artery revascularization.

Monaco and associates studied 208 patients at moderate clinical risk who underwent major vascular surgery and were randomly allocated to either a "selective strategy" group, in whom coronary angiography was performed on the basis of noninvasive test results, or to a "systematic strategy" group, in whom preoperative coronary angiography was systematically performed. The strategy of routine coronary angiography had no effect on the short-term outcome, but the long-term outcome was improved in surgical patients with peripheral arterial disease at medium to high risk.

One issue in interpreting the results is that the length of time between coronary revascularization and noncardiac surgery most likely affects its protective effect and potential risks. Back and colleagues studied 425 consecutive patients undergoing 481 elective major vascular operations at an academic Veterans Affairs Medical Center. Coronary revascularization was classified as "recent" (CABG, <1 year; percutaneous transluminal coronary angioplasty [PTCA], <6 months) in 35 cases, as "previous" (CABG, 1 to 5 years; PTCA, 6 months to 2 years) in 45 cases, and as "remote" (CABG, >5 years; PTCA, >2 years) in 48 cases. Patients with previous PTCA had similar outcomes as those after CABG. Significant differences in adverse cardiac events and mortality were found between patients with CABG performed within 5 years or PTCA within 2 years (6.3% and 1.3%, respectively), individuals with remote revascularization (10.4% and 6.3%, respectively), and nonrevascularized patients stratified at high risk (13.3% and 3.3%, respectively) or intermediate to low risk (2.8% and 0.9%, respectively). The authors concluded that previous coronary revascularization (CABG, <5 years; PTCA, <2 years) provides only modest protection against adverse cardiac events and mortality following major arterial reconstruction.

In our opinion, the randomized controlled trials provide strong evidence of limited to no benefit of preoperative coronary artery revascularization to reduce cardiovascular risk. In the absence of unusual circumstances, percutaneous and surgical revascularization should not be pursued before noncardiac surgery.

Percutaneous Coronary Intervention and Noncardiac Surgery

PCI using coronary stenting poses several special issues (see Chapter 41).[4] Kaluza and colleagues reported the outcome of 40 patients who underwent prophylactic coronary stent placement less than 6 weeks before major noncardiac surgery requiring general anesthesia. They reported seven MIs, 11 major bleeding episodes, and eight deaths. All the deaths and MIs, as well as 8 of the 11 bleeding episodes, occurred in patients subjected to surgery less than 14 days after stenting. Four patients died after undergoing surgery 1 day after stenting. Wilson and colleagues, as cited in the guidelines, reported on 207 patients in whom noncardiac surgery was performed within 2 months of stent placement. Eight patients died or had an MI, and all of them were among

the 168 patients who underwent surgery 6 weeks after stent placement. Vincenzi and coworkers studied 103 patients and reported that the risk for a perioperative cardiac event was 2.11-fold greater in patients with recent stents (<35 days before surgery) than in those undergoing PCI more than 90 days before surgery. These data point to the importance of delaying surgery after stenting, even though the investigators either continued antiplatelet drug therapy or only briefly interrupted it, and all patients received heparin.

Drug-eluting stents may represent an even greater problem during the perioperative period. Emerging data from a series of recent analyses in the nonoperative setting and several perioperative case reports suggest that the risk for thrombosis continues for at least 1 year after insertion. Several reports suggest that drug-eluting stents may represent an additional risk over a prolonged period (up to 12 months), particularly if the use of antiplatelet agents is discontinued.

Schouten retrospectively evaluated 192 patients who underwent noncardiac surgery after successful PCI for unstable CAD within 2 years of the procedure. Drug-eluting stents accounted for 52% of the stents placed. Of the 192 patients, 30 underwent surgery before the recommended discontinuation of dual-antiplatelet therapy for the particular stent (30 days for bare-metal stents and up to 6 months for sirolimus-eluting stents). In patients in whom antiplatelet therapy was stopped before the required time for use of clopidogrel (early-surgery group), the incidence of death or nonfatal MI was 30.7% compared with 0% in patients who continued antiplatelet therapy. The elevated risk for stent thrombosis and cardiovascular events, however, seems to abate over time. In the Evaluation of Drug-Eluting Stents and Ischemic Events (EVENT) registry of 4637 consecutive patients, 4.4% underwent major noncardiac surgery in the ensuing year. A relative 27-fold increased rate of cardiovascular events occurred in the week after surgery versus any other week after stent implantation, but the absolute rate was only 1.9%.

Wijeysundera and colleagues evaluated 8116 patients who underwent noncardiac surgery in Ontario, Canada, and found that 34% had a coronary stent implanted within the 2 years before surgery.[1] Drug-eluting stents represented one third of the stents placed. Patients with bare-metal stents implanted less than 45 days before surgery had a 6.7% cardiovascular event rate, which dropped to 2.6% with a stent implanted 45 to 180 days before surgery. Patients with a drug-eluting stent had a 20.2% cardiovascular event rate in the first 45 days after stent implantation, and the rate became similar to that in patients without stenting when the stent was implanted more than 180 days before surgery. Bangalore and colleagues studied the impact of drug-eluting stents compared with bare-metal stents placed preoperatively in 8415 patients in Massachusetts.[33] In this cohort the death, MI, and bleeding event rate was 8.6% in the first 30 days after PCI, dropping to 5.2% when surgery was performed more than 90 days after coronary revascularization. Using propensity matching to compare the bare-metal stent and drug-eluting stent populations, the death and MI rate was higher in the bare-metal stent cohort.

In a Scotland-wide retrospective cohort analysis, perioperative death and ischemic cardiac events were much more common within the first 6 weeks after stent implantation than after 6 weeks, 42.4% versus 12.8%, respectively.[1] Forty-five percent of the revascularizations in this cohort were performed for an acute coronary syndrome, increasing the baseline risk of the cohort. The event rate was higher in patients who underwent revascularization because of acute coronary syndromes within 6 weeks, in whom it reached 65%. In contrast to other reports, no temporal differences were noted between the bare-metal and drug-eluting stent groups.

Data from more recent large observational studies suggest that the time frame of increased risk of stent thrombosis is on the order of 6 months, regardless of stent type (bare metal or drug eluting). In a large cohort of patients from the Veterans Health Administration hospitals, the increased risk of surgery for the 6 months after stent placement was most pronounced in patients in whom the indication for PCI was an MI.[1]

In 2016, ACC/AHA published a focused update on duration of dual-antiplatelet therapy in CAD patients, including revising the perioperative guidelines.[4] The current recommendations for delay after coronary stent placement include 30 days for bare-metal stent implantation and 6 months after drug-eluting stent placement (Fig. 23.3). The guidelines writing committee noted that elective noncardiac surgery may be considered more than 180 days after drug-eluting stent implantation if the risk of delay is thought to be greater than the risk of stent thrombosis. The guideline committee gave a class IIb recommendation that elective surgery may be considered after 3 months for patients in whom the P2Y12 inhibitor needs to be discontinued if further delay of surgery is greater than the risk of stent thrombosis. In patients with illness requiring more timely surgery, strategies for bridging the cessation of antiplatelet therapy until the procedure include the use of IV eptifibatide and tirofiban, but these strategies lack outcomes data.

Pharmacologic Interventions

Beta-Adrenergic Blocking Agents

Beta-adrenergic blocking agents have undergone extensive study in perioperative risk management. As noted earlier, some of the trial data used to support recent recommendations on the titrated use of beta blockers from Poldermans and colleagues have become uncertain. A recent meta-analysis of all the beta blocker trials demonstrates that beta blockers decrease nonfatal MI but increase stroke and death.[34] As a result, ACC/AHA guidelines[1] suggest that perioperative beta blockers can be considered on a case-by-case basis in patients with significant myocardial ischemia, three or more RCRI risk factors, or a compelling long-term indication for beta blockers. Aggregate impact of beta blockers seems to be low. Of the more than 10,000 participants in the trials, 75 nonfatal MIs were prevented and 19 strokes and 35 deaths instigated (Table 23.4).

Most of these trials did not titrate beta blockers in the same manner as they are used in other conditions, such as HF or hypertension. For example, in the POISE trial, Devereaux and colleagues randomly assigned 8351 high-risk patients undergoing noncardiac surgery to metoprolol succinate, 200 mg daily, or matching placebo.[25] The use of high-dose, long-acting medications may have worsened outcomes by limiting the physician's flexibility to modify treatment on the basis of the rapidly shifting perioperative environment. Other trials used lower doses without titration to hemodynamic parameters as well. Administration of beta blockers as performed in the clinical trials clearly does not provide a benefit sufficient for their routine use.

Current guidelines suggest that beta blockade may be reasonable in patients with intermediate- or high-risk myocardial ischemia reported in preoperative noninvasive testing or patients with three or more RCRI risk factors, although there is no direct evidence to support routine use even in this higher-risk population.[1] If beta blockers are to be used, it is recommended that initiation begin 1 day or more before surgery. Initiation on the day of surgery has been associated with an increase in stroke and mortality.[1] In hospital, short-acting oral or IV beta blockers should be used to permit titration to hemodynamics. No specific BP or HR targets have been validated, although BP control to less than 140/90 mm Hg and HRs of 60 to 80 beats/min may be reasonable when beta blockers are used.

Statin Therapy

Statins are routinely recommended for patients with atherosclerosis and diabetes (see Chapters 25 and 27). Their role in patients undergoing noncardiac surgery is less well defined. In a retrospective analysis of 750 patients, 10% of whom had the composite outcome (30-day death, MI, and AF), statin use was associated with a 45% reduction in adverse events, including a 5% absolute reduction in 30-day mortality. In addition to their cholesterol-lowering properties, statins have anti-inflammatory actions that may provide benefit as well. In an NSQIP study of 7777 patients undergoing various surgeries, statin use was associated with reductions in noncardiac events, including a 47% reduction in respiratory complications, 59% reduction in VTE, and 35% reduction in infectious complications.[35] The evidence suggests that statin therapy should be continued during the perioperative period. Le Manach and associates evaluated the effect of statin discontinuation in a vascular surgery population. When compared with a control population, discontinuation of statins was associated with more than a twofold increase

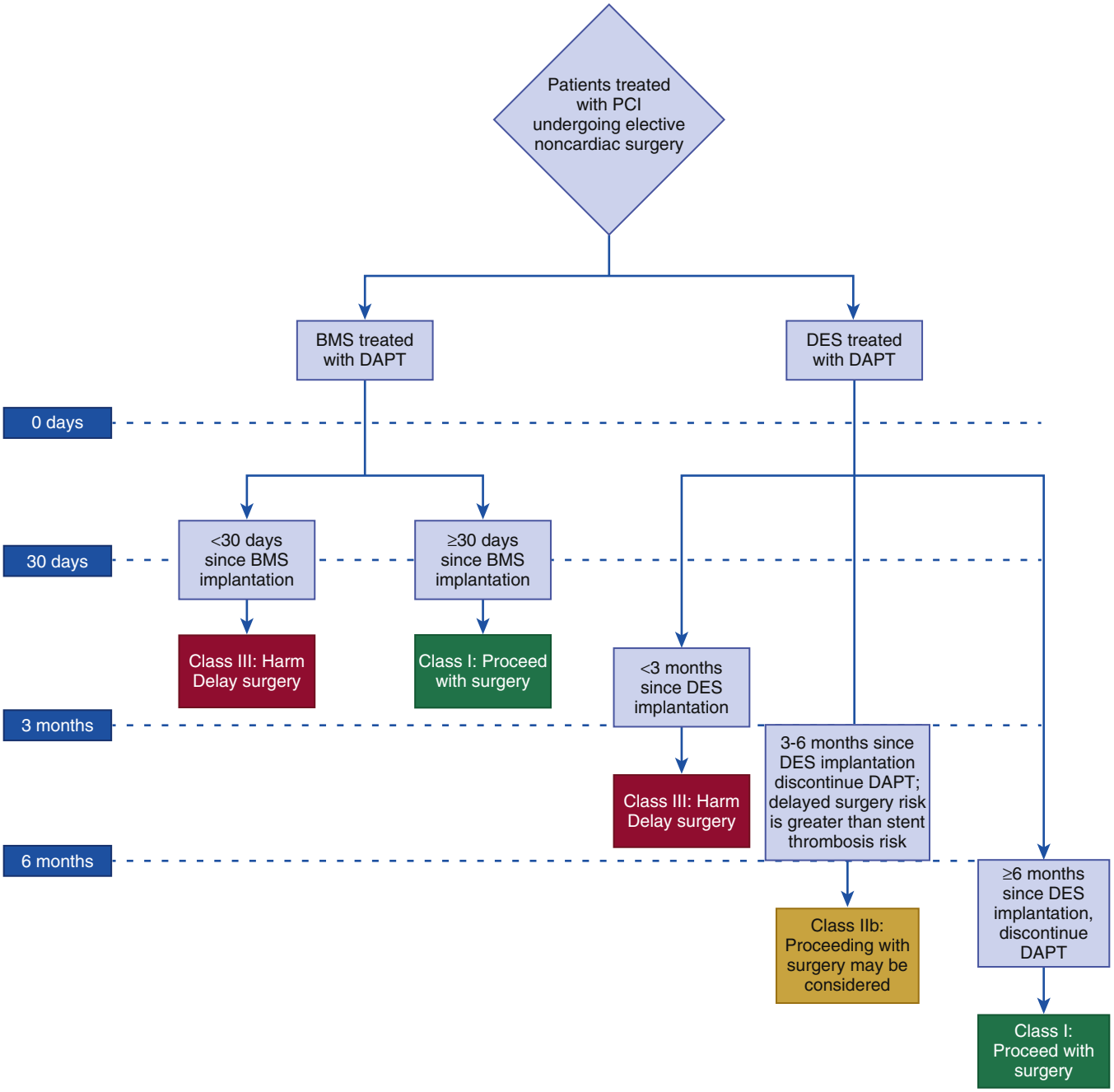


FIGURE 23.3 Treatment algorithm for patients with coronary stents undergoing noncardiac surgery. *BMS,* Bare metal stent; *DAPT,* dual-antiplatelet therapy; *DES,* drug-eluting stent; *PCI,* percutaneous coronary intervention. (From Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2016;68:1082–1115.)

in troponin elevation, whereas continuation reduced the rate of troponin release by more than 40%. In patients already receiving statins, a prospective randomized trial of 500 patients with stable CAD about to undergo emergency surgery randomly received placebo or atorvastatin (80 mg) 2 hours before surgery. In the group who received the statin, cardiac death, MI, or unplanned revascularization occurred in 2.4% of patients compared with 8% in the placebo arm.[36] Indeed, starting statin therapy should be considered in patients who meet ACC/AHA lipid guideline recommendations and in cardiovascular high-risk patients, because they merit this treatment even without surgery.

Other Therapies

POISE 2, a blind randomized trial with a 2 × 2 factorial design, allowed separate evaluation of low-dose clonidine versus placebo and low-dose aspirin versus placebo in 10,010 patients with, or at risk for, atherosclerotic disease who were undergoing noncardiac surgery.[37] Low-dose clonidine did not reduce the rate of death or nonfatal MI but was associated with an increased risk of clinically important hypotension and nonfatal cardiac arrest. Administration of aspirin was not associated with any difference in the rate of death or nonfatal MI but increased the risk of major bleeding.[38]

Two small, randomized trials have evaluated the potential protective effect of prophylactic nitroglycerin in reducing perioperative cardiac complications after noncardiac surgery. Neither established a benefit for the prophylactic use of nitroglycerin. Because prophylactic nitroglycerin has considerable hemodynamic effects and is not known to prevent MI or cardiac death, the data do not support its routine use.

As described above, the MANAGE trial has a 2 × 2 factorial design testing the efficacy of dabigatran and omeprazole in patients undergoing noncardiac surgery who develop an elevated troponin or

TABLE 23.4 Recommendations for Perioperative Therapy with Beta Blockers

Class I
• Continue beta blockers in patients who are receiving beta blockers chronically.
Class IIa
• Guide management of beta blockers after surgery by clinical circumstances.
Class IIb
• In patients with intermediate- or high-risk preoperative tests, it may be reasonable to begin beta blockers.
• In patients with ≥3 Revised Cardiac Risk Index (RCRI) factors, it may be reasonable to begin beta blockers before surgery.
• Initiating beta blockers in the perioperative setting as an approach to reduce perioperative risk is of uncertain benefit in those with a long-term indication but no other RCRI risk factors.*
• It may be reasonable to begin perioperative beta blockers long enough in advance to assess safety and tolerability, preferably >1 day before surgery.
Class III
• Beta blocker therapy should not be started on the day of surgery.

*Clinical risk factors include a history of ischemic heart disease, history of compensated or previous heart failure, history of cerebrovascular disease, diabetes mellitus, and renal insufficiency (defined in the RCRI as a preoperative serum creatinine level of 2 mg/dL).

From Fleisher LA, Beckman JA, Brown KA, 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. *J Am Coll Cardiol*. 2014;64:e77–e137.

CK-MB level with evidence of an ischemic event or no alternative explanation for biomarker elevation.[27] Although a benefit was noted with therapy, the incomplete follow up, change in endpoint, and high discontinuation rate render recommendation of dabigatran in this setting difficult.

NONPHARMACOLOGIC INTERVENTIONS

Temperature

Frank and colleagues, as cited in the guidelines, completed a randomized trial of regional versus general anesthesia for lower extremity vascular bypass procedures and noted an association between hypothermia (temperature <35°C) and myocardial ischemia. They subsequently performed a trial in 300 high-risk patients undergoing a diverse range of intermediate- and high-risk procedures and randomly assigned to maintenance of normothermia or routine care. They observed a significantly reduced incidence of perioperative cardiac morbidity and mortality within 24 hours of surgery in the normothermic group.

Electrocardiographic, Hemodynamic, and Echocardiographic Monitoring

Multiple studies have demonstrated the predictive value of correlating perioperative ST-segment changes and major cardiac events, as described earlier. Furthermore, the duration (cumulative or continuous) of perioperative ST changes strongly predicts poor outcomes. ST-segment monitoring has therefore become standard during the intraoperative and ICU periods for high-risk patients. However, ST-segment changes may also develop in patients at low to moderate risk. These changes may not reflect true myocardial ischemia, as suggested in a recent series.

Postoperative patients may have the greatest risk for a cardiac event when on the ward and unmonitored. Few studies have tested the efficacy of ST-segment telemetric monitoring during the perioperative period. The issue of whether early treatment of prolonged ST-segment changes improves outcomes in this situation remains unresolved.

Much controversy surrounds the value of pulmonary artery (PA) catheterization for noncardiac surgery. Several small, randomized trials did not demonstrate a significant reduction in major cardiac morbidity and mortality in patients so monitored during aortic surgery. In a large-scale cohort study, Polanczyk and colleagues found that patients with PA catheters who were matched to those without catheters by a propensity score also failed to demonstrate significant benefit (see "Classic References"). In fact, they observed an increased incidence of congestive HF and untoward noncardiac outcomes in the catheter group. A total of 1994 patients were randomly allocated to goal-directed therapy guided by a PA catheter or to standard care without the use of a PA catheter in patients undergoing urgent or elective major surgery. No difference in survival occurred, but pulmonary embolism developed at a higher rate in the catheter group than in the standard-care group. Current evidence therefore does not support the routine use of PA catheterization for high-risk patients undergoing major noncardiac surgery. Determining whether these results apply to the high-risk vascular surgical population and whether use of a PA catheter provides benefit in specific clinical situations will require further work.

Transesophageal echocardiography (TEE) represents another means of assessing intraoperative cardiac function (see Chapter 16). This tool sensitively monitors intraoperative wall motion abnormalities and fluid status. In patients undergoing aortic cross-clamping, TEE showed significantly better sensitivity in detecting intraoperative ischemia than electrocardiographic monitoring. For noncardiac surgery, a study of TEE, 2-lead electrocardiography, and 12-lead electrocardiography demonstrated minimal additive value of TEE over 2-lead electrocardiography. TEE monitoring may nonetheless prove valuable in guiding treatment in patients with unstable hemodynamics who have uncertain fluid status and myocardial function.

Transfusion Threshold

Much controversy surrounds the optimal hemoglobin level at which transfusion is indicated in high-risk noncardiac surgical patients. No randomized trials have evaluated the optimal transfusion threshold, although much anecdotal evidence exists. A large-scale trial of transfusion triggers in the ICU did not document increased morbidity or mortality when a hemoglobin concentration lower than 7 g/dL was used as a transfusion threshold, but trends toward increased morbidity emerged in the subset of patients with ischemic heart disease. In the FOCUS (Transfusion Trigger Trial for Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair) trial, Carson and colleagues randomly assigned hip fracture patients to a liberal transfusion strategy (hemoglobin threshold of 10 g/dL) or a restrictive transfusion strategy (symptoms of anemia or at physician's discretion for hemoglobin level <8 g/dL).[1] A liberal transfusion strategy, compared with a restrictive strategy, did not reduce rates of death or inability to walk independently on 60-day follow-up and did not reduce in-hospital morbidity in elderly patients at high cardiovascular risk. The impact of transfusion may depend on the severity of the precipitating anemia. Smilowitz and coworkers followed 3050 patients after orthopedic surgery.[39] In this cohort the presence of anemia, hemorrhage, and transfusion were independently associated with long-term mortality. Interestingly, the effect of transfusion was attenuated by the severity of anemia. For patients with no anemia, transfusion increased the HR 4.4-fold; for those with mild anemia, HR was only 2.3-fold; and for those with moderate/severe anemia (hemoglobin <11 g/dL), there was benefit, with HR of 0.81. These data suggest a restrictive policy of transfusion may be the most beneficial for patients undergoing noncardiac surgery.

CONCLUSION

Three trends are notable in the perioperative management of patients undergoing noncardiac surgery: (1) the rate of MI and cardiovascular death are declining; (2) noncardiovascular death now accounts for the majority of perioperative mortality; and (3) the evidence base supporting current management practices continues to grow rapidly. As overall mortality risk declines over time, the future goal of preoperative assessment will be to identify patients at clinically inapparent increased risk and devise and test interventions to reduce this risk. Additionally, preoperative risk assessment will increasingly serve to determine if the long-term benefits of surgery outweigh the perioperative risks. The predictive value of biomarkers and treatment of biomarker elevations, novel medications, and presurgical rehabilitation (prehabilitation) are currently under investigation and may represent the next frontier in perioperative management.

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