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ACC/AHA GUIDELINE

ACC/AHA 2007 Guidelines on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery)

Developed in Collaboration With the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, and Society for Vascular Surgery

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Preamble

It is important that the medical profession play a significant role in critically evaluating the use of diagnostic procedures and therapies as they are introduced and tested in the detection, management, or prevention of disease states. Rigorous and expert analysis of the available data documenting absolute and relative benefits and risks of those procedures and therapies can produce helpful guidelines that improve the effectiveness of care, optimize patient outcomes, and favorably affect the overall cost of care by focusing resources on the most effective strategies.

The American College of Cardiology (ACC) Foundation and the American Heart Association (AHA) have jointly engaged in the production of such guidelines in the area of cardiovascular disease since 1980. The ACC/AHA Task Force on Practice Guidelines, whose charge is to develop, update, or revise practice guidelines for important cardiovascular diseases and procedures, directs this effort. Writing committees are charged with the task of performing an assessment of the evidence and acting as an independent group of authors to develop, update, or revise written recommendations for clinical practice.

Experts in the subject under consideration have been selected from both organizations to examine subject-specific data and write guidelines. The process includes additional representatives from other medical practitioner and specialty groups when appropriate. Writing committees are specifically charged to perform a formal literature review, weigh the strength of evidence for or against a particular treatment or procedure, and include estimates of expected health outcomes where data exist. Patient-specific modifiers, comorbidities, and issues of patient preference that may influence the choice of particular tests or therapies are considered, as well as frequency of follow-up and cost-effectiveness. When available, information from studies on cost will be considered; however, review of data on efficacy and clinical outcomes will constitute the primary basis for preparing recommendations in these guidelines.

The ACC/AHA Task Force on Practice Guidelines makes every effort to avoid any actual, potential, or perceived conflicts of interest that may arise as a result of an industry relationship or personal interest of the writing committee. Specifically, all members of the writing committee, as well as peer reviewers of the document, were asked to provide disclosure statements of all such relationships that may be perceived as real or potential conflicts of interest. Writing committee members are also strongly encouraged to declare a previous relationship with industry that may be perceived as relevant to guideline development. If a writing committee member develops a new relationship with industry during their tenure, they are required to notify guideline staff in writing. The continued participation of the writing committee member will be reviewed. These statements are reviewed by the parent task force, reported orally to all members of the writing committee at each meeting, and updated and reviewed by the writing committee as changes occur. Please refer to the methodology manual for ACC/AHA guideline writing committees, available on the ACC and AHA World Wide Web sites (http://www.acc.org/qualityandscience/clinical/manual/manual_I.htm and http://circ.ahajournals.org/manual/), for further description of the policy on relationships with industry. Please see Appendix I for author relationships with industry and Appendix II for peer reviewer relationships with industry that are pertinent to these guidelines.

These practice guidelines are intended to assist healthcare providers in clinical decision making by describing a range of generally acceptable approaches for the diagnosis, management, and prevention of specific diseases or conditions. These guidelines attempt to define practices that meet the needs of most patients in most circumstances. Clinical decision making should consider the quality and availability of expertise in the area where care is provided. These guideline recommendations reflect a consensus of expert opinion after a thorough review of the available, current scientific evidence and are intended to improve patient care.

Patient adherence to prescribed and agreed on medical regimens and lifestyles is an important aspect of treatment. Prescribed courses of treatment in accordance with these recommendations will only be effective if they are followed. Because lack of patient understanding and adherence may adversely affect treatment outcomes, physicians and other healthcare providers should make every effort to engage the patient in active participation with prescribed medical regimens and lifestyles.

If these guidelines are used as the basis for regulatory or payer decisions, the ultimate goal is quality of care and serving the patient's best interests. The ultimate judgment regarding care of a particular patient must be made by the healthcare provider and the patient in light of all of the circumstances presented by that patient. There are circumstances in which deviations from these guidelines are appropriate.

The guidelines will be reviewed annually by the ACC/AHA Task Force on Practice Guidelines and will be considered current unless they are updated, revised, or sunsetted and withdrawn from distribution. The executive summary and recommendations are published in the October 23, 2007, issue of the *Journal of the American College of Cardiology* and October 23, 2007, issue of *Circulation*. The full text-guidelines are e-published in the same issue of the journals noted above, as well as posted on the ACC (www.acc.org) and AHA (www.americanheart.org) Web sites. Copies of the full text and the executive summary are available from both organizations.

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1. Definition of the Problem

1.1. Purpose of These Guidelines

These guidelines are intended for physicians and nonphysician caregivers who are involved in the preoperative, operative, and postoperative care of patients undergoing noncardiac surgery. They provide a framework for considering cardiac risk of noncardiac surgery in a variety of patient and surgical situations. The writing committee that prepared these guidelines strove to incorporate what is currently known about perioperative risk and how this knowledge can be used in the individual patient.

The tables and algorithms provide quick references for decision making. The overriding theme of this document is that intervention is rarely necessary to simply lower the risk of surgery unless such intervention is indicated irrespective of the preoperative context. The purpose of preoperative evaluation is not to give medical clearance but rather to perform an evaluation of the patient's current medical status; make recommendations concerning the evaluation, management, and risk of cardiac problems over the entire perioperative period; and provide a clinical risk profile that the patient, primary physician, and nonphysician caregivers, anesthesiologist, and surgeon can use in making treatment decisions that may influence short- and long-term cardiac outcomes. No test should be performed unless it is likely to influence patient treatment. The goal of the consultation is the optimal care of the patient.

1.2. Methodology and Evidence

The ACC/AHA Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery conducted a comprehensive review of the literature relevant to perioperative cardiac evaluation published since the last publication of these guidelines in 2002. Literature searches were conducted in the following databases: PubMed, MEDLINE, and the Cochrane Library (including the Cochrane Database of Systematic Reviews and the Cochrane Controlled Trials Register). Searches were limited to the English language, the years 2002 through 2007, and human subjects. Related-article searches were conducted in MEDLINE to find additional relevant articles. Finally, committee members recommended applicable articles outside the scope of the formal searches.

Major search topics included perioperative risk, cardiac risk, noncardiac surgery, intraoperative risk, postoperative risk, risk stratification, cardiac complication, cardiac evaluation, perioperative care, preoperative evaluation, preoperative assessment, and intraoperative complications. Additional searches cross-referenced these topics with the following subtopics: troponin, myocardial infarction (MI), myocardial ischemia, Duke activity status index, functional capacity, dobutamine, adenosine, venous thrombosis, thromboembolism, warfarin, percutaneous transluminal coronary angioplasty (PTCA), stent, adrenergic beta agonists, echocardiography, anticoagulant, beta blocker, coronary artery bypass surgery, valve, diabetes mellitus, wound infection, blood sugar control, normothermia, body temperature changes, body temperature regulation, hypertension, pulmonary hypertension, anemia, aspirin, arrhythmia, implantable defibrillator, artificial pacemaker, pulmonary artery catheters, Swan-Ganz catheter, and platelet aggregation inhibitors.

As a result of these searches, more than 400 relevant, new articles were identified and reviewed by the committee for the revision of these guidelines. Using evidence-based methodologies developed by the ACC/AHA Task Force on Practice Guidelines, the committee revised the guidelines text and recommendations.

All of the recommendations in this guideline revision were converted from the tabular format used in the 2002 guidelines to a listing of recommendations that has been written in full sentences to express a complete thought, such that a recommendation, even if separated and presented apart from the rest of the document, would still convey the full intent of the recommendation. It is hoped that this will increase the reader's comprehension of the guidelines. Also, the level of evidence, either an A, B, or C, for each recommendation is now provided.

The schema for classification of recommendations and level of evidence are summarized in Table 1, which also illustrates how the grading system provides an estimate of the size of treatment effect and an estimate of the certainty of the treatment effect.

1.3. Epidemiology

The prevalence of cardiovascular disease increases with age, and it is estimated that the number of persons older than 65 years in the United States will increase 25% to 35% over the next 30 years (1). Coincidentally, this is the same age group in which the largest number of surgical procedures is performed (2). Thus, it is conceivable that the number of noncardiac surgical procedures performed in older persons will increase from the current 6 million to nearly 12 million per year, and nearly one fourth of these—major intraabdominal, thoracic, vascular, and orthopedic procedures—have been associated with significant perioperative cardiovascular morbidity and mortality.

1.4. Practice Patterns

There are few reliable data available regarding 1) how often a family physician, general internist, physician extender, specialist, or surgeon performs a preoperative evaluation on his or her own patient without a formal cardiovascular consultation and 2) how often a formal preoperative consultation is requested from either a generalist or a subspecialist such as a cardiologist for different types of surgical procedures and different categories of patients. The actual patterns of practice with regard to the practitioner performing the evaluation and utilization of testing varies widely, suggesting the need to determine which practices lead to the best clinical and economic outcomes (3). There is an important need to determine the relative cost-effectiveness of different strategies of perioperative evaluation. In many institutions, patients are evaluated in an anesthesia preoperative evaluation setting. If sufficient information about the patient's cardiovascular status is available, the symptoms are stable, and further evaluation will not influence perioperative management, a formal consultation may not be required or obtained. This is

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Table 1. Applying classification of recommendations and level of evidence.

"Estimate of Certainty (Precision) of Treatment Effect"	"Size of Treatment Effect"			
	Class I ***Benefit >>> Risk*** **Procedure/Treatment SHOULD be performed/administered**	**Class IIa** ***Benefit >> Risk*** ***Additional studies with focused objectives needed*** **IT IS REASONABLE to perform procedure/administer treatment**	**Class IIb** ***Benefit ≥ Risk*** ***Additional studies with broad objectives needed; Additional registry data would be helpful*** **Procedure/Treatment MAY BE CONSIDERED**	**Class III** ***Risk ≥ Benefit*** ***No additional studies needed*** **Procedure/Treatment should NOT be performed/administered SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL**
Level A *Multiple (3-5) population risk strata evaluated** *General consistency of direction and magnitude of effect*	• Recommendation that procedure or treatment is useful/effective • Sufficient evidence from multiple randomized trials or meta-analyses	• Recommendation in favor of treatment or procedure being useful/effective • Some conflicting evidence from multiple randomized trials or meta-analyses	• Recommendation's usefulness/efficacy less well established • Greater conflicting evidence from multiple randomized trials or meta-analyses	• Recommendation that procedure or treatment not useful/effective and may be harmful • Sufficient evidence from multiple randomized trials or meta-analyses
Level B *Limited (2-3) population risk strata evaluated**	• Recommendation that procedure or treatment is useful/effective • Limited evidence from single randomized trial or non-randomized studies	• Recommendation in favor of treatment or procedure being useful/ effective • Some conflicting evidence from single randomized trial or non-randomized studies	• Recommendation's usefulness/efficacy less well established • Greater conflicting evidence from single randomized trial or non-randomized studies	• Recommendation that procedure or treatment not useful/effective and may be harmful • Limited evidence from single randomized trial or non-randomized studies
Level C *Very limited (1-2) population risk strata evaluated**	• Recommendation that procedure or treatment is useful/effective • Only expert opinion, case studies, or standard-of-care	• Recommendation in favor of treatment or procedure being useful/ effective • Only diverging expert opinion, case studies, or standard-of-care	• Recommendation's usefulness/efficacy less well established • Only diverging expert opinion, case studies, or standard-of-care	• Recommendation that procedure or treatment not useful/effective and may be harmful • Only expert opinion, case studies, or standard-of-care
Suggested phrases for writing recommendations †	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/ beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown /unclear/uncertain or not well established	is not recommended is not indicated should not is not useful/effective/beneficial may be harmful

*Data available from clinical trials or registries about the usefulness/efficacy in different sub-populations, such as gender, age, history of diabetes, history of prior MI, history of heart failure, and prior aspirin use. A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Even though randomized trials are not available, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

†In 2003, the ACC/AHA Task Force on Practice Guidelines developed a list of suggested phrases to use when writing recommendations. All recommendations in this guideline have been written in full sentences that express a complete thought, such that a recommendation, even if separated and presented apart from the rest of the document (including headings above sets of recommendations), would still convey the full intent of the recommendation. It is hoped that this will increase readers' comprehension of the guidelines and will allow queries at the individual recommendation level.

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facilitated by communication between anesthesia personnel and physicians responsible for the patient's cardiovascular care.

1.5. Financial Implications

The financial implications of risk stratification cannot be ignored. The need for better methods of objectively measuring cardiovascular risk has led to the development of multiple noninvasive techniques in addition to established invasive procedures. Although a variety of strategies to assess and lower cardiac risk have been developed, their aggregate cost has received relatively little attention. Given the striking practice variation and high costs associated with many evaluation strategies, the development of practice guidelines based on currently available knowledge can serve to foster more efficient approaches to perioperative evaluation.

2. General Approach to the Patient

This guideline focuses on the evaluation of the patient undergoing noncardiac surgery who is at risk for perioperative cardiac morbidity or mortality. In patients with known coronary artery disease (CAD) or the new onset of signs or symptoms suggestive of CAD, baseline cardiac assessment should be performed. In the asymptomatic patient, a more extensive assessment of history and physical examination is warranted in those individuals 50 years of age or older, because the evidence related to the determination of cardiac risk factors and derivation of a Revised Cardiac Risk Index occurred in this population (4). Preoperative cardiac evaluation must therefore be carefully tailored to the circumstances that have prompted the evaluation and to the nature of the surgical illness. Given an acute surgical emergency, preoperative evaluation might have to be limited to simple and critical tests, such as a rapid assessment of cardiovascular vital signs, volume status, hematocrit, electrolytes, renal function, urine analysis, and ECG. Only the most essential tests and interventions are appropriate until the acute surgical emergency is resolved. A more thorough evaluation can be conducted after surgery. In patients in whom coronary revascularization is not an option, it is often not necessary to perform a noninvasive stress test. Under other, less urgent circumstances, the preoperative cardiac evaluation may lead to a variety of responses, including cancellation of an elective procedure.

2.1. Role of the Consultant

If a consultation is requested, then it is important to identify the key questions and ensure that all of the perioperative caregivers are considered when providing a response. Several studies suggest that such an approach is not always taken. A multiple-choice survey regarding the purposes and utility of cardiology consultations was sent to randomly selected New York metropolitan area anesthesiologists, surgeons, and cardiologists (5). There was substantial disagreement on the importance and purposes of a cardiology consultation; for instance, intraoperative monitoring, "clearing the patient for surgery," and advising as to the safest type of anesthesia were regarded as important by most cardiologists and surgeons but as unimportant by anesthesiologists. In addition, the charts of 55 consecutive patients aged more than 50 years who received preoperative cardiology consultations were examined to determine the stated purpose of the consultation, recommendations made, and concordance by surgeons and anesthesiologists with cardiologists' recommendations. Of the cardiology consultations, 40% contained no recommendations other than "proceed with case," "cleared for surgery," or "continue current medications." A review of 146 medical consultations suggests that the majority of such consultations give little advice that truly impacts either perioperative management or outcome of surgery (6). In only 5 consultations (3.4%) did the consultant identify a new finding; 62 consultations (42.5%) contained no recommendations.

Once a consultation has been obtained, the consultant should review available patient data, obtain a history, and perform a physical examination that includes a comprehensive cardiovascular examination and elements pertinent to the patient's problem and the proposed surgery. The consultant must not rely solely on the question that he or she has been asked to answer but must provide a comprehensive evaluation of the patient's risk. The consultation may have been requested for an ECG anomaly, chest pain, or arrhythmia that may have been thought to be indicative of CAD but that the consultant may determine is noncardiac in origin or benign, therefore requiring no further evaluation. In contrast, the consultation may lead to a suspicion of previously unsuspected CAD or heart failure (HF) in a patient scheduled for an elective procedure, which justifies a more extensive evaluation (7–9). A critical role of the consultant is to determine the stability of the patient's cardiovascular status and whether the patient is in optimal medical condition, within the context of the surgical illness. The consultant may recommend changes in medication, suggest preoperative tests or procedures, or propose higher levels of postoperative care. In some instances, an additional diagnostic cardiac evaluation is necessary on the basis of the results of the initial preoperative test. In general, preoperative tests are recommended only if the information obtained will result in a change in the surgical procedure performed, a change in medical therapy or monitoring during or after surgery, or a postponement of surgery until the cardiac condition can be corrected or stabilized. Before suggesting an additional test, the consultant should feel confident that the information will have the potential to affect treatment. Redundancy should be avoided.

The consultant must also bear in mind that the perioperative evaluation may be the ideal opportunity to effect the long-term treatment of a patient with significant cardiac disease or risk of such disease. The referring physician and patient should be informed of the results of the evaluation and implications for the patient's prognosis. The consultant can also assist in planning for follow-up, such as suggesting additional therapies known to reduce long-term cardiovascular risk or setting up an office appointment. It is the cardiovascular consultant's responsibility to ensure clarity of communication, such that findings and impressions will be incorporated effectively into the patient's overall plan of care. This ideally would include direct communication with the surgeon, anesthesiologist, and other physicians, as well as frank discussion directly with the patient and, if appropriate, the family. The consultant should not use phrases such as "clear for surgery." As is expected for good medical

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care in general, clear documentation in the medical record is appropriate.

2.2. History

A history is crucial to the discovery of cardiac and/or comorbid diseases that would place the patient in a high surgical risk category. The history should seek to identify serious cardiac conditions such as unstable coronary syndromes, prior angina, recent or past MI, decompensated HF, significant arrhythmias, and severe valvular disease (Table 2). It should also determine whether the patient has a prior history of a pacemaker or implantable cardioverter defibrillator (ICD) or a history of orthostatic intolerance. Modifiable risk factors for coronary heart disease (CHD) should be recorded, along with evidence of associated diseases, such as peripheral vascular disease, cerebrovascular disease, diabetes mellitus, renal impairment, and chronic pulmonary disease. In patients with established cardiac disease, any recent change in symptoms must be ascertained. Accurate recording of current medications used, including herbal and other nutritional supplements, and dosages is essential. Use of alcohol, tobacco, and over-the-counter and illicit drugs should be documented.

Table 2. Active Cardiac Conditions for Which the Patient 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 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 uncontrolled ventricular rate (HR greater than 100 bpm at rest)
	Symptomatic bradycardia
	Newly recognized ventricular tachycardia
Severe valvular disease	Severe aortic stenosis (mean pressure gradient greater than 40 mm Hg, aortic valve area less than 1.0 cm^2, or symptomatic)
	Symptomatic mitral stenosis (progressive dyspnea on exertion, exertional presyncope, or HF)

CCS indicates Canadian Cardiovascular Society; HF, heart failure; HR, heart rate; MI, myocardial infarction; NYHA, New York Heart Association.

*According to Campeau (10).

†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 less than or equal to 1 month (within 30 days).

The history should also seek to determine the patient's functional capacity (Table 3). An assessment of an individual's capacity to perform a spectrum of common daily tasks has been shown to correlate well with maximum oxygen uptake by treadmill testing (11). A patient classified as high risk owing to age or known CAD but who is asymptomatic and runs for 30 minutes daily may need no further evaluation. In contrast, a sedentary patient without a history of cardiovascular disease but with clinical factors that suggest increased perioperative risk may benefit from a more extensive preoperative evaluation (8,9,13,14). The preoperative consultation may represent the first careful cardiovascular evaluation for the patient in years or, in some instances, ever. For example, inquiry regarding symptoms suggestive of angina or anginal equivalents such as dyspnea or HF may establish or suggest these diagnoses for the first time.

2.3. Physical Examination

A cardiovascular examination should include an assessment of vital signs (including measurement of blood pressure in both arms), carotid pulse contour and bruits, jugular venous pressure and pulsations, auscultation of the lungs, precordial palpation and auscultation, abdominal palpation, and examination of the extremities for edema and vascular integrity. The presence of an implanted pacemaker or ICD can also be confirmed by physical examination. More detailed observations will be dictated by specific circumstances. The following points are worth emphasizing:

The general appearance provides invaluable evidence regarding the patient's overall status. Cyanosis, pallor, dyspnea during conversation or with minimal activity, Cheyne-Stokes respiration, poor nutritional status, obesity, skeletal deformities, tremor, and anxiety are just a few of the clues of underlying disease or CAD that can be recognized by the skilled physician.

In patients with acute HF, rales and chest X-ray evidence of pulmonary congestion correlate well with elevated pulmonary venous pressure. However, in patients with chronic HF, these findings may be absent. An elevated jugular venous pressure or a positive hepatojugular reflux are more reliable signs of hypervolemia in these patients (15,16). Peripheral edema is not a reliable indicator of chronic HF unless the jugular venous pressure is elevated or the hepatojugular test is positive.

An examination of the carotid and other arterial pulses is essential. The presence of associated vascular disease should heighten suspicion of occult CAD. Cardiac auscultation will often provide useful clues to underlying cardiac disease. When present, a third heart sound at the apical area suggests a failing left ventricle (LV), but its absence is not a reliable indicator of good ventricular function (16). If a murmur is present, the clinician will need to decide whether or not it represents significant valvular disease. Detection of significant aortic stenosis is of particular importance because this lesion poses a higher risk for noncardiac surgery (17). Significant mitral stenosis or regurgitation increases the risk of HF. Aortic regurgitation and mitral regurgitation may be minimal, yet they predispose the patient to infective endocarditis should bacteremia occur after surgery. Recommenda-

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Table 3. Estimated Energy Requirements for Various Activities

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

kph indicates kilometers per hour; MET, metabolic equivalent; and mph, miles per hour.
*Modified from Hlatky et al (11), copyright 1989, with permission from Elsevier, and adapted from Fletcher et al (12).

tions for endocarditis prophylaxis have been published elsewhere (18) (see Section 3.5 Valvular Heart Disease).

2.4. Comorbid Diseases

The consultant must evaluate the cardiovascular system within the framework of the patient's overall health. Associated conditions often heighten the risk of anesthesia and may complicate cardiac management. The most common of these conditions are discussed below.

2.4.1. Pulmonary Disease

The presence of either obstructive or restrictive pulmonary disease places the patient at increased risk of developing perioperative respiratory complications. Hypoxemia, hypercapnia, acidosis, and increased work of breathing can all lead to further deterioration of an already compromised cardiopulmonary system. If significant pulmonary disease is suspected by history or physical examination, determination of functional capacity, response to bronchodilators, and/or evaluation for the presence of carbon dioxide retention through arterial blood gas analysis may be justified. If there is evidence of infection, appropriate antibiotics are critical. Steroids and bronchodilators may be indicated, although the risk of producing arrhythmia or myocardial ischemia by beta agonists must be considered. Recommendations for preoperative chest radiographs can be found elsewhere (19).

2.4.2. Diabetes Mellitus

A variety of metabolic diseases may accompany cardiac disease. Diabetes mellitus is the most common. Its presence should heighten suspicion of CAD, particularly because CAD and myocardial ischemia are more likely in patients with diabetes mellitus (20–22). Lee et al identified insulin therapy for diabetes mellitus as a significant risk factor for cardiac morbidity (4). Older patients with diabetes mellitus are more likely to develop HF postoperatively than those without diabetes mellitus even after adjustment for treatment with angiotensin-converting enzyme (ACE) inhibitors (23). Management of blood glucose levels in the perioperative period may be difficult. Fragile patients with diabetes mellitus need careful treatment with adjusted doses or infusions of short-acting insulin based on frequent blood sugar determinations. Historically, it has been acceptable to maintain relatively high glucose levels perioperatively to avoid the attendant risks of hypoglycemic episodes; however, aggressive perioperative glucose control in coronary bypass surgery patients by a continuous, intravenous insulin infusion was found to be superior to intermittent subcutaneous insulin administration in significantly reducing postoperative wound infection (24). A similar benefit is less well established but may be found in noncardiac surgery (25). A discussion of the perioperative management of blood glucose concentration can be found in Section 8.7.

2.4.3. Renal Impairment

Azotemia is commonly associated with cardiac disease and is associated with an increased risk of cardiovascular events. Maintenance of adequate intravascular volume for renal perfusion during diuresis of a patient with HF is often challenging. Excessive diuresis in combination with initiation of ACE inhibitors or angiotensin receptor blockers may result in an increase in blood urea nitrogen and serum creatinine concentrations. In patients with known vascular disease, a small increase in blood urea nitrogen and creatinine may suggest the presence of renal artery stenosis. However, small increases in blood urea nitrogen and serum creatinine concentrations are not an indication to discontinue these drugs, because they have been shown to improve survival in patients with HF due to systolic dysfunction. Preexisting renal disease (preoperative serum creatinine levels 2 mg per dL or greater or reduced glomerular filtration rate) has been identified as a risk factor for postoperative renal dysfunction and increased long-term morbidity and mortality compared with patients without renal disease (26,27). In coronary artery bypass

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patients who are more than 70 years old, preoperative creatinine levels greater than 2.6 mg per dL place the patient at much greater risk for chronic dialysis postoperatively than creatinine levels below 2.6 mg per dL (28). Intuitively, one might extrapolate these findings to those older patients with comparable creatinine levels who undergo major noncardiac surgical procedures. One large study has shown that a preoperative creatinine level greater than 2 mg per dL is a significant, independent risk factor for cardiac complications after major noncardiac surgery (4).

Creatinine clearance, another indicator of renal function, has been used to predict postoperative complications (29,30). Creatinine clearance incorporates serum creatinine, age, and weight to provide a more accurate assessment of renal function than serum creatinine alone. Kertai and colleagues evaluated 852 subjects undergoing major vascular surgery and demonstrated an increase in mortality as both serum creatinine increased and creatinine clearance decreased, with creatinine clearance providing a more accurate assessment (29). To date, there has been no validation of this relationship by other investigators or in a prospective study. The AHA, in a scientific statement, advocated use of the Modification in Diet in Renal Disease equation to calculate glomerular filtration rate to determine kidney function (27).

2.4.4. Hematologic Disorders

Anemia imposes a stress on the cardiovascular system that may exacerbate myocardial ischemia and aggravate HF (31). Preoperative transfusion, when used appropriately in patients with advanced CAD and/or HF, may reduce perioperative cardiac morbidity. However, with current concern about transfusion reaction, clerical error, or transmission of communicable disease through the use of blood products, a conservative approach with respect to transfusion is warranted. Hematocrits less than 28% are associated with an increased incidence of perioperative ischemia and postoperative complications in patients undergoing prostate and vascular surgery (31–33). In the VA National Surgical Quality Improvement Program database, mild degrees of preoperative anemia or polycythemia were associated with an increased risk of 30-day postoperative mortality and cardiac events in older, mostly male veterans undergoing major noncardiac surgery (34). The adjusted risk of 30-day postoperative mortality and cardiac morbidity begins to rise when hematocrit levels decrease to less than 39% or exceed 51%.

Polycythemia, thrombocytosis, and other conditions that increase viscosity and hypercoagulability may increase the risk of thromboembolism or hemorrhage. Appropriate steps to reduce these risks should be considered and tailored to the individual patient's particular circumstances. Current guidelines are available that address perioperative transfusion practices (35).

2.5. Ancillary Studies

The consultant should review all pertinent available laboratory data. In the present era of cost containment, the laboratory data available may be minimal. Therefore, the consultant may require additional tests such as blood chemistries and a chest x-ray on the basis of history and physical examination. Blood levels of cardiac drugs should be obtained only when there are specific indications, such as changes in renal function, a recent change in dose, or symptoms that suggest toxicity.

The ECG is frequently obtained as part of a preoperative evaluation in all patients over a specific age or undergoing a specific set of procedures. Section 5.2.1 identifies the indications for a preoperative ECG based on the available evidence. An abnormal ECG report is often the reason that consultation is requested, but if not previously done, an ECG should be obtained as part of the consultation. Metabolic and electrolyte disturbances, medications, intracranial disease, and pulmonary disease, among other things, can alter the ECG. Conduction disturbances, such as right bundle-branch block or first-degree atrioventricular block, may lead to concern but usually do not justify further workup. The same is often true of asymptomatic ventricular arrhythmias, even in the presence of structural heart disease (36,37). On the other hand, subtle ECG clues can point to a clinically silent condition of major importance.

2.6. Multivariable Indices to Predict Preoperative Cardiac Morbidity

The basic clinical evaluation obtained by history, physical examination, and review of the ECG usually provides the consultant with sufficient data to estimate cardiac risk. In an attempt to codify those clinical and laboratory factors that influence outcome, numerous investigators have developed risk indices over the past 25 years based on multivariable analyses (17,38–47). Although some authors have suggested a scoring system that assigns more weight to some factors than others and sums these to arrive at a composite risk (17,45,47), most recent articles have suggested simpler criteria (4,38–44). Lee et al derived and validated a "simple index" for the prediction of cardiac risk for stable patients undergoing nonurgent major noncardiac surgery (4). Six independent risk correlates were identified: ischemic heart disease (defined as history of MI, history of positive treadmill test, use of nitroglycerin, current complaints of chest pain thought to be secondary to coronary ischemia, or ECG with abnormal Q waves); congestive HF (defined as history of HF, pulmonary edema, paroxysmal nocturnal dyspnea, peripheral edema, bilateral rales, S_3, or X-ray with pulmonary vascular redistribution); cerebral vascular disease (history of transient ischemic attack or stroke); high-risk surgery (abdominal aortic aneurysm or other vascular, thoracic, abdominal, or orthopedic surgery); preoperative insulin treatment for diabetes mellitus; and preoperative creatinine greater than 2 mg per dL. Increasing numbers of risk factors correlated with increased risk, yet the risk was substantially lower than described in many of the original indices (4). These improvements in outcome most likely reflect selection bias with respect to who presents for elective surgery, advances in surgical technique and anesthesia, and advances in the management of CAD both perioperatively and in general. The Revised Cardiac Risk Index has become one of the most widely used risk indices (4).

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2.7. Clinical Assessment

In the original guidelines, the committee chose to segregate clinical risk factors into major, intermediate, and minor risk factors. There continues to be a group of active cardiac conditions that when present indicate major clinical risk. The presence of 1 or more of these conditions mandates intensive management and may result in delay or cancellation of surgery unless the surgery is emergent (Table 2). These include

- unstable coronary syndromes,
  - unstable or severe angina,
  - recent MI,
- decompensated HF,
- significant arrhythmias, and
- severe valvular disease.

Given the increasing use of the Revised Cardiac Risk Index, the committee chose to replace the intermediate-risk category with the clinical risk factors from the index, with the exclusion of the type of surgery, which is incorporated elsewhere in the approach to the patient. Clinical risk factors include

- history of ischemic heart disease,
- history of compensated or prior HF,
- history of cerebrovascular disease,
- diabetes mellitus, and
- renal insufficiency (4).

A history of MI or abnormal Q waves by ECG is listed as a clinical risk factor, whereas an acute MI (defined as at least 1 documented MI 7 days or less before the examination) or recent MI (more than 7 days but less than or equal to 1 month before the examination) with evidence of important ischemic risk by clinical symptoms or noninvasive study is an active cardiac condition. This definition reflects the consensus of the ACC Cardiovascular Database Committee. In this way, the separation of MI into the traditional 3- and 6-month intervals has been avoided (17,48). Current management of MI provides for risk stratification during convalescence (49). If a recent stress test does not indicate residual myocardium at risk, the likelihood of reinfarction after noncardiac surgery is low. Although there are no adequate clinical trials on which to base firm recommendations, it appears reasonable to wait 4 to 6 weeks after MI to perform elective surgery.

Minor predictors are recognized markers for cardiovascular disease that have not been proven to increase perioperative risk independently, for example, advanced age (greater than 70 years), abnormal ECG (LV hypertrophy, left bundle-branch block, ST-T abnormalities), rhythm other than sinus, and uncontrolled systemic hypertension. The presence of multiple minor predictors might lead to a higher suspicion of CAD but is not incorporated into the recommendations for treatment.

2.7.1. Stepwise Approach to Perioperative Cardiac Assessment

Figure 1 presents, in algorithmic form, a framework for determining which patients are candidates for cardiac testing. The clinician must consider several interacting variables and give them appropriate weight. Since publication of the perioperative cardiovascular evaluation guidelines in 2002 (50), several new randomized trials and cohort studies have led to modification of the original algorithm. Given the availability of this evidence, the writing committee chose to include the level of the recommendations and strength of evidence for each of the pathways.

Step 1: The consultant should determine the urgency of noncardiac surgery. In many instances, patient- or surgery-specific factors dictate an obvious strategy (eg, emergency surgery) that may not allow for further cardiac assessment or treatment. In such cases, the consultant may function best by providing recommendations for perioperative medical management and surveillance. Selected postoperative risk stratification is often appropriate in patients with elevated risk for long-term coronary events who have never had such an assessment before. This is usually initiated after the patient has recovered from blood loss, deconditioning, and other postoperative complications that might confound interpretation of noninvasive test results.

Step 2: Does the patient have 1 of the active cardiac conditions in Table 2? If not, proceed to step 3. In patients being considered for elective noncardiac surgery, the presence of unstable coronary disease, decompensated HF, or severe arrhythmia or valvular heart disease usually leads to cancellation or delay of surgery until the cardiac problem has been clarified and treated appropriately. Examples of unstable coronary syndromes include previous MI with evidence of important ischemic risk by clinical symptoms or noninvasive study, unstable or severe angina, and new or poorly controlled ischemia-mediated HF. Many patients in these circumstances are referred for coronary angiography to assess further therapeutic options. Depending on the results of the test or interventions and the risk of delaying surgery, it may be appropriate to proceed to the planned surgery with maximal medical therapy.

Step 3: Is the patient undergoing low-risk surgery? Many procedures are associated with a combined morbidity and mortality rate less than 1% (see Section 4), even in high-risk patients. Additionally, mortality on the day of surgery, for most ambulatory surgical procedures, is actually lower than mortality on day 30, which suggests that the incremental risk of ambulatory surgery is negligible or may be protective (51). Therefore, interventions based on cardiovascular testing in stable patients would rarely result in a change in management, and it would be appropriate to proceed with the planned surgical procedure.

Step 4: Does the patient have good functional capacity, without symptoms? Functional status has been shown to be reliable for perioperative and long-term prediction of cardiac events (52–56). In highly functional asymptomatic patients, management will rarely be changed based on the results of any further cardiovascular testing. It is therefore appropriate to proceed with the planned surgery. In patients with known cardiovascular disease or at least 1 clinical risk factor, perioperative heart rate control with beta blockade appears appropriate as outlined in Section 7.2.

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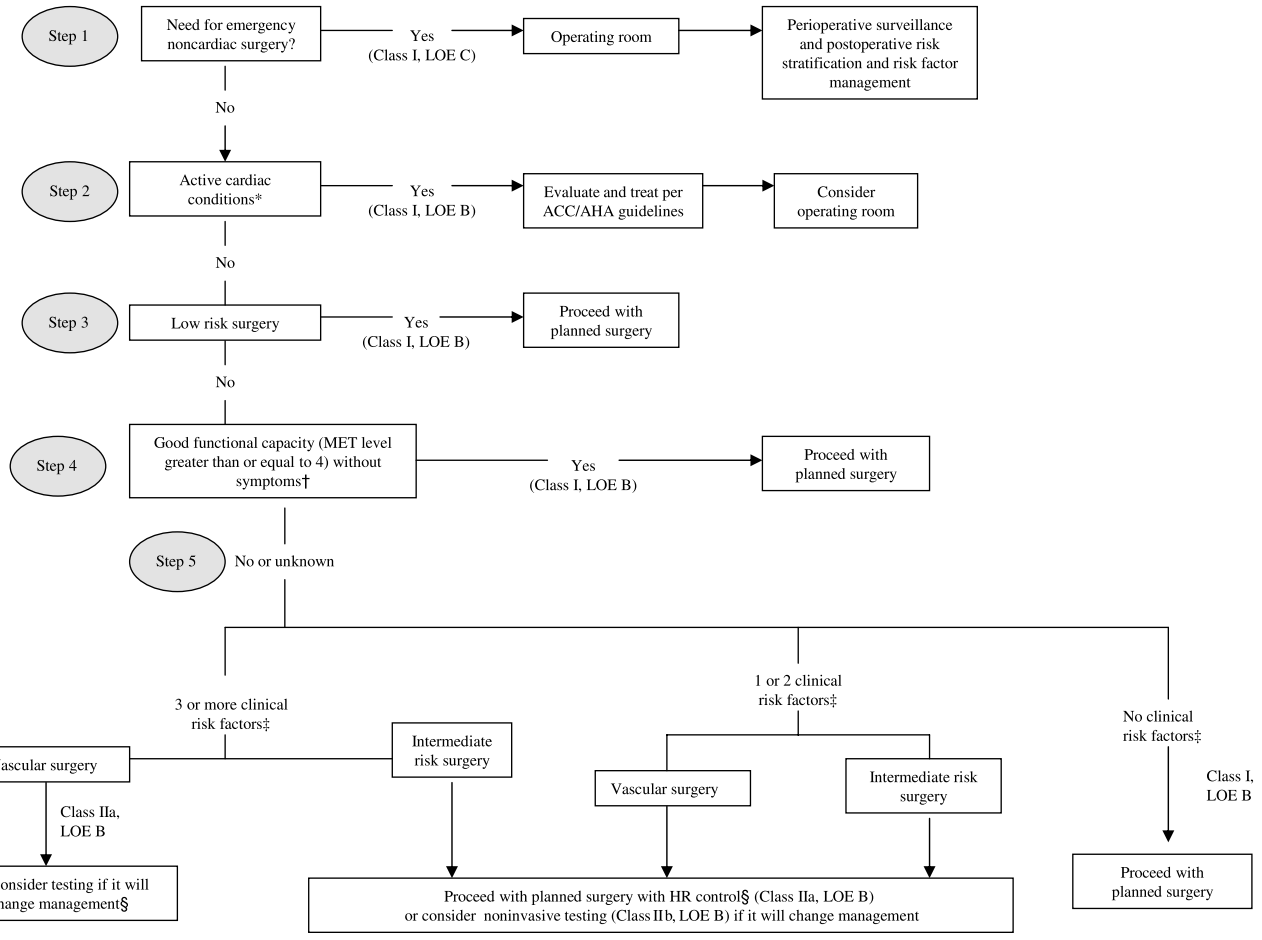

Figure 1. Cardiac evaluation and care algorithm for noncardiac surgery based on active clinical conditions, known cardiovascular disease, or cardiac risk factors for patients 50 years of age or greater. *See Table 2 for active clinical conditions. †See Table 3 for estimated MET level equivalent. ‡Clinical risk factors include ischemic heart disease, compensated or prior HF, diabetes mellitus, renal insufficiency, and cerebrovascular disease. §Consider perioperative beta blockade (see Table 11) for populations in which this has been shown to reduce cardiac morbidity/mortality. ACC/AHA indicates American College of Cardiology/American Heart Association; HR, heart rate; LOE, level of evidence; and MET, metabolic equivalent.

If the patient has not had a recent exercise test, functional status can usually be estimated from the ability to perform activities of daily living (55). Functional capacity can be expressed as metabolic equivalents (METs); the resting or basal oxygen consumption (V_{O_2}) of a 70-kg, 40-year-old man in a resting state is 3.5 mL per kg per min, or 1 MET. For this purpose, functional capacity has been classified as excellent (greater than 10 METs), good (7 to 10 METs), moderate (4 to 7 METs), poor (less than 4 METs), or unknown. Multiples of the baseline MET values provide a uniform terminology across different exercise protocols to express aerobic demands for specific activities. Maximum and submaximum levels of work differ per unit of time according to the exercise protocol used. Thus, 6 minutes of a Naughton protocol is not equivalent to 6 minutes on a standard Bruce protocol in terms of work performed and energy expended. The predicted MET level for a certain activity is influenced by the degree of conditioning and genetic predisposition. Perioperative cardiac and long-term risks are increased in patients unable to meet a 4-MET demand during most normal daily activities (55). In 1 series of 600 consecutive patients undergoing major noncardiac procedures, perioperative myocardial ischemia and cardiovascular events were more common in patients who reported poor exercise tolerance (inability to walk 4 blocks or climb 2 flights of stairs), even after adjustment for baseline characteristics known to be associated with increased risk (55). The likelihood of a serious complication occurring was inversely related to the number of blocks that could be walked ($P=0.006$) or flights of stairs that could be climbed ($P=0.01$). Examples of leisure activities associated with less than 4 METs are slow ballroom dancing, golfing with a cart, playing a musical instrument, and walking at a speed of approximately 2 to 3 mph. Activities that require more than 4 METs include moderate cycling, climbing hills, ice skating, roller blading, skiing, singles tennis, and jogging. The Duke Activity Status Index contains questions that can be used to estimate the patient's functional capacity (11,52). Use of the Duke Activity Status Index or other activity scales (53) and knowledge of the METs levels required for physical activities, as listed above and described in Table 3, provide the clinician with a relatively easy set of questions to estimate whether a patient's functional capacity will be less than or greater than 4 METs. At activity levels less than 4 METs, specific questions to establish risk gradients are less reliable.

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Table 4. Cardiac Risk* Stratification for Noncardiac Surgical Procedures

Risk Stratification	Procedure Examples
Vascular (reported cardiac risk often more than 5%)	Aortic and other major vascular surgery Peripheral vascular surgery
Intermediate (reported cardiac risk generally 1% to 5%)	Intraperitoneal and intrathoracic surgery Carotid endarterectomy Head and neck surgery Orthopedic surgery Prostate surgery
Low† (reported cardiac risk generally less than 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.

Furthermore, a clinical questionnaire only estimates functional capacity and does not provide as objective a measurement as exercise treadmill testing or arm ergometry. Other activity scales have been advocated, including the Specific Activity Scale (57).

Step 5: If the patient has poor functional capacity, is symptomatic, or has unknown functional capacity, then the presence of clinical risk factors will determine the need for further evaluation. If the patient has no clinical risk factors, then it is appropriate to proceed with the planned surgery, and no further change in management is indicated.

If the patient has 1 or 2 clinical risk factors, then it is reasonable to either proceed with the planned surgery, with heart rate control with beta blockade, or consider testing if it will change management. Two studies in vascular surgery patients with 1 to 2 clinical risk factors were unable to demonstrate any difference in outcome in the group who proceeded with the planned surgery with good medical management or tight heart rate control, but there are circumstances in which the clinician may change aspects of care based on the results of the test (58,59).

In patients with 3 or more clinical risk factors, the surgery-specific cardiac risk is important. The surgery-specific cardiac risk (Table 4) of noncardiac surgery is related to 2 important factors. First, the type of surgery itself may identify a patient with a greater likelihood of underlying heart disease and higher perioperative morbidity and mortality. Perhaps the most extensively studied example is vascular surgery, in which underlying CAD is present in a substantial portion of patients. If the patient is undergoing vascular surgery, testing should only be considered if it will change management. Other types of surgery may be associated with similar risk to vascular surgery but have not been studied extensively. For nonvascular surgery, the degree of hemodynamic cardiac stress dictates the surgery-specific risk. Depending on the noncardiac surgical procedure, it may be associated with profound alterations in heart rate, blood pressure, vascular volume, pain, bleeding, clotting tendencies, oxygenation, neurohumoral activation, and other perturbations. The intensity of these coronary and myocardial stressors helps determine the likelihood of perioperative cardiac events. The perioperative morbidity related to the procedures ranges from 1% to 5%. In these patients who are considered ready to undergo intermediate-risk surgery, there are insufficient data to determine the best strategy (proceeding with the planned surgery with tight heart rate control with beta blockade or further cardiovascular testing if it will change management).

3. Disease-Specific Approaches

3.1. Coronary Artery Disease

3.1.1. Patients With Known CAD

In some patients, such as those with an acute MI, prior coronary artery bypass grafting (CABG), coronary angioplasty, or a coronary angiogram that shows luminal obstructions or irregularities, the presence of CAD may be obvious. On the other hand, many patients without cardiac symptoms may have severe double- or triple-vessel disease that is not clinically obvious because the patients may present atypically or are functionally limited by severe arthritis or peripheral vascular disease. A subset of patients who are candidates for revascularization independent of planned noncardiac surgery may benefit from noninvasive evaluation. In patients with known CAD, as well as those with previously occult coronary disease, the questions become 1) What is the amount of myocardium in jeopardy? 2) What is the ischemic threshold, ie, the amount of stress required to produce ischemia? 3) What is the patient's ventricular function? and 4) Is the patient on his or her optimal medical regimen? Clarification of these questions is an important goal of the preoperative history and physical examination, and selected noninvasive testing is used to determine the patient's prognostic gradient of ischemic response during stress testing() (Table 5). Given recent evidence regarding the limited value of coronary revascularization before noncardiac surgery (see Section 7.1), the indication for preoperative testing is limited to the group in whom coronary revascularization may be beneficial independent of noncardiac surgery.

3.1.2. Influence of Age and Gender

Advanced age is a special risk, not only because of the increased likelihood of coronary disease but also because of the effects of aging on the myocardium. The mortality of acute MI increases dramatically in the aged (69). Intraoperative or perioperative MI has a higher mortality in the aged (17,44,45).

Gender is important because premenopausal women have a lower incidence of CAD, and in general, symptomatic CAD occurs 10 or more years later in women than in men (70). Women who have premature menopause, such as after oophorectomy, are an exception to this rule. Women with diabetes mellitus have an increased risk that is equivalent to men of the same age. The mortality rate after acute MI is greater for women than for men, but older age and diabetes mellitus account for much of this difference (71). Whether or not other factors such as coronary artery size or different

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Table 5. Prognostic Gradient of Ischemic Responses During an ECG-Monitored Exercise Test in Patients With Suspected or Proven CAD

Risk Level	Ischemic Response Gradient
High	Ischemia induced by low-level exercise* (less than 4 METs or heart rate less than 100 bpm or less than 70% of age-predicted heart rate) manifested by 1 or more of the following:
	Horizontal or downsloping ST depression greater than 0.1 mV
	ST-segment elevation greater than 0.1 mV in noninfarct lead
	Five or more abnormal leads
	Persistent ischemic response greater than 3 minutes after exertion
	Typical angina
	Exercise-induced decrease in systolic blood pressure by 10 mm Hg
Intermediate	Ischemia induced by moderate-level exercise† (4 to 6 METs or heart rate 100 to 130 bpm [70% to 85% of age-predicted heart rate]) manifested by 1 or more of the following:
	Horizontal or downsloping ST depression greater than 0.1 mV
	Persistent ischemic response greater than 1 to 3 minutes after exertion
	Three to 4 abnormal leads
Low	No ischemia or ischemia induced at high-level exercise† (greater than 7 METs or heart rate greater than 130 bpm [greater than 85% of age-predicted heart rate]) manifested by:
	Horizontal or downsloping ST depression greater than 0.1 mV
	One or 2 abnormal leads
Inadequate test	Inability to reach adequate target workload or heart rate response for age without an ischemic response. For patients undergoing noncardiac surgery, the inability to exercise to at least the intermediate-risk level without ischemia should be considered an inadequate test.

bpm indicates beats per min; CAD, coronary artery disease; and MET, metabolic equivalent.

*Workload and heart rate estimates for risk severity require adjustment for patient age. Maximum target heart rates for 40- and 80-year-old subjects taking no cardioactive medication are 180 and 140 bpm, respectively (61–68).

†Based on Weiner et al (61), Morris et al (62), Chaitman (63), Gianrossi et al (64), Detrano et al (65), Mark et al (66), Mark et al (67), and Gibbons et al (68).

pathophysiology also contribute to the increased risk in women is not yet fully understood.

3.2. Hypertension

Numerous studies (17,38,41,44,72,73) have shown that stage 1 or stage 2 hypertension (systolic blood pressure below 180 mm Hg and diastolic blood pressure below 110 mm Hg) is not an independent risk factor for perioperative cardiovascular complications. However, hypertension is common, and treatment has been shown to be associated with decreased rates of death due to stroke and CHD in the nonsurgical setting. Unfortunately, all too few patients with hypertension are treated, and fewer yet have their hypertension controlled. Accordingly, the perioperative evaluation is a unique opportunity to identify patients with hypertension and initiate appropriate therapy. As a universally measured variable with a recognized association with CAD, hypertension serves as a useful marker for potential CAD (74). In addition, several investigators have demonstrated exaggerated intraoperative blood pressure fluctuation with associated ECG evidence of myocardial ischemia in patients with preoperative blood pressure elevation (75–78). This effect can be modified by treatment (76–81). Because intraoperative ischemia correlates with postoperative cardiac morbidity (72,82), it follows that control of blood pressure preoperatively may help reduce the tendency to perioperative ischemia. Although an elevated blood pressure on an initial recording in a patient with previously undiagnosed or untreated hypertension has been shown to correlate with blood pressure lability under anesthesia (82,83), the definition of the severity of hypertension rests with subsequent recordings in a nonstressful environment (74). In patients undergoing therapy for hypertension, a thorough review of current medications and dosages, along with awareness of known intolerance to previously prescribed drugs, is essential. The physical examination should include a search for target-organ damage and evidence of associated cardiovascular pathology. A funduscopic examination may provide useful data regarding the severity and chronicity of hypertension.

The physical examination and simple laboratory tests can rule out some of the rare but important causes of hypertension. Further evaluation to exclude secondary hypertension is rarely warranted before necessary surgery. If pheochromocytoma is a serious possibility, surgery should be delayed to permit its exclusion. A loud abdominal bruit may suggest renal artery stenosis. A radial to femoral artery pulse delay suggests coarctation of the aorta, whereas hypokalemia in the absence of diuretic therapy raises the possibility of hyperaldosteronism.

If the initial evaluation establishes hypertension as mild or moderate, and there are no associated metabolic or cardiovascular abnormalities, there is no evidence that it is beneficial to delay surgery (84). Several investigators have established the value of effective preoperative blood pressure control among patients with established hypertension (77,78,81,85), and antihypertensive medications should be continued during the perioperative period. Particular care should be taken to avoid withdrawal of beta blockers and clonidine because of potential heart rate or blood pressure rebound (see Sections 7.2.1.3 and 7.2.3). In patients unable to take oral medications, parenteral beta blockers and transdermal clonidine may be used. Medication selection and risks should be assessed on the basis of national guidelines (74).

For stage 3 hypertension (systolic blood pressure greater than or equal to 180 mm Hg and diastolic blood pressure greater than or equal to 110 mm Hg), the potential benefits of delaying surgery to optimize the effects of antihypertensive medications should be weighed against the risk of delaying the surgical procedure. With rapidly acting intravenous agents, blood pressure can usually be controlled within a matter of several hours. One randomized trial was unable to demonstrate a benefit to delaying surgery. Weksler and colleagues studied 989 chronically treated hypertensive pa-

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tients who presented for noncardiac surgery with diastolic blood pressure between 110 and 130 mm Hg who had no previous MI, unstable or severe angina pectoris, renal failure, pregnancy-induced hypertension, LV hypertrophy, previous coronary revascularization, aortic stenosis, preoperative dysrhythmias, conduction defects, or stroke (86). The control group had their surgery postponed, and they remained in the hospital for blood pressure control, whereas the study patients received 10 mg of nifedipine delivered intranasally. They observed no statistically significant differences in postoperative complications, which suggests that this subset of patients without significant cardiovascular comorbidities can proceed with surgery despite elevated blood pressure on the day of surgery. Alternatively, beta blockers appear to be particularly attractive agents for the treatment of preoperative high blood pressure. Several reports have shown that the introduction of preoperative beta-adrenergic blockers leads to effective modulation of severe blood pressure fluctuations and a reduction in the number and duration of perioperative coronary ischemic episodes (76–81). The preoperative administration of beta-adrenergic blocking drugs has been shown to decrease the incidence of postoperative atrial fibrillation (87), and in patients who have or are at risk for CAD who must undergo noncardiac surgery, treatment with beta blockers during hospitalization can reduce mortality and the incidence of cardiovascular complications (88,89). A full discussion of the benefits and risks of beta blockers can be found in Section 7.2.1.

Interestingly, patients with preoperative hypertension appear more likely to develop intraoperative hypotension than nonhypertensive persons; this is particularly true for patients taking ACE inhibitors or angiotensin II receptor antagonists (90). In some patients, this may be related to a decrease in vascular volume. In 1 report, intraoperative hypotension was associated with a greater incidence of perioperative cardiac and renal complications than intraoperative hypertension, although other studies have not shown this (78,91–96). Several authors have suggested withholding ACE inhibitors and angiotensin receptor antagonists the morning of surgery (97–99). Consideration should be given to restarting ACE inhibitors in the postoperative period only after the patient is euvolemic, to decrease the risk of perioperative renal dysfunction.

3.3. Heart Failure

Heart failure has been identified in several studies as being associated with a poorer outcome when noncardiac surgery is performed. In a study by Goldman et al (17), both the presence of a third heart sound and signs of HF were associated with a substantially increased risk during noncardiac surgery. Detsky et al (45) identified alveolar pulmonary edema as a significant risk factor, and in the report by Cooperman et al (47), HF also bestowed a significant risk. Lee et al also identified HF (defined as the presence of any of the following: history of congestive HF, pulmonary edema, or paroxysmal nocturnal dyspnea; physical examination showing bilateral rales or S_3 gallop; or chest X-ray showing pulmonary vascular redistribution) as an independent predictor of risk (4). Every effort must be made to detect unsuspected HF by a careful history and physical examination. If possible, it is important to identify the cause of HF, because this may have implications concerning risk of death versus perioperative HF. For instance, prior HF due to hypertensive heart disease may portend a different risk than prior HF that results from CAD.

3.4. Cardiomyopathy

There is little information on the preoperative evaluation of patients with cardiomyopathy before noncardiac surgery. At this time, preoperative recommendations must be based on a thorough understanding of the pathophysiology of the myopathic process. Every reasonable effort should be made before surgery to determine the cause of the primary myocardial disease. Knowledge of the cause may alter intraoperative and postoperative management of intravenous fluids. In patients with a history or signs of HF, preoperative assessment of LV function may be recommended to quantify the severity of systolic and diastolic dysfunction. This information is valuable for both intraoperative and postoperative management. This assessment frequently includes echocardiography.

Hypertrophic obstructive cardiomyopathy poses special problems. Reduction of blood volume, decreased systemic vascular resistance, and increased venous capacitance may cause a reduction in LV volume and thereby potentially increase a tendency to outflow obstruction, with potentially untoward results. Furthermore, reduced filling pressures may result in a significant fall in stroke volume because of the decreased compliance of the hypertrophied ventricle. Beta-adrenergic agonists should be avoided because they may increase the degree of dynamic obstruction and decrease diastolic filling. In a relatively small series of 35 patients with hypertrophic obstructive cardiomyopathy, there were no deaths or serious ventricular arrhythmias during or immediately after general surgical procedures; 1 patient had major vascular surgery (100). In the 22 patients who underwent catheterization, the mean rest and peak provocable gradients were 30 and 81 mm Hg, respectively. The only patient who had a perioperative MI had 2-vessel coronary disease. Significant arrhythmias or hypotension that required vasoconstrictors occurred in 14% and 13% of patients, respectively (100). In another study, 77 patients with hypertrophic obstructive cardiomyopathy who underwent noncardiac surgery were evaluated. There were no deaths, but these patients had a significant incidence of adverse cardiac events, frequently manifested as HF. Independent risk factors for adverse outcome in all patients included major surgery and increasing duration of surgery. Echocardiographic features, including resting outflow tract gradient, were not associated with adverse cardiac events (101).

3.5. Valvular Heart Disease

Cardiac murmurs are common in patients facing noncardiac surgery. The consultant must be able to distinguish organic from functional murmurs, significant from insignificant murmurs, and the origin of the murmur to determine which patients require prophylaxis for endocarditis and which patients require further quantitation of the severity of the

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valvular lesion. We recommend physicians review all of the available data and use individual clinical judgment when determining whether to recommend prophylaxis. Specific recommendations for endocarditis prophylaxis have been published elsewhere (18).

Severe aortic stenosis poses the greatest risk for noncardiac surgery (17,102,103). If the aortic stenosis is symptomatic, elective noncardiac surgery should generally be postponed or canceled. Such patients require aortic valve replacement before elective but necessary noncardiac surgery. If the aortic stenosis is severe but asymptomatic, the surgery should be postponed or canceled if the valve has not been evaluated within the year. On the other hand, in patients with severe aortic stenosis who refuse cardiac surgery or are otherwise not candidates for aortic valve replacement, noncardiac surgery can be performed with a mortality risk of approximately 10% (104,105). In a database analysis in which severity of aortic stenosis was not defined, the presence of aortic stenosis was associated with an increased risk of acute MI (odds ratio [OR] 1.55) but not death after adjustment for other comorbidities (106). If a patient is not a candidate for valve replacement, percutaneous balloon aortic valvuloplasty may be reasonable as a bridge to surgery in hemodynamically unstable adult patients with aortic stenosis who are at high risk for aortic valve replacement surgery and may be reasonable in adult patients with aortic stenosis in whom aortic valve replacement cannot be performed because of serious comorbid conditions (103,107).

Mitral stenosis, although increasingly rare, is important to recognize. When stenosis is mild or moderate, the consultant must ensure control of heart rate during the perioperative period, because the reduction in diastolic filling period that accompanies tachycardia can lead to severe pulmonary congestion. Significant mitral stenosis increases the risk of HF. However, preoperative surgical correction of mitral valve disease is not indicated before noncardiac surgery unless the valvular condition should be corrected to prolong survival and prevent complications that are unrelated to the proposed noncardiac surgery. When the stenosis is severe, the patient may benefit from balloon mitral valvuloplasty or open surgical repair before high-risk surgery (108).

Aortic regurgitation suspected on examination warrants qualification for long-term follow-up and indicated therapy. If such qualification is not done, the regurgitation needs to be identified, and provide appropriate medical treatment. Attention to volume control and afterload reduction is recommended. In contrast to mitral stenosis, severe aortic regurgitation is not benefited by unusually slow heart rates, which can increase the volume of regurgitation by increasing the duration of diastole. Tachycardia thus reduces the time of regurgitation in severe aortic regurgitation.

Mitral regurgitation has many causes, the 2 most common being mitral valve prolapse that results from myxomatous degeneration and functional mitral regurgitation that complicates postinfarction LV remodeling. Specific recommendations regarding perioperative antibiotic prophylaxis for patients with mitral valve prolapse can be found elsewhere (18).

Patients with severe mitral regurgitation (often manifested clinically by an apical holosystolic murmur, a third heart sound, and a diastolic flow rumble) may benefit from afterload reduction and administration of diuretics to produce maximal hemodynamic stabilization before high-risk surgery. It is also important for the consultant to note even mild reduction of the LV ejection fraction (LVEF) in patients with mitral regurgitation, because LVEF may overestimate true LV performance. In such patients, even a mildly reduced LVEF may be a sign of reduced ventricular reserve. In patients with persistent or permanent atrial fibrillation at high risk for thromboembolism, preoperative and postoperative therapy with intravenous heparin or subcutaneous low-molecular-weight heparin may be considered to cover periods of subtherapeutic anticoagulation (110,111–113). Patients who have severe symptomatic mitral regurgitation or aortic insufficiency should be considered for further evaluation. These topics are discussed in more detail in the AHA/ACC Valvular Heart Disease guidelines (103).

Patients with a mechanical prosthetic valve are of concern because of the need for endocarditis prophylaxis (18) when they undergo surgery that may result in bacteremia and the need for careful anticoagulation management. The Seventh American College of Chest Physicians Consensus Conference on Antithrombotic and Thrombolytic Therapy recommends the following (114): For patients who require minimally invasive procedures (dental work, superficial biopsies), the recommendation is to briefly reduce the international normalized ratio (INR) to the low or subtherapeutic range and resume the normal dose of oral anticoagulation immediately after the procedure. Perioperative unfractionated heparin therapy is recommended for patients in whom the risk of bleeding with oral anticoagulation is high and the risk of thromboembolism without anticoagulation is also high (mechanical valve in the mitral position, Bjork-Shiley valve, recent [ie, less than 1 year] thrombosis or embolus, or 3 or more of the following risk factors: atrial fibrillation, previous embolus at any time, hypercoagulable condition, mechanical prosthesis, and LVEF less than 30% (115). For patients between these 2 extremes, physicians must assess the risk and benefit of reduced anticoagulation versus perioperative heparin therapy.

3.6. Arrhythmias and Conduction Defects

Cardiac arrhythmias and conduction disturbances are not uncommon findings in the perioperative period (17,39,116), particularly in the elderly. Both supraventricular and ventricular arrhythmias have been identified as independent risk factors for coronary events in the perioperative period (17,116). More recent detailed studies using continuous ECG monitoring found that asymptomatic ventricular arrhythmias, including couplets and nonsustained ventricular tachycardia, were not associated with an increase in cardiac complications after noncardiac surgery (37). Nevertheless, the presence of an arrhythmia in the preoperative setting should provoke a search for underlying cardiopulmonary disease, ongoing myocardial ischemia or infarction, drug toxicity, or metabolic derangements.

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Some cardiac arrhythmias, although relatively benign, may unmask underlying cardiac problems; for example, atrial fibrillation and other types of supraventricular arrhythmias can produce ischemia by increasing myocardial oxygen demand in patients with coronary disease. Atrial fibrillation is the most common type of sustained supraventricular tachycardia, particularly in elderly patients who are likely to be undergoing surgical procedures. Rarely, arrhythmias, because of the hemodynamic or metabolic derangements they cause, may deteriorate into more life-threatening rhythm disturbances; for example, atrial fibrillation with a rapid ventricular response in a patient with an accessory bypass pathway may degenerate into ventricular fibrillation. Ventricular arrhythmias, whether single premature ventricular contractions, complex ventricular ectopy, or nonsustained ventricular tachycardia, usually do not require therapy unless they result in hemodynamic compromise. Although frequent ventricular premature beats and nonsustained ventricular tachycardia are considered risk factors for the development of intraoperative and postoperative arrhythmias and sustained ventricular arrhythmias during long-term follow-up, they are not associated with an increased risk of nonfatal MI or cardiac death in the perioperative period (36,37). However, patients who develop sustained and/or nonsustained ventricular tachycardia during the perioperative period should be referred to a cardiologist for further evaluation, including an evaluation of their ventricular function and screening for CAD. Physicians should have a low threshold to institute prophylactic beta-blocker therapy in patients at increased risk of developing a perioperative or postoperative supraventricular or ventricular tachyarrhythmia. Several studies suggest that beta-blocker therapy can reduce mortality and the incidence of cardiovascular complications (including the development of arrhythmias) during surgery and for up to 2 years afterward (87–89,117).

High-grade cardiac conduction abnormalities, such as complete atrioventricular block, if unanticipated, can increase operative risk and may necessitate temporary or permanent transvenous pacing. On the other hand, patients with intraventricular conduction delays, even in the presence of a left or right bundle-branch block, and no history of advanced heart block or symptoms rarely progress to complete heart block perioperatively (118). The availability of transthoracic pacing units makes the decision for temporary transvenous pacing less critical.

3.7. Implanted Pacemakers and ICDs

Each year, more than 250 000 patients undergo placement of a permanent pacemaker, and more than 150 000 patients undergo placement of an ICD. The presence of a pacemaker or ICD has important implications regarding preoperative, intraoperative, and postoperative patient management. The situations in which device malfunction may occur, as well as the techniques that may be used to prevent them, are discussed in Section 7.5.

3.8. Pulmonary Vascular Disease and Congenital Heart Disease

There are no reported studies that specifically assess the perioperative risk associated with pulmonary vascular disease in patients having noncardiac surgery. A number of reports have evaluated cardiovascular function many years after surgery for congenital heart disease. Five years after surgery for ventricular septal defect or patent ductus arteriosus, pulmonary vasoreactivity often remains abnormal, resulting in high pulmonary pressures with hypoxia. Such patients may not tolerate intraoperative or postoperative hypoxia as well as normal individuals.

Patients with congenital heart disease have also demonstrated a reduced cardiac reserve during exercise (119). Postoperative studies of patients with coarctation of the aorta or tetralogy of Fallot have demonstrated findings consistent with underlying ventricular dysfunction (120,121). These observations should be kept in mind when such patients are evaluated before noncardiac surgery. Patients receiving primary cardiac repair at a younger age in the present era may be less prone to postoperative ventricular dysfunction because of improved surgical techniques.

Although most experts agree that pulmonary hypertension poses an increased risk for noncardiac surgery, no major study of this has been performed. The only analogous situation is labor and delivery for women with Eisenmenger syndrome due to a congenital intracardiac shunt. Peripartum mortality was reported to be between 30% and 70% in 1971, but no recent data exist to clarify whether or not this has fallen with improvements in care (122). In patients with severe pulmonary hypertension and a cardiac shunt, systemic hypotension results in increased right-to-left shunting and predisposes the patient to development of acidosis, which can lead to further decreases in systemic vascular resistance. This cycle must be recognized and treated appropriately.

4. Surgery-Specific Issues

Cardiac complications after noncardiac surgery are a reflection of factors specific to the patient, the operation, and the circumstances under which the operation is undertaken. To the extent that preoperative cardiac evaluation reliably predicts postoperative cardiac outcomes, it may lead to interventions that lower perioperative risk, decrease long-term mortality, or alter the surgical decision-making process. Such alterations might include either choosing a lower-risk, less-invasive procedure or opting for nonoperative management (eg, recommending an endovascular rather than open operative approach for a particular aneurysm or occlusive lesion, electing to follow up rather than operate on a moderate-sized [4 to 5 cm] infrarenal aortic aneurysm, or choosing nonoperative treatment for the disabled claudicant who has no limb-threatening ischemia). Although different operations are associated with different cardiac risks, these differences are most often a reflection of the context in which the patient undergoes surgery (stability or opportunity for adequate preoperative preparation), surgery-specific factors (eg, fluid shifts, stress levels, duration of procedure, or blood loss), or patient-specific factors (the incidence of CAD associated with the condition for which the patient is undergoing surgery).

To the extent that preoperative cardiac evaluation can identify potentially reducible cardiac risks, interventions

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directed at reducing those risks might improve both short- and long-term cardiac outcomes. The potential for improvement in long-term outcomes is particularly relevant to operative decision making in patients undergoing surgery directed at long-term goals. When, for example, surgery in asymptomatic individuals is undertaken with the objective of prolonging life (eg, elective repair of aortic aneurysm) or preventing a future stroke (eg, carotid endarterectomy), the decision to intervene must be made with the expectation that the patient will live long enough to benefit from the prophylactic intervention.

4.1. Urgency

Mangano (1) determined that cardiac complications are 2 to 5 times more likely to occur with emergency surgical procedures than with elective operations. This finding is not surprising, because the necessity for immediate surgical intervention may make it impossible to evaluate and treat such patients optimally. For instance, collected data have confirmed that the composite mortality rate for elective repair of patients with asymptomatic abdominal aortic aneurysms is significantly lower (3.5%) than that for ruptured aneurysms (42%) (123). The mortality rate for graft replacements of symptomatic but intact abdominal aortic aneurysms remains relatively high (19%) despite the fact that, like elective cases, they are not associated with antecedent blood loss or hypotension (124). Unfortunately, most true surgical emergencies (eg, symptomatic abdominal aortic aneurysms, perforated viscus, or major trauma) do not permit more than a cursory cardiac evaluation.

In addition, some situations do not lend themselves to comprehensive cardiac evaluation, although surgical care may qualify as semielective. In some patients, the impending danger of the disease is greater than the anticipated perioperative risk. Examples include patients who require arterial bypass procedures for limb salvage or mesenteric revascularization to prevent intestinal gangrene. Patients with malignant neoplasms also pose a diagnostic and therapeutic dilemma with respect to preoperative cardiac evaluation, especially when it is difficult to determine whether the malignancy is curable before surgical exploration. Each of these situations illustrates the importance of close communication among consultant, surgeon, and anesthesiologist to plan an approach for cardiac assessment that is appropriate for the individual patient and the underlying disease.

4.2. Surgical Risk

For elective surgery, cardiac risk can be stratified according to a number of factors, including the magnitude of the surgical procedure. Backer et al (125) encountered no cardiac complications after 288 ophthalmologic procedures in 195 patients with a prior history of MI compared with a reinfarction rate of 6.1% for a number of nonophthalmologic surgeries at the same center. Indeed, large-scale studies have supported the low morbidity and mortality rates in superficial procedures performed on an ambulatory basis. For example, Warner et al (126) determined the perioperative (30 day) incidence of symptomatic MI and cardiac death in 38 500 patients who underwent 45 090 consecutive procedures with anesthetics. Fourteen perioperative MIs occurred (0.03%), of which 2 resulted in death on postoperative day 7 after the infarction. Two MIs occurred either intraoperatively or within the first 8 hours, 1 of which was fatal. Using age- and gender-adjusted annual incidence rates for MIs and sudden death, the authors predicted that 17.8 MIs should have occurred among this population during the study period, which suggests that these events may have occurred independent of the procedure. In contrast, Lee and colleagues (4) reported that major perioperative cardiac events occurred in 1.4% of relatively unselected patients 50 years of age or older undergoing elective noncardiac surgery that required hospital admission. In a pooled analysis of prospective studies in which patients who had or were at risk for cardiac disease underwent at least 1 measurement of a cardiac enzyme or cardiac biomarker after surgery, 3.9% experienced a major perioperative cardiac event (127).

Several large surveys have demonstrated that perioperative cardiac morbidity is particularly concentrated among patients who undergo major thoracic, abdominal, or vascular surgery, especially when they are 70 years of age or older (1,125,128–130). Ashton et al (38) prospectively studied the incidence of perioperative MI associated with thoracic, abdominal, urologic, orthopedic, and vascular surgery in a cohort of 1487 men older than 40 years. The highest MI rate (4.1%; OR 10.39, 95% CI: 2.3 to 47.5) occurred in the subset of patients with an established diagnosis of CAD. Nevertheless, independent significant risk factors for infarction also included age greater than 75 years (OR 4.77, 95% CI: 1.17 to 19.41) and the need for elective vascular surgery even in the absence of suspected CAD (adjusted OR 3.72, 95% CI: 1.12 to 12.37). An exception to this assumption is intrathoracic surgery, notably for pulmonary neoplasm. This group has a high incidence of tobacco consumption, a notable risk factor for both lung cancer and atherosclerosis. In addition, limitations with respect to exercise tolerance can be due to either CAD, lung disease, or both, which makes the assessment of CAD more difficult. It is advisable to have a high index of suspicion of CAD in patients undergoing intrathoracic surgery.

Few procedure-specific data are available regarding perioperative cardiac morbidity in most surgical specialties, perhaps because advanced age and serious, incidental CAD are assumed to be distributed randomly within groups of patients who undergo noncardiac operations in such fields as general surgery, orthopedics, urology, gynecology, and neurosurgery. As shown by Ashton et al (38) and many others, however, patients who require vascular surgery appear to have an increased risk for cardiac complications because 1) many of the risk factors that contribute to peripheral vascular disease (eg, diabetes mellitus, tobacco use, and hyperlipidemia) are also risk factors for CAD; 2) the usual symptomatic presentation for CAD in these patients may be obscured by exercise limitations imposed by advanced age, intermittent claudication, or both; and 3) major open vascular surgery may be associated with substantial fluctuations in intravascular/extravascular fluid volumes, cardiac filling pressures, systemic blood pressure, heart rate, and thrombogenicity (1).

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Several studies have attempted to stratify the incidence of perioperative and long-term mortality and cardiac morbidity according to the original type of vascular surgery performed. Using the Medicare National Inpatient Sample from 1994 through 1999, Birkmeyer et al noted that in high-volume hospitals, the perioperative mortality rates for carotid endarterectomy, lower-extremity bypass, and aneurysm surgery were 1.5%, 4.1%, and 3.9%, respectively (131). In a prospective series of 53 aortic procedures and 87 infrainguinal bypass grafts for which operative mortality rates were nearly identical (9% and 7%, respectively), Krupski et al (132) found that the risk for fatal/nonfatal MI within a 2-year follow-up period was 3.5 times higher (21% versus 6%) among patients who received infrainguinal bypass grafts. This difference probably is related to the fact that diabetes mellitus (44% versus 11%) and history of previous MI (43% versus 28%), angina (36% versus 15%), or HF (29% versus 9%) also were significantly more prevalent in the infrainguinal bypass group. L'Italien et al (133) have presented comparable data regarding the perioperative incidence of fatal or nonfatal MI and the 4-year event-free survival rate after 321 aortic procedures, 177 infrainguinal bypass grafts, and 49 carotid endarterectomies. Slight differences in the overall incidence of MI among the 3 surgical groups, which may have been related to the prevalence of diabetes mellitus, were less significant than the influence of discrete cardiac risk factors (previous MI, angina, HF, fixed or reversible myocardial perfusion imaging defects, and ST-T depression during stress testing) (133).

Although these and other studies (8) suggest that the clinical evidence of CAD in a patient who has peripheral vascular disease appears to be a better predictor of subsequent cardiac events than the particular type of peripheral vascular operation to be performed, the introduction of endovascular alternatives, either alone or in combination with an adjunctive open surgical procedure, has led to a reduction in all-cause perioperative mortality and morbidity. For example, the DREAM (Dutch Randomized Endovascular Aneurysm Management) trial was a multicenter randomized trial of endovascular abdominal aortic aneurysm repair versus open repair in which 351 patients were randomized with aneurysms at least 5 cm in diameter. Patients were enrolled if considered fit for open repair and if they had suitable anatomy. Initial results were reported in 2004 (134) and revealed a 30-day operative mortality rate in favor of endovascular repair (1.7% for endovascular repair versus 4.7% for open repair, relative risk [RR] 3.9, 95% CI: 0.9 to 32.9, $P=0.10$). However, 2-year follow-up (135) demonstrated cumulative survival rates were not significantly different between the 2 approaches (89.6% for open repair versus 87.7% for endovascular repair). Similar results were noted for the EVAR (EndoVascular Abdominal aortic aneurysm Repair)-1 trial conducted in the United Kingdom (136,137). Indeed, in a random sample of inpatient Medicare claims from 2000 to 2003, endovascular abdominal aortic aneurysm repair increased during this period to 41% of all elective repairs in the United States, with a decline in mortality from 5.0% to 3.7% (P less than 0.001) (124). Likewise, recent clinical trials support the notion that endovascular management of thoracic aneurysms dramatically reduces all-cause perioperative mortality and morbidity; however, the underlying cardiovascular disease may lead to similar long-term outcomes (138).

Several studies have suggested that variations in surgical mortality and morbidity are inversely related to hospital volume. Nonetheless, the relative effect of hospital volume is procedure-specific, even among relatively complex operations. Using information from the national Medicare claims database and the Nationwide Inpatient Sample, Birkmeyer et al (131) examined the mortality associated with 6 different types of cardiovascular procedures and 8 types of major cancer resections between 1994 and 1999. Absolute differences in adjusted mortality rates between very-low-volume hospitals and very-high-volume hospitals ranged from more than 12% for pancreatic resection (16.3% versus 3.8%) to only 0.2% for carotid endarterectomy (1.7% versus 1.5%). The absolute differences in adjusted mortality rates between very-low-volume hospitals and very-high-volume hospitals were greater than 5% for esophagectomy and pneumonectomy; 2% to 5% for gastrectomy, cystectomy, repair of a nonruptured abdominal aneurysm, and replacement of an aortic or mitral valve; and less than 2% for coronary artery bypass grafting, lower-extremity bypass, colectomy, lobectomy, and nephrectomy (131). In a follow-up report, the observed associations between hospital volume and operative mortality for many of these procedures were largely mediated by surgeon volume (139). Moreover, these investigators have also noted that the higher operative mortality observed for black patients across a wide range of surgical procedures is due in large part to the higher mortality rates at the hospitals they attend (140).

Some investigators suggest that community-wide quality improvement initiatives may lead to improvement in care processes and outcomes. For example, a significant decrease in the combined event rate (30-day stroke or mortality) for carotid endarterectomy procedures was observed in a random sample of Medicare patients in 10 states during initial (June 1, 1995, to May 31, 1996) and subsequent (June 1, 1998, to May 31, 1999) reviews. Significant state-to-state variation was present, however, with a combined event rate for carotid endarterectomy alone that ranged from 2.7% (Georgia) to 5.9% (Indiana) for all indications combined, from 4.4% (Georgia) to 10.9% (Michigan) in patients with recent transient ischemia or stroke, from 1.4% (Georgia) to 6.0% (Oklahoma) in patients with no symptoms, and from 3.7% (Georgia) to 7.9% (Indiana) in patients with nonspecific symptoms (141). Although this may be related to other factors, quality improvement is likely to be the strongest influence.

Given that the prevalence of CAD contributes substantially to the perioperative risk of major surgical procedures, at least some of the differences in surgical outcome from 1 hospital to another may potentially be related to variations in the degree to which CAD is recognized and treated appropriately. The level of this awareness also has implications regarding survival. In the prospectively randomized Veterans Administration Trial of Carotid Endarterectomy versus Nonoperative Management for Asymptomatic Carotid Stenosis, for example, more than 20% of both randomized cohorts died of cardiac-related complications within a follow-up period of 4

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years (142). Historically, Hertzer (9) observed in a selective review of several thousand open vascular surgical procedures (carotid endarterectomy, aortic aneurysm resection, and lower-extremity revascularization) reported in the English literature from 1970 to 1987 that cardiac complications were responsible for approximately half of all perioperative deaths and that fatal events were nearly 5-times more likely to occur in the presence of standard preoperative indications of CAD. Furthermore, the late (5-year) mortality rate for patients who were suspected to have CAD was twice that for patients who were not (approximately 40% versus 20%). It is intriguing that in this report, both the perioperative and 5-year mortality rates for patients who previously had coronary bypass surgery were similar to the results reported for patients who had no clinical indications of CAD at the time of peripheral vascular surgery. Similarly, in the Coronary Artery Surgery Study (CASS), which included 24 959 participants with known CAD, prior CABG was associated with reduced cardiac risk after noncardiac operations involving the thorax, abdomen, vasculature, and head and neck (postoperative deaths 1.7% versus 3.3%, MI 0.8% versus 2.7%) (60). Nonetheless, results from the randomized, prospective Coronary Artery Revascularization Prophylaxis (CARP) trial demonstrated that coronary artery revascularization before elective major vascular surgery did not improve long-term survival or alter early postoperative outcomes, including death, MI, and length of the hospital stay, among patients with stable CAD (143). However, patients with a stenosis of the left main coronary artery of greater than 50%, an LVEF of less than 20%, and severe aortic stenosis were excluded from the trial. In contrast to the CASS report, the lack of benefit for coronary artery revascularization in the CARP trial was attributed to a significant recent increase in use of beta blockers, antiplatelet agents, ACE inhibitors, and statins (60,143). Indeed, Mangano et al and Poldermans et al documented the cardioprotective effect of perioperative beta blockade in substantially and significantly reducing cardiac morbidity and mortality in high-risk patients undergoing major vascular surgery (88,89). However, despite aggressive perioperative medical management, the risk of early cardiac morbidity and late mortality remains significant after major vascular surgery. For example, in the CARP trial, the incidence of early MI was 8.4%, with a median mortality of 23% at 27 months (143).

Patients undergoing major vascular surgery constitute a particular challenge, because these are high-risk operations in a patient population with a high prevalence of significant CAD. There are, however, other surgical procedures for which the interaction of patient-specific and surgery-specific factors has been examined. Nonthoracic solid organ transplantation generally represents a high-risk procedure in a patient with multiple comorbidities. Significant CAD is common in patients with diabetes mellitus who have end-stage renal disease. In a study of 176 consecutive patients undergoing either kidney or kidney-pancreas transplants, there was a high correlation between adverse postoperative cardiac events and preoperative documentation of reversible defects on intravenous dipyridamole myocardial perfusion imaging in combination with significant CAD on coronary angiograms: 3 of 27 patients (11.1%) versus 1 of 111 patients (0.9%) with a normal dipyridamole myocardial perfusion imaging (144). Similarly, in a review of 2694 adult renal transplants performed at the University of Minnesota between January 1, 1985, and December 31, 1998, there was an overall incidence of cardiac complications of 6.1%, which was significantly related to age greater than 50 years and preexisting cardiac disease (145).

Although the prevalence of CAD is relatively low in patients with end-stage liver disease who are undergoing liver transplantation, 2 studies (146,147) have documented the reliability of dobutamine stress echocardiography (DSE) in predicting post-transplant cardiac events. Stress echocardiography has also been shown to be useful in predicting cardiac outcomes in patients with advanced obstructive pulmonary disease who are undergoing lung volume reduction surgery (148,149).

As Fleisher and Barash (150) have emphasized, the specific surgical setting must be considered within any algorithm regarding preoperative cardiac evaluation. The term "noncardiac operation" is exceedingly broad in its definition; it embraces aging patients with complex technical problems, as well as younger patients scheduled for straightforward surgical procedures. As described above, cardiovascular morbidity and mortality vary not only among procedures but also among institutions for the same procedure. Therefore, in assessing the risks and benefits of a perioperative intervention strategy, risks associated with noncardiac surgery must be individualized. It is important to remember, however, that the indications for coronary intervention should not be redefined simply because a patient who has CAD of marginal significance also happens to require a major noncardiac procedure. Conversely, the long-term implications of severe left main or triple-vessel disease and diminished LV function are no less ominous after a minor noncardiac operation than they are in any other patient situation. In the final analysis, 1 of the ultimate objectives of the preoperative cardiac assessment is to exclude the presence of such serious CAD that some form of direct intervention would be warranted even if no noncardiac operation were necessary. In this regard, the presentation for noncardiac surgery may simply represent the first time that a patient with overt or suspected CHD has had an opportunity for cardiovascular assessment.

In summary, the surgical procedures have been classified as low-risk, intermediate-risk, and vascular surgery. Although coronary disease is the overwhelming risk factor for perioperative morbidity, procedures with different levels of stress are associated with different levels of morbidity and mortality. Superficial and ophthalmologic procedures represent the lowest risk and are rarely associated with excess morbidity and mortality. Major vascular procedures represent the highest-risk procedures and are now considered distinctly in the decision to perform further evaluation because of the large body of evidence regarding the value of perioperative interventions in this population (Figure 1). Both endovascular abdominal aortic aneurysm repair and carotid endarterectomy should be considered within the intermediate-risk category distinct from the open vascular surgery procedures on the basis of preoperative morbidity and mortality rates, but clinicians should incorporate the similarly poor long-term

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survival that accompanies these procedures into their decision-making processes. Within the intermediate-risk category, morbidity and mortality vary depending on the surgical location and extent of the procedure. Some procedures may be short, with minimal fluid shifts, whereas others may be associated with prolonged duration, large fluid shifts, and greater potential for postoperative myocardial ischemia and respiratory depression. Therefore, the physician must exercise judgment to correctly assess perioperative surgical risks and the need for further evaluation.

5. Supplemental Preoperative Evaluation

5.1. Assessment of LV Function

Recommendations for Preoperative Noninvasive Evaluation of LV Function

CLASS IIa

1. It is reasonable for patients with dyspnea of unknown origin to undergo preoperative evaluation of LV function. (*Level of Evidence: C*)
2. It is reasonable for patients with current or prior HF with worsening dyspnea or other change in clinical status to undergo preoperative evaluation of LV function if not performed within 12 months. (*Level of Evidence: C*)

CLASS IIb

1. Reassessment of LV function in clinically stable patients with previously documented cardiomyopathy is not well established. (*Level of Evidence: C*)

CLASS III

1. Routine perioperative evaluation of LV function in patients is not recommended. (*Level of Evidence: B*)

Resting LV function has been evaluated before noncardiac surgery by radionuclide angiography, echocardiography, and contrast ventriculography (46,151–160). Of 9 studies that demonstrated a positive relation between decreased preoperative ejection fraction and postoperative mortality or morbidity, 6 were prospective (151,152,155,158,161,162), and 3 were retrospective (153,154,158).

Halm et al (161) studied a cohort of 339 men either with documented ischemic heart disease or multiple risk factors for CHD; 49% had clinically evident vascular disease. An echocardiographic determination of LVEF less than 40% was associated with all adverse perioperative outcomes (cardiac death, nonfatal MI, unstable angina, congestive HF, and ventricular tachycardia). In multivariable analysis that included the clinical risk factors of definite CAD or history of congestive HF, neither LVEF nor regional wall-motion score added significant independent value in the prediction of individual events such as postoperative cardiac death, nonfatal MI, or HF (161).

In a study of 570 patients having transthoracic echocardiography before major noncardiac surgery, Rohde and colleagues (162) found that any degree of LV systolic dysfunction was marginally associated with postoperative MI or cardiogenic pulmonary edema (OR 2.1, 95% CI: 1.0 to 4.5; $P=0.05$). The finding of any degree of LV dysfunction had a poor sensitivity (43%) and positive predictive value (13%) in predicting these events, with a specificity of 76% and negative predictive value of 94%. This finding is concordant with a subsequent meta-analysis (163) of 8 studies of preoperative resting LV function as assessed by radionuclide angiography. In that study, Kertai et al found that LVEF less than 35% had a sensitivity of 50% and a specificity of 91% in the prediction of perioperative nonfatal MI or cardiac death (163). The greatest risk of complications was observed in patients with an LVEF at rest of less than 35%. In the perioperative phase, poor LV systolic or diastolic function is mainly predictive of postoperative HF and, in critically ill patients, death. It is noteworthy, however, that resting LV function was not found to be a consistent predictor of perioperative ischemic events.

5.2. Assessment of Risk for CAD and Assessment of Functional Capacity

5.2.1. The 12-Lead ECG

Recommendations for Preoperative Resting 12-Lead ECG

CLASS I

1. Preoperative resting 12-lead ECG is recommended for patients with at least 1 clinical risk factor* who are undergoing vascular surgical procedures. (*Level of Evidence: B*)
2. Preoperative resting 12-lead ECG is recommended for patients with known CHD, peripheral arterial disease, or cerebrovascular disease who are undergoing intermediate-risk surgical procedures. (*Level of Evidence: C*)

CLASS IIa

1. Preoperative resting 12-lead ECG is reasonable in persons with no clinical risk factors who are undergoing vascular surgical procedures. (*Level of Evidence: B*)

CLASS IIb

1. Preoperative resting 12-lead ECG may be reasonable in patients with at least 1 clinical risk factor who are undergoing intermediate-risk operative procedures. (*Level of Evidence: B*)

CLASS III

1. Preoperative and postoperative resting 12-lead ECGs are not indicated in asymptomatic persons undergoing low-risk surgical procedures. (*Level of Evidence: B*)

In patients with established or documented coronary disease, the resting 12-lead ECG contains important prognostic information that relates to long-term morbidity and mortality (164–167). The magnitude and extent of Q waves provide a crude estimate of LVEF and are a predictor of long-term mortality (168,169). Horizontal or downsloping ST-segment depression greater than 0.5 mm, LV hypertrophy with a "strain" pattern, and left bundle-branch block in patients with established coronary disease are all associated with decreased life expectancy (164–172). In particular, the presence of LV hypertrophy or ST-segment depression on

*Clinical risk factors include history of ischemic heart disease, history of compensated or prior HF, history of cerebrovascular disease, diabetes mellitus, and renal insufficiency.

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a preoperative 12-lead ECG predicts adverse perioperative cardiac events (173).

The resting 12-lead ECG has been examined both preoperatively and postoperatively to evaluate its prognostic value. To create an index for risk of cardiovascular complications, Lee and colleagues studied 4135 patients aged 50 years or older undergoing major noncardiac surgery (4). Major noncardiac surgery was defined by an expected hospital length of stay of at least 2 days. In this cohort, the presence of a pathological Q wave on the preoperative ECG was associated with an increased risk of major cardiac complications, defined as an MI, pulmonary edema, ventricular fibrillation, primary cardiac arrest, or complete heart block. Pathological Q waves were found in 17% of the patient population.

In contrast to these findings, Liu and colleagues studied the predictive value of a preoperative 12-lead ECG in 513 patients aged 70 years or older undergoing elective or urgent noncardiac surgery (174). In this cohort, 75% of the patients had a baseline ECG abnormality, and 3.7% of the patients died. The causes of death, in decreasing order, were sepsis, multisystem organ failure, bowel perforation, stroke, respiratory failure, and cardiac complications. Electrocardiographic abnormalities were not predictive of any outcome, although no abnormality was examined individually.

The resting 12-lead ECG did not identify increased perioperative risk in patients undergoing low-risk surgery (175). In a study of 18 189 patients at 9 centers undergoing elective cataract surgery, half of the patients underwent basic testing that included a 12-lead ECG, complete blood count, and electrolyte measurement. There was no difference in outcome between the group that had routine testing versus the group that did not. The no-testing group was eligible to undergo a test in response to a specific complaint or physical finding.

Although the optimal time interval between obtaining a 12-lead ECG and elective surgery is unknown, general consensus suggests that an ECG within 30 days of surgery is adequate for those with stable disease in whom a preoperative ECG is indicated.

5.2.2. Exercise Stress Testing for Myocardial Ischemia and Functional Capacity

The aim of supplemental preoperative testing is to provide an objective measure of functional capacity, to identify the presence of important preoperative myocardial ischemia or cardiac arrhythmias, and to estimate perioperative cardiac risk and long-term prognosis. Poor functional capacity in patients with chronic CAD or those convalescing after an acute cardiac event is associated with an increased risk of subsequent cardiac morbidity and mortality (62). Decreased functional capacity may be caused by several factors, including inadequate cardiac reserve, advanced age, transient myocardial dysfunction from myocardial ischemia, deconditioning, and poor pulmonary reserve.

In evaluating the role of exercise testing to assess patients undergoing noncardiac procedures, it is useful to summarize what is known about ECG exercise testing in general. The sensitivity gradient for detecting obstructive coronary disease is dependent on severity of stenosis and extent of disease, as well as the criteria used for a positive test. As many as 50% of patients with single-vessel coronary disease and adequate levels of exercise can have a normal exercise ECG (63). The mean sensitivity and specificity of exercise testing for obstructive coronary disease are 68% and 77%, respectively (64). The sensitivity and specificity are 81% and 66% for multivessel disease and 86% and 53% for 3-vessel or left main coronary disease, respectively (65).

Weiner et al (61) studied 4083 medically treated patients in CASS and identified a high-risk patient subset (12% of the population) with an annual mortality rate greater than or equal to 5% per year when the exercise workload was less than Bruce stage I and the exercise ECG showed ST-segment depression greater than or equal to 1 mm. A low-risk subset (34% of the population) who were able to complete or do more than Bruce stage III with a normal exercise ECG had an annual mortality rate of less than 1% per year over 4 years of follow-up (61). Similar results have been reported by others (66,67).

Table 6 lists publications in which exercise test results and perioperative events were reported. In most series, very-high-risk patients (recent MI, unstable angina, HF, and serious ventricular arrhythmias) were excluded. McPhail et al (184) reported on preoperative exercise treadmill testing and supplemental arm ergometry in 100 patients undergoing surgery for peripheral vascular disease or abdominal aortic aneurysm. Of the 100 patients, 30 were able to reach 85% of age-predicted heart rate maximum, and only 2 had cardiac complications (6%). In contrast, 70% of the population were unable to reach 85% of age-predicted heart rate or had an abnormal exercise ECG. In this group, the cardiac complication rate (MI, death, HF, or ventricular arrhythmia) was 24% (17 patients).

A peak exercise heart rate greater than 75% of age-predicted maximum can be expected in approximately half of all patients who undergo treadmill exercise, with supplemental arm ergometry when necessary for patients limited by claudication (177). The frequency of an abnormal exercise ECG response is dependent on prior clinical history (177,180). Among patients without a cardiac history and with a normal resting ECG, approximately 20% to 50% will have an abnormal exercise ECG. The frequency is greater (35% to 50%) in patients with a prior history of MI or an abnormal rest ECG. The risk of perioperative cardiac events and long-term risk are increased significantly in patients with an abnormal exercise ECG at low workloads (184,177,178).

In contrast to the above-mentioned studies of patients with vascular disease, in a general population of patients in which only 20% to 35% had peripheral vascular disease and who were undergoing noncardiac surgery, Carliner et al (186) reported exercise-induced ST-segment depression greater than or equal to 1 mm in 16% of 200 patients older than 40 years (mean age 59 years) being considered for elective surgery. Only 2 patients (1%) had a markedly abnormal (ST-segment depression of 2 mm or more) exercise test. Of the 32 patients with an abnormal exercise test, 5 (16%) died or had a nonfatal MI. Of 168 patients with a negative test, 157 (93%) did not die or have an MI. In that series, however, the results of preoperative exercise testing were not statistically significant independent predictors of cardiac risk.

Table 5 provides a prognostic gradient of ischemic responses during an ECG-monitored exercise test as developed

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Table 6. Preoperative Exercise Testing Before Major Noncardiac Surgery

Study, Year	n	% of Patients With Abnormal Test	Criteria for Abnormal Test	% Events	Prediction of Cardiac Events		Event	Comments
					% Positive Test	% Negative Test		
Peripheral vascular surgery or abdominal aortic aneurysm repair								
McCabe et al (176), 1981	314	36	STD, CP, or A	38 (15/39)	81 (13/16)	91 (21/23)	D, M, I, H, A	
Cutler et al (177), 1981	130	39	STD	7 (9/130)	16 (8/50)	99 (79/80)	D, M	Less than 75% MPHR increased risk
Arous et al (178), 1984	808	17	STD	NR	21 (19/89)	NR	D, M	
Gardine et al (179), 1985	86	48	STD	11 (2/19)	11 (1/9)	90 (9/10)	D, M	
von Knorring and Lepantalo (180), 1986	105	25	STD, A, or CP	3 (3/105)	8 (2/26)	99 (78/79)	D, M	
Kopecky et al (181), 1986	114	57	Less than 400 kpm	7 (8/110)	13 (8/63)	100 (47/47)	D, M	
Leppo et al (182), 1987*	60	28	STD	12 (7/60)	25 (3/12)	92 (44/48)	D, M	Exercise test results used to refer patients for revascularization
Hanson et al (183), 1988	74	57	STD	3 (1/37)	5 (1/19)	100 (18/18)	D, M	Arm ergometry
McPhail et al (184), 1988*	100	70	Less than 85% MPHR	19 (19/100)	24 (17/70)	93 (28/30)	D, M, A, F	Less than 85% MPHR; $P=0.04$; STD; NS
Urbinati et al (185), 1994	121	23	STD	0	0/28	100 (93/93)	D, M	Carotid endarterectomy patients. STD predicted late death.
Peripheral vascular surgery or major noncardiac surgery								
Carliner et al (186), 1985	200	16	STD	8 (16/200)	16 (5/32)	93 (157/168)	D, M	5 METs (NS)

Numbers in parentheses are number of patients/total number of patients. In references (176, 178, 179, 181, and 183), the total number of patients undergoing peripheral vascular surgery was less than the total number tested. A indicates cardiac arrhythmia; CP, chest pain; D, death; F, failure; H, hypotension; I, myocardial ischemia; kpm, kilometers per hour; M, myocardial infarction; MET, metabolic equivalent; MPHR, maximum predicted heart rate; n, number of patients; NR, not reported; NS, not significant; and STD, exercise-induced electrocardiographic ischemia.

*Studies with prospective collection of postoperative electrocardiogram and cardiac enzymes.

for a general population of patients with suspected or proven CAD (187). The onset of a myocardial ischemic response at low exercise workloads is associated with a significantly increased risk of perioperative and long-term cardiac events. In contrast, the onset of a myocardial ischemic response at high exercise workloads is associated with significantly less risk. The prognostic gradient is also influenced by the age of the patient, the extent of the coronary disease, the degree of LV dysfunction, hemodynamic response to exercise, and presence or absence of chronotropic incompetence. American College of Cardiology/American Heart Association guidelines concerning the indications for and interpretation of exercise stress testing are available (188).

5.2.3. Noninvasive Stress Testing

Recommendations for Noninvasive Stress Testing Before Noncardiac Surgery

CLASS I

1. **Patients with active cardiac conditions (see Table 2) in whom noncardiac surgery is planned should be evaluated and treated per ACC/AHA guidelines† before noncardiac surgery. (*Level of Evidence: B*)**

CLASS IIa

1. **Noninvasive stress testing of patients with 3 or more clinical risk factors and poor functional capacity (less than 4 METs) who require vascular surgery‡ is reasonable if it will change management. (*Level of Evidence: B*)**

†ACC/AHA/ESC Guidelines for the Management of Patients With Atrial Fibrillation (110), ACC/AHA/ACP Guidelines for the Management of Patients with Chronic Stable Angina (189), ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult (190), ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction (49), ACC/AHA/ESC Guidelines for the Management of Patients With Supraventricular Arrhythmias (191), ACC/AHA 2002 Guideline Update for the Management of Patients With Unstable Angina and Non–ST-Segment Elevation Myocardial Infarction (192), ACC/AHA 2006 Guidelines for the Management of Patients With Valvular Heart Disease (103), and ACC/AHA/ESC Guidelines for the Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death (193).

‡Vascular surgery is defined by emergency aortic and other major vascular surgery and peripheral vascular surgery. See Table 4.

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CLASS IIb

1. Noninvasive stress testing may be considered for patients with at least 1 to 2 clinical risk factors and poor functional capacity (less than 4 METs) who require intermediate-risk noncardiac surgery if it will change management. (*Level of Evidence: B*)
2. Noninvasive stress testing may be considered for patients with at least 1 to 2 clinical risk factors and good functional capacity (greater than or equal to 4 METs) who are undergoing vascular surgery. (*Level of Evidence: B*)

CLASS III

1. Noninvasive testing is not useful for patients with no clinical risk factors undergoing intermediate-risk noncardiac surgery. (*Level of Evidence: C*)
2. Noninvasive testing is not useful for patients undergoing low-risk noncardiac surgery. (*Level of Evidence: C*)

The 2 main techniques used in preoperative evaluation of patients undergoing noncardiac surgery who cannot exercise are to increase myocardial oxygen demand (by pacing or intravenous dobutamine) and to induce hyperemic responses by pharmacological vasodilators such as intravenous dipyridamole or adenosine. The most common examples presently in use are DSE and intravenous dipyridamole/adenosine myocardial perfusion imaging with both thallium-201 and technetium-99m.

5.2.3.1. Radionuclide Myocardial Perfusion Imaging Methods

Publications that report the results of stress myocardial perfusion testing before both vascular and nonvascular surgery are summarized in Table 7. The bulk of the studies included were prospectively recruited patient studies, a majority of which involved patients undergoing vascular surgery. Cardiac events in the perioperative period were defined for the purpose of this table as MI or death due to cardiac causes, and information about events and scan results had to be available. These studies have shown that reversible perfusion defects, which reflect jeopardized viable myocardium, carry the greatest risk of perioperative cardiac death or MI. The percentage of patients with evidence of ischemic risk reflected in reversible myocardial perfusion defects ranged from 23% to 69%. The positive predictive value of reversible defects for perioperative death or MI ranged from 2% to 20% in reports that included more than 100 patients. In more recent publications, the positive predictive value of myocardial perfusion imaging has been decreased significantly. This is probably related to the fact that in recent years, the results of preoperative stress nuclear imaging studies have been actively used to select patients for therapeutic interventions such as coronary revascularization, as well as to adjust perioperative medical treatment and monitoring and to select different surgical procedures. The result is a lower cardiac event rate in patients with abnormal studies. However, because of a very high sensitivity of abnormal stress nuclear imaging studies for detecting patients at risk for perioperative cardiac events, the negative predictive value of a normal scan has remained uniformly high at approximately 99% for MI or cardiac death. Most studies have found that fixed perfusion defects do not have significant predictive value for perioperative cardiac events. Even though patients with fixed defects in some studies had increased risk compared with patients with normal images, the risk was significantly lower than in patients with reversible defects.

Shaw et al (224) conducted a meta-analysis of dipyridamole myocardial perfusion imaging for risk stratification before elective vascular surgery (10 studies, 1994 patients) that demonstrated significant prognostic utility for this scintigraphic technique. In addition, they noted that the positive predictive value of perfusion imaging was correlated with the pretest cardiac risk of the patients. Overall, a reversible myocardial perfusion defect predicted perioperative events, and a fixed thallium defect predicted long-term cardiac events. Semiquantitative analysis of myocardial perfusion imaging improved the clinical risk stratification by defining a relationship of increasing risk of cardiac events as defect size increased.

Importantly, the risk of perioperative cardiac events as a function of stress nuclear myocardial perfusion imaging is continuous rather than categorical. Several studies have shown that the risk of cardiac events increases as the extent of reversible defects increases (203,205,225). Abnormal imaging studies with a small degree of reversible defect carry a small risk of cardiac events, whereas the cardiac risk increases significantly as the size of the reversible defect increases to a moderate degree (20% to 25% of LV mass). A meta-analysis of studies examining the relationship of perioperative cardiac risk and semiquantitative assessment of reversible defects on dipyridamole myocardial perfusion imaging in patients undergoing noncardiac vascular surgery was reported by Etchells and colleagues (226). In 9 studies comprising 1179 patients, they found that reversible defects in fewer than 20% of myocardial segments were associated with a small, nonsignificant increased risk of perioperative death or MI. Reversible defects that involved more than 20% of myocardial segments were associated with a significantly higher risk of perioperative cardiac death or MI that increased progressively as the extent of reversible defects increased.

Beattie et al (227) conducted a meta-analysis (68 studies) comparing stress myocardial perfusion imaging versus stress echocardiography in 10 049 patients at risk for MI before elective noncardiac surgery. The authors concluded that both myocardial perfusion imaging and stress echocardiography detected a moderate-to-large defect in 14% of patients (likelihood ratio 8.35, 95% CI: 5.6 to 12.45) and that a moderate-to-large perfusion defect predicted postoperative MI and death.

Mondillo et al (228) sought to compare the predictive value of different noninvasive tests in patients scheduled for noncardiac surgery. A total of 118 patients were risk stratified according to clinical markers and LVEF to low-, moderate-, or high-risk categories and randomly assigned to 1 of 3 noninvasive tests: dipyridamole stress echocardiography, dobutamine stress echocardiography, or dipyridamole perfusion scintigraphy. Although the low-risk group was event-free, 10.4% of the moderate-risk group and 24% of the high-risk group experienced events. Of the clinical risk categories, only the high-risk category was related to cardiac complications (P less than 0.05). Multivariable analysis showed the best

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Table 7. Summary of Studies Examining the Value of Myocardial Perfusion Imaging for Preoperative Assessment of Cardiac Risk

				Perioperative Events*		
Study, Year	n	% of Patients With Ischemia	Events % (MI/ Death)	Ischemia: % Positive Predictive Value	Normal: % Negative Predictive Value	Comments
Vascular surgery						
Boucher et al (194), 1985	48	33 (16)	6 (3)	19 (3/16)	100 (32/32)	First study to define risk of thallium redistribution
Cutler and Leppo (195), 1987	116	47 (54)	10 (11)	20 (11/54)	100 (60/60)	Only aortic surgery
Fletcher and Kershaw (196), 1988	67	22 (67)	4 (3)	20 (3/15)	100 (56/56)	
Sachs et al (197), 1988	46	31 (14)	4 (2)	14 (2/14)	100 (24/24)	
Eagle et al (44), 1989	200	41 (82)	8 (15)	16 (13/82)	98 (61/62)	Defined clinical risk
McEnroe et al (198), 1990	95	36 (34)	7 (7)	9 (3/34)	96 (44/46)	Fixed defects predict events
Younis et al (199), 1990	111	36 (40)	7 (8)	15 (6/40)	100 (51/51)	Included long-term follow-up
Mangano et al (200), 1991	60	37 (22)	5 (3)	5 (1/22)	95 (19/20)	Managing physicians blinded to scan result
Strawn and Guernsey (201), 1991	68	N/A	6 (4)	N/A	100 (21/21)	
Watters et al (202), 1991	26	58 (15)	12 (3)	20 (3/15)	100 (11/11)	Included echocardiographic (TEE) studies
Hendel et al (203), 1992	327	51 (167)	9 (28)	14 (23/167)	99 (97/98)	Included long-term follow-up
Lette et al (41), 1992	355	45 (161)	8 (30)	17 (28/161)	99 (160/162)	Used quantitative scan index
Madsen et al (204), 1992	65	69 (45)	8 (5)	11 (5/45)	100 (20/20)	
Brown and Rowen (205), 1993	231	33 (77)	5 (12)	13 (10/77)	99 (120/121)	Prognostic utility enhanced by combined scan and clinical factors
Kresowik et al (206), 1993	170	39 (67)	3 (5)	4 (3/67)	98 (64/65)	
Baron et al (207), 1994	457	35 (160)	5 (22)	4 (7/160)	96 (195/203) NFMI only	Did not analyze for cardiac deaths; no independent value of scan
Bry et al (208), 1994	237	46 (110)	7 (17)	11 (12/110)	100 (97/97)	Cost-effectiveness data included
Koutelou et al (209), 1995	106	44 (47)	3 (3)	6 (3/47)	100 (49/49)	Used adenosine/SPECT thallium imaging
Marshall et al (210), 1995	117	47 (55)	10 (12)	16 (9/55)	97 (33/34)	Used adenosine thallium and sestamibi; size of ischemic defect enhanced prognostic utility
Van Damme et al (211), 1997	142	34 (48)	2 (3)	N/A	N/A	Used dobutamine SPECT sestamibi and echocardiographic imaging; echocardiographic and nuclear scan prognostic utility was equivalent
Huang et al (212), 1998	106	36 (39)	5 (5)	13 (5/39)	100 (24/24)	Dipyridamole thallium SPECT
Cohen et al (213), 2003	153	31 (48)	4 (6)	4 (2/48)	100 (21/21)	Dipyridamole SPECT sestamibi imaging; perioperative and long-term follow-up. Perfusion defect in the LAD territory was best predictor of long-term death/MI.
Harafuji et al (214), 2005	302	30 (92)	1.3 (4)	2 (2/92)	100 (210/210)	SPECT thallium with adenosine stress in 239 patients; dipyridamole in 63. Summed stress score greater than or equal to 14 (20-segment model) best multivariate predictor of events.
Nonvascular surgery†						
Camp et al (215), 1990	40	23 (9)	15 (6)	67 (6/9)	100 (23/23)	Diabetes mellitus, renal transplant
Iqbal et al (216), 1991	31	41 (11)	11 (3)	27 (3/11)	100 (20/20)	Exercise 86%, diabetes mellitus, pancreas transplant
Coley et al (217), 1992	100	36 (36)	4 (4)	8 (3/36)	98 (63/64)	Define clinical risk factors in patients with known or suspected CAD
Shaw et al (218), 1992	60	47 (28)	10 (6)	21 (6/28)	100 (19/19)	Used adenosine
Takase et al (219), 1993	53	28 (15)	11 (6)	27 (4/15)	100 (32/32)	Patients with documented or suspected CAD; included rest echocardiogram
Younis et al (220), 1994	161	31 (50)	9 (15)	18 (9/50)	98 (87/89)	Intermediate- to high-risk CAD
Stratmann et al (221), 1996	229	29 (67)	4 (10)	6 (4/67)	99 (1/92)	Used dipyridamole sestamibi and noted fixed defect had more prognostic utility than transient defect
Zoghbi et al (222), 2003	87	8 (7)	2 (2)	14 (1/7)	97 (1/79)	Liver transplant cohort
Patel et al (223), 2003	174	31 (54)	7 (12)	15 (8/54)	97 (116/120)	Renal transplant cohort

All studies except those by Coley et al (217) and Shaw et al (218) acquired patient information prospectively. Only in reports by Mangano et al (200) and Baron et al (207) were attending physicians blinded to scan results. Patients with fixed defects were omitted from calculations of positive and negative predictive value. CAD indicates coronary artery disease; LAD, left anterior descending coronary artery; MI, myocardial infarction; n, number of patients who underwent surgery; N/A, not available; NFMI, nonfatal myocardial infarction; SPECT, single-photon emission computed tomography; and TEE, transesophageal echocardiography.

*Positive and negative predictive values are predictive value (number of patients/total number of patients whose test results indicated either ischemia or a normal scan).

†Studies utilizing pharmacological and/or exercise thallium testing.

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predictors of events were the severity and extent of ischemia (dipyridamole, *P* less than 0.01; dobutamine, *P* less than 0.005). Only reversible perfusion defects at scintigraphy were significantly related to perioperative events. The strongest predictor of cardiac events was the presence of more than 3 reversible defects (*P* less than 0.05).

A meta-analysis was performed on 58 studies of 6 preoperative noninvasive tests, including studies on myocardial perfusion scintigraphy (n=23), DSE (n=8), and dipyridamole stress echocardiography (n=4) (163). The summary receiver operating characteristic curve with the end point of prediction of perioperative cardiac death and nonfatal MI was highest with DSE, with a weighted sensitivity of 85% (95% CI: 74% to 97%) and specificity of 70% (95% CI: 62% to 79%). Although DSE performed better than the other tests, statistical significance was only reached compared with myocardial perfusion scintigraphy (relative diagnostic OR: 5.5, 95% CI: 2.0 to 14.9). However, the large majority of the cited nuclear studies involved older planar imaging technology that is generally no longer in use.

The use of techniques to quantify the extent of abnormality and the current routine use of quantitative gated single-photon emission computed tomography perfusion imaging to evaluate LVEF will probably improve the positive predictive nature of myocardial perfusion imaging. Although there are relatively few published reports using adenosine myocardial perfusion imaging in the preoperative risk assessment of patients before noncardiac surgery, its usefulness appears to be equivalent to that of dipyridamole. American College of Cardiology/American Heart Association guidelines concerning indications for and interpretation of stress testing with myocardial perfusion imaging are available (229).

The need for caution in routine screening with dipyridamole myocardial perfusion imaging of all patients before vascular surgery has been raised by Baron et al (207). In this review of patients undergoing elective abdominal aortic surgery, the presence of definite CAD and age greater than 65 years were better predictors of cardiac complications than perfusion imaging. Subsequently, several studies have prospectively examined the impact of preoperative cardiac risk assessment using a methodology that generally followed the recommendations outlined in prior ACC/AHA preoperative guidelines. In a report by Vanzetto et al (230), consecutive patients were evaluated before abdominal aortic surgery. If no major or fewer than 2 intermediate clinical cardiac risk factors were present, patients went directly to elective surgery. The authors noted a 5.6% incidence of cardiac events (death/MI) in those patients with 1 risk factor and a rate of 2.4% in those with no cardiac risk factors. All high-risk patients (2 or more cardiac risk factors) underwent dipyridamole myocardial perfusion single-photon emission computed tomography imaging, and those with a normal scan (38%) had a cardiac event rate of 2% in contrast to a rate of 23% in 43 patients demonstrating reversible thallium defects. Bartels et al (54) also reported that patients referred for elective vascular surgery who had no clinical intermediate or major clinical risk factors had a 2% incidence of cardiac events. Those patients with either intermediate risk factors and a functional capacity of less than 5 METs or high clinical risk underwent stress myocardial perfusion imaging or had intensified medical therapy before elective surgery. Using this ACC/AHA guideline–influenced approach, the overall cardiac mortality for the cohort was only 1%, and there were no significant differences in outcome among patients with low, intermediate, or high clinical risk. Another report (231) also used the clinical risk factor parameters to divide vascular surgery patients into low-, intermediate-, and high-cardiac-risk groups. Those authors did not include functional capacity measurements but noted a 0% death or MI rate in the perioperative period among the low-risk patients.

In summary, stress nuclear myocardial perfusion imaging has a high sensitivity for detecting patients at risk for perioperative cardiac events. Perioperative cardiac risk appears to be directly proportional to the amount of myocardium at risk as reflected in the extent of reversible defects found on imaging. Because of the overall low positive predictive value of stress nuclear imaging, it is best used selectively in patients with a high clinical risk of perioperative cardiac events.

5.2.3.2. Dobutamine Stress Echocardiography

Dobutamine stress echocardiography has become the method of choice for pharmacological stress testing with ultrasound imaging. With incremental infusion of supratherapeutic doses of dobutamine, which increases myocardial contractility and heart rate, significant coronary stenotic disease can be identified with the induction of LV ischemic regional wall-motion abnormalities within the distribution of the affected vessels. The dobutamine infusion is often supplemented with intravenous atropine to optimize chronotropic response to stress. In patients with suboptimal LV endocardial definition, intravenous contrast imaging for LV opacification is now routinely used for image enhancement and improved diagnostic interpretation (232).

Several reports have documented the accuracy of DSE to identify patients with significant angiographic coronary disease (233–238). The use of DSE in preoperative risk assessment was evaluated in 16 studies, all published since 1991 and identified by a computerized search of the English language literature (Table 8) (146,149,160,239–251). The populations predominantly but not exclusively included patients undergoing peripheral vascular surgical procedures. Only 2 studies blinded the physicians and surgeons who treated the patients to the dobutamine stress echocardiography results (160,241). In the remaining studies, the results were used to influence preoperative management, particularly the decision whether or not to proceed with coronary angiography or coronary revascularization before elective surgery. Each study used similar but not identical protocols. The definition of a positive and negative test result differed considerably on the basis of subjective analysis of regional wall motion (ie, worsening of preexisting wall-motion abnormalities was considered by some investigators as a positive finding and by others as a negative finding). The end points used to define clinical outcome varied and included both "soft" (ie, arrhythmia, HF, and ischemia) and "hard" (ie, MI or cardiac death) perioperative events.

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Table 8. Summary of Studies Examining the Value of Dobutamine Stress Echocardiography for Preoperative Risk Assessment

Study, Year	n	Patients With Ischemia, %	Events (MI/Death) (n)	Criteria for Abnormal Test	MI or Death*		Comments
					Positive Predictive Value	Negative Predictive Value	
Lane et al (239), 1991	38	50	8% (3)	New WMA	16% (3/19)	100% (19/19)	Vascular and general surgery
Lalka et al (240), 1992	60	50	15% (9)	New or worsening WMA	23% (7/30)	93% (28/30)	Multivariate analysis
Eichelberger et al (241), 1993	75	36	3% (2)	New or worsening WMA	7% (2/27)	100% (48/48)	Managing physicians blinded to DSE results
Langan et al (242), 1993	74	24	4% (3)	New WMA or ECG changes	17% (3/18)	100% (56/56)	
Poldermans et al (243), 1993	131	27	4% (5)	New or worsening WMA	14% (5/35)	100% (96/96)	Multivariate analysis; managing physicians blinded to DSE results
Dávila-Román et al (244), 1993	88	23	2% (2)	New or worsening WMA	10% (2/20)	100% (68/68)	Included long-term follow-up
Poldermans et al (160), 1995	302	24	6% (17)	New or worsening WMA	24% (17/72)	100% (228/228)	Multivariate analysis
Shafritz et al (245), 997	42	0	2% (1)	New or worsening WMA	N/A	97% (41/42)	
Plotkin et al (146), 1998	80	8	3% (2)	New or worsening WMA, ECG changes, and/or symptoms of chest pain or dyspnea	33% (2/6)	100% (74/74)	Orthotopic liver transplantation
Ballal et al (246), 1999	233	17	3% (7)	New or worsening WMA	0% (0/39)†	96% (187/194)	Included long-term follow-up
Bossone et al (149), 1999	46	9	2% (1)	New or worsening WMA	25% (1/4)	100% (42/42)	Lung volume reduction surgery; included long-term follow-up
Das et al (246), 2000	530	40	6% (32)	New or worsening WMA or failure to develop hyperdynamic function	15% (32/214)	100% (316/316)	Multivariate analysis; nonvascular surgery
Boersma et al (248), 2001	1097	20	4% (44)	New or worsening WMA	14% (30/222)	98% (861/875)	Major vascular surgery; multivariate analysis; long-term follow-up
Morgan et al (249), 2002	78	5	0% (0)	Undefined	0% (0/4)	100% (100%)	High-risk noncardiac surgery in one third of patients
Torres et al (250), 2002	105	47	10% (10)	New or worsening WMA	18% (9/49)	98% (55/56)	Multivariate analysis; vascular surgery in 82% of patients; long-term follow-up
Labib et al (251), 2004	429	7	2% (10)	New or worsening WMA	9% (3/32)	98% (390/397)	Vascular surgery in 30% of patients

DSE indicates dobutamine stress echocardiogram; MI, myocardial infarction; n, number of patients who underwent surgery; and WMA, wall-motion abnormality.
*Numbers in parentheses refer to number of patients/total in group.
†Intervening revascularization in 9 ischemic patients (23%).

The data indicate that DSE can be performed safely and with acceptable patient tolerance. The range of positive test results was 5% to 50%. The predictive value of a positive test ranged from 0% to 33% for hard events (nonfatal MI or death). The negative predictive value ranged from 93% to 100%. In the series by Poldermans et al (160), the presence of a new wall-motion abnormality was a powerful determinant of an increased risk for perioperative events after multivariable adjustment for different clinical and echocardiographic variables. Several studies have suggested that the extent of the wall-motion abnormality and/or wall-motion change at low ischemic thresholds, particularly at a heart rate of less than 60% of age-predicted maximum (243,247), is especially important. These findings have been shown to be predictors of long-term (243,244,252,253) and short-term (254) outcomes.

Integration of the presence of clinical risk factors such as ongoing stable angina, prior MI, HF, and diabetes mellitus with analysis of the ischemic threshold enhances the value of DSE in predicting perioperative nonfatal MI or death. In a study by Das et al (247), an ischemic response at 60% or more of maximal predicted heart rate was associated with only a 4% event rate if no clinical risk factors were present versus a 22% event rate in patients with more than 2 risk factors. The same investigators found a high event rate with an ischemic threshold of less than 60% of maximal predicted

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heart rate (29% in patients with no risk factors compared with 40% in those patients with more than 2 risk factors). In that study, the only multivariable predictors of perioperative nonfatal MI or death were ischemic threshold less than 60% of maximal predicted heart rate (OR: 7.00, 95% CI: 2.8 to 17.6, $P=0.0001$) and congestive HF (OR: 4.66, 95% CI: 1.55 to 14.02, $P=0.006$) (247).

Labib et al (251) investigated the negative predictive value of preoperative patients who did or did not reach 85% of maximum predicted heart rate on a DSE test, as well as the impact of resting wall-motion abnormalities without ischemia for the prediction of perioperative MI. Of the 429 patients, 16% had a peak heart rate less than 85% of the maximum predicted (77% of the group undergoing therapy with beta blockers). Cardiac events were statistically less frequent in the negative-DSE group than in the positive-DSE group (7 of 397 or 1.8% versus 3 of 32 or 9.4%; $P=0.03$). In the negative-DSE group, no difference was seen in clinical events between the maximal and submaximal groups; however, when resting wall motion was compared in patients who had a negative DSE (n=397), patients with a fixed wall-motion abnormality at rest had more clinical events than the group with normal wall motion (7 of 100 or 7% versus 0 of 297 or 0%; $P=0.0001$). Variables associated with postoperative cardiac events (MI or death) included CAD (OR: 5.56, 95% CI: 1.06 to 29.05, $P=0.035$), resting wall-motion abnormality (OR not available, P less than 0.001), and resting ejection fraction less than 35% (OR: 13.78, 95% CI: 2.41 to 78.99, $P=0.019$).

Even in high-risk noncardiac surgery, patients with ischemia induced by DSE have a clearly lower (3% to 7%) risk of perioperative nonfatal MI or death if they are classified as moderate to low risk by clinical risk scoring versus a 3- to 5-fold greater risk in those with a high clinical risk score (4,247,248). This risk may be reduced significantly with beta-blocker therapy (89,248). In patients at low to intermediate clinical risk who are undergoing established and therapeutic beta blockade, DSE is unlikely to impact the early perioperative outcome (248) but contributes to the stratification of long-term cardiac risk (253).

Dobutamine stress magnetic resonance imaging has been used to identify myocardial ischemia in those not well suited for dobutamine stress transthoracic echocardiography (255–257). In more than 500 patients across 6 studies, both the sensitivity and specificity of dobutamine stress magnetic resonance for appreciating 50% coronary arterial luminal narrowings have been demonstrated to range between 83% and 91% (255–260). Results from dobutamine stress magnetic resonance are useful for identifying those at risk for the future occurrence or cardiac death or MI (261). Dobutamine stress magnetic resonance imaging has been used to assess perioperative risk in those individuals undergoing noncardiac surgery (262). In a study of 102 patients with intermediate clinical predictors of a cardiac event during noncardiac surgery (262), the presence of inducible ischemia on a dobutamine stress magnetic resonance stress test was associated with a 20% incidence of adverse cardiac events (MI, cardiac death, or perioperative congestive HF) compared with a 2% incidence in those without inducible ischemia ($P=0.004$).

This difference was significant ($P=0.04$) after adjustment for age greater than 70 years, diabetes mellitus, the presence of stable angina before testing, a history of HF, LVEF, or a Q wave on the resting ECG. As shown with other noninvasive imaging techniques, dobutamine stress magnetic resonance results do not provide incremental prognostic information in individuals with preoperative clinical data indicating a low risk for sustaining a cardiac event during noncardiac surgery (262).

An early meta-analysis (224) has suggested that DSE is superior to dipyridamole-thallium stress testing in the prediction of perioperative cardiac events during vascular surgery. Subsequent large, prospective, individual studies directly comparing stress echocardiography and nuclear imaging in the context of risk stratification for noncardiac surgery, however, have been lacking (263,264).

A recent, much larger meta-analysis by Beattie and colleagues (227). re-examined the predictive value of pharmacological stress testing with echocardiography versus nuclear perfusion scintigraphy. This study did not differentiate between the type of pharmacological stressor used, nor was there a subgroup analysis with regard to the type of noncardiac surgery. The meta-analysis included 25 studies of stress echocardiography (3373 patients) and 50 studies of stress nuclear perfusion imaging (6827 patients). Five studies of dipyridamole stress echocardiography were included with those that used dobutamine stress. Perioperative MI and death were the only end-point events considered. In this analysis, the likelihood ratio, defined as sensitivity/1-specificity, of a perioperative cardiac event with a positive stress echocardiogram was more than twice that of a positive stress nuclear perfusion study (likelihood ratio 4.09, 95% CI: 3.21 to 6.56 versus 1.83, 95% CI: 1.59 to 2.10; $P=0.001$). The finding of a moderate to large ischemic abnormality by either pharmacological stress imaging modality was highly predictive of perioperative MI or death (likelihood ratio 8.35, 95% CI: 5.6 to 12.45), but such an abnormality was detected in only approximately 15% of all patients tested by either method (227).

5.2.3.3. Stress Testing in the Presence of Left Bundle-Branch Block

The tachycardia induced during exercise and conceivably also during dobutamine infusion may result in reversible septal defects even in the absence of left anterior descending artery disease in some patients. This response is unusual with either dipyridamole or adenosine stress testing. Consequently, the specificity of exercise myocardial perfusion imaging in the presence of left bundle-branch block is low (reported to be 33%), and overall diagnostic accuracy varies from 36% to 60% (265,266). In contrast, the use of vasodilators in such patients has a sensitivity of 98%, a specificity of 84%, and a diagnostic accuracy of 88% to 92% (267–269). Comparison of DSE to exercise thallium-201 SPECT imaging for the diagnosis of LAD coronary disease in the setting of left bundle-branch block has also found pharmacologic stress to be superior to exercise, with diagnostic accuracies of

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Table 9. Predictive Value of Preoperative ST-Segment Changes Detected by Ambulatory Monitoring for Perioperative Myocardial Infarction and Cardiac Death After Major Vascular Surgery

Study, Year	n	Patients With Abnormal Test, %	Criteria for Abnormal Test	Perioperative Events, % (n/N)		Comments
				Positive Predictive Value*	Negative Predictive Value	
Raby et al (276), 1989	176	18	A	10% (3/32)	1% (1/144)	24 to 48 hours during ambulation
Pasternack et al (277), 1989	200	39	A	9% (7/78)	2% (2/122)	
Mangano et al (42), 1990	144	18	A,B	4% (1/26)	4% (5/118)	Immediately before surgery
Fleisher and Barash (150), 1992	67	24	A,B	13% (2/16)	4% (2/51)	Immediately before surgery
McPhail et al (275), 1993	100	34	A	15% (5/34)	6% (4/66)	
Kirwin et al (274), 1993	96	9	A	11% (1/9)	16% (14/87)	Definition of MI based on enzymes only
Fleisher et al (278), 1995	86	23	A,B	10% (2/20)	3% (2/66)	Quantitative monitoring not predictive

A indicates ≥1 mm of ST-segment depression; B, ≥2 mm of ST-segment elevation; MI, myocardial infarction; and n, number of patients.
*Positive predictive value for postoperative cardiac events.

92% versus 69% respectively (270). Again these findings were primarily due to the low specificity of exercise perfusion imaging (42%) compared to DSE (92%), despite high sensitivities of 100% and 91% respectively (270). In a study by Mairesse et al (271), dobutamine stress testing with imaging by echocardiography and perfusion scintigraphy were directly compared in 24 patients with left bundle-branch block. For the detection of LAD ischemia, the diagnostic sensitivity of DSE was similar to perfusion imaging (83% versus 75%), with identical specificities (92%) and equivalent diagnostic accuracies (87% versus 83%) respectively. In the presence of left bundle-branch block, the diagnostic accuracy of perfusion scintigraphy in detection of CAD in other coronary distributions ranged from 42% to 75% compared to 79% with DSE (271).

Pharmacologic stress testing with either perfusion scintigraphy or DSE is hence preferred over exercise stress testing for the preoperative evaluation of CAD in patients with left bundle-branch block. Furthermore, exercise should not be combined with dipyridamole in such patients, and synthetic catecholamines will also yield false-positive results (272).

5.2.4. Ambulatory ECG Monitoring

The predictive value of preoperative ST changes on 24- to 48-hour ambulatory ECG monitoring for cardiac death or MI in patients undergoing vascular and nonvascular surgery has been reported by several investigators. The frequency of abnormal ST-segment changes observed in 869 patients reported in 7 series was 25% (range 9% to 39%) (42,273–277). The positive and negative predictive values for perioperative MI and cardiac death are shown in Table 9. In 2 studies, preoperative ST changes had a predictive value similar to dipyridamole myocardial perfusion imaging (275,278).

Although the test has been shown to be predictive of cardiac morbidity, there are several limitations. Differences in the study protocols (24 versus 48 hour, ambulatory versus in-hospital monitoring) may account for the variability in the predictive value of the test. Preoperative ambulatory ECG monitoring for ST-segment changes cannot be performed in a significant percentage of patients because of baseline ECG changes. The test, as currently used, only provides a binary outcome and therefore cannot further stratify the high-risk group in order to identify the subset for whom coronary angiography should be considered (278).

5.3. Recommendations: If a Test Is Indicated, Which Test?

In most ambulatory patients, the test of choice is exercise ECG testing, which can both provide an estimate of functional capacity and detect myocardial ischemia through changes in the ECG and hemodynamic response. Although treadmill exercise stress testing in patients with abdominal aortic aneurysms would cause concern with regard to induced rupture, there is evidence that it can be performed safely in this population. In a series of more than 250 patients with an abdominal aortic aneurysm greater than 4 cm (including 97 that were 6 cm or greater) who underwent treadmill exercise, only a single patient developed subacute aneurysm rupture 12 hours after testing, which was repaired successfully (279).

In patients with important abnormalities on their resting ECG (eg, left bundle-branch block, LV hypertrophy with "strain" pattern, or digitalis effect), stress cardiac imaging should be considered. As discussed with left bundle-branch block, exercise myocardial perfusion imaging has an unacceptably low specificity because of septal perfusion defects that are not related to CAD. For these patients, pharmacologic stress myocardial perfusion scintigraphy or dobutamine stress echocardiography is recommended over exercise stress imaging.

In patients unable to perform adequate exercise, a nonexercise stress test should be considered. In this case, pharmacological stress testing with adenosine, dipyridamole, or dobutamine myocardial perfusion imaging testing and dobutamine echocardiography are commonly used tests. Intrave-

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nous dipyridamole and adenosine should be avoided in patients with significant bronchospasm, critical carotid occlusive disease, or a condition that prevents their being withdrawn from theophylline preparations or other adenosine antagonists. Dobutamine should not be used as a stressor in patients with serious arrhythmias, severe hypertension, or hypotension. For patients in whom echocardiographic image quality is likely to be poor, a myocardial perfusion study is more appropriate. Soft tissue attenuation can also be a problem with myocardial perfusion imaging, although recent development of attenuation correction for acquisition and analysis has been very helpful in reducing this issue. If there is an additional question about valvular dysfunction, the echocardiographic stress test is favored. In many instances, either stress perfusion or stress echocardiography is appropriate. The expertise of the practitioner's available stress laboratory resources in identifying severe coronary disease is as important as the particular type of stress test ordered.

The current evidence does not support the use of an ambulatory ECG as the only diagnostic test to refer patients for coronary angiography, but it may be useful in rare circumstances to direct medical therapy. In general, indications for preoperative coronary angiography are similar to those identified for the nonoperative setting.

6. Implications of Guidelines and Other Risk Assessment Strategies for Costs and Outcomes

The decision to recommend further testing or treatment for the individual patient being considered for noncardiac surgery ultimately becomes a balancing act between the estimated probabilities of effectiveness versus risk. The proposed benefit, of course, is the possibility of identifying and/or treating advanced but relatively unsuspected CAD that might result in significant cardiac morbidity or mortality either perioperatively or in the long term. In the process of further screening and treatment, the risks from the tests and treatments themselves may offset or even exceed the potential benefit of evaluation. Furthermore, the cost of screening and treatment strategies must be considered. Although physicians should be concerned with improving the clinical outcome of their patients, cost is an appropriate consideration when different evaluation and treatment strategies are available that cannot be distinguished from one another in terms of clinical outcome.

Froehlich et al (280) compared test utilization and outcome for aortic surgery patients before and after implementation of the ACC/AHA preoperative assessment guidelines at their center using a comprehensive educational program. They demonstrated dramatic reductions in stress testing after implementation of the guidelines, mostly with nuclear imaging (88% to 47%), cardiac catheterization (24% to 11%), coronary revascularization (24% to 2%), and overall preoperative costs ($1087 to $171). At the same time, perioperative outcome was actually improved as the death/MI rate fell from 11% to 4%. Of note, implementation of the guidelines had the greatest impact in the preoperative evaluation of clinically low-risk patients. This study supports the ACC/AHA guideline approach of clinical assessment of risk followed by selective testing with stress nuclear myocardial perfusion imaging in higher-risk subgroups of patients, and they confirm that cardiac patients at low clinical risk can typically undergo elective surgery with a low event rate without further testing. The approach of selective testing, based on an understanding of test performance, a clinical patient assessment, and the potential impact of test results on clinical decision making, is supported as leading to appropriateness of testing, as outlined in the ACC Foundation/American Society of Nuclear Cardiology proposed method for evaluating the appropriateness of cardiovascular imaging (281).

Formal decision and cost-effectiveness analyses of the value of preoperative cardiac evaluation have been published and have yielded highly varied results (208,282,283). These models were created before the publication of the CARP trial and the DECREASE (Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography)-II trial and assumed that coronary revascularization had benefits in clinical populations that differed from center to center; therefore, it is difficult to determine the exact risks of aggressive screening and treatments versus the benefits in terms of risk reduction. Additionally, the models all demonstrate that the optimal strategy depends on the mortality rates for both cardiac procedures and noncardiac surgeries in the clinically relevant range. One model, which did not support a strategy incorporating coronary angiography and revascularization, used lower mortality rates than those used or reported in the other studies (282,283,284). Therefore, the use of any decision and cost-effectiveness model in a specific situation depends on the comparability of local mortality rates to those of the model.

One report suggested that the cost of a selected coronary screening approach, as described in the present guidelines, was as low as $214 per patient (285). Resource utilization and costs of preoperative evaluation also decreased in patients undergoing elective abdominal aortic surgery in the period of implementation for the initial version of these guidelines compared with historical controls, whereas outcomes were similar (280). Several publications have shown a cost per year of life saved for this selected screening strategy of less than $45 000 when applied to patients undergoing vascular surgery (286,287). However, none of these studies included a strategy of selected screening followed by aggressive beta-blocker treatment in high-risk individuals, as described by Poldermans and colleagues (89).

Available data suggest that implementation of various strategies of beta blockade in patients undergoing major vascular surgery is cost-effective and even cost-saving from the perspective of a short-term provider. Fleisher et al (288) used decision analytic techniques to compare 5 different strategies for implementing beta blockade in patients undergoing abdominal aortic aneurysm surgery. These ranged from 1) no routine beta blockade to 2) oral bisoprolol 7 days preoperatively followed by perioperative intravenous metoprolol and oral bisoprolol, 3) immediate preoperative atenolol with postoperative intravenous then oral atenolol, 4) intraoperative esmolol with conversion to intravenous and then oral atenolol in the immediate postoperative period, and 5) intra-

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operative and postoperative (at 18 hours) esmolol followed by atenolol. Using Medicare costs as a proxy, they found that the institution of an oral beta blocker a minimum of 7 days before surgery was associated with a cost savings of approximately $500 from the hospital's perspective; that is, beta blockade was associated with both better outcomes and lower cost. All other strategies tested were cost saving, but to a lesser degree. Of note, this decision analysis did not include the performance of any screening tests or the costs of such testing. Schmidt et al (289) estimated the impact of a clinical practice guideline for perioperative beta blockers at a medical center in western Massachusetts in high-risk patients with 2 or more cardiac risk factors or known CAD. Using effectiveness data for beta-blocker treatment from Mangano et al (88), they estimated that full use of beta blockers in eligible patients could result in 62 to 89 fewer deaths annually at a cost of approximately $33 000 to $40 000. Prophylactic beta blockade also represents an excellent strategy in patients for whom coronary revascularization for long-term benefit is not a serious consideration.

7. Perioperative Therapy

7.1. Preoperative Coronary Revascularization With CABG or Percutaneous Coronary Intervention

(All of the Class I indications below are consistent with the ACC/AHA 2004 Guideline Update for Coronary Artery Bypass Graft Surgery.)

CLASS I

1. Coronary revascularization before noncardiac surgery is useful in patients with stable angina who have significant left main coronary artery stenosis. (*Level of Evidence: A*)
2. Coronary revascularization before noncardiac surgery is useful in patients with stable angina who have 3-vessel disease. (Survival benefit is greater when LVEF is less than 0.50.) (*Level of Evidence: A*)
3. Coronary revascularization before noncardiac surgery is useful in patients with stable angina who have 2-vessel disease with significant proximal LAD stenosis and either EF less than 0.50 or demonstrable ischemia on noninvasive testing. (*Level of Evidence: A*)
4. Coronary revascularization before noncardiac surgery is recommended for patients with high-risk unstable angina or non–ST-segment elevation MI.§ (*Level of Evidence: A*)
5. Coronary revascularization before noncardiac surgery is recommended in patients with acute ST-elevation MI. (*Level of Evidence: A*)

CLASS IIa

1. In patients in whom coronary revascularization with PCI is appropriate for mitigation of cardiac symptoms and who need elective noncardiac surgery in the subsequent 12 months, a strategy of balloon angioplasty or bare-metal stent placement followed by 4 to 6 weeks of dual-antiplatelet therapy is probably indicated. (*Level of Evidence: B*)
2. In patients who have received drug-eluting coronary stents and who must undergo urgent surgical procedures that mandate the discontinuation of thienopyridine therapy, it is reasonable to continue aspirin if at all possible and restart the thienopyridine as soon as possible. (*Level of Evidence: C*)

CLASS IIb

1. The usefulness of preoperative coronary revascularization is not well established in high-risk ischemic patients (e.g., abnormal dobutamine stress echocardiograph with at least 5 segments of wall-motion abnormalities). (*Level of Evidence: C*)
2. The usefulness of preoperative coronary revascularization is not well established for low-risk ischemic patients with an abnormal dobutamine stress echocardiograph (segments 1 to 4). (*Level of Evidence: B*)

CLASS III

1. It is not recommended that routine prophylactic coronary revascularization be performed in patients with stable CAD before noncardiac surgery. (*Level of Evidence: B*)
2. Elective noncardiac surgery is not recommended within 4 to 6 weeks of bare-metal coronary stent implantation or within 12 months of drug-eluting coronary stent implantation in patients in whom thienopyridine therapy, or aspirin and thienopyridine therapy, will need to be discontinued perioperatively. (*Level of Evidence: B*)
3. Elective noncardiac surgery is not recommended within 4 weeks of coronary revascularization with balloon angioplasty. (*Level of Evidence: B*)

7.1.1. Rationale for Surgical Coronary Revascularization

To understand the value of preoperative evaluation, it is important to understand the pathophysiology of perioperative cardiac morbidity. This topic has been reviewed elsewhere (290). Ellis et al (291) analyzed the coronary angiograms of 63 patients undergoing major nonthoracic vascular surgery in a case-control study that indirectly supported benefit from preoperative coronary bypass surgery and found that a coronary occlusion proximal to viable myocardium was associated with a higher rate of perioperative MI and death, which raises the question of whether revascularizing coronary occlusions might not reduce the frequency of these adverse events. However, in that study, the number of mild, "nonobstructive" lesions was also associated with MI and death. This is consistent with studies that show that the most severe stenoses may not always be responsible for MI and that coronary thrombosis frequently occurs at the site of milder stenoses. Thus, preoperative revascularization of severe stenoses may not reduce perioperative ischemic complications (292).

7.1.2. Preoperative CABG

Until recently, all of the evidence regarding the value of surgical coronary revascularization was derived from cohort studies in patients who presented for noncardiac surgery after

§High-risk unstable angina/non–ST-segment elevation MI patients were identified as those with age greater than 75 years, accelerating tempo of ischemic symptoms in the preceding 48 hours, ongoing rest pain greater than 20 minutes in duration, pulmonary edema, angina with S_3 gallop or rales, new or worsening mitral regurgitation murmur, hypotension, bradycardia, tachycardia, dynamic ST-segment change greater than or equal to 1 mm, new or presumed new bundle-branch block on ECG, or elevated cardiac biomarkers, such as troponin.

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successful cardiac surgery. There are now several randomized trials that have assessed the overall benefit of prophylactic coronary bypass surgery to lower perioperative cardiac risk of noncardiac surgery, the results of which can be applied to specific subsets of patients and will be discussed later.

There have been several cohort studies published. In 1984, results of preoperative coronary angiography were reported in a large series of 1001 patients under consideration for elective vascular surgical procedures at the Cleveland Clinic (293). Severe CAD was identified by routine coronary angiography in 251 patients who met contemporary indications for CABG. In the 216 patients who underwent CABG, the mortality rate after CABG was 5.3%, with a subsequent mortality rate of 1.5% after vascular surgery. In the entire cohort of 1001 patients, operative deaths with vascular surgery occurred in 1 (1.4%) of 74 patients with normal coronary arteries, in 5 (1.8%) of 278 patients with mild to moderate CAD, in 9 (3.6%) of 250 patients with advanced but compensated CAD, and in 6 (14%) of 44 patients with severe, uncorrected, or inoperable CAD (294).

Eagle et al analyzed 3368 patients in the CASS database who underwent noncardiac surgery during more than 10 years of follow-up after entry in the CASS study (60). Patients undergoing urologic, orthopedic, breast, and skin operations had a very low mortality rate, less than 1%, regardless of whether they had undergone prior CABG for CAD. However, patients undergoing thoracic, abdominal, vascular, and head and neck surgery had a much higher risk of death and MI in the 30 days after the surgical procedure. In the subset of patients undergoing these higher-risk surgical procedures, patients who had undergone prior CABG had a lower risk of death (1.7% versus 3.3%, $P=0.03$) and nonfatal MI (0.8% versus 2.7%, $P=0.002$) than patients without prior CABG. Prior CABG before noncardiac surgery demonstrated the most benefit among patients with multivessel CAD and those with more severe angina. These data indicate that patients undergoing low-risk procedures are unlikely to derive benefit from CABG before low-risk surgery but suggest that patients with multivessel disease and severe angina undergoing high-risk surgery might well benefit from revascularization before noncardiac surgery.

Prior to the publication of randomized trials to address this issue, several authors used decision analysis and evaluation of claims databases to determine the value of coronary revascularization before noncardiac surgery. In an attempt to balance the potential risks versus benefits of CABG before vascular surgery, the additional short-term risks and long-term benefits should be understood. Long-term benefits of such strategies were not incorporated into 2 decision models (282,283) that demonstrated that the value of coronary revascularization before noncardiac surgery depended on local mortality rates for both CABG and noncardiac surgery. If the long-term benefits had been included, the value of preoperative coronary revascularization would have been increased. For instance, the European Coronary Surgery Study Group (295) has reported interesting findings in a small subset of 58 patients with peripheral vascular disease within a much larger series of 768 men who were randomly assigned to receive either coronary bypass surgery or medical management for angina pectoris. Although the presence of incidental peripheral vascular disease was associated with reductions in the 8-year survival rates for either surgical or medical management of CAD, its influence was especially unfavorable in patients who received medical therapy alone; that is, the long-term survival rate was 85% after coronary bypass surgery compared with 57% for nonsurgical treatment ($P=0.02$). Rihal and colleagues (296) have reported similar findings in more than 2000 patients enrolled in the CASS study. Compared with coronary bypass surgery in patients with both CHD and peripheral vascular disease, surgically treated patients with 3-vessel disease had significantly better long-term survival than those treated medically after adjustment for all covariates, including clinical measures of disease stability, stress test results, and LV function. In a study at the Cleveland Clinic Foundation, the cumulative 5-year survival rate for the 216 patients who received coronary bypass was 72% (81% in men without diabetes mellitus) compared with 43% ($P=0.001$) for 35 patients in whom coronary bypass was indicated but never performed (294,297). Fatal cardiac events occurred within a mean of 4.6 years in 12% and 26% of these 2 subsets, respectively ($P=0.033$). These later studies illustrate the importance of both perioperative and long-term cardiac risk when one considers whether to recommend coronary bypass surgery before noncardiac surgery.

A study by Fleisher et al (298) of a cohort of Medicare beneficiaries undergoing infrainguinal or abdominal aortic reconstructive surgery found that preoperative stress testing followed by revascularization was associated with improved short- and long-term survival with the higher-risk aortic surgery. However, this association may be confounded by the fact that the cohorts referred for preoperative stress testing were "healthier" patients, as evidenced by the finding that stress testing with or without coronary revascularization was associated with greater short- and long-term survival. On the other hand, a number of retrospective studies have demonstrated that patients who previously have successfully undergone coronary bypass have a low perioperative mortality rate in association with noncardiac procedures and that their mortality rate is comparable to the surgical risk for other patients who have no clinical indications of CAD (299–302).

The first large, randomized trial (CARP) was published by McFalls and colleagues (143), who randomly assigned 510 patients with significant coronary artery stenosis among 5859 patients scheduled for vascular operations to either coronary artery revascularization before surgery or no revascularization before surgery. Indications for vascular operations were expanding aortic abdominal aneurysm in 33% or peripheral vascular occlusive disease in 67%. Patients needing emergent or urgent surgery were excluded, as were patients with unstable coronary syndromes, at least 50% stenosis of the left main coronary artery, LVEF less than 20%, or severe aortic stenosis. One or more major coronary arteries had to have at least 70% stenosis and be suitable for revascularization. Overall, 74% of the 510 patients had 3 or more of the Eagle clinical risk criteria for CAD (44), 2 or more variables as defined by the Revised Cardiac Risk Index (4), or a moderate or large reversible defect on perfusion stress

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imaging. The remaining patients had angina or abnormal results on a stress test.

Two hundred fifty-eight patients were assigned to revascularization, and of the 225 who actually received preoperative coronary artery revascularization and had subsequent vascular surgery, 59% had PCI (PTCA and bare-metal stents) and 41% had CABG, at the discretion of the local investigators. The average number of vessels revascularized was 3.0 plus or minus 0.8 in the CABG patients and 1.3 plus or minus 0.8 in the PCI group. Thirty-three patients had coronary revascularization and did not undergo subsequent vascular surgery. Of these 33 patients, 10 died after CABG or PCI, 18 declined vascular surgery, and 5 developed a severe coexisting condition. Of those proceeding to vascular surgery, 4 deaths occurred in the revascularization group; 3 patients (2 after PCI and 1 after CABG) died after vascular surgery, which was performed during the same admission as the coronary revascularization procedure. Four percent of the patients assigned to the nonrevascularization group underwent coronary revascularization because of a change in their cardiac status. In the revascularization group, a median of 48 days after CABG and 41 days after PCI elapsed before the vascular operation. The types of vascular surgery procedures, anesthesia, and adjunctive medical management were similar between the revascularization and no-revascularization groups. Long-term medical management was similar between the 2 groups.

At 30 days after the vascular operation and analyzing treatment assigned, death had occurred in 3.1% of the revascularization group and 3.4% of the nonrevascularization group ($P=0.87$). Within 30 days of the vascular operation, postoperative MI by biomarker criteria had occurred in 12% of the revascularization group and 14% of the nonrevascularization group ($P=0.37$). At 2.7 years after randomization, mortality was 22% in the revascularization group and 23% in the nonrevascularization group (RR: 0.98, 95% CI: 0.70 to 1.37, $P=0.92$). Analysis with regard to treatment received rather than treatment assigned did not alter the long-term mortality findings. The authors concluded that routine coronary revascularization in patients with stable cardiac symptoms before elective vascular surgery does not significantly alter the long-term outcome or short-term risk of death or MI.

In a subsequent publication from the CARP trial, the authors reported on the subset of 222 patients who underwent elective vascular surgery after coronary revascularization (303). Prior CABG had been performed in 91 patients and prior PCI in 131 patients. Patients were not randomized between CABG and PCI; rather, the type of coronary revascularization was left to the discretion of the local investigator. Completeness of revascularization was defined as the number of coronary vessels revascularized relative to the total number of vessels with a stenosis of 70% or greater. A revascularization rate of greater than 100% could be obtained by this definition. Baseline clinical characteristics, Revised Cardiac Risk Index, results of stress imaging, and medical treatment were similar in the CABG and PCI groups. The CABG group had 3.0 (standard deviation 1.3) significantly stenosed vessels compared with 2.2 (standard deviation 1.4) in the PCI group (P less than 0.001). Completeness of revascularization was 117% (standard deviation 66%) in the CABG group compared with 81% (standard deviation 57%) in the PCI group (P less than 0.001). The incidence of death was not significant between the CABG and PCI groups (2.2% versus 3.8%, respectively; $P=0.497$). The incidence of any MI at 30 days and any MI after vascular surgery was higher in the PCI group than in the CABG group (30 days, 16.8% versus 6.6%, $P=0.024$; after vascular surgery, 32.7% versus 9.9%, $P=0.009$). They also found that the longer the delay between coronary revascularization and the vascular operation, the higher the incidence of MI. In the entire group, MI was inversely related to the completeness of revascularization ($P=0.02$) and occurred more frequently in abdominal than in infrainguinal vascular operations (19% versus 7.5%, $P=0.01$). This study addressed outcomes after vascular surgery in patients who received nonrandomized coronary revascularization procedures and did not address the relative benefit or risk of CABG compared with PCI for preoperative coronary revascularization using intention-to-treat analysis.

In patients in whom coronary revascularization is indicated, timing of the procedure depends on the urgency of the noncardiac surgical procedure balanced against the stability of the underlying CAD. The decision to perform revascularization on a patient before noncardiac surgery to "get them through" the noncardiac procedure is appropriate only in a small subset of very-high-risk patients when long-term outcomes are included.

The DECREASE-II trial (59) was designed to evaluate the utility of cardiac testing in patients undergoing major vascular surgery with intermediate cardiac risk factors and adequate beta-blocker therapy. A composite end point of death and nonfatal MI was assessed at 30 days after vascular surgery. The incidence of the primary end point in patients with extensive ischemia was 14.7%. Extensive ischemia was identified in 34 patients (8.8% of the population studied). Only 12 of 34 patients with extensive ischemia were considered to be candidates for coronary revascularization. The authors found that "in intermediate-risk patients with extensive ischemia, no revascularization compared with revascularization did not improve 30-day outcome (25.0% versus 9.1% events; OR 3.3, 95% CI: 0.5 to 24; p less than 0.32)." The authors went on to state, "The effect of coronary revascularization in intermediate-risk patients with extensive stress-induced ischemia cannot be assessed, owing to the insufficient number of patients studied." This study confirms that extensive cardiac ischemia is a risk factor for perioperative cardiac events, but it was too small to assess the effect of revascularization.

The DECREASE-V pilot study (304) screened 1880 patients scheduled for major vascular surgery and identified a high-risk cohort by the presence of 3 or more clinical risk factors. Of these, 101 showed extensive ischemia on DSE (5 or more ischemic segments, 88% of patients) or dobutamine or dipyridamole perfusion scintigraphy (at least 3 ischemic walls, 13% of patients). An LVEF of 35% or less was observed in 43% of these 101 patients. The 101 patients were randomized to best medical therapy and revascularization or best medical therapy alone before vascular surgery. Best medical therapy included tight heart rate control with beta

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blockers and continuation of antiplatelet therapy. The revascularization group (n=49) underwent catheterization, which revealed 2-vessel disease in 24%, 3-vessel disease in 67%, and left main disease in 8%. Revascularization with PCI was performed in 65% and CABG in 35%. Drug-eluting stents (DES) were used in 94% of the PCI patients, and dual-antiplatelet therapy was continued perioperatively. There was no significant difference in perioperative transfusion requirement in patients with and without antiplatelet therapy. Vascular surgery occurred a median of 29 (range 13 to 65) days after CABG and a median of 31 (range 19 to 39) days after PCI. Two patients died after CABG before vascular surgery owing to ruptured aneurysms. The outcome of 30-day all-cause death or nonfatal MI was similar between the revascularization and medical therapy patients at 43% versus 33% (OR: 1.4, 95% CI: 0.7 to 2.8, $P=0.30$), respectively. Postoperative troponin elevations occurred in 38.8% of revascularized patients versus 34.7% of medically treated patients. The incidence of 1-year all-cause death or MI was high (47%) and similar in both groups at 49% for revascularization and 44% for medical therapy (OR: 1.2, 95% CI: 0.7 to 2.3, $P=0.48$). This study was not sized to definitively answer the question as to the value of preoperative revascularization in high-risk patients; however, the findings are consistent with the previously published literature suggesting a lack of benefit of preoperative coronary revascularization in preventing death or MI.

Patients undergoing elective noncardiac procedures who are found to have prognostic high-risk coronary anatomy and in whom long-term outcome would likely be improved by coronary bypass grafting (305) should generally undergo coronary revascularization before a noncardiac elective vascular surgical procedure or noncardiac operative procedures of intermediate or high risk (Table 4). The cumulative mortality and morbidity of both the coronary revascularization procedure and the noncardiac surgery should be weighed carefully in light of the individual patient's overall health, functional status, and prognosis. The indications for preoperative surgical coronary revascularization, therefore, are essentially identical to those recommended by the ACC/AHA 2004 Guideline Update for Coronary Artery Bypass Graft Surgery and the accumulated data on which those conclusions were based (306).

7.1.3. Preoperative PCI

The role of prophylactic preoperative PCI in reducing untoward perioperative cardiac complications appears limited to patients with unstable active CAD who would be appropriate candidates for emergent or urgent revascularization under the published ACC/AHA PCI and CABG guidelines (306,307). Patients with ST-elevation MI, unstable angina, and non–ST-elevation MI benefit from early invasive management, as outlined in the current ACC/AHA/SCAI (Society for Cardiovascular Angiography & Interventions) 2005 guideline update for PCI (307). Additionally, in such patients in whom noncardiac surgery is imminent, despite an increased risk in the peri-MI period, a strategy of balloon angioplasty or bare-metal stenting should be considered, as discussed below.

Patients with asymptomatic ischemia or stable Canadian Cardiovascular Society class I or II angina do not appear to be candidates for prophylactic preoperative coronary revascularization unless cardiac catheterization reveals high-risk surgical anatomy, as discussed above. The evidence for the use and timing of PCI discussed below is summarized in Table 10.

It is unclear from the literature whether patients with stable but severe Canadian Cardiovascular Society class III angina would benefit from prophylactic preoperative coronary intervention. Indications for PCI for patients with this clinical presentation are outlined in the current ACC/AHA/SCAI 2005 guideline update for PCI (307). The balance of the evidence to date suggests that routine preoperative coronary revascularization in patients with stable class III angina will not alter perioperative risk. High-risk unprotected left main disease in a noncardiac surgical candidate presents a special case for consideration. The reported high rates of restenosis and acute events after balloon angioplasty, atherectomy, and bare-metal stenting in the left main artery suggest that these procedures would be a poor preoperative strategy before noncardiac surgery (320). There have been reports of successful unprotected left main PCI with DES in this group of patients (321), but the need for prolonged and perhaps lifelong dual-antiplatelet therapy to prevent catastrophic subacute thrombosis suggests that this strategy would have limited utility in the preoperative setting as well. Coronary artery bypass grafting should be considered in suitable patients with significant left main stenoses.

Percutaneous intervention as a prophylactic preoperative coronary intervention in stable patients with prior coronary bypass surgery before noncardiac surgery is of unknown value. However, recurrent symptomatic ischemia early after CABG is a class I indication for percutaneous revascularization.

In summary, the present review of the literature suggests that PCI before noncardiac surgery is of no value in preventing perioperative cardiac events, except in those patients in whom PCI is independently indicated for an acute coronary syndrome. However, unscheduled noncardiac surgery in a patient who has undergone a prior PCI presents special challenges, particularly with regard to management of the dual-antiplatelet agents required in those who have received coronary stents.

7.1.4. PCI Without Stents: Coronary Balloon Angioplasty

Several retrospective series of coronary balloon angioplasty before noncardiac surgery have been reported (Table 10). In a 50-patient series reported from Mayo Clinic (309), PTCA using balloons without stents was performed before noncardiac surgery (52% vascular procedures) in patients at high risk for perioperative complications (62% with greater than Canadian Cardiovascular Society class III angina, 76% with multivessel disease, and all with positive functional tests). Urgent CABG was required in 10% of patients after PTCA. The noncardiac operation was performed a median of 9 days after PCI, and the perioperative MI rate was 5.6%, whereas the mortality rate was 1.9%. Whether this result differs from what might have occurred without PTCA is uncertain.

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Table 10. Studies Reporting the Clinical Outcome (Death or Nonfatal MI) of Patients Undergoing Noncardiac Surgery After PCI

Study, Year	No. of Patients Who Underwent PCI	Time From PCI to Surgery	Perioperative Mortality, %	Perioperative Infarction, %	Comments
PCI without stents (coronary balloon angioplasty)					
Allen et al (308), 1991	148	338 days (mean)	2.7	0.7	No increase in events if surgery performed within 90 days of PTCA
Huber et al (309), 1992	50	9 days (mean)	1.9	5.6	CABG needed after balloon angioplasty in 10% of patients; no control group for comparison
Elmore et al (310), 1993	14	10 days (mean)	0	0%	Very small study. Event rate in patients treated with CABG or balloon angioplasty less than in control group. Angioplasty patients had fewer risk factors than patients undergoing CABG
Gottlieb et al (311), 1998	194	11 days (median)	0.5	0.5	Only vascular surgeries included
Posner et al (312), 1999	686	1 year (median)	2.6	2.2	Patients who had undergone PCI had a similar frequency of death and MI but half the angina and HF as matched patients with CAD who had not undergone PCI. Event rates were much higher if PCI had been performed within 90 days
Brilakis et al (313), 2005	350	Within 2 months	0.3	0.6	All events occurred in patients who underwent surgery within 2 weeks of PTCA
Leibowitz et al (314), 2006	216	Early (0 to 14 days)	19	4.7	56% had balloon angioplasty. 44% had stents. No outcome difference between balloon angioplasty and stent groups
		Late (15 to 62 days)	11	7.2	
PCI with coronary stents					
Kaluza et al (315), 2000	40	13 days (mean)	20	16.8	Mortality was 32% among patients operated on less than 12 days after stent placement vs 0 in patients operated on 12 to 30 days after PCI
Hassan et al (316), 2001	251	29 months (median)	0.8	0.8	Among patients who received PCI in BARI, outcome after noncardiac surgery was equivalent to that of BARI patients who had received CABG
McFalls et al (143), 2004	225	54 days (median)	3.1 (revascularization) vs 3.4% (control)	11.6 (revascularization) vs 14.3% (control)	Patients randomized to coronary revascularization (PCI in 59%, CABG in 41%) or not before vascular surgery. No difference in short- or long-term risk of MI or death
Godet et al (317), 2005	78	5 to 8 weeks	4	9	Propensity analysis showed no benefit for preoperative revascularization
Vicenzi et al (318), 2006	103	12 months	5	12	Mix of bare-metal and drug-eluting stents. Cardiac risk within 35 days of stent implantation was increased 2.1-fold compared with after 35 days
Schouten et al (319), 2007	192	Early	13.3	0	Early surgery: 13.3% had MACE; late surgery: 0.6% had MACE. Early surgery and no thienopyridine: 30.7% had MACE
		Late	0.6	0	
Poldermans et al (304), 2007	32 PCI 17 CABG	31 days	22.5 at 30 days	34.7 at 30 days	High-risk patients with significant CAD randomized to revascularization vs medical therapy. No advantage to revascularization in primary end point at 30 days or 1 year

BARI indicates Bypass Angioplasty Revascularization Investigation; CAD, coronary artery disease; CABG, coronary artery bypass surgery; HF, heart failure; MACE, major adverse cardiovascular event(s); MI, myocardial infarction; PCI, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty.

Elmore et al (310) analyzed a cohort of 2452 patients who had abdominal aortic aneurysm surgery between 1980 and 1990, of whom 100 patients (4.1%) required perioperative coronary revascularization (86 had CABG, and 14 had PTCA). No deaths occurred in either group, and the perioperative mortality rate for the 2452 patients was 2.9%. The median number of days between the coronary revascularization and surgery was 10 days for PTCA and 68 days for

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CABG. At 3 years, no statistical difference in survival was seen between the groups (82.8% for CABG and 92.3% for PTCA). The 3-year cardiac event rates were 27.3% for the CABG group and 56.5% for the PTCA group. The small numbers of patients in the PTCA group and the retrospective analysis over a long period of time make interpretation of the results of this study difficult. It appears, however, that candidates for elective abdominal aortic aneurysm surgery who have symptomatic disease (CAD) have a low operative mortality when revascularization is performed before surgery by either PTCA or CABG.

Allen et al (308) performed a retrospective analysis of 148 patients who underwent angioplasty before noncardiac surgery (35% abdominal, 33% vascular, and 13% orthopedic surgery). Surgery occurred within 90 days after angioplasty in 72 patients. There were 4 operative deaths (1 cardiac), and 16 patients experienced cardiac complications during the noncardiac surgery. Cardiac complications were more common in patients older than 60 years. Little information can be gleaned from this small retrospective study except to note the low incidence of cardiac death in patients who had coronary angioplasty sometime before their noncardiac surgery.

Gottlieb et al (311) studied 194 patients with CAD who underwent PTCA before vascular surgery (abdominal aortic, carotid endarterectomy, or peripheral vascular surgery). The median interval between PTCA and surgery was 11 days (interquartile range 3 to 49 days) (311). Twenty-six (13.4%) of the patients had a cardiac complication, but only 1 patient died, and 1 had a nonfatal MI. The variable time interval over which PTCA was performed before surgery and the inability to know whether the clinical outcome of these patients would have been different had a prior PTCA procedure not been performed limit the conclusions that can be drawn from this study.

Massie et al performed a case-control study of 140 patients with abnormal dipyridamole myocardial perfusion imaging scans in 2 or more segments; 70 underwent coronary angiography (of whom 25 were referred for revascularization), and 70 (matched for age, gender, type of vascular surgery, and number of myocardial segments that were suggestive of ischemia on myocardial perfusion imaging scanning) did not (322). A trend toward late benefit associated with preoperative revascularization was offset by a trend toward an early hazard from the risk of the preoperative invasive cardiac evaluation and treatment. There were no significant differences between the angiography group and matched control subjects with respect to the frequency of perioperative nonfatal MI (13% versus 9%) or fatal MI (4% versus 3%) or the frequency of late nonfatal MI (16% versus 19%) or late cardiac death (10% versus 13%).

In a retrospective cohort study by Posner et al (312), adverse events in the 30 days after noncardiac surgery were compared among patients who had undergone preoperative PTCA at any time, patients with nonrevascularized CAD, and patients without known coronary disease ("normal controls"). Patients with CAD had twice the risk of an adverse outcome as normal controls (OR: 1.98, *P* less than 0.001); however, the risk of an adverse outcome among patients who had undergone PTCA was half that of patients with nonrevascularized CAD. The benefit was limited to a reduction in angina and HF; there was no reduction in early postoperative MI or death associated with prior PTCA. The investigators did not control for the severity of coronary disease, comorbid illness, or the medical management used in the PTCA and nonrevascularized CAD groups. No benefit was seen in patients who had a PTCA 90 days or less before noncardiac surgery. The long time frame in which PTCA had been performed preoperatively limits the conclusions that can be drawn from this study.

Leibowitz et al (314) performed a retrospective review of 216 patients who had PCI with balloon angioplasty alone or PCI with stenting within 3 months of noncardiac surgery. Adverse clinical events included acute MI, major bleeding, and death less than 6 months after noncardiac surgery. Overall, 11% of patients died, 12% in the balloon-only group (13/122) versus 14% in the stent group (13/94; *P*=NS). There was no significant difference in either acute MI or bleeding between the balloon-only group (6% and 13%, respectively) and the stent group (7% and 16%, respectively). More deaths occurred in both the balloon-only and stent groups if noncardiac surgery was performed on days 0 to 14 after PCI (19%) than on days 15 to 62 after PCI (11%). However, the retrospective nature of the study did not allow for standardization of medical therapy after PCI, and 46% of patients who died had an ejection fraction less than 30%.

A retrospective analysis by Brilakis et al (313) of 350 patients who underwent balloon angioplasty between 1988 and 2001 in the 2 months before noncardiac surgery found 3 (1.6%) had perioperative MI or death, and all these events occurred in the patients who underwent noncardiac surgery within 2 weeks of balloon angioplasty. The authors concluded that the risk of perioperative death or MI in patients who undergo PCI before noncardiac surgery is low, and PTCA balloon angioplasty should be performed at least 2 weeks before noncardiac surgery.

There are data that permit comparison of the protective effects of revascularization with CABG and balloon angioplasty before noncardiac surgery. In the Bypass Angioplasty Revascularization Investigation, patients with multivessel coronary disease were randomly assigned to undergo balloon angioplasty or CABG (323). In an ancillary study, the results of 1049 surgeries performed in 501 patients subsequent to randomization were analyzed; 250 patients had undergone CABG, and 251 had balloon angioplasty (316). The median time from the most recent coronary revascularization procedure to noncardiac surgery was 29 months. The results of the study revealed that the frequency of death or MI was low in patients with multivessel disease who had undergone either procedure (1.6% in both groups), and there was no difference in the length of hospitalization or hospital cost. The risk of death or MI was lower when the noncardiac surgery was performed less than 4 years after coronary revascularization (0.8% versus 3.6% in patients undergoing surgery 4 or more years after coronary revascularization). These data do not provide insight into which patients require preoperative coronary revascularization, but they do suggest that the risk of perioperative infarction or death is approximately equal in patients who have undergone balloon angioplasty or CABG if

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they had been appropriate for and amenable to either type of coronary revascularization procedure.

After balloon angioplasty, delaying noncardiac surgery for more than 8 weeks increases the chance that restenosis at the angioplasty site will have occurred and theoretically increases the chances of perioperative ischemia or MI. However, performing the surgical procedure too soon after the PCI procedure might also be hazardous. Arterial recoil or acute thrombosis at the site of balloon angioplasty is most likely to occur within hours to days after balloon coronary angioplasty. Delaying surgery for at least 2 to 4 weeks after balloon angioplasty to allow for healing of the vessel injury at the balloon treatment site is supported by the study by Brilakis et al (313). Daily aspirin antiplatelet therapy should be continued perioperatively. The risk of stopping the aspirin should be weighed against the benefit of reduction in bleeding complications from the planned surgery.

7.1.5. PCI: Bare-Metal Coronary Stents

Table 10 also provides data on several studies of PCI with coronary stenting before noncardiac surgery. Godet et al(317) performed an analysis of 1152 patients after abdominal aortic surgery, 308 of whom underwent preoperative coronary angiography and 78 of whom underwent PCI (bare-metal stents in 96%). Patients who underwent coronary angiography without PCI fell into 2 groups: those with minor coronary lesions (n=13) and those with untreatable severe CAD (n=123). This latter group had a high cardiac risk, with severe postoperative coronary events occurring in 14.5% and death in 8.1%. After aortic surgery, compared with a control group of patients without preoperative PCI, the preoperative bare-metal coronary stent group showed no significant differences in death (4% in the control group and 5% in the stent group) or in severe postoperative coronary events (defined as new Q waves, prolonged ST-T changes, or positive troponin I; 6% in the control group and 9% in the stent group). Propensity analysis provided a similar conclusion, with a predicted rate of severe postoperative coronary events of 8.2% versus an observed rate in the bare-metal coronary stent group of 9.0% (nonsignificant) and a predicted rate of death of 6.9% versus an observed rate of 5.1% (nonsignificant).

A retrospective study by Kaluza et al (315) indicated that the frequency of bare-metal stent thrombosis when elective noncardiac surgery is performed within 2 weeks of stent placement is very high, as is the frequency of MI and death. In that study, there were 8 deaths, 7 MIs, and 11 major bleeding episodes in 40 patients who underwent coronary bare-metal stent placement less than 6 weeks (1 to 39 days, average 13 days) before noncardiac surgery. All deaths and MIs occurred in patients who were subjected to surgery less than 14 days after bare-metal stenting, and stent thrombosis accounted for most of the fatal events.

Another retrospective analysis by Wilson et al (324) of patients who underwent major noncardiac surgery in the 2 months after bare-metal coronary stent placement showed death, MI, or stent thrombosis in 8 (4%) of 207 patients, with death occurring in 6 patients (3%). Examination of the interval between coronary stenting and cardiac events revealed that all adverse events occurred in patients who underwent noncardiac surgery within 6 weeks of coronary stenting. Neither bleeding complications nor transfusion rate appeared related to the antiplatelet regimen (324).

Reddy and Vaitkus (325) published a retrospective analysis of 56 patients who received bare-metal coronary stents before noncardiac surgery that showed that 38% of patients who underwent surgery within 14 days of coronary stenting experienced a stent-related MI or cardiovascular death. No patients who underwent noncardiac surgery more than 6 weeks after coronary stenting had stent-related MI or cardiovascular death.

Sharma et al (326) retrospectively reviewed 47 patients who underwent noncardiac surgery within 90 days of bare-metal coronary stent implantation. They noted a 26% mortality rate in patients who had noncardiac surgery within 3 weeks of stent implantation compared with a 5% mortality rate in those in whom noncardiac surgery occurred more than 3 weeks after stent implantation. More importantly, in the early-surgery group, death occurred in 1 (5%) of 20 patients who continued taking thienopyridines perioperatively compared with 6 (85.7%) of 7 patients in whom thienopyridines were discontinued. There were no significant differences in bleeding between those taking or not taking thienopyridines.

If a coronary stent is used in the revascularization procedure, as in the majority of percutaneous revascularization procedures, further delay of noncardiac surgery may be beneficial. Bare-metal stent thrombosis is most common in the first 2 weeks after stent placement and is exceedingly rare (less than 0.1% of most case series) more than 4 weeks after stent placement (327,328). Given that stent thrombosis will result in Q-wave MI or death in the majority of patients in whom it occurs, and given that the risk of bare-metal stent thrombosis diminishes after endothelialization of the stent has occurred (which generally takes 4 to 6 weeks), it appears reasonable to delay elective noncardiac surgery for 4 to 6 weeks to allow for at least partial endothelialization of the stent, but not for more than 12 weeks, when restenosis may begin to occur.

A thienopyridine (ticlopidine or clopidogrel) is generally administered with aspirin for 4 weeks after bare-metal stent placement. The thienopyridines and aspirin inhibit platelet aggregation and reduce stent thrombosis but increase the risk of bleeding. Rapid endothelialization of bare-metal stents makes late thrombosis rare, and thienopyridines are rarely needed for more than 4 weeks after implantation of bare-metal stents. For this reason, delaying surgery 4 to 6 weeks after bare-metal stent placement allows proper thienopyridine use to reduce the risk of coronary stent thrombosis; then, after the thienopyridine has been discontinued, the noncardiac surgery can be performed. However, once the thienopyridine is stopped, its effects do not diminish immediately. It is for this reason that some surgical teams request a 1-week delay after thienopyridines are discontinued before the patient proceeds to surgery. In patients with bare-metal stents, daily aspirin antiplatelet therapy should be continued perioperatively. The risk of stopping the aspirin should be weighed against the benefit of reduction in bleeding complications from the planned surgery. In the setting of noncardiac surgery in patients who have recently received a bare-metal stent, the

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risk of stopping dual-antiplatelet agents prematurely (within 4 weeks of implantation) is significant compared with the risk of major bleeding from most commonly performed surgeries.

7.1.6. PCI: DES

Drug-eluting stents are designed to reduce neointimal formation, thus leading to lower restenosis rates. The currently available DES are coated with either sirolimus or paclitaxel. Several additional agents are in clinical testing. However, the action of these drugs will delay endothelialization and healing and possibly induce hypersensitivity to the drug or polymer and lead to an increased risk of thrombosis (329,330). Thrombosis of DES may occur late and has been reported up to 1.5 years after implantation, particularly in the context of discontinuation of antiplatelet agents before noncardiac surgery (331,332).

Vicenzi et al (318) reported a prospective observational study of 103 patients who underwent noncardiac surgery within 12 months of stent implantation. A mix of bare-metal stents and DES was reported, but in a significant number of patients, the type of stent could not be identified. Antiplatelet agents were either continued perioperatively or discontinued for fewer than 3 days preoperatively. All patients received therapeutic unfractionated heparin or enoxaparin. The main outcome variable was the combined perioperative complication rate at 30 days, which included cardiac complications, bleeding, surgical complications, and sepsis. Cardiac complications included death, MI, repeat revascularization, congestive HF, new unstable angina, new significant arrhythmias, or myocardial cell injury, defined as a positive troponin T without ECG signs or symptoms. Fully 45% of the patients experienced complications, and 4.9% died. The majority (333,334) of complications were cardiac (5% cardiac death, 12% MI, and 22% myocardial cell injury). Only 4% had bleeding complications despite the use of an anticoagulation regimen. Recently implanted stents (less than 35 days before surgery) resulted in a 2.1-fold increase in adverse events compared with those implanted more than 90 days before surgery. Outcomes stratified by type of anticoagulation regimen, type of stent, and type of operation were not reported. The authors estimated that 5% of stented patients from their institutions underwent subsequent noncardiac surgery. This study raises concern that noncardiac surgery, even with continued antiplatelet or anticoagulation regimens, presents a substantial risk of cardiac events in the year after stent implantation.

The CARP trial (143) and DECREASE-V pilot trial (304) used bare-metal stents and DES, respectively, in some of the patients randomized to revascularization in those trials, and neither trial showed an advantage of preoperative PCI with stents in preventing perioperative death or MI. See Section 7.1.2 for details.

Schouten et al (319) reported a single-center registry experience of 192 patients who had noncardiac surgery between 1999 and 2005 who also had a successful PCI for unstable coronary disease within the preceding 2 years. Patients with bare-metal stents received lifelong aspirin and at least 1 month of clopidogrel, and patients with DES received lifelong aspirin and clopidogrel for at least 3 months (sirolimus) or 6 months (paclitaxel), according to the existing guidelines. No protocol for continuation or withholding of antiplatelet agents before noncardiac surgery was in force, and this decision was left to the care providers. The composite end point of major adverse cardiac events (MACE, defined as nonfatal MI or death) at 30 days after noncardiac surgery was analyzed. There was a Revised Cardiac Risk Index of 1 in 34%, 2 in 39%, and 3 or more in 28% of the patients. Beta blockers were being taken preoperatively by 68% of patients. Bare-metal stents were used in 48% and DES in 54% of the patients. The early-surgery group was defined as those whose noncardiac surgery occurred within the time frame when clopidogrel was required (bare-metal stent, 1 month; sirolimus stent, 3 months; and paclitaxel stent, 6 months). Late surgery was defined as noncardiac surgery that occurred after this time. A total of 2.6% of all patients experienced MACE (all fatal), with a 13.3% rate of MACE in the early-surgery group and 0.6% in the late-surgery group. Interruption of antiplatelet therapy was associated with a significantly higher rate of MACE (5.5% versus 0%, $P=0.0023$) in the entire group of patients undergoing noncardiac surgery. Discontinuation of antiplatelet therapy in the early-surgery group resulted in a 30.7% incidence of MACE (all fatal) versus a 0% incidence in early-surgery patients who continued dual-antiplatelet therapy perioperatively. Overall, there was no difference in MACE between patients with bare-metal stents and those with DES. The study reported that all patients with MACE had discontinued antiplatelet therapy before surgery, whereas only 46% without MACE had done so. The study also stated there was no difference in surgical risk between patients in whom antiplatelet agents were discontinued and those in whom they were not. Excessive blood loss occurred in 2 patients, 1 of whom was receiving antiplatelet agents and 1 of whom was not. Transfusions were required in 24% of patients taking antiplatelet therapy and in 20% of those in whom antiplatelet therapy was discontinued ($P=0.50$). The authors concluded that there was an increased rate of MACE in patients undergoing early surgery and that discontinuation of antiplatelet agents may be a major cause of this MACE. This study was reported as research correspondence, and the authors cited the limitation of small numbers in interpretation of the results. Nonetheless, these findings are concordant with other small series and support the conclusion that early surgery and discontinuation of antiplatelet agents are risk factors for cardiac events at the time of noncardiac surgery after stent placement.

7.1.7. Stent Thrombosis and DES

Several reports of stent thrombosis after discontinuation of antiplatelet therapy before noncardiac surgery have been published and raise concern. Iakovou et al (333) followed up 2229 patients after DES implantation. Overall, 1.3% had stent thrombosis, with a case fatality rate of 45%. Subacute thrombosis within 30 days of implantation occurred in 0.6% of patients, and late thrombosis, more than 30 days after implantation, occurred in 0.7%. Independent predictors of stent thrombosis were premature discontinuation of antiplatelet therapy (hazard ratio [HR]: 90, *P* less than 0.001), renal failure (HR: 6.49, *P* less than 0.001), bifurcation lesions

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(HR: 6.42, *P* less than 0.001), diabetes mellitus (HR: 3.71, *P*=0.001), and lower ejection fraction (HR: 1.09 for each 10% decrease, *P* less than 0.001). Thrombosis occurred in 29% of patients who prematurely discontinued dual-antiplatelet therapy. Moreno et al (335) performed a meta-analysis of DES trials and found no significant difference in the rate of stent thrombosis between DES (0.58%) and bare-metal stents (0.54%); however, they noted the absence of thienopyridine therapy to be associated with DES thrombosis.

Ong et al (336) reported on late angiographic DES thrombosis, defined as occurring at least 1 month after stent implantation. They reported an incidence of late stent thrombosis of 0.35% in patients treated with DES; however, of the 8 angiographically confirmed cases of late stent thrombosis in their cohort of 2006 patients, 3 were related to complete cessation of antiplatelet therapy, and 2 additional cases occurred within 1 month of cessation of clopidogrel therapy.

McFadden et al (331) reported 4 cases of stent thrombosis that occurred 343 to 442 days after stent implantation shortly after discontinuation of antiplatelet agents. Nasser et al (332) reported 2 cases in which aspirin was stopped for noncardiac surgery 4 and 21 months after DES implantation; both patients suffered acute stent thrombosis and a large MI, and 1 died.

Spertus et al (337) reported a 19-center study of 500 patients with acute MI designed to examine the prevalence and predictors of thienopyridine discontinuation 30 days after DES treatment. They found that 13.6% stopped thienopyridine therapy within 30 days, and these patients were more likely to die (7.5% versus 0.7%, *P* less than 0.0001) and to be rehospitalized (23% versus 14%, *P*=0.08) by 12 months than those who continued thienopyridine therapy.

The BASKET-LATE study (Basel Stent Cost-Effectiveness Trial–Late Thrombotic Events) (338) reported a significantly greater incidence of death and nonfatal MI in patients who had received DES than in those who received bare-metal stents after clopidogrel had been discontinued at 6 months. A consecutive series of 746 patients with 1133 stented lesions randomly assigned in a 2:1 fashion to DES or bare-metal stents and without events at 6 months were followed up for 12 months after the discontinuation of clopidogrel. Groups were well matched with regard to baseline clinical characteristics, and the cohort included consecutive patients with indications for the procedure of ST-elevation MI in 21.1% and unstable angina in 36.7%. Overall, the 18-month rate of death or MI was not different between the DES and bare-metal stent groups. The rate of death or MI after clopidogrel discontinuation at 6 months was 4.9% in the DES group and 1.3% in the bare-metal stent group (HR: 2.2, *P*=0.03). Documented late stent thrombosis was twice as frequent in the DES group as in the bare-metal stent group (2.6% versus 1.3%), and occurred between 15 and 362 days (median 116 days, interquartile range 53 to 313 days) after discontinuation of clopidogrel. Stent thrombosis was associated with an 88% risk of death or nonfatal MI. Target-vessel revascularization was less frequent in the DES group than in the bare-metal stent group (7.5% versus 11.6%, *P*=0.04). The authors concluded that after the discontinuation of clopidogrel, there is an increased incidence of cardiac death and nonfatal MI in patients receiving DES compared with bare-metal stents, possibly related to stent thrombosis.

A long-term observational study of 24-month clinical outcomes in patients with stents and varying duration of clopidogrel therapy was reported by Eisenstein et al (339). A total of 4666 patients who received bare-metal stents (n=3165) or DES (n=1501) were followed up at 6, 12, and 24 months. Patients were stratified with regard to type of stent and clopidogrel use. Landmark analysis was performed on those patients who were event-free at 6 and 12 months of follow-up and stratified as to clopidogrel use at that time. Adjusted 24-month outcomes based on 6-month clopidogrel use showed that DES patients without clopidogrel at 6 months had significantly higher rates of death (5.3% versus 2.0%, *P*=0.03) and death or MI (7.2% versus 3.1%, *P*=0.02) than patients in the DES group given clopidogrel. The adjusted HR for death in the DES group without clopidogrel was 2.43 (*P*=0.03) compared with the DES with clopidogrel group. There were no significant differences in death or death and MI in patients with bare-metal stents with or without clopidogrel at 6 months. There were fewer events in patients with DES plus clopidogrel at 6 months (death or MI 3.1% versus 6.0%, *P*=0.02) than in patients with bare-metal stents without clopidogrel at 6 months. Adjusted 24-month outcomes based on 12-month clopidogrel use similarly showed that DES patients who did not take clopidogrel had significantly higher rates of death (3.5% versus 0%, *P*=0.004) and death or MI (4.5% versus 0%, *P* less than 0.001) than DES patients who did take clopidogrel at 12 months. There were no significant differences in death or death and MI in patients with bare-metal stents with or without clopidogrel use at 12 months. There were fewer events in patients with DES plus clopidogrel (death or MI 0%, *P* less than 0.001) than in patients with bare-metal stents with (4.7%) or without (3.6%) clopidogrel treatment at 12 months. The authors concluded that the extended use of clopidogrel (up to 12 months) in patients with DES is associated with a reduced risk of death and death or MI at 24 months. They noted that the optimal duration of clopidogrel use beyond 12 months after DES implantation is not currently known.

On December 7 and 8, 2006, the US Food and Drug Administration held advisory panel meetings in Washington, DC, to discuss the safety and stent thrombosis rates associated with DES (340). At the time of this writing, the panel report is yet to be published, but initial conclusions were that 1) there appears to be a numerical excess of late stent thrombosis with DES, but the magnitude is uncertain; 2) there does not appear to be an increase in rates of death or MI when the products are used in accordance with indications listed on the label; 3) the off-label use of DES, like bare-metal stents, is associated with increased risk compared with on-label use; and 4) more data are needed, which will entail studying outcomes in more patients for longer periods of time. The panel concurred with the AHA/ACC guideline recommendation for 12 months of dual-antiplatelet therapy after DES implantation in patients who are not at high risk for bleeding.

The Swedish Coronary Angiography and Angioplasty Registry (SCAAR) study group published a registry study of

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6033 patients treated with DES and 13 738 patients treated with bare-metal stents and followed up for 3 years (341). Over the entire follow-up period, the 2 groups did not differ in the composite outcomes of death or MI. At 6 months, there was a trend toward a lower unadjusted event rate in the DES group. However, after 6 months, patients with DES had a higher event rate, with 12.7 more events per 1000 patients per year than among patients given bare-metal stents (adjusted relative risk 1.2%; 95% CI: 1.05 to 1.37). At 3 years, mortality was higher in patients with DES (adjusted relative risk 1.18%; 95% CI: 1.04 to 1.35). The relative rate of clinical restenosis was 60% lower in the DES patients. This analysis suggests an 18% increase in the relative risk of death in the long term with DES compared with bare-metal stents, which equates to an incremental absolute risk of death of 0.5% per year and an incremental absolute risk of death or MI of 0.5% to 1.0% per year after the initial 6 months.

In January 2007, an AHA/ACC/SCAI/American College of Surgeons (ACS)/American Diabetes Association (ADA) science advisory was issued regarding the prevention of premature discontinuation of dual-antiplatelet therapy in patients with coronary artery stents (342). The advisory notes that the current recommendations of duration of dual-antiplatelet regimens after bare-metal, sirolimus-eluting, and paclitaxel-eluting stent implantation were formulated from trials designed to obtain Food and Drug Administration approval and the anticipated time required for the stent struts to become adequately endothelialized. These trials included low-risk lesions in low-risk patients. It has been observed that only approximately 30% to 40% of DES are implanted in such low-risk lesions in low-risk patients (on-label indications). Approximately 60% to 70% of patients receiving DES in most large contemporary series of coronary intervention are in off-label populations that include patients with multivessel coronary disease, left main disease, aorto-coronary vein grafts, bifurcation lesions, previously stented lesions with in-stent restenosis, prior brachytherapy, small vessels, very long lesions, multiple or overlapping stents, chronic total occlusions, and infarct-related lesions in acute MI. Additionally, reports have suggested that delayed or absent endothelialization (343), localized hypersensitivity (330,344), and late stent thrombosis (see above) may occur with increased frequency in patients with DES.

Several analyses of the randomized trials and postmarketing registries of sirolimus and paclitaxel DES have been published recently. Kastrati et al (345) reported that 4958 patients randomized to DES or bare-metal stents and followed up for 12 to 59 months had no significant difference in the incidence of death or MI, but there was a sustained reduction in the need for reintervention with DES. There was a slight increase in the risk of stent thrombosis with sirolimus-eluting stents after the first year. Mauri et al (346) analyzed 878 patients treated with sirolimus-eluting stents, 1400 treated with paclitaxel-eluting stents, and 2267 patients treated with bare-metal stents over 4 years of follow-up according to a hierarchical classification of stent thrombosis. The incidence of stent thrombosis by any criterion was 3% and did not differ between DES and bare-metal stent patients. Stone et al (347) analyzed randomized trials of DES versus bare-metal stents and found that stent thrombosis occurred in 1.2% of sirolimus-eluting stent patients and 1.3% of paclitaxel-eluting stent patients, neither of which was significantly different from the bare-metal stent control group. Rates of death and MI were similar between the DES and bare-metal stent groups over 4 years. After 1 year, stent thrombosis was more common with DES patients. Spaulding et al (348) analyzed data from 1748 patients in 4 randomized trials of sirolimus-eluting stents compared with bare-metal stents with regard to survival at 4 years. The survival rate was 93.3% in the DES group compared with 94.6% in the bare-metal stent group (P = NS). In patients with diabetes mellitus, the survival rate was better in the bare-metal stent group (95.6% versus 87.8%; HR for death, sirolimus group 2.9, $P=0.008$). Rates of MI and stent thrombosis were similar between the 2 groups.

Stent thrombosis is usually a significant clinical event. The incidence of death or MI was 64.4% in patients with angiographically documented bare-metal stent thrombosis (349). Mortality rates due to presumed or documented DES thrombosis range from 20% to 45% (337–339).

The average reported incidence of subacute (within 1 month of implantation) stent thrombosis is approximately 0.5% to 1.0%. Late stent thrombosis at 1 to 12 months was not seen with bare-metal stents but was reported to occur in 0.19% of patients in a large DES registry (350). In October 2006, an independent patient-level meta-analysis of DES trials was presented that demonstrated an increased rate of DES thrombosis of approximately 0.2% per year between years 1 and 4 after stent implantation compared with bare-metal stents (351). Another meta-analysis (352) of all the published DES trials that examined very late stent thrombosis at more than 1 year after implantation found a rate of 5.0 per 1000 patients (0.5%) compared with 0% in patients with bare-metal stents (relative risk 5.02, $P=0.02$). The incidence of early stent thrombosis (within 30 days of implantation) was 4.4 per 1000 (0.44%) in DES patients compared with 5.0 per 1000 (0.5%) in bare-metal stent patients ($P=0.74$). The incidence of late stent thrombosis (more than 30 days after implantation) was 5.0 per 1000 DES patients compared with 2.8 per 1000 bare-metal stent patients ($P=0.22$). The median time to late sirolimus-eluting stent thrombosis was 15.5 months (range 173 to 773 days), and the median time to paclitaxel-eluting stent thrombosis was 18 months (range 40 to 548 days), whereas the median time to bare-metal stent thrombosis was 3.5 to 4.0 months. Very late stent thrombosis appears to be a phenomenon restricted to DES. These findings have clear implications for the duration of antiplatelet therapy.

Predictors of late stent thrombosis include the clinical factors of advanced age, acute coronary syndrome, diabetes mellitus, low ejection fraction, renal failure, and prior brachytherapy and the angiographic factors of long stents, multiple lesions, overlapping stents, ostial or bifurcation lesions, small vessels, and suboptimal stent results (underexpansion, malapposition, or residual dissection). The optimal duration of clopidogrel therapy after 1 year has not been established and should depend on the physician's judgment of the risk/benefit ratio for the individual patient. Current expert opinion sug-

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gests that continuation of thienopyridine (clopidogrel) therapy beyond 1 year may be considered in patients undergoing DES placement.

A 2007 AHA/ACC/SCAI/ACS/ADA science advisory report (342) concludes that premature discontinuation of dual-antiplatelet therapy markedly increases the risk of catastrophic stent thrombosis and death or MI. To eliminate the premature discontinuation of thienopyridine therapy, the advisory group recommends the following:

1. Before implantation of a stent, the physician should discuss the need for dual-antiplatelet therapy. In patients not expected to comply with 12 months of thienopyridine therapy, whether for economic or other reasons, strong consideration should be given to avoiding a DES.
2. In patients who are undergoing preparation for PCI and who are likely to require invasive or surgical procedures within the next 12 months, consideration should be given to implantation of a bare-metal stent or performance of balloon angioplasty with provisional stent implantation instead of the routine use of a DES.
3. A greater effort by healthcare professionals must be made before patient discharge to ensure that patients are properly and thoroughly educated about the reasons they are prescribed thienopyridines and the significant risks associated with prematurely discontinuing such therapy.
4. Patients should be specifically instructed before hospital discharge to contact their treating cardiologist before stopping any antiplatelet therapy, even if instructed to stop such therapy by another healthcare provider.
5. Healthcare providers who perform invasive or surgical procedures and who are concerned about periprocedural and postprocedural bleeding must be made aware of the potentially catastrophic risks of premature discontinuation of thienopyridine therapy. Such professionals who perform these procedures should contact the patient's cardiologist if issues regarding the patient's antiplatelet therapy are unclear, to discuss optimal patient management strategy.
6. Elective procedures for which there is significant risk of perioperative or postoperative bleeding should be deferred until patients have completed an appropriate course of thienopyridine therapy (12 months after DES implantation if they are not at high risk of bleeding and a minimum of 1 month for bare-metal stent implantation).
7. For patients treated with DES who are to undergo subsequent procedures that mandate discontinuation of thienopyridine therapy, aspirin should be continued if at all possible and the thienopyridine restarted as soon as possible after the procedure because of concerns about late stent thrombosis.

Similar conclusions and recommendations were published online in a clinical alert by the SCAI in January 2007 (351). Given the above reports and recommendations, use of a DES for coronary revascularization before imminent or planned noncardiac surgery that will necessitate the discontinuation of dual-antiplatelet agents is not recommended.

In conclusion, in patients with stable CAD, the indications for PCI in the preoperative setting should be identical to those developed by the joint ACC/AHA Task Force that provided guidelines for the use of PCI in patients with stable angina and asymptomatic ischemia (307). There is no evidence to support prophylactic preoperative percutaneous revascularization in patients with asymptomatic ischemia or stable angina.

Similarly, there is little evidence to show how long a more distant PCI (ie, months to years before noncardiac surgery) protects against perioperative MI or death. Because additional coronary restenosis is unlikely to occur more than 8 to 12 months after PCI (whether or not a stent is used), it is reasonable to expect ongoing protection against untoward perioperative ischemic complications in currently asymptomatic, active patients who had been symptomatic before complete percutaneous coronary revascularization more than 8 to 12 months previously.

7.1.8. Perioperative Management of Patients With Prior PCI Undergoing Noncardiac Surgery

According to the 2005 PCI guidelines, "In patients who have undergone PCI, clopidogrel 75 mg daily should be given for at least 1 month after bare-metal stent implantation (unless the patient is at increased risk for bleeding, then it should be given for a minimum of 2 weeks), 3 months after sirolimus stent implantation, and 6 months after paclitaxel stent implantation, and ideally up to 12 months in patients who are not at high risk of bleeding. (*Level of Evidence: B*)" (307). The newer recommendation by the AHA/ACC/SCAI/ACS/ADA Science Advisory Committee cited above (342) is for 12 months of dual-antiplatelet therapy in patients who have undergone PCI with DES. If there is a contraindication to 12 months of dual-antiplatelet therapy, such as planned noncardiac surgery, then DES should not be implanted.

For patients who have undergone successful coronary intervention with or without stent placement before planned or unplanned noncardiac surgery, there is uncertainty regarding how much time should pass before the noncardiac procedure is performed. One approach is outlined in Figure 2, which is based on expert opinion. Given the reports of late DES thrombosis and the current recommendations discussed above, clinicians should remain vigilant even beyond 365 days after DES placement. The times of 14, 30 to 45, and 365 days for balloon angioplasty, bare-metal stents, and DES, respectively, recommended in Figure 2 are somewhat arbitrary because of a lack of high-quality evidence.

Consideration should be given to continuing dual-antiplatelet therapy in the perioperative period for any patient needing noncardiac surgery that falls within the time frame that requires dual-antiplatelet therapy, particularly those who have received DES. In addition, consideration should be given to continuing dual-antiplatelet therapy perioperatively beyond the recommended time frame in any patient at high risk for the consequences of stent thrombosis, such as patients in whom previous stent thrombosis has occurred, after left main stenting, after multivessel stenting, and after stent placement in the only remaining coronary artery or graft conduit. Even after thienopyridines have been discontinued, serious consideration should be given to continuation of aspirin antiplatelet therapy perioperatively in any patient with

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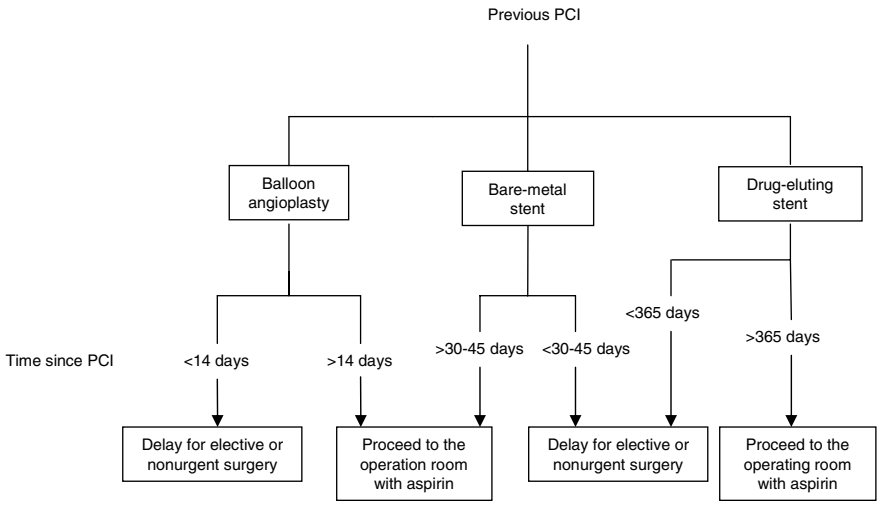

Figure 2. Proposed approach to the management of patients with previous percutaneous coronary intervention (PCI) who require noncardiac surgery, based on expert opinion.

previous placement of a DES. The risk of stopping antiplatelet therapy should be weighed against the benefit of reduction in bleeding complications from the planned surgery. If thienopyridines must be discontinued before major surgery, aspirin should be continued and the thienopyridine restarted as soon as possible. There is no evidence that warfarin, antithrombotics, or glycoprotein IIb/IIIa agents will reduce the risk of stent thrombosis after discontinuation of oral antiplatelet agents (342).

7.1.9. Perioperative Management in Patients Who Have Received Intracoronary Brachytherapy

Intracoronary radiation with gamma or beta brachytherapy has been used in the past to treat recurrent in-stent restenosis. Brachytherapy delays the healing response and inhibits endothelialization of the irradiated coronary segment. Late total occlusion and thrombosis of the irradiated coronary segment occurs at a rate of 6% to 15%, especially after the placement of additional new bare-metal stents. Prolonged antiplatelet therapy is effective in preventing late thrombosis of the irradiated coronary segment, in 1 study reducing the late thrombosis rate to 2.5% with 6 months of therapy versus 9.6% with 1 month of dual-antiplatelet therapy. Additional benefit was demonstrated with 12 months of dual-antiplatelet therapy (late thrombosis rate of 3.3%) (353,354). It is unclear when, if ever, antiplatelet therapy can be safely discontinued in these patients.

Given the considerations above, antiplatelet therapy should be continued as per the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention, with a class IIa recommendation: "It is reasonable that patients undergoing brachytherapy be given daily chronic clopidogrel 75 mg indefinitely and daily chronic aspirin 75 mg to 325 mg indefinitely unless there is significant risk for bleeding. (*Level of Evidence: C*)" (307). Therefore, serious consideration should be given to continuing dual-antiplatelet therapy in the perioperative period for any patient who has received brachytherapy for restenosis or in-stent restenosis, particularly those in whom additional stents (bare-metal or drug-eluting) were placed at the time of or subsequent to the administration of brachytherapy. The risk of stopping antiplatelet therapy should be weighed against the benefit of reduction in bleeding complications from the planned surgery.

7.1.10. Risks Associated With Perioperative Antiplatelet Agents

Dual-antiplatelet therapy with aspirin and clopidogrel carries a 0.4% to 1.0% increased absolute risk of major bleeding compared with aspirin alone (355). Some procedures carry a low risk of bleeding; for example, there is no indication to interrupt dual-antiplatelet therapy for dental procedures (356). The risk of surgical bleeding after administration of aspirin, thienopyridines, and glycoprotein IIb/IIIa inhibitors has been reviewed (334,357). Increased blood loss in patients taking aspirin has been reported in noncardiac surgery, including general surgical, gynecologic, and urologic operations, and in dermatologic surgery in those patients whose bleeding time was prolonged. One study reported that patients taking aspirin who were undergoing emergency general surgery operations did not demonstrate an increased risk of bleeding complications (358). Preoperative aspirin use may not increase the risk of neuraxial anesthesia or analgesia (359).

The authors of a review of this subject (334) concluded that monotherapy with aspirin need not be routinely discontinued for elective noncardiac surgery. Burger et al (360) reviewed the surgical literature with regard to the risks of stopping low-dose aspirin versus the risks of bleeding and found that in the majority of surgeries, low-dose aspirin may result in increased frequency of procedural bleeding (relative risk 1.5) but not an increase in the severity of bleeding complications or perioperative mortality due to bleeding complications. Possible exceptions were intracranial surgery and prostatectomy. They recommended that aspirin should only be discontinued if the known bleeding risks are similar or more severe than the observed cardiovascular risks of aspirin withdrawal.

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In cardiac surgery, perioperative aspirin use results in increased blood loss and need for reoperation but no increase in mortality and is associated with improved saphenous vein bypass graft patency. The ACC/AHA 2004 Guideline Update for Coronary Artery Bypass Graft Surgery reviewed this issue and stated: "In summary, aspirin is the drug of choice for prophylaxis against early saphenous graft thrombotic closure. Perioperative use and/or administration of aspirin within 48 hours of operation should be the standard of care and should be continued indefinitely, given its benefit in the secondary prevention of subsequent clinical events" (306). In noncardiac vascular surgery, preoperative aspirin is routinely used and is associated with improved peripheral bypass graft patency. Few data exist regarding the risks and benefits of the use of aspirin perioperatively in other noncardiovascular surgery.

Likewise, monotherapy with clopidogrel or ticlopidine may not need to be discontinued in elective noncardiac surgery; however, there is conflicting information about the risks of bleeding in patients taking perioperative clopidogrel. Hongo et al reported that a significant increased risk of major perioperative bleeding was found in patients undergoing CABG (361). Another study suggested no increased risk of bleeding complications and mortality in patients taking clopidogrel who were undergoing emergency CABG compared with those treated with aspirin and heparin alone (362). In the Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) trial (363), patients in whom clopidogrel was stopped fewer than 5 days before CABG surgery had a significantly increased (9.6% versus 6.3% in the placebo arm) rate of major bleeding but no significant difference in perioperative mortality. Kapetanakis et al reported that patients receiving clopidogrel before off-pump coronary artery bypass surgery had an OR of 5.1 (95% CI: 2.47 to 10.47, *P* less than 0.01) with regard to the need for hemostatic reoperation and a significant increase in the need for packed red blood cell and platelet transfusions but no difference in surgical mortality (364). In a series of patients undergoing carotid endarterectomy, a reduction in transcranial Doppler–determined emboli was seen with pretreatment with aspirin and clopidogrel, but no increase in bleeding complications or blood transfusions was seen (365).

Cannon et al (366) suggest that for patients receiving clopidogrel, a 5-day interval between stopping the drug and elective surgery is optimal. This is reflected in the ACC/AHA recommendation that clopidogrel should be withheld for at least 5 to 7 days in patients scheduled for elective CABG surgery (306). For urgent and emergent surgery, a delay of surgery until platelet function has recovered is usually not a feasible option. Under these circumstances, some experts recommend platelet transfusions for treatment of hemorrhage that continues despite usual hemostatic techniques, even if platelet count is normal. However, no data demonstrate that transfused platelets reverse the clopidogrel effect. For this reason, it may be more appropriate to reserve platelet transfusion for patients with significant clinical bleeding after usual hemostatic methods are applied. A comprehensive approach for patients taking clopidogrel and aspirin who are undergoing emergent CABG surgery might include the use of aprotinin, aminocaproic acid, or tranexamic acid to promote hemostasis during the early reperfusion period. Early clinical experience suggested that the intraoperative use of aprotinin or tranexamic acid may permit surgery to be conducted safely on patients presenting while taking aspirin and clopidogrel (367,368); however, there is controversy regarding the safety of aprotinin in cardiac surgery (369). Although this result is debated, Mangano and colleagues found that aprotinin used in cardiac surgery was associated with a doubling in the risk of renal failure requiring dialysis among patients undergoing complex coronary artery surgery compared with controls (369). Similarly, the use of aprotinin in the primary surgery group was associated with a 55% increase in the risk of MI or HF (*P* less than 0.001) and a 181% increase in the risk of stroke or encephalopathy ($P=0.001$). Neither aminocaproic acid nor tranexamic acid was associated with an increased risk of renal, cardiac, or cerebral events compared with controls. A later study found that the use of aprotinin was associated with a significant reduction in long-term survival (5-year mortality 20.8% with aprotinin versus 12.7% for controls, OR: 1.48, $P=0.005$) that was not seen in CABG patients treated with aminocaproic acid or tranexamic acid (370). The applicability of this information to other types of surgery is unknown.

7.1.11. Strategy of Percutaneous Revascularization in Patients Needing Urgent Noncardiac Surgery

Patients who require percutaneous coronary revascularization in whom near-term noncardiac surgery is necessary require special consideration (342,371). A potential strategy is outlined in Figure 3. Percutaneous coronary revascularization should not be routinely performed in patients who need noncardiac surgery unless clearly indicated for high-risk coronary anatomy, unstable angina, MI, or hemodynamically or rhythmically unstable active CAD amenable to percutaneous intervention. If PCI is necessary, then the urgency of the noncardiac surgery and the risk of bleeding associated with the surgery in a patient taking dual-antiplatelet agents need to be considered. If there is little risk of bleeding or if the noncardiac surgery can be delayed 12 months or more, then PCI with DES and prolonged aspirin and thienopyridine therapy could be considered if the patient meets the criteria outlined in the AHA/ACC/SCAI/ACS/ADA science advisory group recommendations outlined above (342). If the noncardiac surgery is likely to occur within 1 to 12 months, then a strategy of bare-metal stenting and 4 to 6 weeks of aspirin and thienopyridine therapy with continuation of aspirin perioperatively should be considered. Although the risk of restenosis with this strategy is higher than with DES, restenotic lesions are usually not life-threatening, even though they may present as an acute coronary syndrome (372), and can usually be dealt with by repeat PCI if necessary. If the noncardiac surgery is imminent (within 2 to 6 weeks) and the risk of bleeding is high, then consideration should be given to balloon angioplasty and provisional bare-metal stenting plus continued aspirin antiplatelet monotherapy, with restenosis dealt with by repeat PCI if necessary. If the noncardiac surgery is urgent or emergent, then cardiac risks, the risk of bleeding, and the long-term benefit of coronary revascularization must be

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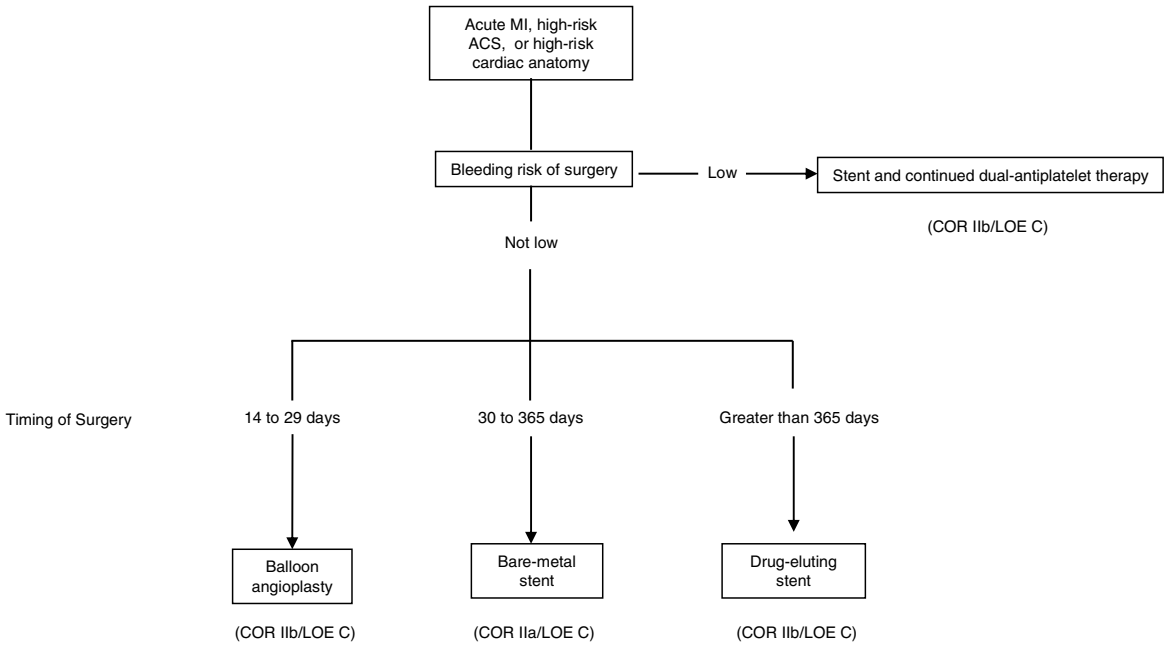

Figure 3. Treatment for patients requiring percutaneous coronary intervention (PCI) who need subsequent surgery. ACS indicates acute coronary syndrome; COR, class of recommendation; LOE, level of evidence; and MI, myocardial infarction.

weighed, and if coronary revascularization is absolutely necessary, CABG combined with the noncardiac surgery could be considered.

7.2. Perioperative Medical Therapy

7.2.1. Perioperative Beta-Blocker Therapy

Recommendations for Beta-Blocker Medical Therapy‖

CLASS I

1. Beta blockers should be continued in patients undergoing surgery who are receiving beta blockers to treat angina, symptomatic arrhythmias, hypertension, or other ACC/AHA class I guideline indications. (*Level of Evidence: C*)
2. Beta blockers should be given to patients undergoing vascular surgery who are at high cardiac risk owing to the finding of ischemia on preoperative testing. (*Level of Evidence: B*)

CLASS IIa

1. Beta blockers are probably recommended for patients undergoing vascular surgery in whom preoperative assessment identifies CHD. (*Level of Evidence: B*)
2. Beta blockers are probably recommended for patients in whom preoperative assessment for vascular surgery identifies high cardiac risk, as defined by the presence of more than 1 clinical risk factor.* (*Level of Evidence: B*)
3. Beta blockers are probably recommended for patients in whom preoperative assessment identifies CHD or high cardiac risk, as defined by the presence of more than 1 clinical risk factor,* who are undergoing intermediate-risk or vascular surgery. (*Level of Evidence: B*)

CLASS IIb

1. The usefulness of beta blockers is uncertain for patients who are undergoing either intermediate-risk procedures or vascular surgery, in whom preoperative assessment identifies a single clinical risk factor.* (*Level of Evidence: C*)
2. The usefulness of beta blockers is uncertain in patients undergoing vascular surgery with no clinical risk factors who are not currently taking beta blockers. (*Level of Evidence: B*)

CLASS III

1. Beta blockers should not be given to patients undergoing surgery who have absolute contraindications to beta blockade. (*Level of Evidence: C*)

Since publication of the ACC/AHA focused update on perioperative beta-blocker therapy, several randomized trials have been published that have not demonstrated the efficacy of these agents. Despite several meta-analyses, some of which reached conflicting conclusions, there are still very few randomized trials of this issue.

Few studies have compared different beta-blocker agents. Studies to determine the ideal target population, duration of preoperative titration, and route of administration are lacking. In addition, practical concerns, such as how, when, how long, and by whom perioperative beta-blocker therapy should ideally or practically be implemented, remain unaddressed. Randomized controlled trials are still needed to explore the observation that there may be some harm associated with beta-blocker therapy in low-risk patients (373). Moreover, there is currently a lack of data regarding which beta blocker to use perioperatively, although longer-acting agents appear superior to shorter-acting agents. In fact, studies involving the shorter-acting agent metoprolol have shown lower or no efficacy (374,375). In summary, the best approach on how to medically protect patients from cardiovascular complications

‖Care should be taken in applying recommendations on beta-blocker therapy to patients with decompensated HF, nonischemic cardiomyopathy, or severe valvular heart disease in the absence of CHD.

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Table 11. Recommendations for Perioperative Beta-Blocker Therapy Based on Published Randomized Clinical Trials

Surgery	No Clinical Risk Factors	1 or More Clinical Risk Factors	CHD or High Cardiac Risk	Patients Currently Taking Beta Blockers
Vascular	Class IIb, Level of Evidence: B	Class IIa, Level of Evidence: B	Patients found to have myocardial ischemia on preoperative testing: Class I, Level of Evidence: B* Patients without ischemia or no previous test: Class IIa, Level of Evidence: B	Class I, Level of Evidence: B
Intermediate risk	. . .	Class IIb, Level of Evidence: C	Class IIa, Level of Evidence: B	Class I, Level of Evidence: C
Low risk	. . .	. . .	. . .	Class I, Level of Evidence: C

See Table 4 for definition of procedures. Ellipses (. . .) indicate that data were insufficient to determine a class of recommendation or level of evidence. See text for further discussion. CHD indicates coronary heart disease.

*Applies to patients found to have coronary ischemia on preoperative testing.

†Applies to patients found to have coronary heart disease.

during noncardiac surgery is still unknown. Limitations in the perioperative beta-blocker literature include the following:

- Most trials are inadequately powered.
- Few randomized trials of medical therapy to prevent perioperative MACE have been performed.
- Few randomized trials have examined the role of perioperative beta-blocker therapy, and there is particularly a lack of trials that focus on high-risk patients.
- Studies to determine the role of beta blockers in intermediate- and low-risk populations are lacking.
- Studies to determine the optimal type of beta blockers are lacking.
- No studies have addressed care-delivery mechanisms in the perioperative setting, identifying how, when, and by whom perioperative beta-blocker therapy should be implemented and monitored.

Although many of the randomized controlled trials of beta-blocker therapy are small, the weight of evidence—especially in aggregate—suggests a benefit to perioperative beta blockade during noncardiac surgery, particularly in high-risk patients (Table 11). Current studies suggest that beta blockers reduce perioperative ischemia and may reduce the risk of MI and death in high-risk patients. Available evidence strongly suggests but does not definitively prove that when possible, beta blockers should be started days to weeks before elective surgery. The dose should be titrated to achieve a resting heart rate of 60 beats per min (bpm) to increase the likelihood the patient will receive the benefit of beta blockade. Rate control with beta blockers should continue during the intraoperative and postoperative period to maintain a heart rate of 60 to 65 bpm, because this regimen has demonstrated efficacy (59,89). Prospective randomized trials are either under way or soon to be presented. These will hopefully shed light on some of the questions regarding perioperative beta-blocker therapy. Per ACC/AHA Task Force on Practice Guidelines methodology, unpublished data cannot be used to formulate guideline recommendations.

7.2.1.1. Evidence on Efficacy of Beta-Blocker Therapy

Several randomized trials examined the effect of perioperative beta blockers on cardiac events surrounding surgery. Poldermans et al examined the effect of bisoprolol on patients undergoing vascular surgery and in patients at high risk for perioperative cardiac complications who were scheduled for vascular surgery (89). Of 846 patients with risk factors for cardiac disease, 173 were found to have new regional wall-motion abnormalities on DSE. Of these patients, 61 were excluded from further study owing to large areas (greater than or equal to 5 segments) of regional wall-motion abnormalities on DSE or because they were already taking beta blockers. The remaining 112 high-risk patients were randomized to standard care or bisoprolol started at least 7 days before surgery and titrated to maintain heart rate less than 60 bpm preoperatively and less than 80 bpm intraoperatively and postoperatively. The rates of cardiac death (3.4% versus 17%; $P=0.02$) and nonfatal MI (0% versus 17%; P less than or equal to 0.001) were lower for the bisoprolol groups than for the placebo groups, respectively. Importantly, owing to the unblinded design and the inclusion of only high-risk patients in this study, the results cannot be generalized to all patients undergoing noncardiac surgery.

Boersma et al subsequently reanalyzed the total cohort of 1351 consecutive patients considered for enrollment in the aforementioned randomized trial of bisoprolol (248). Forty-five patients had perioperative cardiac death or nonfatal MI. Eighty-three percent of the patients had fewer than 3 clinical risk factors. Among this subgroup, patients taking beta blockers had a lower risk of cardiac complications (0.8% [2/263]) than those not taking beta blockers (2.3% [20/855]). In patients with 3 or more risk factors (17%), those taking beta blockers who had a DSE who demonstrated 4 or fewer segments of new wall-motion abnormalities had a significantly lower incidence of cardiac complications (2.3% [2/86]) than those not receiving beta-blocker therapy (9.9% [12/121]). However, among the small group of patients with more extensive ischemia on DSE (5 or more segments), there was no difference in the incidence of cardiac events (4 of 11 for those taking beta blockers versus 5 of 15 for those not taking

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beta blockers). Therefore, beta-blocker therapy was beneficial in all but the subset of patients with more extensive ischemia. Nevertheless, one must be cautious about inferring a class effect from this observation about bisoprolol and the treatment protocol.

The Multicenter Study of Perioperative Ischemia Research Group (88,376) reported on 200 patients undergoing general surgery randomized to a combination of intravenous and oral atenolol versus placebo for 7 days. Although they found no difference in perioperative MI or death, they reported significantly fewer episodes of ischemia by Holter monitoring in the atenolol versus placebo groups (24% versus 39%, respectively; $P=0.03$). They then conducted follow-up on these patients after discharge and documented fewer deaths in the atenolol group over the subsequent 6 months (1% versus 10%; P less than 0.001). It is not clear why such a brief course of therapy could exert such a delayed effect, and the study did not control for other medications given either before or after surgery. Use of ACE inhibitors and beta blockers postoperatively differed significantly between the study groups.

Additional studies have examined the use of perioperative beta blockers but were limited in power to detect cardiac events or were not randomized. More recent randomized trials have looked at beta blockade for the prevention of perioperative cardiac complications during noncardiac surgery. Juul et al (375) randomized 921 diabetic subjects undergoing a range of noncardiac operations to either 100 mg of extended-release metoprolol or placebo in the DIPOM (Diabetic Postoperative Mortality and Morbidity) study. They excluded patients with "conditions indicating beta-blocker treatment," which was not elaborated on. Of those randomized, an equal number of deaths (16%) were observed in both groups. Myocardial infarction rates were not reported separately, and it is unclear at what time point the mortality was compared. Yang et al (377) report a study of 496 subjects undergoing major vascular surgery who were randomized to dose-adjusted metoprolol or placebo. Exclusions in that study included those already taking a beta blocker. They reported similar MI rates (7.7% versus 8.4%) and death rates (0% versus 1.6%) at 30 days in the beta-blocker and placebo groups, respectively. These were not noninferiority analyses but rather simply negative study results. Most importantly for the purposes of these guidelines, the patients included (although diabetic in 1 study and undergoing major vascular surgery in the other) undoubtedly represent a heterogenous risk group without documented CAD. These studies suggest no identifiable benefit for these beta-blocker regimens in this lower-risk group.

Stone et al (76) randomized a group of patients with mild hypertension who underwent predominantly (58%) vascular surgery to oral beta blockers 2 hours before surgery or standard care. Control subjects had a higher frequency (28%) of ST-segment depression (on intraoperative monitoring, as reported by the authors) than treated patients (2%). In a nonrandomized study, Pasternack et al (378) gave oral metoprolol immediately before surgery, followed postoperatively by intravenous metoprolol during abdominal aortic aneurysm repair. Only 3% suffered an acute MI compared with 18% for matched control subjects. Pasternack et al (79) subsequently reported fewer episodes of intraoperative ischemia in patients treated with oral metoprolol before peripheral vascular surgery than in untreated patients. Yeager et al (379) reported a case-control analysis of their experience with perioperative MI during vascular surgery, comparing 53 index cases of perioperative MI with 106 matched control subjects. They found a strong association of beta-blocker use with a decreased likelihood of MI (OR: 0.43; $P=0.01$). In 26 vascular surgery patients with documented preoperative ischemia who were randomized to a protocol of heart rate suppression with intravenous esmolol compared with standard care, Raby et al (380) demonstrated that the esmolol group had fewer episodes of ischemia than control subjects (33% versus 72%; $P=0.055$). Zaugg et al (381) randomized elderly noncardiac surgery patients to preoperative and postoperative atenolol titrated to heart rate, intraoperative atenolol titrated to heart rate, or no beta blockers and detected no episodes of intraoperative myocardial ischemia, ECG changes consistent with MI, or death in any group. Three of 19 patients in the no-beta-blocker group developed significant elevations of cardiac troponin I (cTnI) consistent with a perioperative MI compared with none of 40 patients who received 1 of the atenolol regimens. Brady et al randomized patients undergoing elective vascular surgery to either metoprolol 50 mg twice a day or placebo, from admission to the hospital until 7 days after surgery (382). They found no difference in cardiovascular events, which included MI, unstable angina, ventricular tachycardia, and stroke. This trial may have been underpowered (n=103) to identify a difference in outcomes, particularly hard outcomes of death and MI. Also, by trial design, therapy was initiated the day before vascular surgery, and it is quite possible that those randomized to metoprolol received incomplete beta blockade in the early perioperative period.

Perioperative beta-blocker therapy has been reviewed in several meta-analyses and in a very large cohort population study. Auerbach and Goldman (383) undertook a review of this topic in 2002. They reported on a MEDLINE search and literature review of only 5 studies (all 5 studies are included in Table 12). They calculated a number needed to treat, on the basis of these studies, of only 2.5 to 6.7 to see improvement in measures of myocardial ischemia and only 3.2 to 8.3 in studies reporting a significant impact of beta blockers on cardiac or all-cause mortality. They concluded that the literature supports a benefit of beta blockers on cardiac morbidity and mortality.

A systematic review of the perioperative medical therapy literature by Stevens et al (385) for noncardiac surgery included the results of 11 trials using beta blockers for perioperative therapy. These authors concluded that beta blockers significantly decreased ischemic episodes during and after surgery. Beta blockers significantly reduced the risk of nonfatal MI; however, the results became nonsignificant if the 2 most positive trials were eliminated. Likewise, the risk of cardiac death was significantly decreased with beta-blocker usage. These authors incorporated studies not considered in other meta-analyses, including studies that were not blinded. Results to be quantified were limited to those in the 30-day perioperative period. The authors also reported a

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Table 12. Perioperative Prophylactic Beta Blockers and Anti-Ischemic Medications

					Myocardial Ischemia		MI		Death	
Study, Year	Procedure	n	Control	Drug and Dosage	Control	Drug	Control	Drug	Control	Drug
Studies of beta blockers										
Pasternack et al (378), 1987	Abdominal aortic aneurysmorrhaphy	83	Case-control	Metoprolol 50 mg PO preoperatively			17.6% (9/51)	3.1% (1/32)*		
Pasternack et al (379), 1989	Vascular	200	Unblinded	Metoprolol 50 mg PO preoperatively	1.8±3.2 episodes	0.8±1.6 episodes*				
	Noncardiac	128	Placebo	Labetalol	28.2% (11/39)	2.2% (2/89)*	0% (0/39)	0% (0/89)		
Stone et al (76), 1988				Atenolol Alprenolol PO preoperatively						
Poldermans et al (89), 1999	Vascular	112	Unblinded	Bisoprolol 5 to 10 mg PO			17% (9/53)	0% (0/59)*	17% (9/53)	3.4% (2/59)*
Raby et al (380), 1999	Vascular	26	Placebo	IV esmolol	72.7% (8/11)	33.3% (5/15)*				
Wallace et al (376), 1998, and Mangano et al (88), 1996	Noncardiac	200	Placebo	Atenolol 10 to 20 mg IV or 50 to 100 mg PO	39/101 (38.6%)	24/99 (24.2%)*			(At 6 months) 10/101 1/99 (9.9%) (1.0%)*	
Urban et al (384), 2000	Noncardiac	107	Placebo	IV esmolol on the day of surgery, followed by metoprolol starting at 25 mg PO BID and increased to maintain an HR less than 80 bpm, and continued for the next 48 hours	14.5% (8/55)	5.8% (3/52)	5.4% (3/55)	1.9% (1/52)		
Brady et al (382), 2005	Vascular	103	Placebo	Metoprolol 50 mg PO BID preoperatively until 7 days after surgery	9% (4/44)	9.4% (5/53)	11.3% (5/44)	5.6% (3/53)	2.2% (1/44)	5.6% (3/53)
Juul et al (375), 2006	Noncardiac	921	Placebo	Metoprolol 100 mg sustained release 1 day preoperatively, until up to 8 days postoperatively					16% 72/459)	16% (74/462)
Yang et al (377), 2006	Vascular	496	Placebo	Weight-adjusted metoprolol, 50, 75, or 100 mg			21/250 (8.4%)	19/246 (7.7%)	4/250 (1.6%)	0/246 (0%)

BID indicates twice per day; bpm, beats per minute; HR, heart rate; IV, intravenous; McSPI, Multicenter Study of Perioperative Ischemia; MI, myocardial infarction; n, number of patients; NTG, nitroglycerin; and PO, by mouth.
*$P<0.05$ for drug vs control.

direct relationship between the prevalence of prior MI and the magnitude of risk reduction observed with beta-blocker therapy, suggesting that higher risk confers greater benefit. The number needed to prevent perioperative ischemia was 8 subjects, the number needed to prevent MI was 23, and 32 patients had to be treated to prevent cardiac death. These authors pointed out that given the observation that high-risk patients seemed to receive all the benefit, the target population for beta-blocker therapy is not clear. They also highlighted that schedules of beta-blocker administration varied significantly among the reported studies and acknowledged the potential for a single large, strongly positive study to skew the results of this meta-analysis (385).

In contrast, Devereaux et al (386) published their opinion paper on the clinical evidence regarding the use of beta-blocker therapy in patients undergoing noncardiac surgery for the purpose of preventing perioperative cardiac complications. They expressed the opinion that the literature supporting the use of beta blockers during noncardiac surgery is modest at best and is based on a few small, unblinded studies with a focused patient population. In a review of the literature in 2005, Devereaux et al (387) discussed 22 studies randomizing 2437 patients undergoing noncardiac surgery to beta-blocker therapy or placebo. The Perioperative Beta Blockade (POBBLE) study was not included in this review (382). They found no statistically significant benefit with regard to any of

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the individual outcomes and a "nominally" statistically significant benefit (RR: 0.44, 99% CI 0.16 to 1.24) for the composite outcome of cardiovascular mortality, nonfatal MI, and nonfatal cardiac arrest. The authors believed that these data were inadequate to draw conclusions without a larger, controlled study. This review, however, included a wide variety of studies, patient populations, and beta-blocker regimens. Many of the studies described only a single or double dose of beta blockers preoperatively or at induction of anesthesia. Many of the data, therefore, do not pertain to perioperative beta blockade for the purpose of cardiac risk reduction or are focused on a low-risk population. Additionally, the largest studies included, those reported by Miller et al (388) and preliminary data from Yang et al (377), which together account for almost as many subjects as all the other studies combined, may not have been appropriate to include in this analysis. The first, by Miller et al, was a study of a single intravenous dose of beta blocker for the purpose of blood pressure control during intubation, not reduction of perioperative events. It included follow-up only to the point of discharge from the recovery room. The second, that of Yang et al, was based on an abstract, whereas the full manuscript has now been published. The studies included in this review also varied widely in length of follow-up.

McGory et al (389) performed a meta-analysis of 6 randomized trials of perioperative beta blockade and concluded that therapy was associated with significant reductions in perioperative myocardial ischemia (33% to 15%), MI, cardiac mortality, and long-term cardiac mortality (12% to 2%). These authors used the combined data to derive ORs and CIs for several outcomes. For perioperative overall mortality, the OR for beta-blocker therapy was 0.52 (95% CI: 0.20 to 1.35), and for perioperative cardiac mortality, the OR was 0.25 (95% CI: 0.07 to 0.87). Neither the POBBLE study nor the unpublished findings included in the Devereaux article were included, which explains the marked difference in findings from the other meta-analysis.

A cohort study by Lindenauer et al (373) reviewed records from more than 700 000 patients undergoing noncardiac surgery at 329 hospitals in the United States. Participant hospitals in this cohort study were members of a consortium database measuring quality of care and healthcare use. These authors evaluated all noncardiac surgical cases and compared those who received beta blockers within the first 2 days of hospitalization with those who did not. The authors used propensity score matching techniques in an attempt to reduce confounding. These authors found that for a Revised Cardiac Risk Index score(4) of 3 or more (based on the presence of history of ischemic heart disease, cerebrovascular disease, renal insufficiency, diabetes mellitus, or a patient undergoing high-risk surgery), patients who received beta blockers were significantly less likely to die while in the hospital. This was not true for those with a revised risk index of 2, l, or 0. Those with a risk index of 0 were more likely to die in the hospital if given a beta blocker on day 1 or day 2 of hospitalization. This study was retrospective and not randomized and is therefore subject to potential bias. This is particularly true in terms of reporting bias, because the documentation was based entirely on administrative data sets, using arbitrary definitions of "on" or "off" perioperative beta blockers that were based solely on hospital day of use. Nonetheless, there appears to be an association between improved outcomes and the use of beta blockers in clinically high-risk patients.

Finally, 1 observational cohort study examined the question of which beta blocker may be best for perioperative medical therapy. Redelmeier and colleagues (374) reviewed administrative data related to elective surgery in Ontario, Canada, and documented perioperative beta-blocker usage from April 1992 to April 2002 (10 years). They limited their analysis to patients over 65 years of age who were receiving either atenolol or metoprolol before and after surgery and identified 37 151 subjects. A total of 1038 either had a perioperative MI or died, and the rate of MI or death was significantly lower among those patients receiving atenolol than among those given metoprolol (2.5% versus 3.2%, P less than 0.001). This difference persisted even after adjustment for demographic, clinical, and surgical factors. The inclusion of other long-acting beta blockers in the analysis yielded an identical risk reduction. These data suggest that long-acting beta blockade (when therapy is initiated before surgery), may be superior to short-acting beta blockade. These observations await clinical trial evaluation.

7.2.1.2. Titration of Beta Blockers

Feringa and colleagues performed an observational cohort study of 272 vascular surgery patients (390). Beta-blocker dose was converted to a percentage of the maximum recommended therapeutic dose. In multivariable analysis, higher beta-blocker doses (per 10% increase) were significantly associated with a lower incidence of myocardial ischemia (HR: 0.62, 95% CI: 0.51 to 0.75), troponin T release (HR: 0.63, 95% CI: 0.49 to 0.80), and long-term mortality (HR: 0.86, 95% CI: 0.76 to 0.97). Higher heart rates during ECG monitoring (per 10-bpm increase) were significantly associated with an increased incidence of myocardial ischemia (HR: 2.49, 95% CI: 1.79 to 3.48), troponin T release (HR: 1.53, 95% CI: 1.16 to 2.03), and long-term mortality (HR: 1.42, 95% CI: 1.14 to 1.76). An absolute mean perioperative heart rate less than 70 bpm was associated with the best outcome.

Poldermans and colleagues (59) randomly assigned 770 intermediate-risk patients to cardiac stress testing (n=386) or no testing (n=384). All patients received beta blockers, and the beta-blocker dose was adjusted preoperatively to achieve a resting heart rate of 60 to 65 bpm. In patients with ischemia, physicians aimed to control heart rate below the ischemic threshold. Patients assigned to no testing had a similar incidence of the cardiac events as those assigned to testing. Patients with a heart rate less than 65 bpm had lower risk than the remaining patients (1.3% versus 5.2%; OR 0.24, 95% CI: 0.09 to 0.66, P=0.003). The authors concluded that cardiac testing can safely be omitted in intermediate-risk patients, provided that beta blockers aimed at tight heart rate control are prescribed.

The importance of tight heart rate control in reducing perioperative myocardial ischemia is further supported by a study by Raby et al (380). The lack of tight heart rate control is a potential explanation for the lack of efficacy in some of the randomized trials. Accumulating evidence suggests that

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effective heart rate control with beta blockers should be targeted at less than 65 bpm.

7.2.1.3. Withdrawal of Beta Blockers

Concerns regarding the discontinuation of beta-blocker therapy in the perioperative period have existed for several decades (391). Shammash and colleagues (392) studied a total of 140 patients who received beta blockers preoperatively. Mortality in the 8 patients who had beta blockers discontinued postoperatively (50%) was significantly greater than in the 132 patients in whom beta blockers were continued (1.5%; OR 65.0, *P* less than 0.001). Hoeks and colleagues (393) studied 711 consecutive peripheral vascular surgery patients. After adjustment for potential confounders and the propensity of its use, continuous beta-blocker use remained significantly associated with a lower 1-year mortality than among nonusers (HR: 0.4, 95% CI: 0.2 to 0.7). In contrast, beta-blocker withdrawal was associated with an increased risk of 1-year mortality compared with nonusers (HR: 2.7, 95% CI: 1.2 to 5.9).

As noted in the recommendations, continuation of beta-blocker therapy in the perioperative period is a class I indication, and accumulating evidence suggests that titration to maintain tight heart rate control should be the goal.

7.2.2. Perioperative Statin Therapy

Recommendations for Statin Therapy

CLASS I

1. For patients currently taking statins and scheduled for noncardiac surgery, statins should be continued. (*Level of Evidence: B*)

CLASS IIa

1. For patients undergoing vascular surgery with or without clinical risk factors, statin use is reasonable. (*Level of Evidence: B*)

CLASS IIb

1. For patients with at least 1 clinical risk factor who are undergoing intermediate-risk procedures, statins may be considered. (*Level of Evidence: C*)

Lipid lowering has proven to be highly effective in the secondary prevention of cardiac events. Numerous studies have demonstrated that many patient groups (high-risk patients with a history of MI, high-risk patients without a history of MI, and patients who are simply at high risk) have a lower incidence of MI, stroke, and death when treated with lipid-lowering agents. Specifically, the bulk of this evidence applies to hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase inhibitors, or statin therapy (394,395).

The effectiveness of this class of medications in preventing cardiovascular events among high-risk patients has suggested to many that these agents might similarly improve perioperative cardiac risk. Certainly, the growing evidence that statin therapy improves endothelial function, reduces vascular inflammation, and stabilizes atherosclerotic plaque all supports the concept that these agents may reduce the incidence of cardiovascular events brought on by the stress of surgery in the setting of known atherosclerotic disease.

The evidence relating to statin use in the perioperative period to date is primarily in the form of observational studies (Table 13) (253,396–399,401–404). Hindler and colleagues conducted a meta-analysis to evaluate the overall effect of preoperative statin therapy on postoperative outcomes (405). Preoperative statin therapy was associated with 59% reduction in the risk of mortality after vascular (1.7% versus 6.1%; $P=0.0001$) surgery. When including noncardiac surgery, a 44% reduction in mortality (2.2% versus 3.2%; $P=0.0001$) was observed.

One randomized controlled trial has been performed to evaluate the effectiveness of statin therapy for perioperative cardiovascular risk protection. Durazzo and colleagues randomized 100 patients who were to undergo vascular surgery to atorvastatin 20 mg per day or placebo (406). Subjects in the study received atorvastatin for an average of 30 days before undergoing vascular surgery. The end point studied was a composite of death due to a cardiac cause, MI, unstable

Table 13. Published Studies of Perioperative Statin Use and Outcomes in Noncardiac Surgery

				Adjusted OR (95% CI)	
Study, Year	Design	n (Statin/Total)	Surgery	Perioperative Complications	Perioperative Mortality
Lindenauer et al (396), 2004	Retrospective/ administrative	77 082/ 780 591	Major noncardiac		0.62 (0.58 to 0.67)
Poldermans et al (397), 2003	Case-control	160 Cases, 320 controls	Major vascular		0.22 (0.10 to 0.47)
O'Neil-Callahan et al (398), 2005	Retrospective	526/1163	Major vascular	0.52 (0.35 to 0.77)	
Kertai et al (399), 2004	Retrospective	162/570	AAA surgery	0.24 (0.10 to 0.70) (Death or MI)	
Landesberg et al (400), 2003	Retrospective	502	Major vascular		0.54 (0.26 to 1.11)
Kennedy et al (401), 2005	Retrospective/ administrative	815/2031 Symptomatic	Carotid endarterectomy	0.55 (0.32 to 0.95) (Stroke or death)	0.25 (0.07 to 0.90)
		665/1252 Asymptomatic	Carotid endarterectomy	0.54 (0.13 to 2.24) (Stroke or death)	1.34 (0.61 to 2.93)
Ward et al (402), 2005	Retrospective	72/446	Infrainguinal vascular surgery	0.36 (0.14 to 0.93)	
McGirt et al (403), 2005	Retrospective	657/1566	Carotid endarterectomy	0.35 (0.15 to 0.85) (Stroke)	0.20 (0.04 to 0.99)

AAA indicates abdominal aortic aneurysm; CI, confidence interval; MI, myocardial infarction; n, number of patients; and OR, odds ratio.

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angina, and stroke. Cardiac events occurred in 13 patients (26%) in the placebo group at 6-month follow-up compared with only 4 (8%) in the atorvastatin group ($P=0.31$). Although this study was small, with few end points, and included a composite end point, the investigators did have complete follow-up, and the difference in event rates between the 2 groups was statistically significant.

Poldermans and colleagues evaluated the association between perioperative death and statin use in a case-control study (397). They identified all patients who died during hospitalization for vascular surgery from among 2816 patients who underwent vascular surgery at Erasmus University between 1991 and 2000 (397). For each of the 160 cases of in-hospital death, they matched 2 control subjects based on similar year and type of surgery. Statin use was significantly less in those who died during hospitalization for vascular surgery, with an adjusted OR of 0.22 (95% CI: 0.10 to 0.47). Only 65% of the cases in this study died of vascular causes, although the authors point out that there was no association between statin use and death among those patients who died of bleeding complications. The authors did adjust for medication use, including beta blockers and statins. Although retrospective and observational, these data certainly argue for an association between a lack of statin use and increased mortality after major vascular surgery.

In another similar study, O'Neil-Callahan and colleagues evaluated the association between statin use and cardiac complications during noncardiac surgery (398). They collected information on all patients undergoing major vascular surgery (carotid endarterectomy, aortic surgery, or lower-extremity revascularization) between January 1999 and December 2000 at a single tertiary referral center. The composite end point for this study included death, MI, ischemia, congestive HF, and ventricular tachyarrhythmias. The primary end point occurred in 157 of 1163 patients, significantly more frequently in patients not receiving statin therapy (16.5%) than in those receiving statins (9.9%, $P=0.001$). After adjustment for other predictors of perioperative cardiac events, statin use remained associated with a decreased risk (OR: 0.52, 95% CI: 0.35 to 0.76, $P=0.001$). These authors found that statin use was associated with beta-blocker use, but a propensity score analysis suggested that the effect of statins was independent of that association.

A large administrative database combining patient information from 4 western Canadian provinces was used to examine the relationship between statin use and outcomes in patients undergoing carotid endarterectomy (401). In this study, the authors identified all patients undergoing open surgical treatment for symptomatic carotid disease, examining the association between statin use and perioperative death, perioperative stroke or death, or perioperative cardiovascular outcomes. They found a significant inverse correlation between statin use and perioperative death (OR: 0.25, 95% CI: 0.07 to 0.90) and between statin use and perioperative stroke or death (OR: 0.55, 95% CI: 0.32 to 0.95) but not cardiovascular outcomes (OR: 0.87, 95% CI: 0.49 to 1.54). Interestingly, this group showed no benefit for any of these outcomes in asymptomatic patients undergoing carotid endarterectomy, which suggests that benefit, as expected, is proportional to risk. Similarly, McGirt et al (403) reviewed the results of carotid endarterectomy in 1566 patients at a major academic medical center, documenting a reduced rate of perioperative stroke (OR: 0.35, 95% CI: 0.15 to 0.85) and death (OR: 0.20, 95% CI: 0.04 to 0.99).

Le Manach prospectively collected data in patients undergoing infrarenal aortic surgery and compared a cohort when there were no guidelines for perioperative continuation of statins (discontinuation group, n=491) compared with when guidelines were instituted whereby statin therapy was continued starting as soon as possible after surgery (continuation group, n=178) (407). Postoperative statin withdrawal (more than 4 days) was an independent predictor of postoperative myonecrosis (OR: 2.9, 95% CI: 1.6 to 5.5).

Finally, in the largest such observational study, Lindenauer and colleagues reviewed the hospital and pharmacy records of 780 591 patients over 18 years of age who were undergoing noncardiac surgery (396). These data came from administrative databases in 329 hospitals participating in a quality and benchmarking program. The authors defined statin use as recorded use of statin therapy during the first 2 days of hospitalization. Use after the first 2 days was coded as nonuse of statins. These authors used propensity matching to adjust for baseline demographic and risk factor differences. Hospital mortality was the primary end point and was analyzed in association with statin use, stratified by each patient's calculated Revised Cardiac Risk Index score based on Lee et al (4). Patients who received statins had a lower crude mortality rate (2.13% versus 3.05%, *P* less than 0.001) and a lower mortality rate with matching by propensity score (2.18% versus 3.15%, *P* less than 0.001). Mortality remained lower after adjustment for differences with conditional logistic regression (adjusted OR 0.62, 95% CI: 0.58 to 0.67). The authors estimated that the number needed to treat with statin therapy to prevent in-hospital death was 85 (95% CI: 77 to 98), varying from 186 in the lowest-risk group to 30 in the highest-risk group.

Several other reports also lend support to the association between perioperative statin use and perioperative outcomes. Some of these studies are analyses of reports that included statin use among the independent variables associated with outcomes after noncardiac surgery (404) or are reanalyses of data already discussed (408,409) Additionally, Schouten and colleagues (409) studied 981 patients undergoing major vascular surgery and did not find an association between perioperative statin use and an increased risk of myopathy or any cases of rhabdomyolysis.

In summary, the evidence so far accumulated suggests a protective effect of perioperative statin use on cardiac complications during noncardiac surgery. Most of these data are observational and identify patients in whom time of initiation of statin therapy and duration of statin therapy are unclear. Furthermore, statin dose, target or achieved low-density lipoprotein levels, and indications for statin therapy are also largely unclear. Sufficiently powered randomized trials are needed to determine whether these observed associations translate into a benefit for statin therapy prescribed perioperatively for the purpose of lowering cardiac event rates surrounding noncardiac surgery. Utilizing the periopera-

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tive period as an opportunity to impact long-term health, consideration should be given to starting statin therapy in patients who meet National Cholesterol Education Program criteria (395,410).

7.2.3. Alpha-2 Agonists

CLASS IIb

1. Alpha-2 agonists for perioperative control of hypertension may be considered for patients with known CAD or at least 1 clinical risk factor who are undergoing surgery. (*Level of Evidence: B*)

CLASS III

1. Alpha-2 agonists should not be given to patients undergoing surgery who have contraindications to this medication. (*Level of Evidence: C*)

Several studies examined the role of alpha-agonists (clonidine and mivazerol) for perioperative cardiac protection. Oliver et al (411) reported a large, randomized, placebo-controlled, multicenter trial of the alpha-2 agonist mivazerol in perioperative use. They randomized 2854 patients with known CAD or significant risk factors who were undergoing noncardiac surgery to a 1.5 mcg per kg per hour infusion of mivazerol or placebo. Among patients with an established history of CAD who were undergoing general surgical procedures, the rate of MI was no different between the mivazerol and placebo groups, but the cardiac death rate was reduced (13 of 946 versus 25 of 941; $P=0.04$). Among patients undergoing vascular procedures, both cardiac death rate (6 of 454 versus 18 of 450; $P=0.017$) and the combined end point of death or MI (44 of 454 versus 64 of 450; $P=0.037$) were significantly reduced. The Multicenter Study of Perioperative Ischemia Research Group (412) also reported the results of a placebo-controlled, randomized, double-blind study of perioperative mivazerol. Three hundred patients with known CAD undergoing noncardiac surgery were randomized to high-dose (1.5 mcg per kg per hour) or low-dose (0.75 mcg per kg per hour) mivazerol or placebo. No differences in perioperative death or MI were observed, but the high-dose group had significantly less myocardial ischemia than the placebo group (20 of 98 versus 35 of 103; $P=0.026$). Two randomized, placebo-controlled studies of clonidine for perioperative myocardial protection were performed in 297 patients undergoing vascular surgery (413) and 61 patients undergoing general surgery (414). Both demonstrated a significant decrease in the incidence of myocardial ischemia (35 of 145 versus 59 of 152, P less than 0.01, and 1 of 28 versus 5 of 24, $P=0.05$, respectively).

Wijeysundera and colleagues (415) performed a meta-analysis of perioperative alpha-2 agonist administration through 2002 comprising 23 trials enrolling 3395 patients. Alpha-2 agonists reduced mortality (RR: 0.76, 95% CI: 0.63 to 0.91) and MI (RR: 0.66, 95% CI: 0.46 to 0.94) during vascular surgery.

More recently, Wallace et al (416) conducted a prospective, double-blinded, clinical trial on patients with or at risk for CAD to investigate whether prophylactic clonidine reduced perioperative myocardial ischemia and long-term death in patients undergoing noncardiac surgery. Patients were randomized to clonidine (n=125) or placebo (n=65). Clonidine (0.2 mg orally and by patch) or placebo (tablet and patch) were administered the night before surgery, and clonidine (0.2 mg orally) or placebo (tablet) was administered on the morning of surgery. Patches were left on for 4 days. Prophylactic clonidine administered perioperatively significantly reduced myocardial ischemia during the intraoperative and postoperative period (clonidine 18 of 125 or 14% versus placebo 20 of 65 or 31%; $P=0.01$). Moreover, administration of clonidine had minimal hemodynamic effects and reduced postoperative mortality for up to 2 years (clonidine 19 of 125 or 15% versus placebo 19 of 65 or 29%; RR: 0.43, 95% CI: 0.21 to 0.89, $P=0.035$).

7.2.4. Perioperative Calcium Channel Blockers

A meta-analysis of perioperative calcium channel blockers in noncardiac surgery that was published in 2003 identified 11 studies involving 1007 patients (417). Calcium channel blockers significantly reduced ischemia (RR: 0.49, 95% CI: 0.30 to 0.80, $P=0.004$) and supraventricular tachycardia (RR: 0.52, 95% CI: 0.37 to 0.72, P less than 0.0001). Calcium channel blockers were associated with trends toward reduced death and MI. In post hoc analyses, calcium channel blockers significantly reduced death/MI (RR: 0.35, 95% CI: 0.15 to 0.86, $P=0.02$). The majority of these benefits were attributable to diltiazem. Dihydropyridines and verapamil did not decrease the incidence of myocardial ischemia, although verapamil decreased the incidence of supraventricular tachycardia. The authors concluded that a large-scale trial was needed to define the value of these agents.

7.3. Prophylactic Valvular Intervention Before Noncardiac Surgery

There is little information about the appropriateness of valvular repair or replacement before a noncardiac surgical procedure is undertaken. Clinical experience indicates that patients with valvular heart disease severe enough to warrant surgical treatment should have valve surgery before elective noncardiac surgery. It has been suggested that patients with severe mitral or aortic stenosis who require urgent noncardiac surgery, such as intestinal resection for lesions causing serious gastrointestinal bleeding, may benefit from catheter balloon valvuloplasty at least as a temporizing step to reduce the operative risk of noncardiac surgery (418–421). Unfortunately, there are no controlled studies, and the risks of balloon aortic valvuloplasty in older patients are significant (418), although mitral valvuloplasty performed by experienced operators has been shown to be safe and effective. Experience with managing valvular heart disease during labor and delivery provides insights into the approach to management of the patient for noncardiac surgery. The vast majority of women with regurgitant valvular heart disease can be managed medically during the course of pregnancy, including labor and delivery, because the decrease in peripheral vascular resistance that occurs with pregnancy tends to decrease regurgitant lesions (422). Increased arterial afterload is not well tolerated in patients with aortic and mitral regurgitation. Therefore, increases in blood pressure should be prevented, and LV afterload should be optimized with vasodilators. In contrast, patients with significant aortic or mitral stenosis

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often do not do well with the increased hemodynamic burden of pregnancy. If the stenosis is severe, percutaneous catheter balloon valvotomy should be considered as definitive therapy or as a bridge to care for the patient through pregnancy, labor, and surgical delivery. Excessive changes in intravascular volume should be avoided (see also Section 3.5, Valvular Heart Disease).

7.4. Perioperative Arrhythmias and Conduction Disturbances

In the perioperative setting, cardiac arrhythmias or conduction disturbances often reflect the presence of underlying cardiopulmonary disease, drug toxicity, or metabolic derangements. In patients with documented hemodynamically significant or symptomatic arrhythmias, electrophysiologic testing and catheter ablation, particularly for supraventricular arrhythmias, may be indicated to prevent arrhythmia recurrence (423–425). In patients with documented hemodynamically significant or symptomatic arrhythmias, acute treatment is indicated. Sustained supraventricular arrhythmias may require electrical or pharmacological cardioversion. Alternatively, in atrial fibrillation or atrial flutter, a rate-control strategy can be accomplished with beta-adrenergic blockers, calcium channel blockers, or digoxin (oral or intravenous). Of these 3 types of medications, digitalis is the least effective agent and beta blockers are the most effective agent for controlling the ventricular response during atrial fibrillation (426). An additional benefit of beta blockers is that they have been shown to accelerate the conversion of postoperative supraventricular arrhythmias to sinus rhythm compared with diltiazem (427). In select cases, electrophysiologic testing and catheter ablation, particularly for supraventricular arrhythmias, may be indicated.

Patients with chronic atrial fibrillation or a history of paroxysmal atrial fibrillation before surgery often take chronic oral anticoagulants. It may be necessary to discontinue this anticoagulation from a few to several days before surgery. Bridging anticoagulation with either low-molecular-weight or unfractionated heparin may be indicated if the thromboembolic risk assessment warrants. If time does not allow and it is important that the patient not be taking anticoagulants, the effect of warfarin can be reversed by parenteral vitamin K or fresh frozen plasma (428).

Ventricular arrhythmias, whether simple premature ventricular contractions, complex ventricular ectopy, or nonsustained tachycardia, usually do not require therapy unless they are associated with hemodynamic compromise or occur in the presence of ongoing or threatened myocardial ischemia or LV dysfunction. Studies have shown that although nearly half of all high-risk patients undergoing noncardiac surgery have frequent premature ventricular contractions or asymptomatic nonsustained ventricular tachycardia, the presence of these ventricular arrhythmias is not associated with an increase in nonfatal MI or cardiac death (36,37). Nevertheless, the presence of an arrhythmia in the preoperative setting should provoke a search for underlying cardiopulmonary disease, ongoing myocardial ischemia or infarction, drug toxicity, or metabolic derangements. Physicians should also have a low threshold at which they institute prophylactic beta-blocker therapy in patients at increased risk of developing a perioperative or postoperative arrhythmia (including those in whom arrhythmias are present during the preoperative evaluation).

Several studies have demonstrated that beta-blocker therapy can reduce the incidence of arrhythmias during the perioperative period (87,117). Sustained or symptomatic ventricular tachycardia should be suppressed preoperatively with intravenous lidocaine, procainamide, or amiodarone, and a thorough search should be conducted for underlying causes and appropriate short- and long-term therapy.

The indications for temporary pacemakers are almost identical to those previously stated for long-term permanent cardiac pacing (429). Patients with intraventricular conduction delays, bifascicular block (right bundle-branch block with left anterior or posterior hemiblock), or left bundle-branch block with or without first-degree atrioventricular block do not require temporary pacemaker implantation in the absence of a history of syncope or more advanced atrioventricular block (118).

7.5. Intraoperative Electromagnetic Interference With Implanted Pacemakers and ICDs

It is important to be aware of the potential for adverse interactions between electrical/magnetic activity and pacemaker or ICD function that may occur during the operative period. These interactions result from electrical current generated by electrocautery or cardioversion, as well as the impact of metabolic derangements, antiarrhythmic agents, and anesthetic agents on pacing and sensing thresholds. The probability of these adverse interactions can be minimized if certain precautions are taken. Although this topic has been analyzed in a number of review articles and book chapters (430–433), no formal guidelines have been developed by the ACC, the AHA, or the Heart Rhythm Society. Of note, however, is a practice advisory that has been published by the American Society of Anesthesiology (434).

Electrocautery involves the use of radiofrequency current to cut or coagulate tissues. It is usually applied in a unipolar fashion between the cautery device and an indifferent plate attached to the patient's skin. The indifferent plate is often placed on the patient's thigh. Although bipolar cautery systems are available, they are not widely used. The potential for electromagnetic interference with an implanted device is related to the amount of current generated in the vicinity of the pacemaker or ICD device. In general, high current is generated if the cautery device is close to the pacemaker, particularly if the current path of the cautery lies along the axis of the pacemaker or ICD lead. The electrical current generated by electrocautery can cause a variety of responses by the implanted device, including the following: 1) temporary or permanent resetting to a backup, reset, or noise-reversion pacing mode (eg, a dual-chamber pacemaker may be reset to VVI pacing at a fixed rate); 2) temporary or permanent inhibition of pacemaker output; 3) an increase in pacing rate due to activation of the rate-responsive sensor; 4) ICD firing due to activation by electrical noise; or 5) myocardial injury at the lead tip that may cause failure to

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sense and/or capture. Cardioversion can have similar effects on pacemaker or ICD function. Although the probability of any of these adverse interactions occurring has fallen dramatically owing to the almost universal use of bipolar leads (which greatly reduces the probability of electromagnetic interference) and improved pacemaker and ICD design, they still may occur (430–433,435).

The likelihood and potential clinical impact of adverse interactions occurring in patients with ICDs and pacemaker devices will be influenced by a number of factors, including whether the patient is pacemaker dependent, whether the pacemaker has unipolar or bipolar leads, whether the electrocautery is bipolar or unipolar, and the relative distance from and orientation of the electrocautery relative to the pacemaker and pacemaker lead. These factors, combined with the urgency and type of surgery (interactions are far more likely to occur with surgical procedures that involve the chest or abdomen) and the availability of expertise in pacing and/or ICDs, will ultimately determine the type and extent of evaluation that is performed in a particular institution. Patients with pacemakers must be assessed as to whether they are pacer dependent. This may be determined by a chart review and examination of the ECG, as opposed to requiring the interrogation of the device. When the patient is not pacer dependent and/or the cautery is remote and will be administered in brief bursts, and the operative team can monitor the ECG and pulse oximeter (which allows pulse determination even when electrical interference by cautery interferes with the ECG), it may be unnecessary to interrogate the pacer at all.

Several general recommendations can be made concerning the preoperative and operative management of patients with implanted devices who are undergoing surgical procedures (436). Patients with implanted ICDs or pacemakers need to be identified before surgery so that appropriate records from the device clinic that is monitoring the patient's device can be obtained. In addition, the original indication for device placement should be identified before surgery. Patients with permanent pacemakers, who are pacemaker dependent, should have their device evaluated within 3 to 6 months before significant surgical procedures, and also after surgery. Significant surgical procedures include major abdominal or thoracic surgery, particularly when the surgery involves large amounts of electrocautery. This evaluation should include 1) determining the type of device, 2) determining whether the patient is pacemaker dependent for antibradycardia pacing, and 3) determining device programmed settings and battery status. If a patient is pacemaker dependent, the device should be reprogrammed to an asynchronous mode during surgery (VOO or DOO), or a magnet should be placed over the device during surgery. Implantable cardioverter defibrillator devices should have their tachyarrhythmia treatment algorithms programmed off before surgery and turned on after surgery to prevent unwanted shocks due to spurious signals that the device might interpret as ventricular tachycardia or fibrillation. During the period of time when device therapy has been inactivated, the patient should be monitored continuously for a life-threatening arrhythmia. All patients with implanted devices should have both continuous ECG monitoring and continuous pulse monitoring during surgery. This reflects the fact that electrocautery may interfere with ECG monitoring and make it difficult or impossible to determine the patient's rhythm. Efforts should be made to minimize the chance for interactions by careful management of potential sources of electromagnetic interference. These include 1) the use of a bipolar electrocautery system if possible, 2) the use of short and intermittent bursts of electrocautery at the lowest possible energy levels, 3) maximization of the distance between the electrocautery and the device, and 4) if a unipolar cautery is to be used, placement of the ground patch in a position so as to minimize current flow through the pacemaker or ICD device. Finally, if emergency cardioversion is required, the paddles should be placed as far from the implanted device as possible and in an orientation likely to be perpendicular to the orientation of the device leads (anterior-posterior paddle position is preferred). After the surgery, the function of the implanted device should be assessed and in some cases formally evaluated. If the pacemaker or ICD was reprogrammed before surgery, it should be programmed back to its original settings after surgery. In the case of an ICD, an interrogated programmer printout should be produced to verify that its antitachycardia function has been restored to its active status.

Placement of a magnet over an implanted device has variable effects depending on the type of device, its manufacturer, and its model. Most bradycardia pacemakers will respond to magnet application with asynchronous pacing at a pre-prescribed rate. However, this magnet function can, in a minority of pacemaker models, be programmed off, and therefore, a magnet may not elicit a response from those models. If a magnet will be used during surgery in a patient with a pacemaker who is pacemaker dependent, it should be applied before surgery to be certain that appropriate asynchronous pacing is triggered by the magnet. Unlike bradycardia pacemakers, a magnet will not change the pacing function of an ICD. Magnet application will affect only the antitachycardia function of an ICD. With some models of ICDs, the magnet will first suspend the antitachycardia (shocking) function and then actually turn the therapy off. With other ICD models, the magnet will only temporarily disable the shock function (while the magnet is in place), and the therapy will then become active again on its removal (either intentional or unintentional). Programming the shock function off with an ICD programmer (and turning it back on after the surgery) is the preferred method of addressing these issues. Because some patients with ICDs are also pacemaker dependent, the pacing function of the ICD may need to be programmed to an asynchronous mode (eg, VOO or DOO) during surgery to prevent electromagnetic interference–induced inhibition. Communication of the status of the pacemaker or ICD to the anesthesiologist, surgeon, and intensivist is imperative.

7.6. Preoperative Intensive Care

CLASS IIb

1. **Preoperative intensive care monitoring with a pulmonary artery catheter for optimization of hemodynamic status might be considered; however, it is rarely required and should be restricted to a**

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Table 14. Levels of Thromboembolism Risk in Surgical Patients Without Prophylaxis

	Deep Vein Thrombosis, %		Pulmonary Embolism, %		
Level of Risk	Calf	Proximal	Clinical Events	Fatal Events	Successful Prevention Strategies
Low	2	0.4	0.2	Less than 0.01	No specific prophylaxis; early and "aggressive" mobilization
Minor surgery in patients less than 40 years old with no additional risk factors					
Moderate	10 to 20	2 to 4	1 to 2	0.1 to 0.4	LDUH (every 12 hours), LMWH (less than or equal to 3400 U daily), GCS, or IPC
Minor surgery in patients with additional risk factors					
Surgery in patients aged 40 to 60 years with no additional risk factors					
High	20 to 40	4 to 8	2 to 4	0.4 to 1.0	LDUH (every 8 hours), LMWH (more than 3400 U daily), or IPC
Surgery in patients more than 60 years old or aged 40 to 60 years with additional risk factors (prior VTE, cancer, molecular hypercoagulability)					
Highest	40 to 80	10 to 20	4 to 10	0.2 to 5.0	LMWH (more than 3400 U daily), fondaparinux, oral VKAs (INR 2 to 3), or IPC/GCS plus LDUH/LMWH
Surgery in patients with multiple risk factors (age greater than 40 years, cancer, prior VTE)					
Hip or knee arthroplasty, HFS					
Major trauma; SCI					

GCS indicates graduated compression stocking; HFS, hip fracture surgery; INR, international normalized ratio; IPC, intermittent pneumatic compression; LDUH, low-dose unfractionated heparin; LMWH, low-molecular-weight heparin; SCI, spinal cord injury; U, unit; VKA, vitamin K antagonist; and VTE, venous thromboembolism.
Adapted with permission from Geerts et al (114).

very small number of highly selected patients whose presentation is unstable and complex and who have multiple comorbid conditions. (*Level of Evidence: B*)

Preoperative invasive monitoring in an intensive care setting can be used to optimize and even augment oxygen delivery in patients at high risk. It has been proposed that indexes derived from the pulmonary artery catheter (PAC) and invasive blood pressure monitoring can be used to maximize hemodynamic function which may lead to a reduction in organ dysfunction or morbidity.

There are limited numbers of studies evaluating intensive care monitoring before noncardiac surgery. Two prospective randomized trials evaluating the use of PACs and hemodynamic optimization arrived at different conclusions regarding its impact on morbidity and mortality (437,438). A meta-analysis of hemodynamic optimization by Poeze et al (439) found an overall decreased mortality rate (RR: 0.75, 95% CI: 0.54 to 0.81) in all studies. Kavarana et al (440) performed a retrospective analysis investigating preoperative optimization of cardiovascular function using a PAC in elderly patients (greater than 65 years) undergoing elective colon resection and found reduced mortality (5% versus 15.8%) only in patients with a cardiac risk index greater than 10. Kern and Shoemaker's (441) meta-analysis of 21 randomized controlled trials with various approaches found reduced mortality with hemodynamic optimization.

7.7. Venothromboembolism/Peripheral Arterial Disease

Two peripheral vascular disorders that merit attention preoperatively are venous thromboembolism and, in the elderly, chronic occlusive peripheral arterial disease. Prophylactic measures need to be planned and in some cases started preoperatively for persons with clinical circumstances associated with postoperative venous thromboembolism. These correlates of thromboembolic risk include advanced age; prolonged immobility or paralysis; prior venous thromboembolism; malignancy; major surgery, particularly operations involving the abdomen, pelvis, or lower extremities; obesity; varicose veins; HF; MI; stroke; fractures of the pelvis, hip, or leg; congenital or acquired aberrations in hemostatic mechanisms (hypercoagulable states); and, possibly, high-dose estrogen use as suggested by the American College of Chest Physicians (114). The choice of prophylactic measure or agent—graded-compression elastic stockings, low-dose subcutaneous heparin, low-molecular-weight heparin, warfarin, or intermittent pneumatic compression—will depend on the risk of venous thromboembolism and the type of surgery planned. Table 14 provides published recommendations for various types of surgical procedures (442).

The noninvasive techniques—impedance plethysmography and real-time compression ultrasonography—are effective objective tests to exclude clinically suspected deep venous thrombosis and are best used for this purpose (443,444).

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Table 15. Randomized Clinical Trials of Volatile Anesthetics in Patients Undergoing Coronary Artery Surgery

Study, Year	n	Anesthetic	Control	Surgical Technique	End Point
Slogoff and Keats (451), 1989	1012	Enflurane Halothane Isoflurane	High-dose sufentanil	CPB	No difference in ischemia, MI, or death
Leung et al (452), 1991	186	Isoflurane	High-dose sufentanil	CPB	No difference in ischemia
Helman et al (453), 1992	200	Desflurane	High-dose sufentanil	CPB	Increased ischemia during induction of anesthesia
Belhomme et al (454), 1999	20	Isoflurane before aortic cross-clamping	No volatile anesthetic	CPB	No difference in TnI activation of PKC
Penta de Peppo et al (455), 1999	22	Enflurane before CPB	No volatile anesthetic	CPB	Improved LV function
Tomai et al (456), 1999	40	Isoflurane before CPB	No volatile anesthetic	CPB	Decreased TnI in subset of patients with EF less than 50%
Haroun-Bizri et al (457), 2001	49	Isoflurane before CPB	No volatile anesthetic	CPB	Improved LV function
De Hert et al (458), 2002	20	Sevoflurane	Propofol	CPB	Decreased TnI; improved LV function
De Hert et al (459), 2003	45	Sevoflurane Desflurane	Propofol	CPB; elderly; EF less than 50%	Decreased TnI; improved LV function
Julier et al (460), 2003, and Garcia et al (461), 2005	72	Sevoflurane before aortic cross-clamping	No volatile anesthetic	CPB	No difference in TnI at 72 hours; decreased BNP; decreased late cardiac events in the same study population
Conzen et al (462), 2003	20	Sevoflurane	Propofol	OPCAB	Decreased TnI
De Hert et al (463), 2004	320	Sevoflurane or desflurane	Propofol or midazolam	CPB	Decreased TnI; decreased ICU and hospital LOS
Forlani et al (464), 2004	60	Isoflurane before CPB	No volatile anesthetic	CPB	Decreased TnI and CK-MB
Bein et al (465), 2005	52	Sevoflurane	Propofol	MIDCAB	Improved LV function

BNP indicates brain natriuretic peptide; CK-MB, MB isoenzyme of creatine kinase; CPB, cardiopulmonary bypass; EF, ejection fraction; ICU, intensive care unit; LOS, length of stay; LV, left ventricle; MI, myocardial infarction; MIDCAB, minimally invasive direct coronary artery bypass; OPCAB, off-pump coronary bypass; n, number of patients; PKC, protein kinase C; and TnI, troponin I.

Routine screening of all postoperative patients with a noninvasive technique is not as cost-effective or efficient as appropriate antithrombotic prophylaxis for moderate- and high-risk patients (445,446).

The prevalence of chronic occlusive peripheral arterial disease rises with increasing age, affecting more than 10% of the general population older than 65 years (447) and as many as half of all persons with CAD (448). Patients with this condition may be at increased risk of perioperative cardiac complications, even for a given degree of coronary disease (449). This may warrant particular attention to the preoperative evaluation and intraoperative therapy of such patients. Protection of the limbs from trauma during and after surgery is as important for those with asymptomatic arterial disease as for those with claudication.

8. Anesthetic Considerations and Intraoperative Management

The pathophysiological events that occur with the trauma of surgery and the perioperative administration of anesthetic and pain-relieving drugs often affect the physiology of cardiac function and dysfunction to great degrees. Specific integration of these changes with the consultative evaluation is a field unto itself and beyond the scope of these guidelines. The information provided by the cardiovascular consultant needs to be integrated by the anesthesiologist, surgeon, and postoperative caregivers in preparing an individualized perioperative management plan. The diagnosis of an MI has been redefined by the Joint European Society of Cardiology/ACC Committee for the Redefinition of MI, but the definition of a perioperative MI in noncardiac surgery was not specifically addressed (450).

There are many different approaches to the details of the anesthetic care of the cardiac patient, including the use of specific anesthetic agents (Table 15) or anesthetic techniques (eg, general, regional, or monitored anesthesia care). Each has implications regarding anesthetic and intraoperative monitoring. In addition, no study has clearly demonstrated a change in outcome from the routine use of the following techniques: a PAC, ST-segment monitor, transesophageal echocardiography (TEE), or intravenous nitroglycerin. Therefore, the choice of anesthetic technique and intraoperative monitors is best left to the discretion of the anesthesia care team. Intraoperative management may be influenced by the perioperative plan, including the need for postoperative monitoring, ventilation, analgesia, and the perioperative use of anticoagulants or antiplatelet agents. Therefore, a discussion of these issues before the planned surgery will allow for a smooth transition through the perioperative period.

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8.1. Choice of Anesthetic Technique and Agent

Recommendations for Use of Volatile Anesthetic Agents

CLASS IIa

1. It can be beneficial to use volatile anesthetic agents during noncardiac surgery for the maintenance of general anesthesia in hemodynamically stable patients at risk for myocardial ischemia. (*Level of Evidence: B*)

Multiple studies have examined the influence of anesthetic drugs and techniques on cardiac morbidity. In a large-scale study of unselected patients, coexisting disease and surgical procedure were important determinants of outcome (466). All anesthetic techniques and drugs are associated with known effects that should be considered in the perioperative plan. Opioid-based anesthetics were previously popularized because of the cardiovascular stability associated with their use. The use of high doses of opioids, however, is associated with the need for prolonged postoperative mechanical ventilation, and their use may increase length of stay in the intensive care unit (ICU).

All inhaled volatile anesthetic agents have cardiovascular effects, including depression of myocardial contractility and afterload reduction. The similarities between the agents are greater than their differences. Early studies demonstrated that volatile anesthetic agents did not influence outcome compared with high-dose opioid techniques (451–453). However, as summarized in Table 15, randomized clinical trials in patients undergoing CABG surgery indicate that volatile anesthetics decrease troponin release and enhance LV function compared with propofol, midazolam, or balanced anesthesia techniques with opioids. These data can likely be generalized to patients with CAD who are undergoing noncardiac surgery. Of the 15 trials performed (451–465), the use compared with the nonuse of volatile anesthetics was associated with a decrease in troponin release in 6 trials, preservation of early LV function in 5, decreased ICU length of stay in 1, and decreased late cardiac events in 1. Although decreases in troponin levels reflect the cardioprotective actions of volatile anesthetics, none of the trials were powered to evaluate MI or death as an outcome. Volatile anesthetics have been shown in animal studies to precondition and postcondition the heart against infarction by activating specific intracellular signal transduction pathways (467). Decreased troponin levels in cardiac surgery patients receiving volatile anesthetics may reflect this preconditioning or postconditioning effect. De Hert et al (468) demonstrated that sevoflurane administered throughout surgery decreased troponin and ICU length of stay compared with patients who received propofol, whereas no differences in troponin levels were observed in patients receiving sevoflurane when this volatile anesthetic was administered solely as either a preconditioning or postconditioning agent. Similarly, low doses (0.25 to 0.5 minimum alveolar concentration [MAC]) of sevoflurane and isoflurane have been demonstrated to provide cardioprotection in animal models; however, the dose dependence or class effect of volatile anesthetics to produce cardioprotection in humans has not been specifically investigated.

Neuraxial anesthetic techniques include spinal and epidural approaches. Both techniques can result in sympathetic blockade, resulting in decreases in both preload and afterload. The decision to use neuraxial anesthesia for the high-risk cardiac patient may be influenced by the dermatomal level of the surgical procedure. Infrainguinal procedures can be performed under spinal or epidural anesthesia with minimal hemodynamic changes if neuraxial blockade is limited to those dermatomes. Abdominal procedures can also be performed with neuraxial techniques; however, high dermatomal levels of anesthesia may be required and may be associated with significant hemodynamic effects. High dermatomal levels can potentially result in hypotension if preload becomes compromised or blockade of the cardioaccelerators occurs. A meta-analysis reviewed the impact of central neuraxial analgesia on outcome after coronary artery bypass surgery (469). The use of thoracic epidural analgesia decreased postoperative pulmonary complications but did not influence the incidence of MI or overall mortality. Seven randomized clinical trials conducted in patients undergoing vascular surgery demonstrated no differences in outcome when regional and general anesthesia techniques were compared (470–476). One trial of 168 patients undergoing abdominal aortic surgery specifically examined the relative importance of intraoperative versus postoperative epidural anesthesia and analgesia compared with general anesthesia on outcomes (475). No differences in major morbidity, length of stay, or mortality rate were observed. There was no overall difference in death or major complications in 1021 patients randomized to receive general anesthesia/opioid analgesia or combined general/epidural anesthesia and analgesia for intra-abdominal aortic, gastric, biliary, or colon surgery (477). In the subgroup of patients undergoing aortic surgery, the incidence of MI was decreased ($P=0.05$) from 7.9% in the general anesthesia/opioid analgesia group to 2.7% in the general/epidural anesthesia group; however, the use of beta blockers in the 2 groups was not reported. The MASTER (Multicenter Australian Study of Epidural Anesthesia) trial randomized 915 patients undergoing major abdominal surgery to receive either combined general and epidural anesthesia/epidural analgesia or general anesthesia with opioid analgesia (478). Epidural anesthesia/analgesia did not decrease death or cardiovascular outcomes but modestly improved pulmonary outcomes compared with the general anesthesia group. In a subgroup analysis of patients undergoing aortic surgery, there was no effect of perioperative epidural analgesia on major outcomes (476).

"Monitored anesthesia care" by an anesthesia caregiver includes the use of local anesthesia supplemented with intravenous sedation/analgesia. In a large-scale study, monitored anesthesia care was associated with the highest incidence of 30-day mortality (466). This finding may reflect a strong selection bias in which patients with significant coexisting disease were selected for surgery with monitored anesthesia care rather than other anesthetic techniques. Although this technique can eliminate some of the undesirable effects of general or neuraxial anesthesia, it provides poor

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blockade of the stress response unless the local anesthetic provides profound anesthesia of the affected area. If the local anesthetic block is less than satisfactory or cannot be used at all, monitored anesthesia care could result in an increased incidence of myocardial ischemia and cardiac dysfunction compared with general or regional anesthesia. To achieve the desired effect, excess sedation can occur. Therefore, there may be no significant difference in overall safety with monitored anesthesia care, and general or regional anesthesia may be preferable. In general, the cardiovascular consultant should be aware of these issues, but it is the role of the anesthesiologist to select the best approach with integration and consideration of all medical perspectives and sometimes even patient preference.

8.2. Perioperative Pain Management

From the cardiac perspective, pain management may be a crucial aspect of perioperative care. Because the majority of cardiac events in noncardiac surgical patients occur postoperatively, the postoperative period may be the time during which ablation of stress, adverse hemodynamics, and hypercoagulable responses are most critical. Although no randomized controlled study specifically addressing analgesic regimens has demonstrated improvement in outcome, patient-controlled analgesia techniques are associated with greater patient satisfaction and lower pain scores. Epidural or spinal opiates are becoming more popular and have several theoretical advantages. Several studies have evaluated differing combinations of general and epidural anesthesia and intravenous and epidural analgesia (470,471,473,474,479). Patients having epidural anesthesia/analgesia have demonstrated lower opiate dosages, better ablation of the catecholamine response, and a less hypercoagulable state (480,481). In 1 study of patients undergoing lower-extremity vascular bypass procedures (471), the use of epidural anesthesia/analgesia was associated with a lower incidence of cardiac morbidity; however, this finding was not confirmed in 2 other studies (474,479). In a study of 124 patients undergoing aortic surgery, there was no difference in the incidence of myocardial ischemia in patients randomized to postoperative intravenous analgesia versus epidural analgesia (473). An effective analgesic regimen must be included in the perioperative plan and should be based on issues unique to a given patient undergoing a specific procedure at a specific institution.

8.3. Prophylactic Intraoperative Nitroglycerin

CLASS IIb

1. The usefulness of intraoperative nitroglycerin as a prophylactic agent to prevent myocardial ischemia and cardiac morbidity is unclear for high-risk patients undergoing noncardiac surgery, particularly those who have required nitrate therapy to control angina. The recommendation for prophylactic use of nitroglycerin must take into account the anesthetic plan and patient hemodynamics and must recognize that vasodilation and hypovolemia can readily occur during anesthesia and surgery. (*Level of Evidence: C*)

Nitroglycerin has been shown to reverse myocardial ischemia intraoperatively; however, the intraoperative prophylactic use of nitroglycerin in patients at high risk may have no effects or may actually lead to cardiovascular decompensation through decreases in preload. Topical nitroglycerin may have uneven absorption intraoperatively, so when clinically indicated, it is reasonable to administer nitroglycerin intravenously. The venodilating and arterial dilating effects of nitroglycerin are mimicked by some anesthetic agents, so that the combination of agents may lead to significant hypotension and myocardial ischemia. Therefore, nitroglycerin should be used only when the hemodynamic effects of other agents being used and intravascular volume status have been considered.

Four controlled studies have evaluated prophylactic nitroglycerin infusions for high-risk patients, including 2 studies in noncardiac surgery patients (482–485). Only 1 study, performed in patients with stable angina undergoing carotid endarterectomy, demonstrated a reduced incidence of intraoperative myocardial ischemia in the group receiving 1 mcg of nitroglycerin per kilogram of weight per minute. Neither of the 2 small studies demonstrated any reduction in the incidence of MI or cardiac death. In a retrospective analysis of patients with rest anginal symptoms who were undergoing CABG surgery, preoperative use of intravenous nitroglycerin had no effect on outcomes such as MI, death, or use of an intra-aortic balloon pump (486).

8.4. Use of TEE

CLASS IIa

1. The emergency use of intraoperative or perioperative TEE is reasonable to determine the cause of an acute, persistent, and life-threatening hemodynamic abnormality. (*Level of Evidence: C*)

Transesophageal echocardiography has become increasingly common in the operating room for cardiac surgery but is less frequently used in noncardiac surgery. Multiple investigations have documented the improved sensitivity of TEE for detection of myocardial ischemia compared with ECG or pulmonary capillary wedge pressure measurements. Most studies have used offline analysis of the TEE images, however, and automated, online detection may increase its value.

There are few data regarding the value of TEE-detected wall-motion abnormalities to predict cardiac morbidity in noncardiac surgical patients. In 2 studies from the same group, intraoperative wall-motion abnormalities were poor predictors of cardiac morbidity (487,488). In 1 study involving 322 men undergoing noncardiac surgeries, TEE demonstrated an OR of 2.6 (95% CI: 1.2 to 5.7) for predicting perioperative cardiac events (487). Although regional wall-motion abnormalities in a high-risk patient suggest myocardial ischemia, resolution of myocardial ischemia may not result in improvement of wall motion.

There is emerging evidence demonstrating the utility of TEE to alter the management of patients undergoing cardiac surgery; however, interpretation of TEE requires additional education. Many anesthesiologists are expert in this technique, but others have limited or no training. Currently, there is insufficient evidence to determine the cost-effectiveness of TEE for its use as a diagnostic monitor or to guide therapy during noncardiac surgery; therefore, the routine use of TEE in noncardiac surgery does not appear warranted. In contrast,

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emergent use of intraoperative or perioperative TEE to determine the cause of an acute, persistent, and life-threatening hemodynamic abnormality is indicated. Guidelines for the appropriate use of TEE have been developed by the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists (489).

8.5. Maintenance of Body Temperature

Recommendations for Maintenance of Body Temperature

CLASS I

1. Maintenance of body temperature in a normothermic range is recommended for most procedures other than during periods in which mild hypothermia is intended to provide organ protection (eg, during high aortic cross-clamping). (*Level of Evidence: B*)

Hypothermia is common during the perioperative period in the absence of active warming of patients. In a retrospective analysis of a prospective randomized trial comparing 2 different anesthetic techniques for infrainguinal revascularization surgery, hypothermia (temperature less than 35 degrees Celsius) was associated with an increased risk of myocardial ischemia compared with patients who had a core temperature greater than or equal to 35 degrees Celsius (normothermic group) in the postanesthesia care unit (490). Several methods of maintaining normothermia are available in clinical practice, the most widely studied being forced-air warming.

One randomized clinical trial was performed in 300 high-risk patients undergoing noncardiac surgery in which patients were randomized to active warming via forced air (normothermic group) or routine care (hypothermic group) (491). Perioperative morbid cardiac events (unstable angina/ischemia, cardiac arrest, and MI) occurred less frequently in the normothermic group than in the hypothermic group (1.4% versus 6.3%; $P=0.02$). In addition, ventricular tachycardia occurred less frequently in the normothermic group (2.4% versus 7.9%; $P=0.04$) (491). Hypothermia was an independent predictor of morbid cardiac events by multivariable analysis (RR: 2.2, 95% CI: 1.1 to 4.7, $P=0.04$), indicating a 55% reduction in risk when normothermia was maintained.

8.6. Intra-Aortic Balloon Counterpulsation Device

Placement of an intra-aortic balloon counterpulsation device has been suggested as a means of reducing perioperative cardiac risk in noncardiac surgery. Several case reports have documented its use in patients with unstable coronary syndromes or severe CAD who are undergoing urgent noncardiac surgery (492–495). Although the rate of cardiac complications is low compared with other series of patients at similarly high risk, there are no randomized trials to assess its true effectiveness. Additionally, the use of intra-aortic balloon counterpulsation is associated with complications, particularly in patients with peripheral vascular disease. There is currently insufficient evidence to determine the benefits versus risks of prophylactic placement of an intra-aortic balloon counterpulsation device for high-risk noncardiac surgery.

8.7. Perioperative Control of Blood Glucose Concentration

Recommendations for Perioperative Control of Blood Glucose Concentration

CLASS IIa

1. It is reasonable that blood glucose concentration be controlled¶ during the perioperative period in patients with diabetes mellitus or acute hyperglycemia who are at high risk for myocardial ischemia or who are undergoing vascular and major noncardiac surgical procedures with planned ICU admission. (*Level of Evidence: B*)

CLASS IIb

1. The usefulness of strict control of blood glucose concentration¶ during the perioperative period is uncertain in patients with diabetes mellitus or acute hyperglycemia who are undergoing noncardiac surgical procedures without planned ICU admission. (*Level of Evidence: C*)

Hyperglycemia is an independent predictor of cardiovascular risk, and severity of hyperglycemia is directly related to mortality rate during MI. The impact of perioperative control of blood glucose concentration on morbidity and mortality has been investigated recently. Table 16 summarizes the results of 13 clinical trials evaluating the relationship between blood glucose concentration and outcome in critically ill patients with and without diabetes mellitus (496–499,501–509). Eight retrospective analyses conducted in patients undergoing coronary artery surgery and in patients admitted to a medical-surgical ICU for a variety of surgical and nonsurgical conditions indicated that increased blood glucose concentration was an important predictor of morbidity and mortality. These results were confirmed by a randomized clinical trial of critically ill patients (63% cardiac surgical patients) admitted to a surgical ICU who received intensive treatment with intravenous insulin to control blood glucose concentrations between 80 and 110 mg per dL, who were compared with conventionally treated patients who received insulin only if blood glucose exceeded 215 mg per dL (496). Aggressively treated patients with a prolonged length of stay in the ICU demonstrated significant decreases in morbidity and mortality. Glucose-insulin-potassium was also shown to improve outcomes in cardiac surgery patients when blood glucose concentrations were well controlled (497) but not when blood glucose concentrations were inadequately controlled (498). The benefit of glucose-insulin-potassium to produce cardioprotection in nonhyperglycemic cardiac surgery patients is controversial and may not be similar to the use of insulin to specifically control blood glucose concentration (506). The role of intraoperative glycemic control with a standardized insulin protocol to modulate outcomes was investigated in a prospective observational study of patients with diabetes mellitus undergoing CABG surgery. Although postoperative blood glucose concentrations were similar,

¶Blood glucose less than 150 mg per dL appears to be beneficial.

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Table 16. Impact of Perioperative Blood Glucose Concentration on Outcomes

Study, Year	Study Type	No. of Patients	Study Design	Mean Glucose, mg/dL	% of Patients With Diabetes	Major Findings
van den Berghe et al (496), 2001	RCT	1548 Surgical ICU pts	Intensive intravenous insulin vs conventional treatment	Intensive 103±19 vs conventional 153±33	13 vs 13	Intensive insulin compared with conventional treatment decreased mortality (8.0% to 4.6%) and major morbidity.
Lazar et al (497), 2004	RCT	141 On-pump CABG pts	GIK vs SQ insulin	GIK 134±4 vs SQ insulin 267±6	100	GIK improved 5-year survival and decreased major morbidity.
Lell et al (498), 2002	RCT	46 Off-pump CABG pts	GIK vs saline	GIK 386±152 vs saline 211±75	28 vs 45	No differences were seen in TnI or CK-MB between groups; study terminated because of concerns of persistent hyperglycemia in the GIK group.
Finney et al (499), 2003	Prospective observational	531 ICU pts	Intravenous insulin	N/A	16	Increased administration of insulin was an independent predictor of ICU mortality; regression models demonstrated a mortality benefit if blood glucose was maintained less than 144 to 200 mg/dL.
Ouattara et al (500), 2005	Prospective observational	200 On-pump CABG pts	Insulin by standardized protocol	Tightly controlled 147±42 vs poorly controlled 208±54	100	Poor intraoperative control of blood glucose was an independent predictor of severe morbidity; mortality rate was increased in patients with poorly controlled glucose (11.4%) vs those with tightly controlled glucose (2.4%).
McGirt et al (501), 2006	Retrospective	1201 Pts undergoing CEA	Postoperative insulin use was nonstandardized	N/A	27	Multivariate analysis demonstrated that preoperative glucose greater than 200 mg/dL was an independent predictor of 2.8-, 4.3-, and 3.3-fold increases in risk of stroke/TIA, MI, or death.
Gandhi et al (502), 2005	Retrospective	409 Cardiac surgery pts	Nonstandardized intraoperative use of insulin in 6%	Any adverse event 141±37 vs no events 127±25	28.6 vs 18	Multivariate analysis demonstrated that mean and maximal intraoperative glucose predicted increased mortality. A 20-mg/dL increase in mean intraoperative glucose was associated with a 30% increase in adverse events.
Krinsley (503), 2004	Retrospective	1600 Med-Surg ICU pts	Historical control vs standardized glucose control protocol	Historical 152±93 vs protocol 131±55	16 vs 18	Decreased mortality, renal insufficiency, and ICU length of stay were observed in the standardized insulin protocol compared with the historical group.
Hill et al (504), 2000	Retrospective	2862 CABG pts	Nonstandardized glucose management	79-653	31	Univariate analysis showed no association between maximum blood glucose concentration and mortality.
Krinsley (505), 2003	Retrospective	1826 Med-Surg ICU pts	Nonstandardized glucose management	Survivors 138 vs nonsurvivors 172	22	Progressive increase in in-hospital mortality rate as blood glucose concentration increased, up to 42.5% among patients with mean glucose values in excess of 300 mg/dL.
Furnary et al (506), 2003	Retrospective	3554 CABG pts	SQ insulin vs continuous intravenous insulin	SQ 213±41 vs intravenous 177±30	100	Continuous intravenous insulin was an independent predictor of survival.
Estrada et al (507), 2003	Retrospective	1574 CABG pts	Nonstandardized glucose management	Diabetes 214±47 vs no diabetes 157±37	35	Hyperglycemia did not predict increased mortality but was associated with increased resource utilization.
McAlister et al (508), 2003	Retrospective	1574 CABG pts	92% received intravenous insulin by protocol	164–209	100	Hyperglycemia was an independent predictor of adverse outcomes.

CABG indicates coronary artery bypass graft; CEA, carotid endarterectomy; CK-MB, creatine kinase MB fraction; GIK, glucose insulin potassium; ICU, intensive care unit; Med-Sur, medical-surgical; MI, myocardial infarction; N/A, not available; pts, patients; RCT, randomized, controlled trial; SQ, subcutaneous; TIA, transient ischemic attack; and TnI, troponin I.

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those patients who achieved tight control of blood glucose concentrations intraoperatively demonstrated decreased morbidity and mortality compared with patients whose blood glucose was poorly controlled (4 consecutive blood glucose measurements exceeding 200 mg per dL despite insulin therapy) (500). A retrospective analysis similarly identified intraoperative blood glucose concentration as an independent predictor of adverse outcome in cardiac surgery patients (502). The risks of stroke, MI, and death were also shown to be independently increased 3- to 4-fold by preoperative hyperglycemia (glucose concentration in excess of 200 mg per dL) in patients undergoing carotid endarterectomy (501). Although clinical trials demonstrated the deleterious effects of perioperative hyperglycemia, the ideal target for and cardiovascular benefit of intraoperative and postoperative glycemic control are not entirely clear. Results of regression analyses (499) suggest that blood glucose concentrations controlled to less than 150 mg per dL in the perioperative period may improve outcome and minimize the risk of severe hypoglycemia in anesthetized patients (510,511). The American College of Endocrinology recently published a position statement recommending that preprandial glucose concentration should be less than 110 mg per dL, with maximal glucose not to exceed 180 mg per dL in hospitalized patients and that blood glucose concentration should be controlled to less than 110 mg per dL in the ICU (511). The use of intravenous insulin therapy to maintain glycemic control in the perioperative period was recommended.

9. Perioperative Surveillance

Although much attention has been focused on the preoperative preparation of the high-risk patient, intraoperative and postoperative surveillance for myocardial ischemia and infarction, arrhythmias, and venous thrombosis should also lead to reductions in morbidity. Postoperative myocardial ischemia has been shown to be the strongest predictor of perioperative cardiac morbidity and is rarely accompanied by pain (1). Therefore, it may go untreated until overt symptoms of cardiac failure develop.

The diagnosis of a perioperative MI has both short- and long-term prognostic value. Traditionally, a perioperative MI has been associated with a 30% to 50% perioperative mortality and reduced long-term survival (42,512–514). Therefore, it is important to identify patients who sustain a perioperative MI and to treat them aggressively, because it may reduce both short- and long-term risk.

9.1. Intraoperative and Postoperative Use of PACs

Recommendations for Perioperative Use of PACs

CLASS IIb

1. Use of a PAC may be reasonable in patients at risk for major hemodynamic disturbances that are easily detected by a PAC. However, the decision must be based on 3 parameters: patient disease, surgical procedure (ie, intraoperative and postoperative fluid shifts), and practice setting (experience in PAC use and interpretation of results), because incorrect interpretation of the data from a PAC may cause harm. (*Level of Evidence: B*)

CLASS III

1. Routine use of a PAC perioperatively, especially in patients at low risk of developing hemodynamic disturbances, is not recommended. (*Level of Evidence: A*)

Use of a PAC may provide significant information critical to the care of the cardiac patient; however, the potential risk of complications and cost associated with catheter insertion and use must be considered. Practice guidelines for PAC, as well as methods to perform perioperative optimization of the high-risk surgical patient, have been developed and reported elsewhere (515,516). Several studies have evaluated the benefit of PAC use in both randomized trials and those using historical controls. In patients with prior MI, when perioperative care included PAC and intensive care monitoring for 3 days postoperatively, there was a lower incidence of reinfarction than in historical controls (512). Other changes in management occurred during the period under study, however, including the increased use of beta-adrenergic sympathetic blockade. In particular, patients with signs and symptoms of HF preoperatively, who have a very high (35%) postoperative incidence of HF, might benefit from invasive hemodynamic monitoring (116).

Although a great deal of literature has evaluated the utility of the PAC during the perioperative period in noncardiac surgery, relatively few controlled studies have evaluated PAC use in relation to clinical outcomes. Evidence of benefit of PAC use from controlled trials is equivocal, and a large-scale cohort study demonstrated potential harm (517). Nevertheless, PAC use may benefit high-risk patients. Berlauk et al (437), in comparing outcomes associated with PAC insertion 12 hours before surgery, 3 hours before surgery, or no planned insertion, found the PAC group had fewer adverse intraoperative events and less postoperative cardiac morbidity (P less than 0.05 for both). However, Bender et al (438) found no decrease in morbidity or mortality with routine PAC use in elective surgery. In studies using appropriate patient selection, no differences in cardiac morbidity (MI or cardiac death) were detected (438,518–521). A meta-analysis by Poeze et al (439) found that hemodynamic optimization of critically ill patients decreased mortality (RR: 0.75, 95% CI: 0.62 to 0.90) when all studies were combined, and this effect was attributed to the decreased mortality observed in studies specifically conducted to evaluate the benefit of perioperative interventions (RR: 0.66, 95% CI: 0.54 to 0.81).

Polanczyk et al performed an observational study of 4059 patients aged 50 years or older who underwent major elective noncardiac procedures with an expected length of stay of 2 or more days (522). Major cardiac events occurred in 171 patients (4.2%); those who underwent right heart catheterization had a 4-fold increased incidence of major postoperative cardiac events (34 [15.4%] versus 137 [3.6%]; P less than 0.001). In a case-control analysis of a subset of 215 matched pairs of patients in this trial who did and did not undergo right heart catheterization, adjusted for propensity of right heart catheterization and type of procedure, patients who underwent perioperative right heart catheterization also had in-

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creased risk of postoperative congestive HF (OR: 2.9, 95% CI: 1.4 to 6.2) and major noncardiac events (OR: 2.2, 95% CI: 1.4 to 4.9) (522).

A randomized, multicenter clinical trial of goal-directed therapy with a PAC in 1994 elderly patients (American Society of Anesthesiologists class 3 or 4) who underwent major noncardiac surgery demonstrated no differences in survival or cardiovascular morbidity compared with a standard care group (77% had a central venous catheter placed) (523). Although mortality and hospital length of stay were similar in both groups, the PAC group demonstrated higher rates of pulmonary embolism (0 events in the standard care group versus 8 events in the PAC group; $P=0.004$) (523).

Several surveys have shown physician and nurse understanding of PAC catheterization data are extremely variable, which may account for the higher rate of postoperative congestive HF and greater perioperative net fluid intake observed in some studies. This finding led some to recommend re-evaluation of current accreditation and teaching practices (524–527). The American Society of Anesthesiologists Task Force on Pulmonary Artery Catheterization has recently provided an update to the practice guidelines for pulmonary artery catheterization (515). Given the above-described studies and the accumulating data from the nonsurgical arena, in which the use of a PAC has not shown benefit, the decision to place a PAC should carefully weigh the potential for harm with any potential benefit from the information obtained from the monitor.

9.2. Intraoperative and Postoperative Use of ST-Segment Monitoring

CLASS IIa

1. Intraoperative and postoperative ST-segment monitoring can be useful to monitor patients with known CAD or those undergoing vascular surgery, with computerized ST-segment analysis, when available, used to detect myocardial ischemia during the perioperative period. (*Level of Evidence: B*)

CLASS IIb

1. Intraoperative and postoperative ST-segment monitoring may be considered in patients with single or multiple risk factors for CAD who are undergoing noncardiac surgery. (*Level of Evidence: B*)

The presence of intraoperative and postoperative ST-segment changes has been associated with cardiac morbidity and mortality in high-risk patients undergoing noncardiac surgery. Most contemporary operating rooms and ICU monitors incorporate algorithms that perform real-time analysis of the ST segment. Numerous studies have demonstrated the limited ability of physicians to detect significant ST-segment changes compared with computerized or offline analysis. Computerized ST-segment trending is superior to visual interpretation in the identification of ST-segment changes. Because the algorithms used to measure ST-segment shifts are proprietary, variability in accuracy between the different monitors has been evaluated in several studies compared with offline analysis of standard Holter recordings (528–530). ST-segment trending monitors were found to have an average sensitivity and specificity of 74% (range 60% to 78%) and 73% (range 69% to 89%), respectively, compared with Holter ECG recordings (529). Several factors have been identified that decreased the accuracy of the monitors and have been discussed in detail elsewhere. Additionally, the lead system used affects the incidence of ischemia detected, with leads II and V_5 detecting only 80% of all episodes detected by a 12-lead ECG in 1 study (531), whereas another study found that V_4 was the most sensitive lead (83.3%) (532).

Virtually all studies examining the predictive value of intraoperative and postoperative ST-segment changes have been performed with ambulatory ECG recorders. Using retrospective analysis, investigators have found postoperative ST-segment changes indicative of myocardial ischemia, primarily ST-segment depression, to be an independent predictor of perioperative cardiac events in high-risk noncardiac surgery patients in multiple studies, with changes of prolonged duration (greater than 30 minutes per episode or greater than 2 hours cumulative duration in different studies) being particularly associated with increased risk (42,72,290,533,534). In a review of studies involving more than 2400 patients between the years 1990 and 2003, Landesberg reported a sensitivity of perioperative ischemia in predicting postoperative cardiac events of 55% to 100%; the specificity was 37% to 85%, the positive predictive value was 7% to 57%, the negative predictive value was 89% to 100%, and the relative risk of suffering a postoperative cardiac event, including cardiac death, in patients with ischemia ranged between 2.2% and 73% (535). Postoperative ST-segment changes, particularly of a prolonged duration, have been shown to predict worse long-term survival in high-risk patients (290,513).

In a cohort of patients older than 45 years with 1 risk factor but without known CAD, the presence of intraoperative and postoperative ST-segment changes was not associated with either ischemia on an exercise stress test or cardiac events within 1 year (536). The total cohort of patients was small, which may limit the ability to generalize these findings.

Intraoperative ST-segment changes may also occur in low-risk populations. ST-segment depression has been shown to occur during elective cesarean sections in healthy patients (537,538). Because these changes were not associated with regional wall-motion abnormalities on precordial echocardiography, in this low-risk population, such ST-segment changes may not be indicative of myocardial ischemia and CAD.

Thus, although there are data to support the contention that ST-segment monitoring detects ischemia, no studies have addressed the issue of the effect on outcome when therapy is based on the results of ST-segment monitoring. However, general consensus is that early treatment, such as control of tachycardia, could lead to a reduction in cardiac morbidity.

9.3. Surveillance for Perioperative MI

CLASS I

1. Postoperative troponin measurement is recommended in patients with ECG changes or chest pain typical of acute coronary syndrome. (*Level of Evidence: C*)

CLASS IIb

1. The use of postoperative troponin measurement is not well established in patients who are clinically stable and have undergone vascular and intermediate-risk surgery. (*Level of Evidence: C*)

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CLASS III

1. Postoperative troponin measurement is not recommended in asymptomatic stable patients who have undergone low-risk surgery. (*Level of Evidence: C*)

Multiple studies have evaluated predictive factors for a perioperative MI. The presence of clinical evidence of coronary artery or peripheral vascular disease has been associated with an increased incidence of perioperative MI. Factors that increase the risk of a perioperative MI have been discussed previously. Because of the increased risk of both short- and long-term mortality from a perioperative MI, accurate diagnosis is important.

Perioperative MI can be documented by assessing clinical symptoms, serial ECGs, cardiac-specific biomarkers, comparative ventriculographic studies before and after surgery, radioisotopic or magnetic resonance studies specific for myocardial necrosis, and autopsy studies. The criteria used to diagnose infarction in various studies differ not only in the level of cardiac biomarkers that determine abnormality but also in the frequency with which these biomarkers are sampled after noncardiac surgery. The cardiac biomarker profile after infarction exhibits a typical rise and fall that differs among different biomarkers. Daily sampling may miss detection of a cardiac biomarker rise (such as the MB isoenzyme of creatine kinase [CK-MB]), thus underestimating the incidence of perioperative infarction. The ECG criteria used to define infarction may also differ not only in the definition of a Q wave but also with respect to the magnitude of ST-T wave shifts that determine an abnormal response. In the analysis of cardiac biomarker criteria, numerous assays are available to measure CK-MB, cTnI, and, to a lesser extent, cardiac troponin T. Creatine kinase–MB may be released from noncardiac sources in patients with ischemic limbs or those undergoing aortic surgery, the group at highest risk for a perioperative MI. Additionally, other tissues may release CK-MB into the circulation, such as many from the gastrointestinal tract. Renal insufficiency may affect the ability to clear these enzymes and therefore decrease the specificity of an abnormal result. The use of cTnI or cardiac troponin T offers the potential for enhanced specificity (539–544).

An increasing number of studies have examined the outcome using protocol-specific criteria for perioperative MI after noncardiac surgery. The topic of surveillance for perioperative MI was reviewed in 2005 and a set of criteria proposed (127). Charlson et al (545) reported on 232 patients, most of whom were hypertensive or had diabetes mellitus, who were undergoing elective noncardiac surgery. Serial ECGs and CK-MB were collected for 6 days postoperatively. The incidence of perioperative MI varied greatly depending on the diagnostic criteria used. A strategy of using an ECG immediately after the surgical procedure and on the first and second days postoperatively had the highest sensitivity. Two studies have demonstrated the prognostic significance of a postoperative 12-lead ECG. Rinfret and colleagues, examining the same population set as described above in the study by Lee et al (542), investigated the information provided by a postoperative ECG performed in the recovery room after operation (546). Of the 3750 patients evaluated, 7.5% had significant ECG changes. Significant changes included ST-segment elevation, ST-segment depression, and T-wave changes. The presence of these changes conferred a 2.2-fold increase in major cardiac complications, increasing the rate from 1.9% in patients who did not have these signs to 6.7% in those who did (*P* less than 0.001). The increase in event rate was maintained when stratified by the author's Revised Cardiac Risk Index (4). In fact, the RR of an adverse event associated with ECG changes was higher in the lower-risk group, increasing the events more than 4-fold compared with 2-fold in the high-risk subset. Bottiger and colleagues (547) investigated the value of 12-lead ECGs obtained 15 minutes, 20 hours, 48 hours, 72 hours, and 84 hours after operation in 55 patients. For study entry, patients had operations that required more than 1 hour of anesthesia and a history of CAD or 2 cardiovascular disease risk factors. Of the 55 patients, 19 had perioperative ischemia, and 2 required cardiac catheterization. Electrocardiographic changes of ischemia were noted in 24 patients, of which 88% were noted in the first postoperative evaluation. Moreover, early ECG changes were concordant with cardiac biomarker evidence of myocardial damage.

Strategies that included the serial measurement of CK-MB had higher false-positive rates (ie, lower specificity) without higher sensitivities. In contrast, Rettke et al reported that overall survival was associated with the degree of CK-MB elevation in 348 patients undergoing abdominal aortic aneurysm repair, with higher levels associated with worse survival (548). Yeager et al evaluated the prognostic implications of a perioperative MI in a series of 1561 major vascular procedures (514). These authors found that the incidence of subsequent MI and coronary artery revascularization was significantly higher in patients who had a perioperative MI, except in the subset who only demonstrated an elevated CK-MB without ECG changes or cardiovascular symptoms.

Over the last decade, the diagnosis of myocardial damage has become more sensitive with the application of cardiac biomarkers. Measurement of troponin T or I facilitates the recognition of myocardial damage with much smaller amounts of injury. Because of the augmentation of sensitivity, the threshold to diagnosis of an MI is lower and the frequency greater (290). On the basis of the increase in sensitivity, many studies have been performed to determine whether screening troponin measurements convey important prognostic information.

The largest screening study by Lee and colleagues evaluated troponin T measured in 1175 noncardiac surgical patients (542). Troponin T was measured in the recovery room after operation and on the next 2 postoperative mornings. In this population, an MI was diagnosed in 1.4% (n=17) of the patients using CK-MB fraction and ECG for diagnosis. Troponin T was elevated in 87% of the patients with MI and 16% of the patients without MI.

Martinez and colleagues studied 467 high-risk patients requiring noncardiac surgery (549). The diagnosis of myocardial injury was determined by biomarkers combined with either postoperative changes on 12-lead ECG or 1 of 3 clinical symptoms consistent with MI (chest pain, dyspnea, or requirement for hemodynamic support). The incidence of MI was 9.0%

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by the criterion of cTnI greater than or equal to 2.6 ng per mL, 19% by cTnI greater than or equal to 1.5 ng per mL, 13% by CK-MB mass, and 2.8% by CK-MB%. If surveillance of cTnI greater than or equal to 2.6 ng per mL was used to detect MI, then the strategy with the highest diagnostic yield was surveillance on postoperative days 1, 2, and 3.

The pattern of cardiac specific troponin elevation may also be important. Le Manach and colleagues performed intense cardiac cTnI surveillance after abdominal aortic surgery in 1136 consecutive patients to better evaluate the incidence and timing of postoperative MI (cTnI greater than or equal to 1.5 ng per mL) or myocardial damage (abnormal cTnI less than 1.5 ng per mL) (550). Abnormal cTnI concentrations were noted in 163 patients (14%), of whom 106 (9%) had myocardial damage and 57 (5%) had perioperative MI. In 34 patients (3%), perioperative MI was preceded by a prolonged (greater than 24 hours) period of increased cTnI (delayed perioperative MI), and in 21 patients (2%), the increase in cTnI lasted less than 24 hours (early perioperative MI). The authors concluded that abnormal but low postoperative cTnI is associated with increased mortality and may lead to delayed perioperative MI.

Data like these highlight the difficulty of using cardiac specific troponin to distinguish myocardial damage from infarction. The variability in the rate of MI based on troponin cutoff and other studies highlights the fact that there is a poor relationship between cardiac specific troponin elevation and postoperative ECG changes (551). It is already known that one third of coronary arterial ischemic events occur distal to areas of noncritical stenosis and that critical stenoses are uncommon in the pathogenesis of MI (291). Although the extent of coronary artery atherosclerosis, as determined by the number of vessels with significant stenoses, predicts frequency of perioperative MI, individual lesion stenosis does not (552).

Studies regarding the predictive value of postoperative cardiac specific troponin elevations for long-term outcome have been inconsistent. Investigations have shown that postoperative elevations in cardiac specific troponin are associated with increased cardiovascular morbidity and mortality at 30 days (553,554), 6 months (543,555), 1 year (556), and beyond 1 year (554,557). However, other studies have shown no association with intermediate or long-term cardiovascular outcomes (558), and none of the studies above demonstrate a relationship at the other time points.

On the basis of the available literature, routine measurement of cardiac specific troponin after surgery is more likely to identify patients without acute MI than with MI. Moreover, studies of cardiac specific troponin elevations neither consistently show associations with adverse cardiovascular outcomes at any time point nor provide insight into the effect of treatment on outcomes in patients with an elevated cardiac specific troponin level. Although it is known that elevations in cardiac specific troponin are more likely to occur in patients with more extensive CAD, the role of revascularization in patients with an elevated cardiac specific troponin level but no other manifestation of MI remains unclear. Until each of these issues has been addressed, routine cardiac specific troponin measurement cannot be recommended. Perioperative surveillance for acute coronary syndromes with routine ECG and cardiac serum biomarker measurement is unnecessary in clinically low-risk patients undergoing low-risk operative procedures.

Further evaluation regarding the optimal strategy for surveillance and diagnosis of perioperative MI is required. On the basis of current evidence, in patients without documented CAD, surveillance should be restricted to those who develop perioperative signs of cardiovascular dysfunction. In patients with high or intermediate clinical risk who have known or suspected CAD and who are undergoing high- or intermediate-risk surgical procedures, the procurement of ECGs at baseline, immediately after the surgical procedure and daily on the first 2 days after surgery appears to be the most cost-effective strategy. The use of cardiac specific troponin measurements to supplement the diagnosis in these symptomatic patients is warranted. Additional research is needed to correlate long-term outcome results to the magnitude of isolated cardiac specific troponin elevations.

9.4. Postoperative Arrhythmias and Conduction Disorders

Postoperative arrhythmias are often due to remedial noncardiac problems such as infection, hypotension, metabolic derangements, and hypoxia. The approach taken to the acute management of postoperative tachycardias varies depending on the likely mechanism. If the patient develops a sustained, regular, narrow-complex tachycardia, which is likely due to atrioventricular nodal re-entrant tachycardia or atrioventricular reciprocating tachycardia, the tachycardia can almost always be terminated with vagal maneuvers (Valsalva maneuver or carotid sinus massage) or with intravenous adenosine. Most antiarrhythmic agents (especially beta blockers, calcium channel blockers, and type 1a or 1c antiarrhythmic agents) can be used to prevent further recurrences in the postoperative setting. A somewhat different approach is generally recommended for atrial fibrillation and atrial flutter. The initial approach to management generally involves the use of intravenous digoxin, diltiazem, or a beta blocker in an attempt to slow the ventricular response. Among these 3 types of medications, digitalis is least effective and beta blockers are most effective for controlling the ventricular response during atrial fibrillation (426). An additional benefit of beta blockers is that they have been shown to accelerate the conversion of postoperative supraventricular arrhythmias to sinus rhythm compared with diltiazem (427). Cardioversion of atrial fibrillation/flutter is generally not recommended for asymptomatic or minimally symptomatic arrhythmias until correction of the underlying problems has occurred, which frequently leads to a return to normal sinus rhythm. Also, cardioversion is unlikely to result in long-term normal sinus rhythm if the underlying problem is not corrected. The avoidance of an electrolyte abnormality, especially hypokalemia and hypomagnesemia, may reduce the perioperative incidence and risk of arrhythmias, although acute preoperative repletion of potassium in an asymptomatic individual may be associated with greater risk than benefits (559–562). Unifocal or multifocal premature ventricular contractions do not merit therapy. Very frequent ventricular ectopy or pro-

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longed runs of nonsustained ventricular tachycardia may require antiarrhythmic therapy if they are symptomatic or result in hemodynamic compromise. Patients with an ischemic or nonischemic cardiomyopathy, particularly those with an ejection fraction of less than 35%, a history of HF, and nonsustained ventricular tachycardia in the perioperative period, may benefit from ICD therapy for primary prevention of sudden cardiac death (evaluation by an electrophysiologist may be indicated) (563–565). Ventricular arrhythmias may respond to intravenous beta blockers, lidocaine, procainamide, or amiodarone (378,566–568). Electrical cardioversion should be used for sustained supraventricular or ventricular arrhythmias that cause hemodynamic compromise.

Bradyarrhythmias that occur in the postoperative period are usually secondary to some other cause, such as certain medications, an electrolyte disturbance, hypoxemia, or ischemia. On an acute basis, many will respond to intravenous medication such as atropine, and some will respond to intravenous aminophylline. Bradyarrhythmias due to sinus node dysfunction and advanced conduction abnormalities such as complete heart block will respond to temporary or permanent transvenous pacing or permanent pacing. The indications are the same as those for elective permanent pacemaker implantations.

10. Postoperative and Long-Term Management

Advances in preoperative risk assessment, surgical and anesthetic techniques, and better implementation of medical therapy have served to decrease the frequency of cardiovascular complications associated with noncardiac surgery. Appropriate use of therapies that decrease the frequency of cardiovascular complications in patients with CAD, including beta-adrenergic blockers, antiplatelet therapies, statins, and modifiers of the renin-angiotensin system (ACE inhibitors and/or angiotensin receptor blockers), directed noninvasive evaluations of the coronary anatomy, and selective use of coronary artery revascularization have resulted in reduced rates of perioperative MI and death compared with outcomes in recent decades (569).

Despite these advances, cardiovascular complications represent the most common and most treatable adverse consequences of noncardiac surgery. Those patients who have a symptomatic MI after surgery have a marked increase in the risk of death, reaching as high as 40% to 70% (570). Because the consequences of infarction are so severe, management of patients must continue after risk assessment in the postoperative setting. As described in sections above, postoperative ECG changes suggestive of MI predict poor outcome, and postoperative management is an active process that requires frequent intervention.

10.1. MI: Surveillance and Treatment

In contrast to clinically silent elevations in troponin, the development of coronary artery plaque rupture that results in thrombotic coronary artery occlusion requires rapid intervention. Among eligible patients, rapid reperfusion therapy is the cornerstone of therapy (571). Fibrinolytic therapy markedly reduces mortality when administered to patients who have MI unrelated to a surgical procedure. However, because of the substantial risk of bleeding at the surgical site, patients who have recently undergone surgery have been excluded from all trials of fibrinolytic therapy, and recent surgery is generally considered a strong contraindication to fibrinolytic therapy. Although fibrinolytic therapy has been administered to patients for life-threatening pulmonary embolus shortly after noncardiac surgery, the fibrinolytic dosage has generally been less and has been administered over a longer time interval than is standard for the treatment of acute MI (572,573). Immediate coronary angioplasty has been favorably compared with fibrinolytic therapy in the treatment of acute MI (574), but of greater importance is that the risk of bleeding at the surgical site is believed to be less with direct angioplasty than with fibrinolytic therapy. Only a single small study (575) has evaluated the role of immediate angiography and angioplasty among 48 patients who were believed able to take aspirin and intravenous heparin and to undergo immediate angiography and PCI. This study suggested that such a strategy is feasible and may be beneficial. However, time to reperfusion is a critical determinant of outcome in acute MI, and any hope of benefiting patients who have a perioperative acute MI due to an acute coronary occlusion requires that angiography and revascularization be performed rapidly (ie, within 12 hours of symptom onset) (575,576). In addition, these reperfusion procedures should not be performed routinely on an emergency basis in postoperative patients in whom MI is not related to an acute coronary occlusion. For instance, in cases of increased myocardial demand in a patient with postoperative tachycardia or hypertension, lowering the heart rate or blood pressure is likely to be of greater benefit and is certain to carry less risk. Moreover, because of the requirements for periprocedural anticoagulation and postrevascularization antiplatelet therapy, the benefits of revascularization must be weighed against the risk of postoperative bleeding, individualizing the decision for referral.

Although reperfusion therapy is an important therapy in acute ST-segment elevation MI, the emphasis on reperfusion therapy should not detract from pharmacological therapy, which is also very important and has been shown to reduce adverse events in such patients, as well as in patients with non–ST-elevation acute coronary syndromes. Therapy with aspirin, a beta blocker, and an ACE inhibitor, particularly for patients with low ejection fractions or anterior infarctions, may be beneficial, whether or not the patients are rapidly taken to the catheterization laboratory (49). An extensive evidence-based review of therapy for ST-segment elevation MI can be found in the ACC/AHA Guidelines for the Management of Patients With ST-Segment Elevation Myocardial Infarction (577). Although not intended specifically for patients who have a postoperative MI, these guidelines are nonetheless appropriate for these high-risk patients. Similarly, the ACC/AHA Guidelines for Unstable Angina and Non–ST-Segment Elevation Myocardial Infarction represent an important template for management of this condition in the postoperative setting (192).

In the approach to the long-term postoperative management of noncardiac surgery patients, one should first appreciate that the occurrence of an intraoperative nonfatal MI

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carries a high risk for future cardiac events that are often dominated by cardiovascular death (513,578). Patients who sustain a perioperative MI should have evaluation of LV function performed before hospital discharge, and standard postinfarction medical therapy should be prescribed as defined in the ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction (49). The ACC/AHA guidelines for post-MI evaluation in these types of patients should be followed as soon as possible after surgical recovery. The use of pharmacological stress (579) or dynamic exercise (if feasible) for risk stratification should also be a priority in patients to help determine who would benefit from coronary revascularization. In all cases, the appropriate evaluation and management of complications and risk factors such as angina, HF, hypertension, hyperlipidemia, cigarette smoking, diabetes mellitus (hyperglycemia), and other cardiac abnormalities should commence before hospital discharge. It is also important to communicate these new observations and determinations of cardiac status and risk to the physician and nonphysician providers who will be responsible for arranging subsequent medical care and follow-up.

10.2. Long-Term Management

Although the occasion of noncardiac surgery brings a period of increased cardiovascular risk, physicians should also use the opportunity to ensure appropriate cardiovascular medical therapy. Indeed, the requirement for vascular surgery indicates a high cardiovascular risk alone. In a trial of 1404 patients with critical limb ischemia that investigated the possible benefit of a molecular therapy to reduce bypass graft failure, there was a 16% mortality rate at 1 year (404). Medical therapy was lacking in many patients at study entry: 33% were not taking antiplatelet therapy, 54% were not receiving lipid-lowering therapy, and 52% were not prescribed beta-blocker medications.

Other risk factors may provide additional prognostic insight. In studies of vascular surgery patients who had follow-up for 40 to 48 months, cardiac events were significantly more frequent in those who had a reduced LVEF of less than 35% or 40% and who demonstrated at least a moderate area of ischemia on dipyridamole myocardial perfusion imaging (578,580). Therefore, the perioperative cardiovascular risk represents the most visible but not the largest portion of morbidity and mortality that can be ameliorated by the institution of recommended medical therapy.

These types of observations should encourage us to pay closer attention to the medical outcome of patients seen for perioperative evaluations, especially in the context of vascular surgery. In the recently released ACC/AHA guidelines for the management of patients with peripheral arterial disease, treatment with a statin to achieve a low-density lipoprotein level of less than 100 mg per dL, control of blood pressure to less than 140/90 mm Hg, cigarette smoking cessation, and antiplatelet therapy all received class 1 indications (581). Institution of medical therapy in the hospital is associated with increased compliance (582), which makes early initiation preferable.

In other noncardiac surgical populations, it is clear that preoperative clinical risk assessment, as determined by the clinical criteria, LVEF, coronary angiography, dipyridamole myocardial perfusion imaging, and dobutamine echocardiography, provides information concerning a patient's long-term cardiac risk. Cardiac mortality in the postoperative period increases with higher clinical risk, lower LVEF (less than 35%), multivessel CAD, abnormal myocardial perfusion imaging scans, or multiple ischemic segments on dobutamine echocardiography studies. Other studies (41,278,583) also confirm the value of semiquantitative analysis of myocardial perfusion imaging when these types of perioperative tests are used to predict future cardiac events. All of these studies have the ability to combine an assessment of myocardial ischemia and LV function into a more useful clinical index; however, the extent of ischemia or reduction in ventricular function achieves the best level of prognostic utility for future cardiac events (209,263,584). Overall, a normal or near-normal stress imaging study suggests a relatively small risk, but the positive predictive accuracy of abnormal studies is greatly enhanced by the establishment of a progressive gradient for that abnormality.

In general, the indications for additional screening or testing in postoperative patients depend on individual patient characteristics. It is important that the care team responsible for the long-term care of the patient be provided with complete information about any cardiovascular abnormalities or risk factors for CAD identified during the perioperative period.

11. Conclusions

Successful perioperative evaluation and management of high-risk cardiac patients undergoing noncardiac surgery requires careful teamwork and communication between surgeon, anesthesiologist, the patient's primary caregiver, and the consultant. In general, indications for further cardiac testing and treatments are the same as in the nonoperative setting, but their timing is dependent on several factors, including the urgency of noncardiac surgery, patient-specific risk factors, and surgery-specific considerations. The use of both noninvasive and invasive preoperative testing should be limited to those circumstances in which the results of such tests will clearly affect patient management. Finally, for many patients, noncardiac surgery represents their first opportunity to receive an appropriate assessment of both short- and long-term cardiac risk. Thus, the consultant best serves the patient by making recommendations aimed at lowering the immediate perioperative cardiac risk, as well as assessing the need for subsequent postoperative risk stratification and interventions directed at modifying coronary risk factors. Future research should be directed at determining the value of routine prophylactic medical therapy versus more extensive diagnostic testing and interventions.

12. Cardiac Risk of Noncardiac Surgery: Areas in Need of Further Research

Much progress has been made over the last few years regarding perioperative evaluation of noncardiac surgery. Eagle et al found that patients undergoing low-risk procedures are unlikely to derive benefit from CABG before low-risk surgery; however, patients with multivessel disease and severe angina undergoing high-risk surgery might well

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benefit from revascularization before noncardiac surgery (60). Trials that identify specific subsets of patients in whom preoperative coronary revascularization reduces perioperative and long-term MI and death are needed. The most effective method of preoperative coronary revascularization and the value of complete revascularization are unknown at this time.

The benefit of cardiac testing and preoperative cardiac evaluation, especially in those patients with established CAD, has been established (see Sections 5.2.3 and 5.3); what is unknown is the cost-effectiveness and value of the various methods of cardiac testing for reducing cardiac complications. Further studies in this area are welcomed. The implementation of various strategies of beta blockade in patients undergoing major vascular surgery is cost-effective and even cost-saving from a short-term provider perspective (288), yet the efficacy and cost-effectiveness of various medical therapies for specific subsets of patients (eg, the role of beta blockers in those patients without a positive stress test) are unknown.

Intraoperative and postoperative use of ST-segment monitoring can be useful to monitor patients with known CAD or those who are undergoing vascular surgery, with computerized ST-segment analysis, when available, used to detect myocardial ischemia during the perioperative period, and this type of monitoring may be considered in patients with single or multiple risk factors for CAD who are undergoing noncardiac surgery. Although postoperative troponin measurement is recommended in patients with ECG changes or chest pain typical of acute coronary syndrome, its use is not well established in patients who are clinically stable and have undergone vascular and intermediate-risk surgery. The efficacy of monitoring patients for myocardial ischemia and infarction, particularly the role of monitoring in affecting treatment decisions and outcomes, is unknown.

Although randomized trials have examined the effect of perioperative beta blockers on cardiac events surrounding surgery, and observational studies have shown the benefit of statins during the perioperative period, further evidence is needed with regard to the length of time medical therapy needs to be initiated before noncardiac surgery to be effective. This includes management of antiplatelet agents in the perioperative period.

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APPENDIX I. ACC/AHA Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery: Author Relationships With Industry

Committee Member	Consultant	Research Grant	Scientific Advisory Board	Speakers' Bureau	Other
Joshua A. Beckman	Bristol-Myers Squibb		Sanofi-Aventis	Bristol-Myers Squibb*; Merck & Co; Eli Lilly; Sanofi-Aventis*	None
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Elliott Chaikof	None	None	None	None	None
Kirsten E. Fleischmann	None	None	None	None	Pfizer (QI/CME Initiatives)
Lee A. Fleisher	None	None	None	None	None
William K. Freeman	None	None	None	None	None
James B. Froehlich	Pfizer	None	Sanofi-Aventis	Sanofi-Aventis; Otsuka; Pfizer; Merck & Co	None
Edward K. Kasper	Scios	None	None	None	None
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Barbara Riegel	None	None	None	None	None
John F. Robb	None	None	None	None	None

This table represents the actual or potential relationships with industry that were reported on May 11, 2007. This table was updated in conjunction with all meetings and conference calls of the writing committee. QI/CME indicates quality improvement/continuing medical education.

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APPENDIX II. ACC/AHA 2007 Guidelines on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery: Peer Reviewer Relationships With Industry

Peer Reviewer	Representation	Consultant Fees/ Honoraria	Speakers Bureau	Ownership/ Partnership/ Principal	Research Grant	Salary	Institutional or Other Financial Benefit	Expert Witness or Consultant
Peter Alagona	Official Reviewer: Board of Trustees	None	None	None	None	None	None	None
Joseph Alpert	Official Reviewer: AHA Reviewer	Exeter Inc; Novartis; Sanofi-Aventis	None	None	None	None	None	None
Vincent Carr	Official Reviewer: Board of Governors	None	None	None	None	None	None	None
Bruce Lytle	Official Reviewer: ACCF/AHA Task Force on Practice Guidelines	None	None	Johnson & Johnson	None	None	None	None
L. Kristin Newby	Official Reviewer: AHA Reviewer	Biosite, Inc; Inverness Medical Innovations Inc; Procter & Gamble	Sanofi-Aventis/ Bristol-Myers Squibb	None	Millennium Pharmaceuticals*; Roche Diagnostics*; Sanofi-Aventis/Bristol-Myers Squibb*; Schering-Plough*	None	None	None
Frank Sellke	Official Reviewer: AHA Reviewer	None	Bayer Pharmaceuticals Corp	None	Ikaria Pharmaceuticals*	None	None	None
Susan Begelman	Organizational Reviewer: Society for Vascular Medicine and Biology	Bristol-Myers Squibb*; GlaxoSmithKline*; Sanofi-Aventis*	Bristol-Meyers Squibb*; GlaxoSmithKline*; Sanofi-Aventis*	Nuvelo	None	Nuvelo*	None	None
John Butterworth	Organizational Reviewer: American Society of Anesthesiologists	Eli Lilly	None	None	None	None	None	Represented plaintiff in regard to epidural mass (2005); represented defendant in case of death after bilateral knee arthroplasty (2006); represented defendant in case of brain damage after shoulder surgery (2005); represented defendant in case of postoperative polyneuropathy (2005); represented defendant in case of cardiac arrest before outpatient toe surgery (2006); represented plaintiff in case of stroke after central line placed in carotid artery (2006)
Simon Body	Organizational Reviewer: Society of Cardiovascular Anesthesiologists	None	None	None	None	None	None	None
Myron Gerson	Organizational Reviewer: American Society of Nuclear Cardiology	None	None	None	GE Healthcare*	None	None	None
Bengt Herweg	Organizational Reviewer: Heart Rhythm Society	None	None	None	None	None	None	None
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Scott Kinlay	Organizational Reviewer: Society for Vascular Medicine and Biology	Merck & Co; Merck/Schering-Plough; Pfizer*	Merck; Merck/Schering-Plough; Pfizer*	None	Pfizer*	None	None	None
Luis Molina	Organizational Reviewer: Heart Rhythm Society	None	None	None	None	None	None	None
Anton Sidawy	Organizational: American College of Surgeons	None	None	None	None	None	None	None
Mark Turco	Organizational Reviewer: Society for Cardiovascular Angiography and Interventions	None	None	None	None	None	None	None
Barry Uretsky	Organizational Reviewer: Society for Cardiovascular Angiography and Interventions	None	None	None	None	None	None	None
Neil Weissman	Organizational Reviewer: American Society of Echocardiography	None	None	None	None	None	None	None
Mazen Abu-Fadel	Content Reviewer: ACCF Cardiac Catheterization Committee	None	None	None	None	None	None	None
Barbara Bentz	Content Reviewer: ACCF Clinical Electrophysiology Committee	None	None	None	None	None	None	None
Blase Carabello	Content Reviewer: AHA Council on Clinical Cardiology Leadership Committee	None	None	None	None	None	None	None
Michael Chen	Content Reviewer: ACCF Peripheral Vascular Disease Committee	None	None	None	None	None	None	None
Leslie Cho	Content Reviewer: ACCF Peripheral Vascular Disease Committee	None	Sanofi-Aventis/Bristol-Myers Squibb	None	None	None	None	None
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N.A. Mark Estes III	Content Reviewer: AHA Council on Clinical Cardiology Leadership Committee	None	Boston Scientific/Guidant; Medtronic; St. Jude Medical	None	None	None	None	None
Paul Fedak	Content Reviewer: AHA Council on Cardiovascular Surgery and Anesthesia Leadership Committee	None	None	None	None	None	None	None
W. Gregory Hundley	Content Reviewer: ACCF Cardiovascular Imaging Committee	None	None	MRI Cardiac Services, Inc	Bracco Diagnostics, Inc*	None	None	None
Bradley Knight	Content Reviewer: ACCF Clinical Electrophysiology Committee; AHA Council on Clinical Cardiology Electrocardiography and Arrhythmias Committee; AHA Council on Clinical Cardiology Leadership Committee	Boston Scientific; CardioOptics, Inc; Medtronic	Boston Scientific	None	Boston Scientific; Medtronic; St. Jude Medical	None	None	None
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Harlan Krumholz	Content: ACC/AHA Task Force on Practice Guidelines	None	None	None	None	None	None	None
Fred Kushner	Content: ACC/AHA Task Force on Practice Guidelines	None	CV Therapeutics; Novartis	None	None	None	Pfizer; Sanofi-Aventis	None
Jerrold Levy	Content Reviewer: AHA Council on Cardiovascular Surgery and Anesthesia Leadership Committee	Alexion Pharmaceuticals, Inc; Dianon Systems	PDL BioPharma	None	Abbott Laboratories; Alexion Pharmaceuticals, Inc; The Medicines Co; Novo Nordisk			Defense work; all revenues go to charitable trust with Fidelity
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C. Noel Bairey Merz	Content Reviewer: AHA Council on Clinical Cardiology Leadership Committee	Bayer*; CV Therapeutics; Fuijisara; Merck & Co; Kos Pharmaceuticals, Inc; Sanofi-Aventis	Merck & Co; Pfizer	Boston Scientific*; Eli Lilly*; Johnson & Johnson*; Medtronic*	None	None	None	None
Debabrata Mukherjee	Content Reviewer: ACCF Cardiac Catheterization Committee	None	None	None	None	None	None	None
Rick Nishimura	Content Reviewer: ACC/AHA Task Force on Practice Guidelines	None	None	None	None	None	None	None
Don Poldermans	Content Reviewer: Individual Reviewer	Merck/Novartis	None	None	None	None	None	None
Robert Safford	AHA: Council on Clinical Cardiology Leadership Committee	None	None	None	None	None	None	None
Jay Silverstein	Content Reviewer: ACCF Cardiovascular Imaging Committee	None	None	None	None	None	None	None
Kim Williams	Content Reviewer: ACCF Cardiovascular Clinical Imaging Committee	CV Therapeutics*; GE Healthcare*; King Pharmaceuticals, Inc*	Astellas Healthcare*; GE Healthcare*	None	Bristol-Myers Squibb*; CV Therapeutics*; GE Healthcare*; Molecular Insight Pharmaceuticals, Inc*	None	None	None
Stuart Winston	Content Reviewer: AHA Clinical Electrophysiology Committee	Boston Scientific/Guidant	None	None	Biotronik; Boston Scientific/Guidant; Medtronic	None	None	None
Janet Wyman	Content Reviewer: ACCF Cardiac Catheterization Committee	None	None	None	None	None	None	None

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†Spousal relationship.

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APPENDIX III. Abbreviations List

Abbreviation	Definition
ACC	American College of Cardiology
ACE	angiotensin-converting enzyme
ACS	American College of Surgeons
ADA	American Diabetes Association
AHA	American Heart Association
bpm	beats per minute
CABG	coronary artery bypass graft
CAD	coronary artery disease
CARP	Coronary Artery Revascularization Prophylaxis
CASS	Coronary Artery Surgery Study
CHD	coronary heart disease
CI	confidence interval
CK-MB	creatine kinase–myocardial band
cTnI	cardiac troponin I
DECREASE	Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography
DES	drug-eluting stent(s)
DSE	dobutamine stress echocardiography
ECG	electrocardiogram
HF	heart failure
HR	hazard ratio
ICD	implantable cardioverter-defibrillator
ICU	intensive care unit
LV	left ventricle/left ventricular
LVEF	left ventricular ejection fraction
MACE	major adverse cardiac event(s)
MET	metabolic equivalent
MI	myocardial infarction
OR	odds ratio
PAC	pulmonary artery catheter
PCI	percutaneous coronary intervention
POBBLE	Perioperative Beta Blockade Study
PTCA	percutaneous transluminal coronary angioplasty
RR	relative risk
SCAI	Society for Cardiovascular Angiography and Interventions
TEE	transesophageal echocardiography

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CORRECTION

In the ACC/AHA Guideline by Fleisher LA, Beckman JA, Brown KA, et al, "2007 Guidelines on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery)," which first published online on September 27, 2007 (DOI: 10.1016/j.jacc.2007.09.003), two changes were made.

1. On page e173, the last paragraph in the first column, the second sentence "Perioperative antibiotic prophylaxis is recommended for patients with mitral valve prolapse who have clinical evidence of mitral valve regurgitation or echocardiographic evidence of thickening and/or redundancy of the valve leaflets (109)." should read "Specific recommendations regarding perioperative antibiotic prophylaxis for patients with mitral valve prolapse can be found elsewhere (18)."
2. In the References section, reference 109 should be deleted.

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