

Preparation of the Cardiac Patient for Noncardiac Surgery

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Approximately 20 to 40 percent of patients at high risk of cardiac-related morbidity develop myocardial ischemia perioperatively. The preferred approach to diagnostic evaluation depends on the interactions of patient-specific risk factors, surgery-specific risk factors, and exercise capacity. Stress testing should be reserved for patients at moderate to high risk undergoing moderate- or high-risk surgery and those who have poor exercise capacity. Further cardiovascular studies should be limited to patients who are at high risk, have poor exercise tolerance, or have known poor ventricular function. Medical therapy using beta blockers, statins, and alpha agonists may be effective in high-risk patients. The evidence appears to be the strongest for beta blockers, especially in high-risk patients with proven ischemia on stress testing who are undergoing vascular surgery. Many questions remain unanswered, including the optimal role of statins and alpha agonists, whether or not these therapies are as effective in patients with subclinical coronary artery disease or left ventricular dysfunction, and the optimal timing and dosing regimens of these medications. (*Am Fam Physician* 2007;75:656-65. Copyright © 2007 American Academy of Family Physicians.)

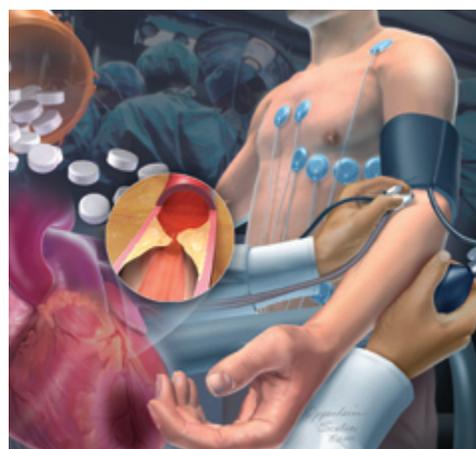


ILLUSTRATION BY BERT OPPENHEIM AND CHRIS SCALICI

Periodic myocardial infarction (MI) is a major cause of morbidity and mortality in patients who have noncardiac surgery. Of the 27 million patients undergoing anesthesia annually, an estimated 50,000 (0.19 percent) experience a perioperative MI.¹ The 1996 American College of Cardiology/American Heart Association (ACC/AHA) Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery provide an evidence-based approach to perioperative evaluation and management of these patients; these guidelines were updated in 2002.² Since then, further studies have increased our knowledge of how to minimize the risk of morbidity and mortality in these patients. The additional evidence includes validation of the algorithms in the original recommendations, studies that prioritize individual therapies based on patient risk, studies that reinforce the role of beta blockers, further definition of the role of statins, and new

data that may support additional medical therapies.

Case Scenario

R.J. is a 76-year-old man who is scheduled for a right hip arthroplasty in two weeks. He presents at the request of his orthopedic surgeon for a medical consultation before surgery. He had an inferior MI one year ago for which he received antithrombotic therapy with complete resolution of his symptoms. He has never smoked, has no history of cerebrovascular disease or diabetes, has a normal ejection fraction, and normal renal function. R.J. usually walks one to two miles in the morning, but his function has been severely limited over the past two months because of hip pain. He is taking hydrochlorothiazide (Esidrix) and simvastatin (Zocor). Although his primary care physician prescribed a beta blocker after his MI, R.J. stopped taking it after a bout of bronchitis two weeks ago. He is asymptomatic from a cardiac and respiratory

SORT: KEY RECOMMENDATIONS FOR PRACTICE

<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
Beta blockers should be given perioperatively to patients with known ischemic heart disease undergoing vascular surgery or who have previously taken beta blockers.	A	12-19, 24
Beta blockers generally are not recommended for patients with low to moderate risk of perioperative cardiovascular complications.	B	22, 24, 41
Statin use is associated with a reduction in perioperative risk in patients with preexisting coronary artery disease, although randomized trial data are lacking.	B	30-33
Alpha ₂ -agonists such as clonidine (Catapres) are a possible alternative to beta blockers to reduce perioperative risk of cardiac complications in high-risk patients.	B	34, 38-40

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 603 or <http://www.aafp.org/afpsort.xml>.

standpoint. His vital signs are normal except for a blood pressure of 157/92 mm Hg. His physical examination is within normal limits, and electrocardiography demonstrates Q waves inferiorly. Should he undergo cardiovascular stress testing before surgery, and is he a candidate for perioperative beta blockade or other medical therapy?

Summary of the ACC/AHA Guidelines

The physician must first assess whether the situation requires emergency surgery. If not, further assessment can be pursued. The ACC/AHA guidelines recommend

that physicians begin with an assessment of the patient's risk factors for perioperative morbidity and mortality (Table 1).² Patients are classified as having minor, intermediate, or major risk factors, and further evaluation is based on the highest category for which the patient has a risk factor (Figure 1).²

The physician also should assess the risk associated with the type of surgery (Table 2).² This information is used to determine the need for diagnostic testing (Figure 1).² If there has been a recent cardiac evaluation (usually within six months in a stable patient) or

TABLE 1
Clinical Predictors of Increased Perioperative Cardiovascular Risk

Major	Intermediate	Minor
Unstable coronary syndromes	Mild angina pectoris (Canadian class I or II [‡])	Advanced age (older than 75 years)
Acute or recent* MI with evidence of important ischemic risk by clinical symptoms or noninvasive study	Previous MI by history or pathologic Q waves	Abnormal electrocardiography results (e.g., left ventricular hypertrophy, left bundle branch block, ST-T abnormalities)
Unstable or severe† angina (Canadian class III or IV [‡])	Compensated or prior heart failure	Rhythm other than sinus (e.g., atrial fibrillation)
Decompensated heart failure	Diabetes mellitus (particularly insulin-dependent)	Low functional capacity (e.g., inability to climb one flight of stairs with a bag of groceries)
Significant arrhythmias	Renal insufficiency	History of stroke
High-grade atrioventricular block		Uncontrolled systemic hypertension
Symptomatic ventricular arrhythmias in the presence of underlying heart disease		
Supraventricular arrhythmias with uncontrolled ventricular rate		
Severe valvular disease		

MI = myocardial infarction.

*—The American College of Cardiology National Database Library defines recent MI as greater than seven days but less than or equal to one month (30 days); acute MI is within seven days.

†—May include "stable" angina in patients who are usually sedentary.

‡—Campeau L. Grading of angina pectoris. *Circulation* 1976;54:522-3.

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Preoperative Cardiac Assessment

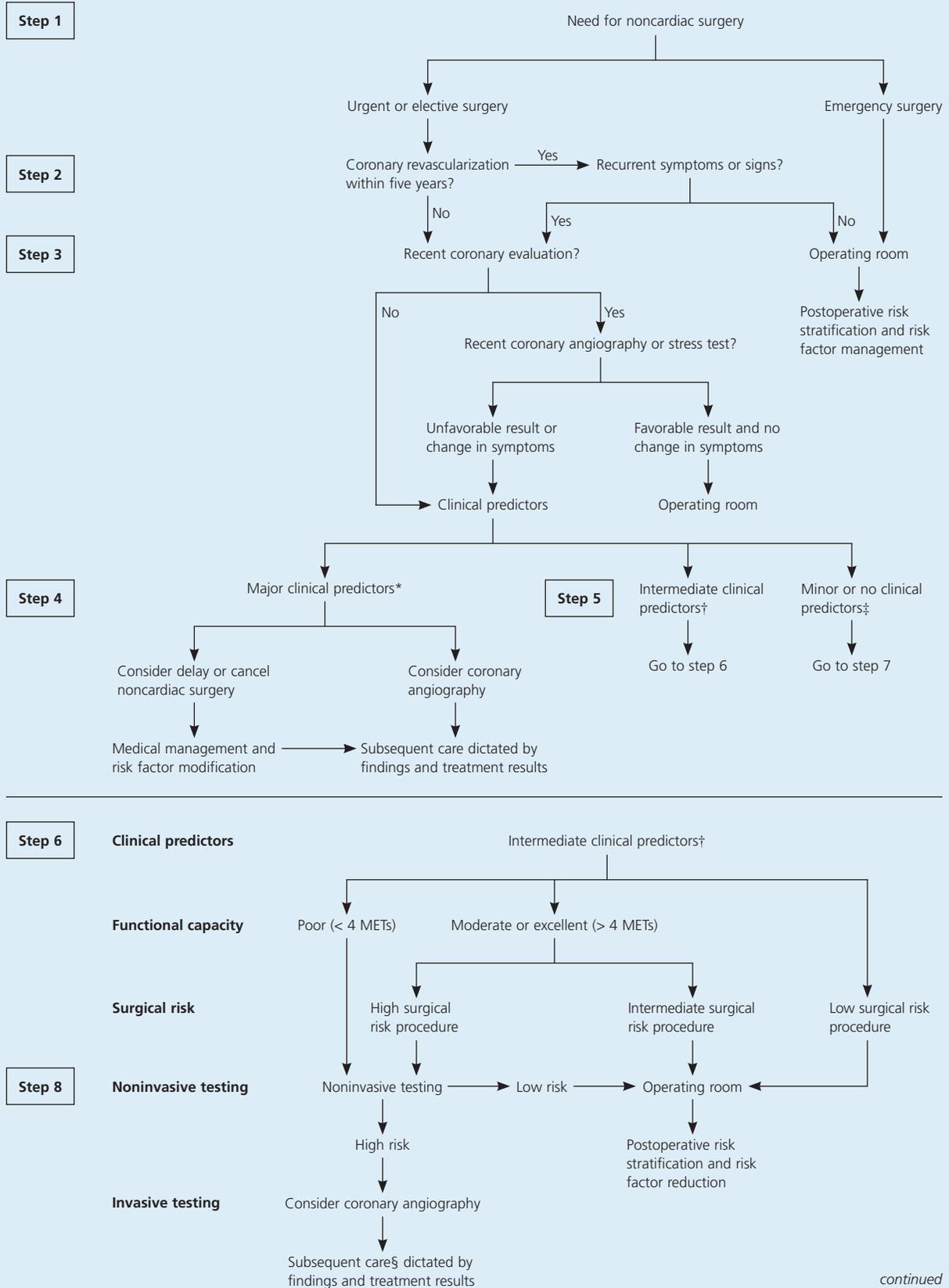
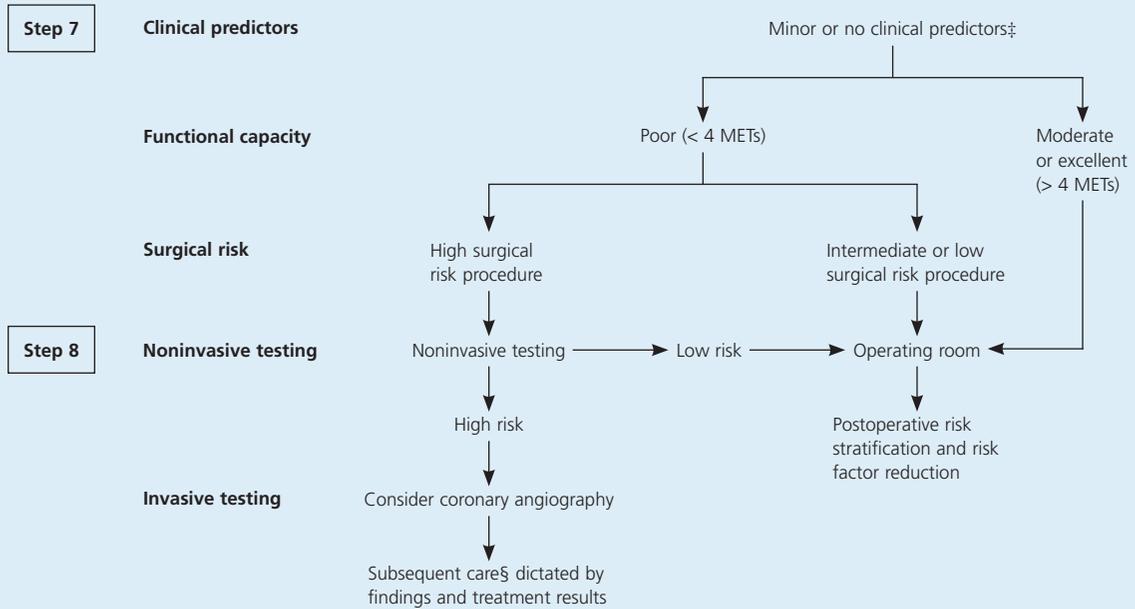


Figure 1. Stepwise approach to preoperative cardiac assessment. (MET = metabolic equivalent; CHF = congestive heart failure)

Preoperative Cardiac Assessment (continued)



*—Major clinical predictors: unstable coronary syndromes, decompensated CHF, significant arrhythmias, severe valvular disease.

†—Intermediate clinical predictors: mild angina pectoris, prior myocardial infarction, compensated or prior CHF, diabetes mellitus, renal insufficiency.

‡—Minor clinical predictors: advanced age, abnormal electrocardiography, rhythm other than sinus, low functional capacity, history of stroke, uncontrolled systemic hypertension.

§—Subsequent care may include cancellation or delay of surgery, coronary revascularization followed by noncardiac surgery, or intensified care.

Figure 1. Stepwise approach to preoperative cardiac assessment. (MET = metabolic equivalent; CHF = congestive heart failure)

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revascularization procedure and no change in symptoms, further evaluation is generally unnecessary. The aim of preoperative testing is to measure functional capacity, to identify the presence of myocardial ischemia or cardiac arrhythmias, and to estimate perioperative cardiac risk. The 2002 ACC/AHA guidelines are available for handheld computers at no charge (STAT Cardiac Clearance, <http://www.statcoder.com/cardiac1.htm>).

Exercise tolerance is one of the most important determinants of perioperative risk and the need for invasive monitoring (Figure 1).² Poor functional capacity in patients with chronic coronary artery disease (CAD) or those convalescing after an acute cardiac event is associated with an increased risk of subsequent cardiac morbidity and mortality.³ If a patient has excellent exercise tolerance, even if he or she has stable angina, this suggests that the myocardium can be stressed without becoming dysfunctional. The authors of one study found that the likelihood of a serious complication was inversely proportional to the number of blocks that could be walked or flights of stairs that could be climbed.⁴ Myocardial

perfusion imaging for patients undergoing vascular surgery has a positive predictive value (PPV) for ischemia between 4 and 20 percent and a negative predictive value (NPV) of 95 to 100 percent.² The same test for patients undergoing nonvascular surgery has a PPV for ischemia between 8 and 67 percent and an NPV between 98 and 100 percent.² Stress echocardiography using dobutamine (Dobutrex) has a PPV for ischemia between 10 and 24 percent and an NPV between 93 and 100 percent.² Because the range for accuracy overlaps among tests, the specific type of stress test chosen should depend on local expertise and availability.

Application of the ACC/AHA Guidelines in Practice

Since the initiation of the ACC/AHA guidelines, several studies have shown that the incidence of preoperative stress testing, cardiac catheterization, and coronary revascularization decreased in institutions where the baseline rate for testing was high. No increase in mortality or morbidity has since been described.⁵

TABLE 2
Cardiac Risk* Stratification for Noncardiac Surgical Procedures

High (reported cardiac risk often >5 percent)

Emergent major operations, particularly in patients older than 75 years

Aortic and other major vascular surgery

Peripheral vascular surgery

Anticipated prolonged surgical procedure associated with large fluid shifts and/or blood loss

Intermediate (reported cardiac risk generally 1 to 5 percent)

Carotid endarterectomy

Head and neck surgery

Intraperitoneal and intrathoracic surgery

Orthopedic surgery

Prostate surgery

Low† (reported cardiac risk generally <1 percent)

Endoscopic procedures

Superficial procedures

Cataract surgery

Breast surgery

*—Combined incidence of cardiac death and nonfatal myocardial infarction.

†—Do not generally require further preoperative cardiac testing.

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However, the Coronary Artery Revascularization Prophylaxis (CARP) study forces us to reconsider these recommendations. In this study, 5,859 patients with CAD risk factors who were undergoing elective major vascular surgery were assigned to one of two groups: those who had received coronary artery revascularization (i.e., percutaneous coronary intervention or bypass surgery) before surgery and those who had not had revascularization before surgery.⁶ Patients with an ejection fraction of less than 20 percent, stenosis of the left main coronary artery, or severe aortic stenosis were excluded.

Investigators found that 30 days after surgery, 12 percent of patients in the revascularization group and 14 percent of those in the nonrevascularization group suffered a postoperative MI as defined by elevated troponin levels. Nearly three years later, the mortality rate was 22 percent in the

revascularization group and 23 percent in the nonrevascularization group. The authors conclude that coronary artery revascularization before elective vascular surgery on moderate-risk patients does not significantly alter the long-term outcome and cannot be recommended. These findings call into question some of the recommendations of the most recent ACC/AHA guidelines,² in particular, aggressive diagnostic testing and revascularization in patients at intermediate risk of coronary complications.

Several smaller observational studies suggest that the interval between revascularization and surgery may be important. In a study of 40 patients, mortality was much higher when surgery was performed within two weeks of stent placement (32 versus 0 percent after two weeks).⁷ The authors of a second study of 207 patients found that the risk of major adverse cardiac events was 4.8 percent when surgery occurred within six weeks of stent placement and 0 percent after this period.⁸

OTHER APPROACHES TO ASSESSING CARDIAC RISK

One of the first attempts to stratify risk was the Goldman criteria, published in 1977.⁹ This was followed by Detsky's clinical risk index in 1986¹⁰ and Lee's revised cardiac risk index, published in 1999.¹¹ The latter is described in Table 3, with its interpretation.¹¹

Medications to Reduce Morbidity and Mortality

BETA BLOCKERS

When the 2002 ACC/AHA guidelines were published, the use of prophylactic beta blockade was recommended for patients with ischemic risk on preoperative stress testing who were to have vascular surgery and in patients currently taking beta blockers. Data supporting the use of these medications in patients with risk factors for CAD or those undergoing intermediate-risk surgery were less compelling.

The data summarizing the various beta-blocker trials, the doses used, and outcomes measured are summarized in Table 4.¹²⁻¹⁹ In a recent study, 921 patients with diabetes mellitus and without documented CAD undergoing major noncardiac surgery were randomized to metoprolol (Lopressor) or placebo. In this group of low- to moderate-risk patients, no differences were noted in all-cause mortality, acute MI, unstable angina, or congestive heart failure.²⁰

A more recent retrospective cohort study of 663,635 patients found that beta-blocker therapy two days before a major noncardiac surgical procedure was associated with a reduced risk of in-hospital death in high-risk patients but not in low-risk patients. Those who had a revised cardiac index (RCI) score of 0 or 1 did not benefit from beta blockade, whereas those with a score

of 2 or greater had a reduction of in-hospital mortality (odds ratio: 0.88 for an RCI score of 2, 0.71 for an RCI score of 3, and 0.58 for an RCI score of 4 or more).²¹ Finally, a meta-analysis found that although beta blockers may reduce the risk of major cardiovascular events, they also increase the risk of bradycardia and hypotension, resulting in subsequent treatment.²² These studies support the use of perioperative beta blockade to reduce cardiovascular morbidity and mortality only in patients with known cardiovascular disease undergoing vascular surgery and previously on beta blockers.

Most investigators believe that beta blockade is appropriate for patients with active ischemic heart disease undergoing major procedures. Based on the available evidence, most experts advocate a target heart rate in the 60s perioperatively.^{13,23} The use of these therapies in patients without active CAD or those undergoing less invasive procedures is advocated as a class 2 recommendation by the 2006 ACC/AHA guidelines Focus Update on Perioperative Beta Blockade (i.e., moderate-quality evidence).²⁴ This

issue should be further clarified by two ongoing studies (i.e., the POISE [Perioperative Ischemic Evaluation Study] trial and the DECREASE-IV [Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography] study); these are expected to be completed within the next four years.

In March 2006, the ACC/AHA released a focused update on perioperative beta-blocker therapy.²⁴ It recommends the use of beta blockers for patients undergoing surgery who are already receiving beta blockers to treat angina, symptomatic arrhythmias, hypertension, or other ACC/AHA-recommended indications and for patients undergoing vascular surgery who are at high cardiac risk because of the finding of ischemia on preoperative testing. The guideline authors found that the weight of evidence is also in favor of beta blockers in patients undergoing vascular surgery in whom preoperative assessment identifies coronary disease; high cardiac risk, as defined by the presence of multiple cardiac risk factors; or coronary disease or high cardiac risk, as defined by the presence of multiple cardiac risk factors in patients who are undergoing intermediate- or high-risk procedures.

The usefulness of perioperative beta blockade is less well established in patients who are undergoing intermediate or high-risk procedures or vascular surgery and in whom preoperative assessment identifies intermediate cardiac risk as defined by the presence of a single clinical risk factor. It is also less well established in patients with low cardiac risk who are not currently on beta blockers and are undergoing vascular surgery. The update also notes that studies to determine the ideal target population, beta-blocking drug, dose, and route of administration are not currently available. Some data suggest that long-acting beta blockers may prove more beneficial than shorter-acting agents.²⁵

STATINS

Statins are believed to act via multiple mechanisms to improve atherosclerotic plaque stability (e.g., antithrombotic, antiproliferative) as well as inhibit leukocyte adhesion.²⁶⁻²⁸ The authors of a retrospective observational study found that a combination of statins and beta blockers in patients undergoing surgery for abdominal aortic aneurysm was associated with a reduced incidence of

Observational studies have found an association between statin use perioperatively and improved outcomes in patients with cardiac risk factors.

TABLE 3
Lee's Revised Cardiac Risk Index

Clinical variable	Points
High-risk surgery (i.e., intraperitoneal, intrathoracic, or suprainguinal vascular surgery)	1
Coronary artery disease	1
Congestive heart failure	1
History of cerebrovascular disease	1
Insulin treatment for diabetes mellitus	1
Preoperative serum creatinine level greater than 2.0 mg per dL (180 μ mol per L)	1
Total:	_____

Interpretation of Risk Score

Risk class	Points	Risk of complications* (%)
I. Very low	0	0.4
II. Low	1	0.9
III. Moderate	2	6.6
IV. High	3 +	11.0

*—Myocardial infarction, pulmonary embolism, ventricular fibrillation, cardiac arrest, or complete heart block.

Adapted with permission from Lee TH, Marcantonio ER, Mangione CM, Thomas EJ, Polanczyk CA, Cook EF, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation* 1999;100:1047.

Preoperative Cardiac Evaluation

perioperative mortality and nonfatal MI.²⁹ This was particularly evident in the high-risk patients. Other observational studies have found similar outcomes in patients undergoing vascular surgery.^{30,31}

In a small randomized trial in which 100 patients were given atorvastatin (Lipitor) or placebo an average of 30 days before vascular surgery, there was a significant reduction in the risk of cardiac death, nonfatal MI, unstable angina, and stroke (8 versus 26 percent; $P = .031$; number needed to treat [NNT] = 5).³² In a retrospective cohort study of 77,082 patients who received lipid-lowering therapy preoperatively, researchers found a 38 percent reduction in the odds of in-hospital mortality among patients undergoing major noncardiac surgery.³³ Unfortunately, no other trials have been conducted. No significant differences were noted between groups, but the study was underpowered. Although statins were not addressed in the 2002 update, the current evidence provides preliminary support for these agents in patients at high risk of perioperative mortality.

ALPHA₂-AGONISTS

Alpha₂-agonists also have been investigated for their perioperative effects. A randomized, double-blind study with 297 patients demonstrated a reduction in the incidence of perioperative myocardial ischemic episodes from 39 to 24 percent (NNT = 7; $P < .01$), although the incidence of fatal cardiac events was not different.³⁴ A number of meta-analyses have demonstrated that alpha₂-agonists reduce cardiac complications in patients undergoing vascular surgery.³⁵⁻³⁷ A recent study of 190 patients found that clonidine (Catapres; 0.2 mg orally and as a patch), started on the morning before surgery and continued four days postoperatively, reduced perioperative myocardial ischemia complications (14 versus 21 percent; $P = .01$; NNT = 14).³⁸ Table 5^{32,34,38-40} compares the current randomized trials of alpha agonists and statins.

OTHER AGENTS

Other agents such as calcium channel blockers and nitrates have also been evaluated to determine if they can reduce the risk of

TABLE 4

Randomized Trials of Perioperative Prophylactic Beta Blockers and Cardiac Morbidity

Author (year)	Procedure	Number of patients	Type of control
Stone (1988) ¹⁵	Noncardiac	128	Placebo
Mangano (1996) ¹² ; Wallace (1998) ¹⁷	Noncardiac	200	Placebo
Poldermans (1999) ¹³	Vascular	112	Unblinded
Raby (1999) ¹⁶	Vascular	26	Placebo
Zaugg (1999) ¹⁸	Noncardiac	63 (59 analyzed)	No perioperative beta blockers
Urban (2000) ¹⁹	Noncardiac	107	Placebo
Brady (2005) ¹⁴	Vascular	103 (97 underwent surgery)	Placebo

NA = not applicable; IV = intravenously.

*— $P < .05$ for drug versus control.

Information from references 12 through 19.

TABLE 5

Randomized Placebo-Controlled Trials of Perioperative Prophylactic Alpha Agonists and Statins

Author (year)	Procedure	Number of patients
Alpha agonists		
Wallace (2004) ³⁸	Noncardiac	190
Stuhmeier (1996) ³⁴	Vascular	297
Ellis (1994) ³⁹	Noncardiac	61
McSPI (1997) ⁴⁰	Noncardiac	300
Statins		
Durazzo (2004) ³²	Vascular	100

NA = not applicable.

*— $P < .05$ for drug versus control.

Information from references 32, 34, and 38 through 40.

<i>Drug/dosage</i>	<i>Myocardial ischemia</i>		<i>Myocardial infarction</i>		<i>Death</i>	
	<i>Control</i>	<i>Drug</i>	<i>Control</i>	<i>Drug</i>	<i>Control</i>	<i>Drug</i>
Labetalol (Normodyne), atenolol (Tenormin)	11/39 (28%)	2/89* (2%)	0/39 (0)	0/89 (0)	NA	NA
Atenolol, 10 to 20 mg IV or 50 or 100 mg orally	39/101 (39%)	24/99* (24%)	NA	NA	10/101 (10%)	1/99* (1%)
Bisoprolol (Zebeta), 5 to 10 mg orally	NA	NA	9/53 (17%)	0/59* (0)	9/53 (17%)	2/59* (3%)
Esmolol (Brevibloc), IV	8/11 (73%)	5/15* (33%)	NA	NA	NA	NA
Atenolol targeted to maintain heart rate (1) pre- and postoperatively or (2) intraoperatively	NA	NA	3/19 (16%)	0/40 (0)	NA	NA
Esmolol IV on the day of surgery, followed by metoprolol (Lopressor), starting at 25 mg orally twice daily and increased to maintain a heart rate less than 80 beats per minute, and continued for the next 48 hours	8/55 (15%)	3/52 (6%)	3/55 (5%)	1/52 (2%)	NA	NA
Metoprolol, orally 50 mg twice daily preoperatively until seven days after surgery	4/44 (9%)	5/53 (9%)	5/44 (11%)	3/53 (6%)	1/44 (2%)	3/53 (6%)

<i>Drug/dosage</i>	<i>Myocardial ischemia</i>		<i>Myocardial infarction</i>		<i>Death</i>	
	<i>Control</i>	<i>Drug</i>	<i>Control</i>	<i>Drug</i>	<i>Control</i>	<i>Drug</i>
Clonidine (Catapres), 0.2 mg oral and patch	20/65 (31%)	18/125* (14%)	NA	NA	NA	NA
Clonidine, 2 mcg per kg orally	59/152 (39%)	35/145 (24%)	4/152 (3%)	0/145 (0)	2/152 (1%)	1/145 (0.7%)
Clonidine for 72 hours after surgery, then 0.3 mg orally 60 to 90 minutes before surgery	5/26 (19%)	6/28 (21%)	NA	NA	NA	NA
Mivazerol (not available in the United States), 1.5 mcg per kg per hour	Intraoperative 34/99 (34%)	37/180 (20%)	6/103 (6%)	3/197 (2%)	NA	NA
Atorvastatin (Lipitor), 20 mg	1/50 (2%)	0/50 (0)	8/50 (16%)	3/50 (6%)	2/50 (4%)	1/50 (2%)

Preoperative Cardiac Evaluation

perioperative cardiac complications. To date, however, they do not seem to offer any additional benefit.^{41,42}

Resolution of the Case

Hip arthroplasty is an intermediate-risk surgery. Based on the Lee revised cardiac risk index (*Table 3*),¹¹ the patient in the case scenario receives 1 point for CAD, putting him at low risk. Because his functional status was good before his recent hip problems and he is having no cardiovascular symptoms, after referring to *Figure 1*² and considering the results of the CARP study, the physician decides in collaboration with the patient that cardiovascular stress testing is not necessary. Because he was taking beta blockers before his recent illness and should remain on them because of his CAD whether or not he is having surgery, the physician chooses to resume them. However, the patient would not otherwise be a candidate for beta blockade. Continuing statin therapy would neither harm nor benefit him for his current surgery.

The authors thank Katherine Musselman and Liana Borau for their assistance with the preparation of the manuscript.

This article is one in a series developed in collaboration with the American Heart Association. Coordinator of the series is Sidney C. Smith, Jr., M.D., Chief Science Officer, American Heart Association, Dallas, Tex. The series coordinator for *AFP* is Sumi Sexton, M.D.

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Author disclosure: Dr. Fleisher was a member of the original and update committees for the American Heart Association Guideline on Perioperative Cardiovascular Evaluation for Noncardiac Surgery and is chair of the current committee.

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