Reducing Perioperative Cardiac Complications in Patients Undergoing Noncardiac Surgery

Case Study and Commentary, Darryl K. Potyk, MD

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Program Audience
Primary care physicians.

Educational Needs Addressed
Cardiac events are common complications of elective noncardiac surgery and increase the mortality and costs associated with these procedures. Recent insight into the pathophysiology of perioperative myocardial ischemia has led to an emphasis on preoperative risk stratification as well as postoperative management. As a result, preoperative cardiac risk evaluation has become an integral part of contemporary clinical practice. Although there is agreement that clinical markers can identify high-risk patients, the approach to risk reduction has been controversial. Good data are becoming available to help guide clinical decision making. Primary care physicians should be able to perform most preoperative cardiac evaluations and recommend risk-reduction strategies without subspecialty referral. To do so, physicians must understand perioperative myocardial ischemia, be familiar with the published guidelines and data in the area of risk assessment, and use an evidence-based approach to risk reduction in high-risk patients.

Educational Objectives
1. Recognize the characteristics of perioperative myocardial ischemia and how they relate to postoperative myocardial infarction
2. Understand the appropriate role of preoperative coronary revascularization
3. Describe first-line medical therapy for decreasing perioperative cardiac complications
4. Know second-line and emerging medical therapies for high-risk patients
5. Understand the value of perioperative pulmonary artery catheterization

Of the 25 million people in the United States who underwent noncardiac surgery in 1998, Mangano [1] estimated that 8 million of them had known cardiac disease, major cardiac risk factors, or were older than 65 years of age [1]. Not surprisingly, perioperative cardiac events were common among these patients. Estimates of serious perioperative cardiac morbidity vary between 1% and 10%, depending on the subset of patients and the type of surgical procedure [1].

Continuous electrocardiographic monitoring with ST segment analysis has provided insight into the pathophysiologic features and frequency of perioperative myocardial ischemia [2,3]. The Perioperative Ischemia Research Group used continuous electrocardiographic monitoring before, during, and after noncardiac operations and found a 41% incidence of myocardial ischemia in the early postoperative period, compared with incidences of 25% and 20%, respectively, during the intraoperative and preoperative periods [2]. Postoperative ischemia has been well characterized. Its peak incidence is within 48 hours of surgery, which correlates with the peak incidence of postoperative myocardial infarction (MI). The ischemic episodes are not associated with tachycardia and follow a circadian rhythm, with most ischemia occurring in the early morning hours. Postoperative ischemia is more severe than ischemia detected during the preoperative or intraoperative period and is clinically silent in more than 90% of cases [3–5]. Silent postoperative ischemia has been reported to be present for more than 50 minutes before each clinical event [3].

Perioperative myocardial ischemia usually occurs in the presence of fixed severe coronary artery stenoses, which limit oxygen delivery during the stressful perioperative period. In one study, all postoperative MIs were preceded by prolonged ST-segment depression and an increase in heart rate [6]. Although prolonged stress-induced ischemia accounts for most perioperative MIs, some are caused by acute thrombosis. Histopathologic analysis of coronary arteries in patients who suffered fatal perioperative MIs has demonstrated the disruption

From the Internal Medicine Residency, Deaconess Medical Center, and University of Washington School of Medicine, Spokane, WA.
of unstable coronary plaques within mild to moderately stenosed vessels [7]. Plaque disruption leads to platelet aggregation and subsequent coronary artery thrombosis. The postoperative period is accompanied by activation of neurohumoral pathways, increases in catecholamine levels, reduced levels of endogenous tissue plasminogen activator, and platelet activation, all of which have been postulated to contribute to perioperative myocardial ischemia. These insights into the complex pathophysiology of perioperative myocardial ischemia have led to an emphasis on postoperative management in addition to preoperative risk stratification.

The evaluation of cardiac risk before noncardiac surgery has become an integral part of contemporary medical practice. Primary care physicians can perform most preoperative cardiac evaluations without subspecialty referral. Because most postoperative medical complications are cardiac or pulmonary in origin, a thorough history and physical examination focusing on cardiopulmonary disorders and an electrocardiogram (ECG) supplemented by judicious laboratory testing are usually sufficient. Primary care physicians should have an understanding of perioperative myocardial ischemia, be familiar with the published guidelines in this area, and use an evidence-based approach to risk reduction in high-risk patients.

**CASE STUDY**

**Initial Presentation**

A 72-year-old man presents to his primary care physician’s office for preoperative cardiac evaluation prior to undergoing elective aortobifemoral reconstruction for occlusive peripheral vascular disease.

**Preoperative Clinical Evaluation**

The patient has chronic stable angina, and his exercise tolerance is limited to walking 1 block due to symptoms of lower extremity claudication. Six months ago the patient was able to walk 4 blocks without cardiopulmonary symptoms; he gave up bowling 3 months ago because of his lower extremity symptoms. The patient has been told that he has congestive heart failure (CHF) due to lower extremity edema. He has not had an echocardiogram, and he currently denies orthopnea, paroxysmal nocturnal dyspnea, and dyspnea on exertion. He has no history of MI. The patient does report that he had bronchospasm in the past, resulting in prior hospitalization for chronic obstructive pulmonary disease (COPD). He recalls that he underwent pulmonary function tests and was prescribed β-agonist therapy for his bronchospasm. There is no history of diabetes mellitus or ventricular arrhythmias.

Physical examination reveals no jugular venous distension, S₃, rales, or wheezes and no peripheral edema. An ECG in the office today shows small Q waves in the inferior leads.

- What is this patient’s risk for a perioperative cardiac event?
- Is further noninvasive testing indicated for this patient prior to surgery?

**Risk Stratification**

Many studies have shown that patients at increased risk for perioperative cardiac events can be identified on the basis of a thorough history, physical examination, and ECG in combination with a risk stratification tool. The most commonly used risk stratification schemes include the American College of Cardiology/American Heart Association (ACC/AHA) guideline [8], the American College of Physicians (ACP) guideline [9], the Revised Cardiac Index [10], and the clinical model developed by Eagle et al [11]. Each of these risk stratification approaches has been validated in terms of identifying high-risk patients. Unlike the ACC/AHA and ACP guidelines, the Revised Cardiac Index and Eagle’s criteria do not provide guidance regarding risk-reduction strategies.

The ACC/AHA and ACP guidelines have been criticized because they are largely based on retrospective or observational data and on extrapolation from information about cardiovascular disease in the nonoperative setting. These guidelines differ in some of their recommendations, but the significance of these differences is unclear. A recent study stratified patients according to both the ACC/AHA and ACP guidelines; disparate recommendations were found in up to 17% of cases [12]. A recent survey of cardiologists revealed that they frequently differed in their approach to standardized patients and that their recommendations deviated from published guidelines up to 40% of the time [13].

Outcome data are lacking to determine whether one guideline is superior to another. Although neither is perfect, the ACC/AHA guideline incorporates the most recent data and represents an authoritative consensus opinion. This guideline outlines a stepwise approach (Figure) to preoperative cardiac risk assessment taking into account the urgency of the surgery and patient-specific risk factors, including functional capacity and risk of the specific surgical procedure (Tables 1–3). The ACC/AHA guideline is currently the preferred guideline.

It is illustrative to risk stratify the case patient with these different tools. According to the Revised Cardiac Index, the case patient has 3 cardiac risk factors (ie, high-risk surgery, ischemic heart disease, CHF) and would therefore be categorized as high risk [10]. As previously noted, the Revised Index does not provide guidance on further management of high-risk patients. The case patient also would be categorized as high risk.
using the clinical model developed by Eagle et al [11], because he has 3 risk factors (ie, age > 70 years, angina, Q waves on ECG). In this setting, the authors of this model do not recommend noninvasive testing but state that consideration should be given to cardiac catheterization [11]. Using the ACP guideline, this patient also would be classified as high risk; he is over age 70 years and has angina that may be severe [9]. It is difficult to classify the patient’s angina because his peripheral vascular disease limits him. It is therefore prudent to assume the worst-case scenario, which would place the patient in a high-risk category due to ischemic heart disease. Because he is unable to stress his heart in the presence of severe peripheral vascular disease, the recommendation would be to further investigate the degree of his coronary artery disease (CAD) prior to noncardiac surgery [9]. According to the ACC/AHA guideline, the case patient has 2 intermediate clinical predictors (ie, angina, CHF) but no major clinical predictors of perioperative cardiac risk; however, because he has poor functional capacity and is scheduled to undergo high-risk surgery, this guideline would recommend noninvasive cardiac testing to further assess his risk [8].

Noninvasive Testing

Noninvasive tests available to refine perioperative cardiac risk include exercise electrocardiography, exercise or dobutamine echocardiography, and exercise- or pharmacologically induced stress myocardial perfusion imaging. When noninvasive testing is necessary, the choice of the tests should be determined by patient characteristics and local expertise.

For most ambulatory patients, the test of choice is an exercise ECG, which provides information regarding the patient’s functional capacity and his or her hemodynamic response to exercise in addition to detecting myocardial ischemia. This test would not be suitable for the case patient because his ability to exercise would be limited by his peripheral vascular disease. It is important to keep in mind that an abnormal resting ECG (ie, left bundle branch block, left ventricular hypertrophy with strain pattern, or digitalis effect) impairs the interpretation of a stress ECG; in the presence of an abnormal resting ECG, other noninvasive techniques should be used [9,14].

Dipyridamole myocardial perfusion imaging and dobutamine echocardiography are the most commonly used pharmacologic stress tests [9]. These tests have similar abilities to predict postoperative cardiac complications [9,15]. Dobutamine should be avoided in patients with serious arrhythmias, severe hypertension, or suspected critical aortic stenosis. Dipyridamole should be avoided in patients with a
Further cardiac testing should be done only if the results will alter perioperative management. Once a patient is identified as being at high risk for perioperative cardiac complications, either by clinical criteria or by noninvasive testing, risk-reduction strategies must be considered. The options for reducing postoperative cardiac complications include a revascularization procedure (ie, coronary artery bypass grafting [CABG] or percutaneous coronary intervention [PCI]) or medical therapy.

Cardiac Testing

A dobutamine echocardiogram is performed and demonstrates areas of ischemia. On coronary angiography, the patient has 2-vessel disease involving the right coronary artery and the distal left anterior descending artery. His left ventricular ejection fraction is 45%. These results indicate that the patient is at increased risk for perioperative cardiac complications after major vascular surgery. He is apprised of the risks associated with surgery, but he wishes to proceed with vascular surgery because he finds the alternatives unacceptable due to the current limitations on his daily functioning.

- What is the current state of the evidence in support of interventions to lower risk for cardiac complications of noncardiac surgery?

Table 3. Cardiac Risk Stratification for Noncardiac Surgical Procedures

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Procedures</th>
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<tbody>
<tr>
<td>High risk (reported risk &gt; 5%)*</td>
<td>Emergent major operations, particularly in the elderly</td>
</tr>
<tr>
<td></td>
<td>Aortic and other major vascular surgery</td>
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<tr>
<td></td>
<td>Peripheral vascular surgery</td>
</tr>
<tr>
<td></td>
<td>Anticipated prolonged surgical procedure with large fluid shifts and/or blood loss</td>
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<tr>
<td>Intermediate risk (reported risk &lt; 5%)*</td>
<td>Carotid endarterectomy</td>
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<tr>
<td></td>
<td>Head and neck surgery</td>
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<tr>
<td></td>
<td>Intraperitoneal and intrathoracic surgery</td>
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<tr>
<td></td>
<td>Orthopedic surgery</td>
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<tr>
<td></td>
<td>Prostate surgery</td>
</tr>
<tr>
<td>Low risk (reported risk &lt; 1%)*</td>
<td>Endoscopic procedures</td>
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<tr>
<td></td>
<td>Superficial procedures</td>
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<tr>
<td></td>
<td>Cataract surgery</td>
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<td>Breast surgery</td>
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*Combined incidence of cardiac death and nonfatal myocardial infarction.

tients who were randomized to CABG or PCI and then subsequently underwent noncardiac surgery [18]. The rates of cardiac complications after noncardiac surgery were similar in both groups for approximately 4 years, but after 4 to 5 years the risk of noncardiac surgery began to increase again. Although this study demonstrated the equivalence of CABG and PCI in this setting, it did not provide any data regarding the relative risk reductions of preoperative coronary revascularization versus medical therapy [18]. This issue was recently addressed in a landmark multicenter study [19]. Patients with clinically significant but stable CAD undergoing elective major vascular surgery were randomly assigned to undergo coronary revascularization (PCI or CABG, 258 patients) or receive medical therapy alone (252 patients). Four deaths were related to the preoperative revascularization procedure, 2 each in the CABG and PCI groups. After elective vascular surgery, there were no significant differences in perioperative death (3%), perioperative MI (8%), or length of stay in the intensive care unit (2 days) between the group that underwent preoperative coronary revascularization and the group that did not. At a median follow-up of 2.7 years, there was no difference in mortality between the 2 groups (22%). It is important to keep in mind the exclusion criteria for this study when considering the implications of these results. Patients
were enrolled only if they had stable coronary symptoms and were excluded if they had at least 50% stenosis of the left main coronary artery, a left ventricular ejection fraction less than 20%, or severe aortic stenosis. Even given these limitations, this study was methodologically sound and provides good evidence that prophylactic preoperative revascularization offers no benefit for prevention of cardiac complications among a high-risk population [19]. Other studies have reported that coronary artery stent implantation within 1 to 2 months prior to noncardiac surgery is associated with increased perioperative cardiac morbidity and mortality [20,21]. Thus, prophylactic revascularization prior to elective surgery does not reduce perioperative cardiac complications and should not be recommended.

**Medical Therapy**

Several recent well-conducted clinical trials indicate that aggressive medical therapy can provide myocardial protection and should be the therapy of choice to reduce perioperative cardiac events.

**β Blockers**

In the first randomized controlled trial of perioperative β blockers, 200 patients with or at risk for CAD who were undergoing noncardiac surgery received placebo or intravenous atenolol 30 minutes before surgery and intravenous or oral atenolol for the duration of their hospital stay [22,23]. Although there was no difference in short-term mortality, the atenolol group had a 40% decrease in postoperative myocardial ischemia and a significant survival advantage at 2 years. In addition to these primary endpoints, diabetic patients receiving atenolol had a fourfold reduction in risk compared with diabetic patients receiving placebo [22]. In another study, 112 high-risk patients undergoing vascular surgery were randomized to receive perioperative bisoprolol or standard perioperative care [24]. The fact that these were all high-risk patients undergoing high-risk surgery resulted in an increased incidence of cardiac complications and increased statistical power. An independent safety committee halted the study early because of a striking benefit demonstrated in the bisoprolol group. Perioperative death occurred in 3.4% of patients in the bisoprolol group compared with 17% of patients in the standard care group, whereas nonfatal MI did not occur in the bisoprolol group but occurred in 17% of the standard care group. These combined primary endpoints occurred in 3.4% of patients in the bisoprolol group and 34% of patients in the standard care group. These studies are methodologically sound and provide good evidence that perioperative β blockers reduce short- and long-term cardiac complications.

There is a tendency to view effective perioperative β blockade as providing sufficient cardioprotection to preclude preoperative risk stratification and cardiac testing. To determine whether this was indeed the case, another recent study looked at the interaction of preoperative stress testing (dobutamine stress echocardiography) and perioperative β blockers [25]. This study showed for the first time that low-risk patients, in addition to high-risk patients undergoing vascular surgery, benefited from β-blocker administration. Similar benefits were seen whether patients had been on long-term β-blocker therapy or had begun these medications just prior to surgery. Unfortunately, this study identified a small group of patients for whom β blockers were not protective. Patients with stress echocardiograms demonstrating widespread severe ischemia (> 5 new abnormal segments) had similar cardiac complication rates regardless of whether they received perioperative β blockers or placebo [25]. Whether it is possible to intervene to decrease perioperative cardiac complications among this very high-risk group and how to identify this group in a cost-effective manner are questions under active investigation.

To summarize the effectiveness of perioperative β-blockade, a recent meta-analysis was performed and concluded that β blockers decrease perioperative ischemia and perioperative cardiac death [26]. The primary adverse effect was bradycardia, which required treatment in a minority of patients. The authors calculated a favorable number needed to treat between 2 and 8. It was recommended that all patients at increased risk for cardiac complications undergoing noncardiac surgery be given β blockers [27]. Some authors, however, advise caution in enthusiastically embracing perioperative β-blocker therapy and note that none of the trials to date have included large numbers of patients and that the beneficial effects reported seem implausibly large [28]. These investigators are currently attempting to enroll 10,000 patients in a randomized trial of perioperative β blockers to definitively establish the degree of benefit as well as the potential risks associated with perioperative β-blocker therapy.

At this time, it seems reasonable to treat high-risk patients with perioperative β blockers, recognizing the limitations of the current data. Starting β blockers 1 to 2 weeks prior to elective surgery and then continuing them during the postoperative period may be more practical than introducing a new medication just prior to surgery. Questions that remain to be answered with future research include what degree of benefit is conferred by β blockers, are all β blockers equally efficacious, what are optimal dosing schedules, and which patients will benefit most from these medications.

**Alternative Agents**

Not all patients can take β blockers, and so there has been interest in other agents that may attenuate the stress response to surgery. Evidence to date suggests that prophylactic calcium channel blockers or clonidine may be alternatives for...
high-risk patients unable to take β blockers. The prophylactic use of nitroglycerin, however, has not been shown to decrease myocardial ischemia or cardiac complications [29,30].

Calcium channel blockers. Calcium channel blockers are widely used and have been studied in the perioperative setting. The studies to date have enrolled small numbers of patients, have different endpoints, and have yielded conflicting results. Data from these studies have recently been pooled for analysis, with disparate conclusions. A meta-analysis found benefit of calcium channel blockers in the perioperative setting [31], whereas another systematic review found no benefit [30]. Large-scale randomized controlled trials are necessary to determine the usefulness of calcium channel blockers in this setting.

Clonidine. The centrally acting α2-agonist clonidine has been shown to reduce hypertension, tachycardia, and norepinephrine release associated with surgical stress. Clonidine has been used in several small studies in an attempt to decrease perioperative cardiac complications. When data from these studies were pooled for analysis, the incidence of postoperative MI and death was decreased among patients taking clonidine, but these trends did not reach statistical significance [30,32]. A more recent trial, however, did show beneficial effects of clonidine [33]. This prospective, double-blind trial involved 190 patients with either known CAD or more than 2 coronary risk factors who were randomized to perioperative clonidine or placebo. Oral and transdermal clonidine were started on the night before surgery and continued for 4 days. The clonidine group had a significant reduction of perioperative myocardial ischemia. At 30 days there was a nonsignificant trend toward fewer deaths in the clonidine group, but at 2 years mortality was significantly reduced in the clonidine group (15% versus 29%) [33]. Larger studies are necessary to confirm this benefit and to determine the magnitude of benefit compared with β-blocker therapy.

Statins. It is increasingly apparent that mechanisms other than increased adrenergic activity contribute to perioperative cardiac complications, and interest in statins and their benefits beyond lowering cholesterol has led to a consideration of perioperative statin use. Statins appear to have a variety of effects that stabilize vulnerable coronary plaques. In nonoperative settings, statins have been associated with decreased in-hospital deaths in patients with acute coronary syndromes and decreased periprocedural MI following PCI. To date, several large observational studies have suggested an association between perioperative statin use and decreased cardiac complication rate after noncardiac surgery [34–36]. One randomized prospective trial has used statins in an attempt to reduce cardiac complications after elective vascular surgery [37]. In this study, 100 patients were randomized to 20 mg/day of atorvastatin or placebo for 45 days perioperatively. Patients had vascular surgery at a mean of 31 days after the start of the study medication. Patients taking atorvastatin had a lower risk for the composite endpoint of cardiovascular events (ie, cardiac death, nonfatal MI, unstable angina, or ischemic stroke) than did patients randomized to placebo. There were no significant differences among the individual components of the composite endpoint between the 2 groups. Approximately half of the patients in both groups of this study received β blockers perioperatively [37]. The sample size was not large enough for subset analysis to determine whether the beneficial effects of atorvastatin were influenced by β-blocker administration or other factors. Once again, larger randomized controlled trials are necessary to confirm this benefit and to determine the degree of benefit. Other unanswered questions include how long should a patient be treated with a statin before and after surgery and what is optimal dosing.

- Given this patient’s level of cardiac risk, clinical history, and preference to undergo vascular surgery, what would be the best treatment option for him?

Although this patient’s coronary anatomy may be amenable to CABG, there is no evidence that CABG will offer him a mortality benefit. In the absence of such a benefit, medical therapy in this setting should be pursued. Unfortunately, the case patient’s history of severe bronchospasm is an absolute contraindication to β-blocker administration. Other contraindications include a history of asthma, bradycardia, or cardiac conduction abnormalities. Thus, consideration needs to be given to alternative medications to reduce his cardiac risks. Calcium channel blockers, clonidine, and/or statins administered during the perioperative period appear to be reasonable options, although current data on the benefit of these treatments are far from conclusive. Further, evidence regarding combination therapy is lacking, and the relative contributions of different medications in this setting are unclear. The patient could be offered combination therapy with a calcium channel blocker or clonidine plus a statin, provided that the limited data on these options are disclosed in a straightforward manner prior to embarking on such a plan.

- Should the patient have a pulmonary artery catheter placed perioperatively to further reduce his cardiac risks?

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Pulmonary Artery Catheterization

The value of pulmonary artery (PA) catheters in high-risk surgical patients has been controversial. Early uncontrolled studies reported benefit compared with historical controls [38]. A small prospective study involving 89 patients undergoing vascular surgery reported lower mortality and decreased early graft thrombosis in patients whose hemodynamic status was optimized with a PA catheter compared with those who did not undergo PA catheter placement [39]. A subsequent observational study of 221 patients reported that perioperative PA catheterization did not improve outcomes and was associated with prolonged hospitalization [40].

A rigorous randomized controlled trial on the use of PA catheters was recently published. In this study, 1994 high-risk patients (ie, age > 60 years or American Society of Anesthesiologists class III or IV) undergoing urgent or elective noncardiac surgery were randomized to receive a PA catheter or usual care [41]. The authors used a predefined protocol and physiologic goals for patients receiving a PA catheter. There were no differences in in-hospital mortality or mortality at 1 year between the invasively monitored group and the standard care group. Similarly, there were no differences between groups for a variety of secondary endpoints, including MI, CHF, arrhythmias, and catheter-related complications [41]. This large randomized controlled trial, together with observational studies, establishes that the use of PA catheters does not decrease perioperative morbidity or mortality and should not be recommended as a risk reduction strategy in high-risk surgical patients. Thus, a PA catheter should not be recommended for this patient.

Perioperative Course

The patient elects to proceed with the planned vascular surgery after being advised of his increased risk for perioperative cardiac complications. Because of his contraindication to β-blocker therapy, he is treated with clonidine and atorvastatin 2 weeks before surgery, and these medications are continued postoperatively. His postoperative course is uneventful. Three months after surgery, the patient is able to walk 4 blocks without claudication or cardiopulmonary symptoms. His CAD has been managed medically, but referral for PCI for better symptomatic relief of his anginal symptoms is being considered.

CONCLUSION

The evaluation of cardiac risk before elective noncardiac surgery has become an integral part of contemporary medical practice. Although there is agreement that clinical markers can identify high-risk patients, the approach to risk reduction has been controversial. Good data are becoming available to help guide clinical decision making.

There is a paucity of data indicating that preoperative coronary revascularization with CABG or PCI offers benefit in terms of risk reduction unless these procedures are indicated independently of the need for noncardiac surgery. Conversely, data from randomized controlled trials regarding medical therapies are very promising. β Blockers decrease perioperative myocardial ischemia and decrease cardiac complications among patients undergoing high-risk surgery. While several trials have confirmed these results, definitive large-scale trials are lacking. At present, it seems prudent to treat high-risk patients without contraindications with β blockers during the perioperative period. For patients who cannot tolerate β blockers, perioperative calcium channel blockers or clonidine may reduce cardiac morbidity. Treatment with a statin perioperatively also appears to be beneficial and may be considered in high-risk patients. Whether adding a statin to these other medications further reduces perioperative complications is unclear and deserves further study. The use of PA catheters does not decrease perioperative complications in high-risk patients and should not be routinely recommended.

The studies to date have involved high-risk patients undergoing high-risk surgery. Whether these data can be extrapolated to high- and intermediate-risk patients undergoing intermediate-risk surgery is unclear. Large numbers of patients will need to be studied with attendant careful risk/benefit analyses. Until such trials are available, consideration should be given to treating high-risk patients undergoing intermediate-risk surgery with the medications discussed.

Corresponding author: Darryl K. Potyk, MD, Deaconess Medical Center, 800 West 5th Ave., PO Box 248, Spokane, WA 99210-0248; potykdf@empirehealth.org.

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