Lesson 270: PreAnesthetic Assessment of the Cardiac Patient for Noncardiac Surgery (Part 2)

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NEEDS STATEMENT

As the population ages and elderly patients and their families seek to improve the quality and length of life via surgery, the prevalence of heart disease in surgical patients will likely increase. Improvements in the medical therapy of patients with chronic coronary artery disease and congestive heart failure may mean that such patients come to surgery better prepared than in the past. Recent guidelines from the American College of Cardiology/American Heart Association (ACC/AHA) address preventive measures, including the management of antiplatelet medications and pharmacologic protection with β-blockers, statins, and aspirin. Anesthesiologists are critically involved in the preanesthetic preparation of such patients and the implementation of these therapies, and thus they should be aware of the current thinking.

TARGET AUDIENCE

Anesthesiologists

LEARNING OBJECTIVES

At the end of this activity, the participant should be able to:
1. Outline the general mechanisms by which β-blockers and statins may reduce perioperative cardiac morbidity.
2. Provide medical perioperative optimization with β-blockade and administration of statins to patients who might benefit.
3. Apply the updated ACC/AHA algorithm to determine which patients may need noninvasive testing before surgery.
4. List the 3 cardiac variables that cause perioperative ischemic events.
5. Assess the result of catecholamine-induced sympathetic stimulation.
6. Explain the main effects of hydroxyethylglutaryl-coenzyme A reductase inhibitors.
7. List the adverse effects of statins.
8. Apply the recent ACC/AHA guidelines to case management.
9. Discuss the difference between β-receptor specific antagonists and nonspecific β-antagonists.
10. Summarize the findings of the CARP (Coronary Artery Revascularization Postesthesia) trial.

CASE HISTORY

A 63-year-old woman presented for left femoral-popliteal bypass surgery. Her medical history was significant for peripheral vascular disease, poorly controlled insulin-dependent diabetes, and end-stage renal disease requiring hemodialysis. Ambulation had been difficult for the past 3 months, and she was unable to climb stairs or walk more than half a block. A stress test 18 months earlier showed no ischemic changes and an absence of arrhythmias, in addition to normal wall motion with an ejection fraction of 95%. She denied symptoms of coronary ischemia. Results of preoperative laboratory tests included hemoglobin, 8.6 g/dL; hematocrit, 25.1%; potassium, 4.5 mEq/L; blood urea nitrogen, 22 mg/dL; creatinine, 5.9 mg/dL; and normal coagulation. She was receiving antibiotics, insulin (both regular and lente, 40 U), atorvastatin, furosemide, and hydrochlorothiazide. Vital sign measurements were blood pressure, 139/60 mm Hg; pulse, 72 beats per minute; respiratory rate, 36 breaths per minute; and SpO2, 95% on room air. She weighed 98 kg; physical examination findings were otherwise unremarkable.

CALL FOR WRITERS

If you would like to write a CME lesson for Anesthesiology News, please send an e-mail to Elizabeth A.M. Frost, MD, at ElizFrost@msin.com.

I n Part 1 of this 2-part series, an overview of the assessment and projected incidence of cardiac disease in the United States was presented (Anesthesiology News December 2007, pages 67-70). The means to identify patients at higher risk were discussed. The mechanisms behind perioperative myocardial infarction and nonoperative ischemic events were differentiated. Guidelines from the American College of Cardiology/American Heart Association (ACC/AHA) were outlined as based on medical history, functional status, and surgery-specific risk. The indications for appropriate stress testing and myocardial revascularization were explored. In Part 2, perioperative medical management is discussed. An algorithm for management of the case presented is outlined in a 5-step format. Recommendations according to the 2007 ACC/AHA updated guidelines are offered.

Medical Management

Perioperative ischemic events are the result of both an increase in vascular inflammation and an imbalance in the relationship between the supply and demand of oxygen in the coronary vasculature. Catecholamine-induced stimulation of the sympathetic nervous system is the primary cause of metabolic imbalance.1 Increased sympathetic activity manifests as augmented heart rate, myocardial contractility, afterload, and preload. The first 3 cardiac variables can be favorably manipulated with pharmacologic therapy. In addition to their modulation of the sympathetic nervous system, β-blockers and statins attenuate endothelial dysfunction caused by inflammation.13 β-blockers work by decreasing the responsiveness of β-adrenergic receptors to catecholamines. This effect is desirable because β2-receptor activation has been linked to

PREANESTHETIC ASSESSMENT

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diastolic dysfunction, an early sign of ischemia. In addition to impaired relaxation, myocardial ischemia may facilitate cardiac rupture when nonischemic cardiac myocytes become hyperkinetic relative to adjacent ischemic, hypokinetic myocytes. The use of β-blockers may prevent this effect.

The activation of β-receptors also causes attraction of neutrophils and other leukocytes along with platelet aggregation around the areas of coronary inflammation; this leads to an increase in tissue damage, vascular endothelial growth, and coronary luminal narrowing. Moreover, catecholamine-induced stress leads to vasoconstriction in diseased coronary vasculature and the liberation of thromboxane A2.

Finally, fibrinolytic activity is decreased by the activation of β-receptors. β-blockade attenuates all these effects. On the other hand, stimulation of β-receptors has marked anti-inflammatory effects and can counter β-receptor activity. Hence, antagonists that are specific to β-receptors are selectively nonselective β-antagonists.

Several studies support the use of perioperative β-blockade. However, it appears that perioperative β-blockade is neither necessary nor appropriate for the general population. A 2005 retrospective study by Lindemauer et al showed that in patients who had major noncardiac surgery, those at higher risk (eg, stroke history, ischemic heart disease, renal insufficiency) had an associated higher risk of in-hospital death. In these high-risk patients, the in-hospital death rate was reduced by perioperative β-blockade. This benefit was not observed in the low-risk patients who received perioperative β-blockade.

Of great significance is the fact that only 33 patients who had at least 4 revised cardiac risk index factors needed to receive perioperative β-blockade to prevent an in-hospital death. In a prospective randomized trial (N=112), Poldermans et al demonstrated that beginning therapy 1 week before vascular surgery and continuing it for 1 month after surgery in high-risk patients reduced the relative risk for either perioperative ischemia or nonfatal myocardial infarction (MI) by 91%. In a follow-up study of the same group of patients, those who had continued to receive β-blocker therapy postoperatively for an average of 22 months experienced an absolute decrease of 45% in either fatal or nonfatal MI during the 2-year study period. In a larger prospective, randomized double-blind trial that compared perioperative atenolol with placebo, patients who received the β-blocker had absolute reductions in all-cause death and cardiac death 24 months postoperatively. Additionally, patients in the treatment group experienced less new-onset congestive heart failure, revascularization, unstable angina, or MI at 6, 12, and 24 months.

Similar to β-blockers, hydroxymethylglutaryl-coenzyme A reduce inhibitors (statins) also help prevent perioperative myocardial injury. Statins exert their main effects by decreasing inflammation, plaque rupture, and endothelial dysfunction. Acute-phase reactants such as C-reactive protein exacerbate thrombosis in injured endothelium by stimulating leukocyte adhesion. Other inflammatory mediators, like interferon, inhibit collagen deposition and promote the weakening of endothelium overlying atheromas. Similar to β-blockers, hydroxymethylglutaryl-coenzyme A reduce inhibitors (statins) also help prevent perioperative myocardial injury. Statins exert their main effects by decreasing inflammation, plaque rupture, and endothelial dysfunction. Acute-phase reactants such as C-reactive protein exacerbate thrombosis in injured endothelium by stimulating leukocyte adhesion. Other inflammatory mediators, like interferon, inhibit collagen deposition and promote the weakening of endothelium overlying atheromas. Statins prevent the action of these acute-phase reactants and may reduce perioperative myocardial ischemia by stimulating an accumulation of endothelial nitric oxide synthase, thus preventing endothelial dysfunction. Nitric oxide synthase inhibits the proliferation of smooth muscle cells and platelet adhesion to damaged endothelium. Statins assist in preventing vascular constriction by preventing the liberation of thromboxane A2. Statins also prevent inflammation-mediated decreases in thromboxidin and plasmin, both of which promote blood fluidity and antagonize coagulation factors.

Durazzo et al evaluated the effects of perioperative statin on the prevention of nonfatal acute MI, congestive heart failure, unstable angina, or death from any cardiac cause in patients undergoing vascular surgery. Patients received 20 mg of atorvastatin beginning, on average, 31 days before surgery for a total of 45 days. After the protocol ended, all patients with increased levels of low-density lipoprotein were advised to continue taking the statin. Although no differences in preoperative characteristics were noted, at the end of 6 months, 8.6% of the treated patients experienced adverse cardiac events versus 26.5% in the placebo group.

In a retrospective study of 77,082 patients, the probability of dying in the hospital was 40% less in those who received statins within the first 48 hours after undergoing major noncardiac surgery (any surgery requiring a median hospital stay of at least 48 hours) compared with patients who did not receive statins. The number of risk factors correlated directly with the benefit from statin therapy. For patients with at least 4 revised cardiac risk index factors, the odds of inhospital death were decreased by 86% compared with nontreated patients with the same number of risk factors. Because the use of both β-blockers and statins is likely beneficial, the appropriate timing and duration of use should be defined. The optimal perioperative timing for administration of β-blockers has not been established. Poldermans et al defined a 30-day preoperative period as being ideal, whereas Mangano et al found immediate preoperative administration to be sufficient.

Although β-blockers and statins are important for the prevention of ischemia, the adverse effects of these drugs must be minimized to optimize patient compliance and safety. The adverse event rate for β-blockade was less than 10% in the Mangano study. The use of β-blockers can cause varying levels of hypotension and bradycardia. In Mangano’s study, no patients were treated for bradycardia despite 13 instances of preoperative or immediate postoperative bradycardia. There were 6 instances of preoperative or immediate postoperative hypotension—none requiring intervention. In a 2006 randomized trial by Yang et al that evaluated metoprolol versus placebo in elective vascular surgery, the incidence rates of intraoperative hypotension and bradycardia were both statistically significant (with a higher incidence in the metoprolol group). Furthermore, in the metoprolol group, 13% of patients required treatment for hypotension and 34% required treatment for bradycardia.

Adverse events related to the use of statins include rhabdomyolysis and myopathies at very low rates. In one study, the incidence of rhabdomyolysis was between 0.04% and 0.2%, and the incidence of myopathy was between 0.1% and 0.5%. When 211 statin users undergoing elective vascular surgery were studied, no cases of rhabdomyolysis were found and there were no statistically significant differences in creatinine kinase levels between statin and nonstatin users.

The validity and general application of some key β-blocker trials have been called into question recently. The DIPOM (Diabetic Postoperative Mortality and Morbidity) trial found no reduction in cardiac events in 921 patients who received 100 mg of extended-release oral metoprolol or placebo for 4 to 5 days perioperatively. The median heart rate was reduced by 11% in the treatment group (83 beats per minute [bpm] in the placebo group and 74 bpm in the metoprolol group on postoperative day 1). The authors concluded that “the evidence is insufficient to recommend perioperative β-blockers for patients at risk of cardiac morbidity.”

In the recent British (Perioperative Beta-Blockade) trial examined the effects of oral metoprolol on myocardial ischemia (72 bpm using Holter monitoring) and cardiac events in 103 patients undergoing infrarenal vascular surgery. The study did not show a benefit of cardioprotection; however, hospital stay was 2 days shorter in the metoprolol group—an important outcome.

In the MaVS (Metoprolol after Vascular Surgery) study, 496 patients undergoing vascular surgery were enrolled in a randomized trial of metoprolol versus placebo. In MaVS, the average heart rate postoperatively was reduced from 79.1 bpm in the placebo group to 69.4 bpm in the metoprolol group; intraoperative bradycardia and hypotension were more common in the group treated with metoprolol. The investigators found that metoprolol did not reduce 30-day and 6-month postoperative cardiac event rates, and suggested that “prophylactic use of perioperative β-blockers in all vascular patients is not indicated.” However, the study had included a majority of patients undergoing regional or combined regional/general anesthesia, and the patient population was relatively healthy.

Other studies support the use of perioperative β-blockade in appropriate surgical patients. In the CARP (Coronary Artery Revascularization Prophylaxis) trial, routine aggressive medical therapy with β-blockers, statins, and aspirin produced equivalent outcomes in patients undergoing vascular surgery when compared with prophylactic coronary revascularization (coronary artery bypass surgery or percutaneous coronary intervention). In a large retrospective study of 663,635 patients, those with the highest cardiac risk scores benefited from perioperative β-blockade.

In another retrospective study, the use of high doses of β-blockers (6.6 mg/kg of oral metoprolol per day, or the equivalent) and lower heart rates were associated with reduced myocardial ischemia and a release of troponin T in vascular surgery patients.

The results of the POISE (Perioperative Ischemic Evaluation) trial, involving almost 10,000 patients, were reported at the 2007 AHA meeting as this review went to press. The findings indicate that fixed-dose treatment with long-acting metoprolol started immediately before surgery reduce myocardial ischemia, but increase stroke. We therefore believe that it is preferable to begin β-blockade in advance of surgery, or perhaps to titrate based on the hemodynamics of each patient.

**Management of the Case Presented**

To review the case presented, the 5 steps outlined in the 2007 ACC/AHA guidelines for perioperative evaluation for noncardiac surgery are considered (Figure).

**Step 1: Is this an emergency noncardiac surgery?** Although this case is not an emergent procedure, the patient’s history indicates that her vascular disease is getting progressively worse. The clinician should bear in mind that any recommendations that may delay surgery should be weighed against the risk for progressive ischemia to the left lower extremity.

**Step 2: Does the patient have active cardiac conditions?** This patient does not have any active cardiac conditions (unstable coronary syndromes, uncomplicated heart failure, significant arrhythmias, or severe valvular disease).

**Step 3: Is this a low-risk surgery?** No; peripheral vascular surgery is considered a high-risk surgery.

**Step 4: Does the patient have good functional capacity (metabolic equivalent of the task [MET] level ≥ 2) without symptoms?** Ambulation is progressively difficult for this patient. She is unable to climb a flight of stairs and would be considered to have a MET level below 4 (Table).

**Step 5: How many clinical risk factors does the patient have?** At this point in the algorithm, further management is determined by the patient’s clinical risk factors and type of surgery. For this patient (with poor functional status, 2 risk
Step 1

Need for emergency noncardiac surgery?

Yes (Class I, LOE C)

Operating room

Perioperative surveillance and postoperative risk stratification and risk-factor management

No

Step 2

Active cardiac conditions?

Yes (Class I, LOE B)

Evaluate and treat per ACC/AHA guidelines

Consider perioperative monitoring

No

Step 3

Low-risk surgery

Yes (Class I, LOE B)

Proceed with planned surgery

Step 4

Good functional capacity (MET level ≥ 4) without symptoms?

Yes (Class I, LOE B)

Proceed with planned surgery

Step 5

No or unknown

3 or more clinical risk factors?

Yes (Class I, LOE B)

Proceed with planned surgery with HR control (Class IIa, LOE B) or consider noninvasive testing (Class IIb, LOE B) if it will change management

1 or 2 clinical risk factors?

Yes (Class I, LOE B)

Vascular surgery

Intermediate-risk surgery

Vascular surgery

Intermediate-risk surgery

No clinical risk factors

Class I, LOE B

Consider testing if it will change management

Proceed with planned surgery

Vascular surgery

Intermediate-risk surgery

Class I, LOE B

Proceed with planned surgery

Figure. A 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 older.

Step 1: Need for emergency noncardiac surgery?

- Yes (Class I, LOE C): Operating room
- No

Step 2: Active cardiac conditions?

- Yes (Class I, LOE B): Evaluate and treat per ACC/AHA guidelines
- No

Step 3: Low-risk surgery

- Yes (Class I, LOE B): Proceed with planned surgery
- No

Step 4: Good functional capacity (MET level ≥ 4) without symptoms?

- Yes (Class I, LOE B): Proceed with planned surgery
- No

Step 5: No or unknown

- 3 or more clinical risk factors: Proceed with planned surgery with HR control (Class IIa, LOE B) or consider noninvasive testing (Class IIb, LOE B) if it will change management
- 1 or 2 clinical risk factors: Consider testing if it will change management
- No clinical risk factors: Proceed with planned surgery

Factors, and undergoing vascular surgery), the 2007 revision of the AHA/ACC guidelines recommend that she either directly undergo surgery with control of heart rate (presumably with β-blockade) or undergo noninvasive testing (if it will change patient management). The AHA/ACC guidelines were written to support clinicians who might elect either option, since the 2006 study by Poldermans et al25 and the CARP trial26 both suggested similar outcomes with the use of medical therapies (with heart rate control) and a strategy that includes stress testing (followed by coronary revascularization in appropriate situations). The guidelines suggest that control of heart rate is a somewhat more recommended strategy (IIa, level of evidence B) compared to noninvasive testing (IIb, level of evidence B).

If our patient had unstable angina, the step 2 recommendation is that she would be treated according to separate AHA/ACC guidelines for unstable angina, which would then potentially include noninvasive testing, coronary catheterization, and/or myocardial revascularization.

Conclusion

Anesthesiologists are often asked to provide a preoperative cardiac evaluation of patients before noncardiac surgery. The goals of such evaluations should include an assessment of the patient’s current cardiovascular, medical, and surgical status; an estimation of functional capacity; and an estimation of the risk associated with the surgical procedure. After weighing the risks and benefits, the clinician must decide whether to recommend that the patient proceed to surgery, undergo a further evaluation of coronary artery disease with appropriate noninvasive stress testing or coronary angiography with the potential for revascularization, or be medically optimized before proceeding to surgery. A patient’s management may include several of the aforementioned pathways of management.

To reduce the uncertainty in determining the most beneficial and cost-effective method to evaluate patients, the ACC/AHA has published guidelines. It is important to make the distinction that these are guidelines, not standards or mandates. Practitioners must use their clinical judgment when deciding on appropriate workups for patients that are in line with the goals of the patient, family, surgeon, primary care provider, and cardiologist for short- and long-term medical management. At each step, the clinician should ask if the information being sought would influence the perioperative or long-term medical management of the patient. In light of an increasing number of studies questioning the benefits of coronary revascularization in reducing perioperative cardiac events (as opposed to aggressive medical management), we are faced with several pathways to providing care. Ultimately, wise management depends on good communication between physicians and patients. In the absence of any agreement about the superiority of one line of
management versus another (medical management vs. revascularization), physicians should rely on their clinical judgment and local experience to supplement published, evidence-based guidelines. Documentation of all conversations, results, and decisions is essential.

References

Post-test

1. A 58-year-old woman with a history of myocardial infarction 2 years previously, diabetes mellitus, and hypertension is scheduled for a right thoracotomy and lung resection for recently diagnosed lung cancer. She has no angina or congestive heart failure. She reports she is the caretaker for her elderly mother. The next appropriate step is to:
   a. proceed to surgery
   b. delay the case for further noninvasive stress testing
c. ensure that the patient is on appropriate perioperative medications (β-blocker and statin), then proceed to surgery
d. recommend cardiac catheterization and possible revascularization

2. Statins may produce cardioprotection by the following mechanisms, except by decreasing:
   a. heart rate
d. endothelial dysfunction

3. β-selective β-blockers reduce all of the following, except:
   a. coronary vasodilation
c. fibrinolytic activity
c. attraction of neutrophils and other leukocytes, in addition to platelet aggregation, around areas of coronary inflammation
d. diastolic dysfunction, an early sign of ischemia

4. The following classes of drugs may be cardioprotective in patients with coronary disease undergoing surgery, except:
   a. sodium nitroprusside
   b. aspirin
c. metoprolol
d. atorvastatin

5. Perioperative ischemic events are the result of:
   a. increased vascular inflammation
   b. imbalance in the oxygen supply and demand of coronary vessels
c. catecholamine-induced sympathetic stimulation
d. all of the above

6. Which of the following is a true statement regarding the POBBLE (Perioperative Beta-Blockade) trial?
   a. It proved that oral metoprolol is beneficial for patients undergoing all types of vascular surgery.
b. It showed that hospital stay could be shortened.
c. It proved nothing.
d. It dealt only with the intravenous use of β-blockade.

7. Which of the following is a true statement regarding the MaVS (Metoprolol after Vascular Surgery) study?
   a. It looked only at patients with cardiac disease.
b. It indicated that perioperative β-blockade is not useful for all vascular patients.
c. It covered only patients undergoing general anesthesia.
d. It showed that cardiac events are reduced both at 30 days and 6 months postoperatively in all patients.

8. Guidelines are:
   a. standards set for the community practitioner
   b. mandates for all cardiac anesthesiologists
   c. presented after reasoning by several professional organizations
d. none of the above

9. A patient with a history of revascularization within the previous 5 years:
   a. requires further stress testing
   b. may not need to undergo further investigation if he/she has no signs or symptoms of ischemia
c. mandates the prophylactic administration of statins and metoprolol
d. can be managed by ignoring the medical history

10. The major clinical predictors for cardiac risk are least likely to include:
    a. decompensated congestive heart failure
   d. atrial fibrillation with a ventricular response rate of 100
   b. severe valvular disease
   c. previous successful coronary artery bypass graft

Table. Estimated Energy Requirements for Various Activities

<table>
<thead>
<tr>
<th>Activity</th>
<th>METs</th>
<th>Calories</th>
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<tbody>
<tr>
<td>Walking indoors</td>
<td>2</td>
<td>100</td>
</tr>
<tr>
<td>Walking on level ground at 3 mph</td>
<td>3</td>
<td>150</td>
</tr>
<tr>
<td>Running</td>
<td>6</td>
<td>250</td>
</tr>
<tr>
<td>Cycling</td>
<td>7</td>
<td>350</td>
</tr>
<tr>
<td>Swimming</td>
<td>8</td>
<td>450</td>
</tr>
</tbody>
</table>

MET, metabolic equivalent of the task.