Study Activity: Perioperative Cardiac Risk Management

Peter Kallas, MD
Assistant Professor of Medicine, Medical Director, Perioperative Medicine Consult Service, Northwestern University, Feinberg School of Medicine, Chicago, IL.

Instructions
This study activity consists of 6 sections. Each section contains a question and then didactic content. Explanations are provided for each answer to help identify areas you may need to focus on and increase your overall knowledge of the topic; they are not part of the CME test.

To participate, read each question and select your answer. If the answer is incorrect, a red box will appear with the explanation. When you select the correct answer, a green box will appear with the explanation, followed by the didactic content. The didactic content will not appear until the corresponding question(s) has been answered correctly. You may want to select the wrong answers as well to see the explanation for why they are incorrect.

All questions need to be answered correctly to move to the CME post-test and evaluation.

Section 1: Management of Patients at Elevated Perioperative Risk for Cardiac Events

Question 1
A 69-year-old male with diabetes with a creatinine of 3 mg/dL, who had a drug-eluting stent placed in his mid-right coronary artery 9 months ago, must now undergo a partial colon resection for diverticulitis in 7 days. Your medical student recommends 4 possible therapies that might reduce the risk of perioperative cardiac events in this patient, but he is unsure whether there is sufficient research to back up his claim. Which of the following statements is MOST CORRECT?

A. Clonidine has not been studied extensively for this indication.

Incorrect. Multiple studies have addressed the use of this drug in preventing perioperative cardiac events. The mechanism is thought to be the blunting of sympathetic output during the perioperative period.

B. ß blockers have not been studied extensively for this indication.

Incorrect. Many observational studies show a significant reduction in perioperative cardiac events in patients who are on chronic ß blockade.

C. Aspirin has not been studied extensively for this indication.

Incorrect. Aspirin and/or clopidogrel withdrawal perioperatively within the 12-month interval after drug-eluting stent placement has been shown to significantly increase the risk of perioperative cardiac events, including in-stent thrombosis.

D. Nitrates have not been studied extensively for this indication.

Correct! The use of nitrates to prevent perioperative cardiac events has not been studied extensively.
Management of Patients at Elevated Perioperative Risk for Cardiac Events

The most extensive clinical research has been performed with the β blockers atenolol, bisoprolol (mainly a European drug), metoprolol, and extended-release metoprolol. Early positive studies by Mangano et al1 and the DECREASE (Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography) studies2,3 have recently come under scrutiny since the publication of the DIPOM (Diabetic Postoperative Mortality and Morbidity) trial,4 the MaVS (Metoprolol After Vascular Surgery) trial5, and the early results of the POISE (Perioperative Ischemic Evaluation) trial.6,7

The American College of Cardiology/American Heart Association (ACC/AHA) guidelines8 published online in September of 2007 for the perioperative management of cardiac risk factors recommends that a β blocker should be considered for those patients undergoing an intermediate- or high-risk noncardiac surgery if they have at least 2 clinical risk factors that were derived from the Revised Cardiac Risk Index.9 These factors include a history of ischemic heart disease, a history of congestive heart failure, a history of stroke or transient ischemic attack, diabetes mellitus, or renal insufficiency.

It is fairly well accepted that β blockers are indicated for high-risk patients (those with ≥2 clinical risk factors) undergoing intermediate-risk or vascular surgery and that they should not be considered in low-risk surgeries. We also do not recommend starting β blockers in patients without clinical risk factors, regardless of the risk of surgery. Lindenauer et al demonstrated in his database analysis of 782 000 patients that β blockers given perioperatively in a low-risk population could possibly be detrimental (Figure 1).10 The initiation of β blockers for patients with only 1 clinical risk factor remains controversial. It is unclear whether patients with 1 clinical risk factor undergoing vascular surgery benefit from β blockade.

Figure 1. Adjusted OR for In-Hospital Death Associated with Perioperative β Blocker Therapy Among Patients Undergoing Major Noncardiac Surgery*

<table>
<thead>
<tr>
<th>Propensity-Matched Cohort</th>
</tr>
</thead>
</table>
| RCRI score 0            | 1.43 (1.29–1.58)  
| RCRI score 1            | 1.13 (0.99–1.30)  
| RCRI score 2            | 0.90 (0.75–1.08)  
| RCRI score 3            | 0.71 (0.56–0.91)  
| RCRI score >4           | 0.57 (0.42–0.76)  

<table>
<thead>
<tr>
<th>Entire Study Cohort</th>
</tr>
</thead>
</table>
| RCRI score 0        | 1.36 (1.27–1.45)  
| Hypertension        | 0.96 (0.82–1.13)  
| RCRI score 1        | 1.09 (1.01–1.19)  
| Diabetes            | 1.28 (1.10–1.50)  
| Ischemic heart disease | 1.12 (0.95–1.31)  
| Renal insufficiency | 1.03 (0.82–1.23)  
| Cerebrovascular disease | 1.01 (0.76–1.35)  
| High-risk surgery   | 0.94 (0.84–1.05)  
| RCRI score 2        | 0.88 (0.80–0.98)  
| RCRI score 3        | 0.71 (0.63–0.80)  
| RCRI score >4       | 0.58 (0.50–0.67)  

OR for Death in the Hospital (95% confidence interval)

*According to the RCRI score and the presence of other risk factors in the propensity-matched cohort and the entire study cohort. Open boxes represent patient subgroups within the listed RCRI category. OR = odds ratio; RCRI = Revised Cardiac Risk Index.

The overall benefit of starting a \( \beta \) blocker within 24 hours of surgery is unclear. There is a concern that this approach may increase the risk for perioperative stroke while still decreasing the risk of cardiac events. The risk of stroke may be greater in certain populations, such as the elderly and those with cerebrovascular disease. Given the uncertainty, be extremely judicious when starting \( \beta \) blockers within 1 day of surgery and err on the side of avoiding hypotension (Table 1).\(^3\text{-}^6,^{11,12}\)

### Table 1. Summary of Stroke Risk Associated with Perioperative \( \beta \) Blockers

<table>
<thead>
<tr>
<th>Study</th>
<th>BB Type</th>
<th>Days Prior</th>
<th>CVA, Placebo</th>
<th>CVA , BB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poldermans et al(^3)</td>
<td>PO bisoprolol</td>
<td>37</td>
<td>0/53</td>
<td>0/59</td>
</tr>
<tr>
<td>Wallace et al(^{11})</td>
<td>IV atenolol</td>
<td>0</td>
<td>1/101</td>
<td>4/99</td>
</tr>
<tr>
<td>DiPOM(^4)</td>
<td>PO metoprolol CR/XL</td>
<td>1</td>
<td>0/459</td>
<td>2/462</td>
</tr>
<tr>
<td>MaVS(^5)</td>
<td>PO metoprolol</td>
<td>0</td>
<td>4/250</td>
<td>5/246</td>
</tr>
<tr>
<td>POBBLE(^{12})</td>
<td>PO/IV metoprolol</td>
<td>1</td>
<td>0/44</td>
<td>1/53</td>
</tr>
<tr>
<td>POISE(^6)</td>
<td>PO metoprolol CR</td>
<td>0</td>
<td>19/4177</td>
<td>41/4174</td>
</tr>
</tbody>
</table>

\( \beta \) = \( \beta \) blocker; CVA = cerebrovascular accident; CR = continued release; DiPOM = Diabetic Postoperative Mortality and Morbidity; IV = intravenous; MaVS = Metoprolol After Vascular Surgery; PO = orally; POISE = Perioperative Ischemic Evaluation; POBBLE = Perioperative \( \beta \)-Blockade; XL = extended release.

Data from Poldermans et al\(^3\); Juul et al\(^5\); Yang et al\(^6\); Nainggolan\(^7\); Wallace et al\(^{11}\); and POBBLE Trial Investigators.\(^{12}\)

\( \beta \) blockers should be titrated to a heart rate of less than 65 bpm days to weeks in advance of surgery. This study by Poldermans et al shows the effect of aggressive heart rate control with \( \beta \) blockade on perioperative cardiac outcomes (Figure 2).\(^{13}\)

#### Figure 2. The Relation Between Heart Rate and Perioperative Cardiovascular Events

Reprinted with permission from Poldermans et al. J Am Coll Cardiol. 2006;48:964-969.\(^{13}\)
Long acting β blockers may have an advantage over short-acting ones, as seen in this large Canadian database analysis comparing short-acting metoprolol to atenolol (Figure 3).\textsuperscript{14}

Theoretically, long-acting β blockers may have a lower potential for β blocker withdrawal as compared to their short-acting counterparts (Table 2).\textsuperscript{8}

![Figure 3. Absolute Risk of Death in the Hospital Within 30 Days of Elective Surgery Comparing Atenolol with Metoprolol](image)

Data expressed as cumulative number of deaths/1000 admissions on corresponding day. \(P\) values compare death rate with atenolol relative to metoprolol for entire interval and for consecutive 14 day intervals, using log-rank test. Reprinted with permission from Redelmeier et al. \textit{BMJ}. 2005;331:932.\textsuperscript{14}

| Table 2. Recommendations for Perioperative β-Blocker Therapy Based on Published Randomized Clinical Trials |
|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|
| Surgery                                          | Clinical Risk Factors, \(n\)                      | ≥1 Clinical Risk Factor                          | CHD or High Cardiac Risk                         | Patients Currently Taking β 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\textsuperscript{*} | 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                  |

\textsuperscript{*} Applies to patients found to have coronary ischemia on preoperative testing.

Ellipses (.) indicate that data were insufficient to determine a class of recommendation or level of evidence.

CHD = coronary heart disease.

Reprinted with permission from Fleisher et al. \textit{Circulation}. 2007;116:e418-e499.\textsuperscript{8}
Clonidine has been shown to have value in cardiac risk reduction perioperatively. The mechanism of action is thought to lie in clonidine’s ability to blunt the surge in adrenergic output of the central nervous system during the stress of surgery. In a small 2004 study, acutely starting clonidine seemed beneficial. There are no formal recommendations regarding dose titration or timing and duration of therapy. There is a randomized, placebo-controlled trial of clonidine that started in June 2006 to test whether “the addition of clonidine to chronic β blockade will reduce mortality and cardiac morbidity among intermediate-to-high risk patients undergoing noncardiac surgery.” Currently, the ACC/AHA guidelines recommend considering treating patients with known coronary artery disease (CAD) or at least 1 clinical risk factor undergoing surgery with an α2-agonist.

The evidence to support aspirin use in this patient lies in the studies that show the detrimental effects of aspirin and clopidogrel withdrawal in cardiac patients with a drug-eluting stent placed within 1 year of surgery. Little has been done to look at nitrates perioperatively. Those studies that have looked at intraoperative intravenous nitroglycerine have not shown an effect on perioperative ischemia in noncardiac surgery.

In summary, β blockers are indicated for patients already taking them and those who have 2 or more clinical risk factors and are undergoing intermediate-risk or vascular surgery. The benefit of β blockade in patients who have 1 risk factor and are undergoing vascular surgery is unclear. Start the β blocker at least 1 week prior to surgery. Starting the medication on the day of surgery may cause more harm than good. If you feel that you need to start a β blocker within 24 hours of surgery, be extremely judicious with it. Titrate the β blocker to a heart rate of less than 65 bpm. It is unclear which β blocker is best. We recommend a longer acting medication like atenolol.

Currently, we believe there are not enough data to recommend treating patients with an α2-agonist. However, the ACC/AHA guidelines recommend considering treating patients with known CAD or at least 1 clinical risk factor undergoing surgery with an α2-agonist. Eventually, results from the EPIC (Evaluating Perioperative Ischemia Reduction by Clonidine) trial will help to clarify this issue.

Continue aspirin as long as possible in patients who have a coronary stent.

Section 2: The Role of Statins in Perioperative Cardiac Risk Reduction

Question 2

Chai is evaluated by the consult service after he sustained a fracture of the left femoral neck while ice fishing. He is a 65-year-old with a medical history significant for congestive heart failure, hypertension, and 60-pack-years of cigarette smoking. His baseline creatinine is 2.5 mg/dL and his low-density lipoprotein (LDL) level is 120 mg/dL, giving him a Framingham Risk Score of 17% for 10 years. Your astute medical student asks whether the patient should be started on a statin before his surgery. He has 1 known clinical risk factor. Which of the following statements is the MOST CORRECT response?

A. Yes. Because he has 1 risk factor and is undergoing an intermediate-risk procedure, a statin may help.

Correct! The ACC/AHA guidelines recommend considering treating patients with statins if they have 1 or more clinical risk factors and are undergoing intermediate-risk surgery.

B. No. There are only animal data that evaluate the use of statins in this setting.

Incorrect. There are animal data, in addition to many human observational studies and 1 randomized controlled trial evaluating statins in the perioperative setting.

C. Yes. Based on the National Cholesterol Education Program (NCEP) guidelines, his LDL should be 70 mg/dL or less.

Incorrect. The guidelines recommend that a patient with 2 or more risk factors or a 10-year risk of 10% to 20% should have an LDL lower than 130 mg/dL with an optional goal of less than 100 mg/dL.
D. Yes. Because this is a high-risk surgery, statins are indicated.

Incorrect. Although statins are likely indicated for most high-risk surgeries, an orthopedic surgery is usually considered intermediate risk.

The Role of Statins in Perioperative Cardiac Risk Reduction

Statins are considered by many to be the next great hope in preventing perioperative cardiac events. Studies have shown a 78% and 29% reduction in perioperative mortality for patients undergoing vascular surgery\(^2\)\(^1\) and noncardiac surgery,\(^2\)\(^2\) respectively (Table 3).\(^8\)

<table>
<thead>
<tr>
<th>Study, yr</th>
<th>Design</th>
<th>n, (Statin/Total)</th>
<th>Surgery</th>
<th>Perioperative Complications</th>
<th>Adjusted OR (95% CI) Perioperative Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lindenauer et al, 2004*</td>
<td>Retrospective/</td>
<td>77 082/780 591</td>
<td>Major noncardiac</td>
<td></td>
<td>0.62 (0.58–0.67)</td>
</tr>
<tr>
<td></td>
<td>administrative</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poldermans et al, 2003†</td>
<td>Case-control</td>
<td>160 cases, 320</td>
<td>Major vascular</td>
<td></td>
<td>0.22 (0.1–0.47)</td>
</tr>
<tr>
<td></td>
<td>controls</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>O’Neil-Callahan et al, 2005‡</td>
<td>Retrospective</td>
<td>526/1163</td>
<td>Major vascular</td>
<td>0.52 (0.35–0.77)</td>
<td></td>
</tr>
<tr>
<td>Kertai et al, 2004§</td>
<td>Retrospective</td>
<td>162/570</td>
<td>AAA surgery</td>
<td>0.24 (0.1–0.7)</td>
<td>(Death or MI)</td>
</tr>
<tr>
<td>Landesberg et al, 2003†</td>
<td>Retrospective</td>
<td>502</td>
<td>Major vascular</td>
<td></td>
<td>0.54 (0.26–1.11)</td>
</tr>
<tr>
<td></td>
<td>administrative</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kennedy et al, 2005¶</td>
<td>Retrospective/</td>
<td>815/2031 symptomatic</td>
<td>Carotid endarterectomy</td>
<td>0.55 (0.32–0.95)</td>
<td>(Stroke or death)</td>
</tr>
<tr>
<td></td>
<td>administrative</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>665/1252 asymptomatic</td>
<td></td>
<td>Carotid endarterectomy</td>
<td>0.54 (0.13–2.24)</td>
<td>(Stroke or death)</td>
</tr>
<tr>
<td>Ward et al, 2005#</td>
<td>Retrospective</td>
<td>72/446</td>
<td>Infrainguinal vascular surgery</td>
<td>0.36 (0.14–0.93)</td>
<td></td>
</tr>
<tr>
<td>McGirt et al, 2005**</td>
<td>Retrospective</td>
<td>657/1566</td>
<td>Carotid endarterectomy</td>
<td>0.35 (0.15–0.85)</td>
<td>(Stroke)</td>
</tr>
</tbody>
</table>


AAA = abdominal aortic aneurysm; CI = confidence interval; MI = myocardial infarction; OR = odds ratio.

The one randomized placebo-controlled trial by Durazzo et al\(^2\)\(^3\) was a single center, prospective, double-blind clinical trial of atorvastatin 20 mg daily versus placebo in 100 patients undergoing noncardiac arterial vascular surgery. The intervention group received atorvastatin for at least 2 weeks prior to surgery, and it was continued for at least 45 days. In this small study, the rates of the primary end point—a composite of death from cardiovascular causes, nonfatal acute myocardial infarction (MI), ischemic stroke, or unstable angina at 6 months—were 26% for the placebo group and 8% for the atorvastatin-treated patients. The difference was statistically different. Three patients in the atorvastatin group had cardiac events in the first 10 days following surgery as compared to 11 patients in the placebo group. Thirteen of the 17 total cardiac events took place within the first 10 days of surgery.

Though no formal guidelines exist for starting statins preoperatively, statins have been shown to affect cardiac C-reactive protein (CRP) levels within 8 weeks\(^2\)\(^4\) and improve endothelial function\(^2\)\(^5\) within 1 month of starting the drug.

Most package inserts for statins recommend caution in continuing these drugs perioperatively for fear of exacerbating its effects on the liver and musculature. However, Schouten et al did not show an increase in...
incidence of myopathy or rhabdomyolysis in 981 patients undergoing major vascular surgery.\textsuperscript{26} For patients undergoing vascular surgery, we advocate starting statins in the perioperative period, at least 2 weeks in advance of surgery if possible, to take advantage of their rapid-acting pleiotropic effects. The statin should be continued for the long term given the well-documented benefits of chronic therapy. This recommendation mirrors the ACC/AHA 2007 perioperative guidelines that state “for patients undergoing vascular surgery with or without clinical risk factors, statin use is reasonable.”\textsuperscript{8} The risk of harm overall appears to be minimal and certainly less than the likelihood of benefit. Moreover, patients already taking statins should definitely not have their statins discontinued if at all possible.

For patients undergoing major nonvascular surgery, first satisfy yourself that the patient does not have an indication for statin therapy based on current NCEP guidelines (Table 4).\textsuperscript{27} If there is no clear indication for the initiation of statin therapy based on NCEP guidelines, we endorse the recently released ACC/AHA perioperative guidelines that state that patients with 1 or more of the clinical risk factors who are undergoing intermediate-risk procedures could consider statin therapy. Moreover, we fully support the ACC/AHA’s strongest recommendation that patients who are already receiving statins and are undergoing noncardiac surgery should not have their statin discontinued.

<table>
<thead>
<tr>
<th>Table 4. Proposed Modifications to NCEP Guidelines for Statin Therapy</th>
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<tbody>
<tr>
<td><strong>LDL-C Goal, mg/dL</strong></td>
</tr>
<tr>
<td>High risk and very high risk</td>
</tr>
<tr>
<td>Moderately high risk</td>
</tr>
</tbody>
</table>

\textsuperscript{*}CHD: History of MI, unstable angina, stable angina, coronary artery procedures, or evidence of clinically significant myocardial ischemia.
\textsuperscript{†}CHD risk equivalents: Clinical manifestations of noncoronary forms of atherosclerotic disease (peripheral arterial disease, abdominal aortic aneurysm, and carotid artery disease), diabetes, and 2+ risk factors with 10-year risk for CHD >20%.
\textsuperscript{‡}Risk factors: Cigarette smoking, hypertension (BP ≥140/90 mm Hg or on antihypertensive medication), low HDL-C (<40 mg/dL), family history of premature CHD (CHD in male first-degree relative <55 years of age; CHD in female first-degree relative <65 years of age), and age (men ≥45 years; women ≥55 years).

CHD = coronary heart disease; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; MI = myocardial infarction. Adapted with permission from Grundy et al. Arterioscler Thromb Vasc Biol. 2004;24:e149-e161.\textsuperscript{27}

It is unclear which statin is best, what is the safest and most effective starting dose, when the statin should be started, and exactly how to monitor patients in the perioperative period. Given the lack of evidence to guide us, it is prudent to watch patients very closely in the postoperative time period and have a low threshold for checking creatine kinase and liver function tests, especially if complications, such as acute renal failure, hepatic failure, or sepsis, ensue.

In summary, we recommend continuing statins for any patient already on them chronically. Furthermore, we recommend starting a statin at least 2 weeks ahead of time for any patient who should be treated with one based on the NCEP guidelines, those undergoing vascular surgery, and those with 1 or more clinical risk factors who are undergoing intermediate surgery. Starting a statin in the acute setting appears to be safe. Follow the patients closely in the postoperative period for any signs of statin side effects or changes in clinical status.
Question 3

A 75-year-old woman, Ima, is scheduled for an open repair of a 6-cm abdominal aortic aneurysm. She has a history of insulin-dependent diabetes and a 2-vessel coronary bypass surgery 4 years ago. She undergoes a preoperative dobutamine stress echo, which shows a moderate-size inferior wall defect with dobutamine infusion only. Her coronary angiogram shows an 80% lesion in her native right coronary artery with no distal bypass grafting to this vessel. You discuss medical options with Ima, and she asks you which treatment or factor has the greatest likelihood of reducing her risk of a perioperative MI?

A. Placement of a drug-eluting stent

Incorrect. Recent studies show no impact on cardiac outcomes with this strategy. Rather, the placement of drug-eluting stents preoperatively poses the risk of stent thrombosis if aspirin and/or clopidogrel are discontinued.

B. Placement of a bare-metal stent

Incorrect. Recent studies show no impact on cardiac outcomes with this strategy. Rather, the placement of bare-metal stents preoperatively poses the risk of stent thrombosis if aspirin and/or clopidogrel are discontinued.

C. Bypass grafting of the current right coronary stenosis

Incorrect. Recent studies have not demonstrated benefit with this approach in preventing perioperative cardiac events.

D. Her history of bypass grafting less than 5 years ago reduced her risk.

Correct! A retrospective study has shown that a history of coronary bypass surgery up to 6 years in the past can keep the cardiac event rate perioperatively as low as 0.6%.

Coronary Interventions in Preoperative Patients with Documented Ischemia on Noninvasive Cardiac Testing

There has yet to be a study that has shown that revascularization, whether with balloon angioplasty, stenting, or bypass surgery, can reduce the risk of perioperative cardiac events. In fact, the contrary has been shown in recent studies.

The CARP (Coronary Artery Revascularization Prophylaxis) trial demonstrated no survival benefit in revascularizing patients who had significant 1- or 2-vessel coronary disease prior to major vascular surgery, as shown in Figure 4.28.
The DECREASE-V study added to this literature by prospectively evaluating a sicker population of 101 patients with 2- or 3-vessel disease undergoing major vascular surgery. Forty-nine of the patients were revascularized preoperatively: 17 underwent coronary artery bypass graft and 32 had a percutaneous intervention. All patients with new stents received dual antiplatelet therapy, which was continued through surgery. There was no difference in all-cause mortality at 30 days or 1 year, as shown in Figure 5.

Figure 4. Long-Term Survival Among Patients Assigned to Undergo Coronary-Artery Revascularization or No Coronary-Artery Revascularization Before Elective Major Vascular Surgery

![Graph showing survival rates for patients with and without coronary artery revascularization.](image)

At risk, n
Revascularization 226 175 113 65 18 7
No revascularization 229 172 108 55 17 12


Figure 5. Incidence of All-Cause Death or MI During 1-Year Follow-Up *

![Graph showing incidence of all-cause death or MI.](image)

*According to the Allocated Strategy in Patients with ≥3 Cardiac Risk Factors with Extensive Stress-Induced Ischemia. MI = myocardial infarction.

Because surgery is a prothrombotic state, it is possible that stenting before major surgery, particularly with a drug-eluting stent, could create a nidus for clot. A clot could lead to an MI, making stenting potentially more harmful than helpful, especially if antiplatelet therapy is withheld. A prospective trial evaluating the outcomes of 103 patients with coronary stents (mix of bare-metal and drug-eluting stents) placed within 1 year of a non-cardiac surgery illustrates this risk. Aspirin and clopidogrel were continued through 87% and 43% of the surgeries, respectively. Twenty-one percent of the patients had an MI and 8.8% died from cardiac causes; both outcomes were relatively high. The duration of wait time did matter, as seen in the graphs below (Figure 6).

One theory is that the myocardial territory that one typically considers susceptible to injury due to a significant coronary stenosis may not be the territory that suffers the perioperative MI. The smaller, softer plaque that is not identified on coronary angiography may be even more vulnerable to rupture and thrombosis. Dawood et al analyzed autopsy specimens on 42 perioperative fatal MI patients and found that 55% of these patients had plaque disruption as the cause of their MI and not demand ischemia. In a small autopsy study, Poldermans et al showed that 9 of their 16 patients who died of a perioperative MI had an infarct in the nonischemic territory, as shown in their preoperative dobutamine stress echo, possibly indicating that it may not be the clinically significant stenoses that are causing the MIs.

The fact that a patient with significant coronary disease wants or needs a noncardiac surgery should not influence whether he is revascularized. You should ask yourself, would this patient be revascularized for the sake of overall prognosis, independent of the upcoming surgery? The recent ACC/AHA guidelines state, “The present review of the literature suggests that PCI [percutaneous coronary intervention] 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.”

On the other hand, Eagle et al looked at 3768 patients retrospectively who had a cardiac catheterization and a subsequent noncardiac surgery an average of 4.1 years later. They showed that a history of coronary bypass surgery reduces the cardiac event rate to 0.6% for noncardiac surgeries in the subsequent 6 years (Table 5).
Hence, a history of revascularization proves beneficial when assessing one’s risk of a perioperative cardiac event, but we do not recommend revascularization for asymptomatic patients to “get the patient through” a noncardiac surgery. Only patients experiencing an acute coronary syndrome should be evaluated for revascularization.

In summary, coronary revascularization should only take place if the patient has indications for it separate from the upcoming surgery. Do not send patients for revascularization to “optimize” them for noncardiac surgery.

Section 4: Perioperative Management of Antiplatelet Therapy for Patients with Cardiac Stents

Question 4

The outpatient consult team is evaluating Mr. Jones, who is scheduled for a total hip replacement. While reviewing his history, the resident discovers that Mr. Jones had a drug-eluting stent placed in his left anterior descending artery recently. Your resident wants to “clear” him for surgery but asks you how long after the stent was initially placed should we wait before allowing the orthopedist to discontinue the dual antiplatelet therapy. Which answer is MOST CORRECT?

A. 1 month

Incorrect. The ACC/AHA recommends waiting 12 months before discontinuing dual antiplatelet therapy because of the excess risk of stent thrombosis during this interval.

B. 3 months

Incorrect. The ACC/AHA recommends waiting 12 months before discontinuing dual antiplatelet therapy because of the excess risk of stent thrombosis during this interval.

C. 6 months

Incorrect. The ACC/AHA recommends waiting 12 months before discontinuing dual antiplatelet therapy because of the excess risk of stent thrombosis during this interval.

D. 12 months

Correct! It is recommended by the ACC/AHA the physicians should wait 12 months before considering discontinuation of dual antiplatelet therapy prior to elective surgery.

Table 5. How Long Does Prior CABG Protect Against Perioperative MI or Death After Noncardiac Surgery

<table>
<thead>
<tr>
<th>Years from CABG to Surgery</th>
<th>MI Risk, %</th>
<th>Death Risk, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–2</td>
<td>0.7</td>
<td>1.7</td>
</tr>
<tr>
<td>2–4</td>
<td>1.1</td>
<td>0.6</td>
</tr>
<tr>
<td>4–6</td>
<td>0.6</td>
<td>1.7</td>
</tr>
<tr>
<td>&gt;6</td>
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CABG = coronary artery bypass graft; MI = myocardial infarction. Adapted with permission from Eagle et al. Circulation. 1997;96:1882-1887.33

Perioperative Management of Antiplatelet Therapy for Patients with Cardiac Stents

The ACC/AHA recommendation is to continue dual antiplatelet therapy (aspirin and clopidogrel) for 12 months after the placement of a drug-eluting stent and to postpone elective surgery until after this time, if possible.19 Discontinuing dual antiplatelet therapy significantly increases the risk of stent thrombosis, MI, and death. In a prospective observation study, 2229 consecutive patients between the years 2002 and 2004 were followed.34 Premature discontinuation of dual antiplatelet therapy resulted in a hazard ratio of 89.7 for cumulative stent thrombosis.
Physicians should wait at least 6 weeks after the placement of a bare-metal stent before discontinuing aspirin and/or clopidogrel before surgery. A retrospective study from the Mayo Clinic in 2003 reviewed the clinical outcomes of 207 patients who underwent surgery within 60 days of bare-metal stent placement (Figure 7). Thirty-five percent of the patients used aspirin only through surgery, and 26% used dual antiplatelet therapy. Of note, only 2 patients had excessive bleeding. All events occurred in the first 5 weeks post-stent placement.

In a study by Kaluza et al, 40 patients underwent noncardiac surgery within 6 weeks of the placement of bare-metal coronary stents. Seven patients suffered a perioperative MI and 8 died. Six of the 7 MIs were confirmed either angiographically or by electrocardiogram (ECG) territory to be the result of in-stent thrombosis. All but 1 of the patients who died had their antiplatelet therapy discontinued perioperatively. All major complications occurred in the first 2 weeks after stent placement. Figure 8 shows the ACC/AHA proposed approach to the management of patients with previous PCI.

In nonelective surgeries, continue dual antiplatelet therapy through surgery, if possible, for those with sirolimus stents in the first 3 months and with paclitaxel stents in the first 6 months. After these time intervals, it is reasonable to treat with aspirin alone for surgeries that cannot be postponed.

If aspirin is discontinued before surgery, stop it 7 days in advance of surgery to allow for the production of enough platelets to prevent significant bleeding perioperatively. Based on coronary bypass data from the CURE (Clopidogrel in Unstable angina to prevent Recurrent ischemic Events) trial, stopping clopidogrel 5 days in advance of surgery appears to be adequate to avoid significant surgical blood loss. However, according to anesthesia guidelines, clopidogrel should be stopped 7 days before the placement of an epidural catheter.

In summary, delay elective surgeries and continue dual antiplatelet therapy for at least 6 weeks and 1 year after bare-metal and drug-eluting stent placement, respectively. After that time period, elective surgery should be performed with aspirin continued if possible.
Section 5: Typical Presentation of Postoperative MI: The Utility of Screening Measures

Question 5

Two days after a total hip replacement, Mr Jackson, a 75-year-old man with CAD, became delirious. His ECG showed new T-wave inversions and subsequent troponin I levels peaked at 3.5 ng/mL. The patient denied chest pain at the time of his MI, and he did not develop a pathological Q wave. What percent of postoperative MIs present with chest pain?

A. 90% to 100%

Incorrect. Studies show that chest pain occurs much less often in the perioperative setting.

B. 60% to 70%

Incorrect. Studies show that chest pain occurs much less often in the perioperative setting.

C. 30% to 40%

Incorrect. Studies show that chest pain occurs less often in the perioperative setting.

D. 10% to 20%

Correct! Studies show that the perioperative MIs have atypical presentations.

Typical Presentation of Postoperative MI: The Utility of Screening Measures

Studies analyzing signs and symptoms of perioperative MI have shown that chest pain can occur in as little as 10% to 20% of the patients who rule in by enzymes, ECG, or scintigraphy.\(^3^9\)\(^4^0\) Possible reasons for this atypical presentation of coronary events include the use of perioperative sedation and high-dose narcotics. Moreover, anginal equivalents, such as nausea, diaphoresis, and hypotension, may be misinterpreted as typical postoperative symptoms related to the procedure and/or anesthesia.

Most perioperative MIs occur in the first 3 days postoperatively and tend to be non-Q wave MIs.\(^4^1\) The sensitivity of immediate postoperative ECGs has been found to be as low as 22% for predicting major cardiac events,\(^4^2\) making the use of troponin screening in high-risk patients a consideration.

Lopez-Jimenez et al studied 772 patients undergoing major noncardiac surgery by following postoperative troponin T levels and creatine kinase-MB enzymes.\(^4^3\) They found that 12% of the patients had a troponin elevation without meeting criteria for the diagnosis of an MI. Those with a troponin T elevation above 0.1 ng/mL had a significant risk for a cardiac event in the following 6 months (adjusted odds ratio 4.6 \(P < .05\)). Hence, though a small troponin elevation does not indicate an MI, it may predict future cardiac events. Aside from aggressive risk factor management, no formal recommendations to address the care of patients with mild troponin elevations postoperatively have been published.

The ACC/AHA guidelines recommend, “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 guidelines do not give formal recommendations regarding the use of troponin measurements postoperatively except in those who have cardiac symptoms.

In summary, cardiac events are difficult to detect in the postoperative time period. Following and comparing the ECGs to baseline of patients with 2 or more clinical risk factors immediately after intermediate- or high-risk surgery and for the first 2 postoperative days are reasonable. We recommend routinely following troponin in patients with symptoms of an acute coronary syndrome. The utility of the routine measurement of troponins in very high-risk patients for the first 2 postoperative days is unknown.
Section 6: The Importance of Continuing Cardiac Medications Postoperatively

Question 6

The medical reconciliation process reveals that Mr Jones was taking atenolol before his gastrointestinal surgery. Knowing that he will be nothing by mouth after surgery, which statement regarding β blocker therapy is MOST CORRECT?

A. Recommend restarting his β blocker immediately after surgery.
   
   **Correct! Studies have shown that β-blocker withdrawal can have life-threatening consequences.**

B. Recommend restarting his β blocker if he becomes hypertensive or tachycardic.
   
   **Incorrect. In the postoperative setting, concern for β-blocker withdrawal typically becomes a more important issue than hypertension.**

C. Recommend restarting his β blocker if he has chest pain.
   
   **Incorrect. β blockers will likely aid in preventing postoperative ischemia and withdrawal from β blockers will likely contribute to the occurrence of angina.**

D. Do not recommend restarting his β blocker because they are likely to result in hypotension or bradycardia.
   
   **Incorrect. Recent studies have questioned the utility of initiating β blockers just before surgery because an elevated stroke incidence has been seen in some patients who start the drug within 24 hours of surgery. For patients on chronic β blockade, it is recommended to continue them perioperatively to avoid the consequences of withdrawal.**

The Importance of Continuing Cardiac Medications Postoperatively

There is only one small retrospective study showing the effects of β-blocker withdrawal after surgery. Of 8 vascular patients who did not have their β blocker resumed after surgery, 4 died, whereas 98.5% of those who continued therapy survived.

Though there is much controversy regarding the initiation of β blockade before noncardiac surgery for cardiac protection, there is no question that patients who are already on β blockers preoperatively should also receive this drug postoperatively, even if the patient is nothing by mouth. Intravenous β blockade would be reasonable in the NPO patient. Typically, β blockers are given the day of surgery with a sip of water along with other important medications. Postoperatively, β blockers are held only if the pulse is less than 50 bpm and the systolic blood pressure is less than 100 mm Hg. Low systolic blood pressures may not be as well tolerated by individuals who are accustomed to much higher blood pressures. For those whose “usual” blood pressures are significantly elevated, it is reasonable to maintain the systolic blood pressure within 20% of the patient’s baseline.

Recent and upcoming publications, such as the POISE trial, have questioned the safety of β-blocker administration perioperatively. The trial documents an elevation in perioperative strokes in β blocked patients. However, these studies refer to the initiation of β blockers in the perioperative period. As a result of these trials, we do not recommend initiating β blockers on the day of surgery. They should ideally be started at least 1 week before surgery. These studies do not cast doubt on the continuation of chronic β blockers, which is considered not only safe, but mandatory.

Clonidine has well-recognized withdrawal issues that are typically associated with severe rebound hypertension. Physicians should have a similar concern for postoperative cardiac events in patients who withdraw from clonidine, although no formal studies have addressed this concern. The clonidine patch offers an alternative to the oral form of clonidine.

Regarding statin withdrawal, Le Manach et al showed that among 569 patients undergoing infrarenal aortic surgery, statin withdrawal for more than 4 days was an independent predictor of postoperative myonecrosis.

In summary, withdrawal of β blockers, clonidine, and statins is dangerous. We recommend continuing patients on these medications in the perioperative period if they are taking them chronically.
References


