Series Editor: Kamal M.F. Itani, MD

Prevention of Perioperative Cardiac Events in Noncardiac Surgery

Haytham M.A. Kaafarani, MD
Martin J. London, MD

Patients undergoing major noncardiac surgery are at a higher risk for postoperative cardiovascular events and death if they have preexisting coronary artery disease (CAD) or multiple risk factors for CAD (eg, diabetes, hypertension, advanced age, lipid abnormalities, smoking).[1] Perioperative cardiac complications such as myocardial infarction (MI), cardiac arrest, and stroke remain among the leading causes of morbidity and mortality, increased resource utilization, and decreased long-term survival in patients undergoing noncardiac surgery.[1–3] More specifically, perioperative MI (PMI) is reported to occur in between 1% and 2% of veterans undergoing noncardiac surgery, a rate that increases to 4% to 6% in those with known CAD, and 6% to 10% in those undergoing vascular surgery.[1,4–9] The incidence of PMI varies substantially among individual studies, partly due to differences in criteria used for defining MI.[1,4–9] For example, some studies use cardiac arrest as a poor surrogate for MI, while data currently are being collected on troponin elevations as a more sensitive marker for myocardial events.

TAKE HOME POINTS

- Suggested mechanisms for perioperative cardiac events include hyperadrenergic, hypercoagulable, and proinflammatory states around the time of surgery.
- Evaluation of preoperative risk for cardiac events in patients undergoing noncardiac surgery involves assessing specific patient-related and procedure-related risk factors and the circumstances surrounding the operation.
- According to the American College of Cardiology and American Heart Association guidelines, the best evidence for administering perioperative β-blockers is in patients already receiving β-blockers and in high-risk patients undergoing vascular surgery.
- Preoperative revascularization is reserved for patients who would benefit from revascularization regardless of the upcoming noncardiac surgery.

Suggested mechanisms for perioperative cardiac events include the hypercoagulable and proinflammatory states associated with anesthesia and surgical trauma as well as a hyperadrenergic state related to perioperative stress, hypoxia, and hypovolemia leading to increased myocardial oxygen demand.[10] Landesberg et al[11] observed that PMI, manifested primarily by ST depression and troponin spillage, was invariably associated with significant increases in heart rate in 185 patients undergoing vascular surgery, although classic MI with ST elevation can and does occur at normal heart rates. Circulating catecholamines and vasoconstrictors increase perioperatively, particularly during anesthesia emergence and extubation and for the first 24 to 48 hours postoperatively.[12] Postulated theories for PMI speculate that with increased catecholamines and subsequent tachycardia and hypertension, intravascular shear stress increases, predisposing the already vulnerable plaque to rupture.[13] Other theories suggest that direct damage to the vulnerable subendocardium occurs, leading to troponin release.

Current strategies to reduce postoperative cardiac morbidity and mortality are instituted based on preoperative risk stratification using clinical risk factors for ischemia and cardiac work-up.[6,14] This article, which is

Dr. Itani is a professor of surgery, Boston University; an associate chief of surgery, Boston Medical Center and Brigham & Women's Hospital; and chief of surgery, Boston Veteran's Administration Health Care System, Boston, MA. Dr. Kaafarani is a resident physician, Department of Surgery, University of South Florida, Tampa, FL. Dr. London is a professor, Department of Anesthesia and Perioperative Care, University of California San Francisco, San Francisco, CA.

Table 1. The Revised Cardiac Risk Index

High-risk surgical procedures	
	Intraperitoneal
	Intrathoracic
	Pelvic vascular (suprainguinal)
Ischemic heart disease	
	History of myocardial infarction
	History of positive exercise test
	History of or current angina
	Use of sublingual nitroglycerin therapy
	Electrocardiogram with Q waves
Congestive heart failure	
	History of congestive heart failure
	Pulmonary edema by history or chest radiography
	Paroxysmal nocturnal dyspnea
	Bilateral rales or S_3 gallop
Cerebrovascular disease	
	History of transient ischemic attack or stroke
Preoperative treatment with insulin (diabetes mellitus)	
Preoperative serum creatinine > 2.0 mg/dL	

Note: Each risk factor is assigned 1 point.

*Low risk is defined as the presence of 1 risk factor or no risk factors. Intermediate risk is defined as 2 to 3 risk factors. High risk is defined as more than 3 risk factors.

Data from Lee TH, Marcantonio ER, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. Circulation 1999;100:1043–9.

the fourth in a series addressing recent evidence-based recommendations for improving the quality and safety of surgical care, reviews the current approaches to preoperative assessment and management of patients undergoing noncardiac surgery. An illustrative case is provided to demonstrate these principles.

INITIAL PREOPERATIVE EVALUATION: ASSESSING CARDIAC RISK

Case Presentation

After being diagnosed with symptomatic cholelithiasis, a 69-year-old man scheduled for laparoscopic cholecystectomy was referred for preoperative evaluation. The patient's past medical history was significant for diabetes mellitus, hypertension, and previous heavy smoking. He reported being able to perform daily household tasks without difficulties. In addition, he was able to walk half a mile and climb 1 flight of stairs before becoming short of breath. He denied any orthopnea or paroxysmal nocturnal dyspnea. Over the past several months, the patient experienced several episodes of chest pain radiating to his left arm that occurred while he was walking in a nearby park. The episodes spontaneously resolved within 5 minutes. His medications included glipizide and captopril. His physical examination was within normal limits.

Patient-Related Risk Factors

Perioperative cardiac complications are the result of an intricate and dynamic relationship among patient-related risk factors including the patient's functional capacity, procedure-related risk factors (eg, type of procedure being performed), and the circumstances surrounding the operation (eg, its urgency or nonurgency). Preoperative patient evaluation begins with obtaining a detailed history and physical examination. A careful preoperative evaluation is crucial to detect modifiable patient-related risk factors and to optimize the perioperative condition in an effort to improve surgical outcomes and decrease postoperative mortality and morbidity.[15] Several cardiac risk classification indices have been developed to aid in this process. This article discusses 2 of the most widely used indices.

Revised Cardiac Risk Index. In 1977, Goldman et al[16] suggested an index of cardiac risk classification for noncardiac surgeries based on 9 risk factors that independently affect postoperative cardiac complications. In 1986, Detsky et al[17] revised the Goldman risk classification, validated it, and added new variables, such as angina, pulmonary edema, and remote history of MI. Another widely used and better validated revision of the Goldman cardiac risk classification is the Revised Cardiac Risk Index (RCRI).[7] This 1999 landmark study identified 6 independent predictors of cardiac complications in noncardiac surgery: (1) high-risk procedures, (2) history or presence of ischemic heart disease, (3) history or presence of congestive heart failure, (4) history of cerebrovascular disease, (5) preoperative treatment with insulin, and (6) serum creatinine exceeding 2.0 mg/dL (**Table 1**). The risk of perioperative cardiac events increased predictably and cumulatively with the presence of 0, 1, 2, 3, or more criteria.

The popularity of the original RCRI is based on its simple linear additive scale, despite the fact that its predictive ability varied substantially among similar surgical procedures (eg, intraperitoneal surgeries).[7] According to the RCRI, the case patient has risk factors mostly in the intermediate risk group. However, the presence of relatively new-onset exertional chest pain may be indicative of unstable angina, which warrants further cardiac evaluation.

Table 2. Clinical Predictors of Increased Perioperative Cardiovascular Risk

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

Adapted with permission from Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2006 guideline update on perioperative cardiovascular evaluation for noncardiac surgery: focused update on perioperative beta-blocker therapy: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery): developed in collaboration with the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society for Vascular Medicine and Biology. Circulation 2006;113:2666.

ECG = electrocardiogram; MI = myocardial infarction.

*The American College of Cardiology National Database Library defines recent MI as > 7 days but ≤ 1 month (30 days); acute MI is within 7 days.

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

‡Campeau L. Grading of angina pectoris. Circulation 1976;54:522–3.

The American College of Cardiology (ACC) and the American Heart Association (AHA) guidelines. The ACC/AHA practice guidelines for risk classification and work-up of patients undergoing noncardiac surgery are published every 5 to 7 years.[14] The latest version of these guidelines was published in 2002; interim guidelines on perioperative β-blocker use were published in 2006.[18] An updated set of complete recommendations is expected to be published in late 2007. According to the current guidelines, patients undergoing noncardiac surgery are classified into high, intermediate, and low cardiac risk categories based on the presence of comorbidities (**Table 2**). These patient-related risk factors differ slightly from the more commonly used RCRI variables. In regards to the case patient, the ACC/AHA guidelines also place him in the intermediate risk group, with final risk classification depending on the results of further cardiac work-up.

The ACC/AHA guidelines also focus on the patient's functional capacity, including the patient's ability to perform routine daily activities independently. A patient with a remote history of CAD who is able to perform routine daily activities without difficulty might be at a lesser risk and likely warrants a less aggressive cardiac work-up than a patient with no previous overt history of CAD but who maintains a sedentary lifestyle. **Table 3** presents a validated way of evaluating functional capacity based on

Table 3. Estimated Energy Requirements for Functional Capacity Evaluation

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

Adapted with permission from Eagle KA, Berger PB, Calkins H, et al. ACC/AHA guideline update for perioperative cardiovascular evaluation for noncardiac surgery—executive summary a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1996 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). Circulation 2002;105:1261.

MET = metabolic equivalent.

Table 4. Cardiac Risk Stratification for Noncardiac Surgical Procedures

High	
	Emergent major operations, particularly in the elderly
	Aortic and other major vascular surgery
	Peripheral vascular surgery
	Anticipated prolonged surgical procedures associated with large fluid shifts and/or blood loss
Intermediate	
	Carotid endarterectomy
	Head and neck surgery
	Intraperitoneal and intrathoracic surgery
	Orthopedic surgery
	Prostate surgery
Low	
	Endoscopic procedures
	Superficial procedure
	Cataract surgery
	Breast surgery

Adapted with permission from Eagle KA, Berger PB, Calkins H, et al. ACC/AHA guideline update for perioperative cardiovascular evaluation for noncardiac surgery—executive summary a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1996 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). Circulation 2002;105:1262.

a detailed patient history.[14] The case patient's functional capacity seems low to moderate and does not add significant risk to the perioperative period, as he is still able to ambulate independently and climb a flight of stairs and is not oxygen dependent or homebound.

Procedure-Related Risk Factors

The circumstances surrounding surgery can have a notable effect on the patient's risk for developing cardiac events. Cardiac complications are 2 to 5 times more likely to occur in urgent operations than in elective procedures.[19] The increased risk associated with urgent procedures results from the limited opportunity to adequately assess and optimize the preoperative status of the patient as well as from the hemodynamic changes and overall level of physiologic stress that dictated the urgency of the intervention.

Surgical procedures can be classified as high, intermediate, or low risk based on consensus-derived estimates of the overall cardiac risk of the procedure (**Table 4**). The cardiac risk associated with noncardiac surgery is not only related to the nature of the procedure but is also intimately correlated with the duration of the procedure, the amount of fluid shifts, and the associated blood loss. High-risk procedures (eg, major vascular surgeries) can be associated with a cardiac risk exceeding 5%, while low-risk procedures (eg, endoscopic surgery or breast surgery) are associated with less than 1% cardiac risk.[14] A recent study suggested that the ACC/AHA procedure-related risk classification is a better predictor of 30-day postoperative mortality than the patient-related ACC/AHA cardiac risk classification.[20]

The RCRI incorporates procedural risk as a variable in the overall point-based risk assessment but uses risk classification criteria different from the criteria used in the ACC/AHA guidelines, as evidenced by the case patient. The case patient's procedure is an intra-abdominal surgery, which qualifies as a high-risk procedure according to the RCRI but as an intermediate-risk procedure according to the ACC/AHA guidelines. Whether the procedure is considered to be high risk according to the ACC/AHA cardiac risk classification upon conversion to the open technique depends mainly on the duration of the procedure, associated iatrogenic injuries (if any), degree of blood loss, and the resulting amount of fluid shifts. Boersma et al[21] recently adapted the RCRI to account for major advances in surgery that have markedly decreased procedural risk. This modified index, which has demonstrated enhanced predictive ability, was derived from a retrospective cohort of over 100,000 patients and incorporates the use of endovascular or laparoscopic techniques and the ACC/AHA surgical classification. However, further analytic work is needed to develop accurate and widely usable indices as surgical and anesthetic technology continues to evolve.

Case Continued

The patient undergoes 12-lead resting electrocardiogram (ECG), which reveals the presence of a left bundle branch block (LBBB). A cardiology consult is requested for further patient evaluation.

Electrocardiogram

The 12-lead ECG remains a valuable tool for initial evaluation of patients undergoing noncardiac surgery.[14] The presence of specific ECG changes (eg, ST-segment depression or left ventricular hypertrophy) in intermediate- or high-risk patients may indicate increased perioperative and long-term cardiac morbidity.[22] The effect of bundle branch block on outcome, however, is controversial. In a retrospective observational analysis, Dorman et al[23] suggested that neither right nor LBBB affected perioperative cardiac outcome, although the presence of a LBBB was associated with a higher overall mortality.

APPROACH TO PREOPERATIVE CARDIAC RISK EVALUATION

Determining the Necessity for Additional Cardiac Work-up

Several algorithms for preoperative cardiac work-up have been published in the last 2 decades, including the ACC/AHA and the American College of Physicians (ACP) guidelines.[24] A thorough discussion of these algorithms and guidelines is beyond the scope of this review. In brief, implementation of the ACC/AHA preoperative assessment guidelines has been shown by several single-center nonrandomized studies to improve surgical outcome and decrease resource utilization.[25–27] However, the ACC/AHA algorithm is used as a framework to guide but not dictate management, as each patient's condition and care should be individualized. The decision to perform further cardiac work-up depends on the patient's risk factors, the patient's functional capacity, and the procedure-related risk factors (including its urgency). Any patient who meets at least 2 of the following criteria should at least undergo further noninvasive cardiac work-up: (1) intermediate clinical predictors, (2) poor functional capacity, and (3) high-risk surgical procedure. The case patient has intermediate to high clinical predictors of risk and low to moderate functional capacity (4 metabolic equivalents) and is undergoing an intermediate-risk procedure. In addition, LBBB was found on ECG. He probably would benefit from further cardiac work-up.

Noninvasive Cardiac Work-up

Transthoracic echocardiography (TTE). TTE is often performed as part of the perioperative cardiac risk evaluation, although its prognostic significance is unclear. An early observational analysis found limited prognostic or predictive value of preoperative echocardiography,[28] but a more recent study by Rohde et al[29] suggested that echocardiographic evidence of systolic dysfunction, left ventricular hypertrophy, or valvular disease were associated with increased perioperative events. Given that it is easily and safely performed, preoperative TTE should be a first-line screening tool in patients with suspected ventricular dysfunction or valvular dysfunction. The clinician should nonetheless appreciate the limitations of a static nonstress echocardiographic examination in detecting CAD.

Stress testing. Exercise ECG testing is abnormal in approximately 20% to 50% of patients with no significant cardiac history and with a normal resting ECG.[22,30] The risk of postoperative cardiac events is higher in patients with abnormal exercise testing, especially at low workloads.[22,31,32] Commonly used alternatives to exercise stress testing in patients unable to exercise include dobutamine stress echocardiography and dipyridamole/adenosine myocardial perfusion imaging. Several studies, including a meta-analysis, compared the 2 pharmacologic tests in predicting postoperative cardiac complications and found comparable predictive values.[33] Stress testing appears to be indicated for the case patient. Due to the preexisting LBBB, the use of dipyridamole or adenosine is the test of choice over exercise or dobutamine echocardiographic evaluation. The use of these vasodilators has a reported sensitivity of 98% and a specificity of 84%. In addition, these vasodilators do not cause tachycardia-induced reversible septal defects.[34–37]

Case Continued

Stress testing with adenosine is performed, and the results are negative. The cardiologist indicates that the patient is an intermediate- to high-risk patient and can undergo an intermediate-risk procedure with no need for further work-up.

PERIOPERATIVE RISK MANAGEMENT

Perioperative risk management involves modifying risk factors for cardiac events. In intermediate-risk patients, optimization of medical therapy including perioperative β-blocker and statin therapy is considered essential. In high-risk patients, the benefit of myocardial revascularization to confer cardiac protection remains controversial.

Perioperative Medical Management

β-Blockers. Various agents have been investigated to maintain heart rate control, such as α_2-agonists and β-blockers. α_2-Agonists reduce central sympathetic outflow, whereas β-blockers block the adverse effects of catecholamines at the peripheral receptor.[38]

In the late 1980s, 2 clinical studies generated considerable interest in using perioperative β-blockade to decrease the risk for cardiac events in patients undergoing noncardiac surgery. Pasternack et al[39] reported that an aggressive preoperative dosing regimen with metoprolol resulted in a significantly lower incidence of PMI in 32 patients undergoing abdominal aortic aneurysm resection as compared with a historical control group of 53 patients. Shortly thereafter, Stone et al[40] reported that a single dose of labetalol, atenolol, or oxprenolol administered orally prior to anesthetic induction in patients with poorly controlled hypertension resulted in less tachycardia and a significantly lower incidence of ischemia.

Mangano et al[5] were the first to report a randomized, double-blind, placebo-controlled trial on the use of perioperative β-blockers. This study adopted the protocol used by Pasternack et al,[39] except that the long-acting agent labetalol was substituted for metoprolol and the 200-patient cohort received long-term follow-up (2 yr). The findings of this study remain controversial. Despite a striking 68% reduction in postdischarge cardiac death (mostly within the first 6–8 mo), there were no differences in any of the assessed perioperative outcomes between treated and placebo groups. This study did not perform an intention-to-treat analysis. The statistical effect of β-blockers on perioperative mortality was purported to be eliminated when data on deaths prior to hospital discharge (which were actually higher in the atenolol group) were included in the analysis.[41,42] In another influential but similarly controversial study, Poldermans et al[9] reported a 91% decrease in perioperative death and nonfatal Q-wave MI in high-risk patients receiving bisoprolol, a β_1-selective agent. This cohort study utilized the small subgroup of the vascular surgery population with a positive dobutamine stress test. Multiple critics of the study stressed that it was unblinded, did not utilize a placebo-controlled cohort, and excluded patients with markedly positive stress testing.

Despite their ambiguities, these pioneer studies led to the implementation of perioperative β-blocker guidelines in many major medical centers. The cardioprotective effect of β-blockade, particularly for lower risk patients, has been more seriously challenged in several recent studies. The Canadian MaVS study[43] utilized perioperative weight-based metoprolol in 496 patients undergoing vascular surgery and found no significant difference over placebo in reducing perioperative cardiac events or death at 30 days or 6 months. An additional placebo-controlled study of 921 diabetic patients undergoing primarily orthopedic or general surgery utilized a fixed once-daily dose of long-acting metoprolol succinate. This study again resulted in a statistically nonsignificant cardioprotective effect at 30 days and up to 18 months postoperatively.[44] Lindenauer et al[45] conducted a large retrospective observational trial that included over 700,000 patients who underwent noncardiac surgery. In the subset of patients with RCRI scores of 2 or higher, β-blockers significantly reduced in-hospital mortality. In the 580,665 patients with an RCRI score of 0 or 1, β-blockade was not only associated with no benefit but was possibly harmful. Potential adverse effects include perioperative bradycardia and hypotension, although the magnitude or clinical significance of these events is unknown.[46] More recently, Feringa et al[47] have shown that tight heart rate control may be key to the perioperative risk reduction with β-blockers. Nonetheless, it is unclear if more aggressive lowering of heart rate may result in an increase in perioperative congestive heart failure or other adverse events. The 2006 ACC/AHA update on β-blockers concluded that the best evidence for use of β-blockade is in patients already receiving β-blockers (eg, angina, arrhythmias, hypertension) and in high-risk patients undergoing vascular surgery.[18]

In summary, high-risk patients might benefit the most from perioperative β-blockers, while their use in intermediate-risk patients, such as the case patient, is still highly debated and considered to be optional due to a lack of definitive evidence.[48,49] A large multinational trial is currently accruing patients undergoing noncardiac surgery and will compare a 30-day protocol of perioperative metoprolol succinate with placebo, which will likely provide more definitive data for determining clinical guidelines.[50]

For patients who will receive perioperative β-blockade, β_1-blockers (eg, atenolol, metoprolol, bisoprolol) are considered the best choice, since nonselective agents might have undesired pulmonary or systemic effects. Although most perioperative studies were performed using β_1-blockers only, it should be noted that nonselective agents (eg, labetalol) are commonly used in the perioperative setting with a low incidence of side effects. Carvedilol, another nonselective agent, has potent anti-inflammatory and antioxidant properties and is considered by many cardiologists to be the preferred agent for chronic congestive heart failure. The ACC/AHA 2006 update on β-blockers noted the lack of studies addressing the choice of β-blocking agents.[18] A recent retrospective pharmacoepidemiologic analysis of more than a decade of outpatient pharmacy data suggested that patients receiving long-acting β-blockers, specifically atenolol, have a lower perioperative cardiac risk than patients receiving short-acting β-blockers, specifically metoprolol.[51] Further randomized studies are needed to confirm this finding. Titration of β-blocker doses for tight heart rate control (~60 bpm) is generally recommended despite a lack of validated outcome data.[18]

Statins. Evidence is emerging regarding the role of the 3-hydroxy-3-methylglutaryl coenzyme A inhibitors, otherwise known as statins, in perioperative cardiac protection.[21,52–54] The cardioprotective advantage of statins is related to their lipid-lowering abilities, anti-inflammatory and antithrombotic effects, and stabilizing effects on coronary plaques. In addition to several observational studies suggesting a role for statins in perioperative cardioprotection, a single randomized clinical trial demonstrated a statistically significant reduction in postoperative cardiac events with the use of atorvastatin perioperatively in patients undergoing vascular surgery.[55] A recent study evaluated the strength of evidence for using statins perioperatively and concluded that the perioperative cardioprotective effect is preserved after adjustment for covariates such as gender; however, it also observed that most studies were not blinded, did not use the same statin dose or duration, and did not control or account for study patients' compliance.[56]

Given that statins are among the most commonly prescribed medications in the world, many patients are already receiving them preoperatively. It is important that patients are restarted on their statins as soon as possible postoperatively. In fact, a recent observational cohort suggested a higher incidence of PMI if patients' statins were restarted late (> 4 days postoperatively) after major vascular surgery.[57]

The safety of statins in the perioperative period remains very controversial. Schouten et al[58] reported a decent safety profile with use of perioperative statins in major vascular surgery, despite an increase in the incidence of creatine kinase release in both users and nonusers prior to surgery as compared with the medical populations.

Although some studies have suggested rapid onset of potentially beneficial effects of statins, the general consensus is that a treatment period of 6 to 8 weeks is required for optimal plaque stabilization prior to surgery. The DECREASE IV trial is currently testing the strategies needed for the cardioprotective effects of β-blockers and statins in an ongoing randomized trial of 6000 patients undergoing noncardiac surgery in Europe.[59]

Antiplatelet agents. Finally, antiplatelet agents such as aspirin and clopidogrel are usually contraindicated perioperatively. However, these agents may have distinct indications in selected high-risk patients; a discussion of this topic is beyond the scope of this review.

Preoperative Revascularization

Only a small proportion of patients undergoing noncardiac surgery will benefit from preoperative angiography. As a principle, angiography should be performed only for patients with clearly abnormal noninvasive testing. Of these patients, an even smaller subgroup will undergo further revascularization.[25] Further revascularization with percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) should be performed only on patients who would benefit from revascularization regardless of the upcoming noncardiac surgery, generally those with left main disease, severe 3-vessel disease, or poor ventricular function. The following discussion reviews the evidence behind this recommendation.

The Coronary Artery Revascularization Prophylaxis (CARP) trial[60] evaluated patients at an increased risk for perioperative cardiac events (based on clinical indicators or noninvasive testing) who were undergoing major vascular surgery and found no long-term benefit from preoperative revascularization. In this trial, 510 patients were randomized to undergo medical therapy versus preoperative revascularization. In the group undergoing revascularization, 41% underwent CABG while 59% underwent PCI. There was no statistical difference in PMI or long-term mortality rates between the medical and the revascularization groups. The results of this trial have been challenged based on its inability to evaluate the benefit of revascularization in high-risk cardiac subgroups, in particular patients with 3-vessel disease who are the group most commonly referred to cardiologists for preoperative revascularization.

Percutaneous coronary intervention. The role of PCI prior to noncardiac surgery remains to be determined despite the results of the CARP trial. In addition to being powered only to detect differences in long-term outcome, this trial has its own critics because it was conducted prior to the advent of drug-eluting stents. Drug-eluting stents may provide a better safety profile in terms of risk for stent restenosis; however, this concept has recently been challenged in the literature and by the news media as numerous adverse safety reports of early and delayed stent thrombosis have been made following the dramatically increased usage of drug-eluting stents.[61,62]

Several nonrandomized studies suggested that the risk of perioperative cardiac events is higher in patients who undergo coronary stenting within 6 weeks of their noncardiac surgery, especially within the first 2 weeks.[63,64] This increased risk is primarily caused by the discontinuation of antiplatelet therapy around the time of surgery, leading to increased risk of stent restenosis. In surgeries that cannot be delayed, coronary angioplasty without stent implantation might be a reasonable alternative in patients whose operation mandates interruption of antiplatelet therapy due to significant risk of bleeding. In these patients, surgery can be delayed for only 1 week postangioplasty.[14] In patients who have received drug-eluting stents, it is essential to delay elective surgery for as long as possible and use the most aggressive antiplatelet regimen perioperatively based on the type of surgery. For example, some vascular procedures are now being performed while patients receive clopidogrel to decrease the risk of stent thrombosis despite recognition of potentially increased transfusion requirements. It is unclear if heparin infusions alone are of value in this setting, and clearly more research is indicated.

Coronary artery bypass grafting. The Coronary Artery Surgery Study (CASS) suggested that the potential cardioprotective benefit of a preoperative CABG in the setting of noncardiac surgery is counterbalanced by the increased mortality associated with the CABG procedure.[65] Therefore, the indications for a preoperative CABG are similar to the well-known indications for CABG, such as 2-vessel disease with left ventricular dysfunction or left main coronary artery stenosis.[66]

Case Conclusion

The patient underwent laparoscopic cholecystectomy without complications. His heart rate was maintained between 60 and 80 bpm intraoperatively and postoperatively with β-blockade. He was discharged home on postoperative day 1 and maintained on β-blockers for 4 weeks postoperatively.

CONCLUSION

Prevention of perioperative cardiac events in patients undergoing noncardiac surgery is an evolving area of study. The approach to preventing perioperative cardiac events entails careful risk assessment and modification of patient-related and procedure-related risk factors. Current evidence-based guidelines provide insights to medical and surgical management of risk factors but also reveal controversies and discordance between guidelines, thus indicating a need for further research. **HP**

Corresponding author: Martin J. London, MD, San Francisco VA Medical Center, Anesthesia (129), 4150 Clement St., San Francisco, CA 94121.

REFERENCES

1. Mangano DT, Browner WS, Hollenberg M, et al; The Study of Perioperative Ischemia Research Group. Association of perioperative myocardial ischemia with cardiac morbidity and mortality in men undergoing noncardiac surgery. N Engl J Med 1990;323:1781–8.
2. Mangano DT, Hollenberg M, Fegert G, et al. Perioperative myocardial ischemia in patients undergoing noncardiac surgery—I: incidence and severity during the 4 day perioperative period. The Study of Perioperative Ischemia (SPI) Research Group. J Am Coll Cardiol 1991;17:843–50.
3. McFalls EO, Ward HB, Santilli S, et al. The influence of perioperative myocardial infarction on long-term prognosis following elective vascular surgery. Chest 1998;113:681–6.
4. Ashton CM, Petersen NJ, Wray NP, et al. The incidence of perioperative myocardial infarction in men undergoing noncardiac surgery. Ann Intern Med 1993;118:504–10.
5. Mangano DT, Layug EL, Wallace A, Tateo I; Multicenter Study of Perioperative Ischemia Research Group. Effect of atenolol on mortality and cardiovascular morbidity after noncardiac surgery [published erratum appears in N Engl J Med 1997;335:1039]. N Engl J Med 1996;335:1713–20.
6. Badner NH, Knill RL, Brown JE, et al. Myocardial infarction after noncardiac surgery [published erratum appears in Anesthesiology 1999;90:644]. Anesthesiology 1998;88: 572–8.
7. Lee TH, Marcantonio ER, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. Circulation 1999;100:1043–9.
8. Harpole DH, DeCamp MM, Daley J, et al. Prognostic models of thirty-day mortality and morbidity after major pulmonary resection. J Thorac Cardiovasc Surg 1999;117: 969–79.
9. Poldermans D, Boersma E, Bax JJ, et al. The effect of bisoprolol on perioperative mortality and myocardial infarction in high-risk patients undergoing vascular surgery. Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group. N Engl J Med 1999;341:1789–94.
10. Devereaux PJ, Goldman L, Cook DJ, et al. Perioperative cardiac events in patients undergoing noncardiac surgery: a review of the magnitude of the problem, the pathophysiology of the events and methods to estimate and communicate risk. CMAJ 2005;173:627–34.
11. Landesberg G, Mosseri M, Zahger D, et al. Myocardial infarction after vascular surgery: the role of prolonged stress-induced, ST depression-type ischemia. J Am Coll Cardiol 2001;37:1839–45.
12. Parker SD, Breslow MJ, Frank SM, et al. Catecholamine and cortisol responses to lower extremity revascularization: correlation with outcome variables. Perioperative Ischemia Randomized Anesthesia Trial Study Group. Crit Care Med 1995;23:1954–61.
13. London MJ. Multilead precordial ST-segment monitoring: “the next generation?” [editorial]. Anesthesiology 2002;96:259–61.
14. Eagle KA, Berger PB, Calkins H, et al. ACC/AHA guideline update for perioperative cardiovascular evaluation for noncardiac surgery—executive summary a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1996 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). Circulation 2002; 105:1257–67.
15. Grayburn PA, Hillis LD. Cardiac events in patients undergoing noncardiac surgery: shifting the paradigm from noninvasive risk stratification to therapy. Ann Intern Med 2003;138:506–11.
16. Goldman L, Caldera DL, Nussbaum SR, et al. Multifactorial index of cardiac risk in noncardiac surgical procedures. N Engl J Med 1977;297:845–50.
17. Detsky AS, Abrams HB, Forbath N, et al. Cardiac assessment for patients undergoing noncardiac surgery. A multifactorial clinical risk index. Arch Intern Med 1986; 146:2131–4.
18. Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2006 guideline update on perioperative cardiovascular evaluation for noncardiac surgery: focused update on perioperative beta-blocker therapy: a report of the American College of Cardiology/American Heart Association

Task Force on Practice Guidelines (Writing Committee to Update the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery): developed in collaboration with the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society for Vascular Medicine and Biology. Circulation 2006;113:2662–74.

19. Mangano DT. Perioperative cardiac morbidity. Anesthesiology 1990;72:153–84.
20. Kaafarani HM, Itani KM, Thornby J, et al. Thirty-day and one-year predictors of death in noncardiac major surgical procedures. Am J Surg 2004;188:495–9.
21. Boersma E, Kertai MD, Schouten O, et al. Perioperative cardiovascular mortality in noncardiac surgery: validation of the Lee cardiac risk index. Am J Med 2005;118:1134–41.
22. Cutler BS, Wheeler HB, Paraskos JA, Cardullo PA. Applicability and interpretation of electrocardiographic stress testing in patients with peripheral vascular disease. Am J Surg 1981;141:501–6.
23. Dorman T, Breslow MJ, Pronovost PJ, et al. Bundle-branch block as a risk factor in noncardiac surgery. Arch Intern Med 2000;160:1149–52.
24. Palda VA, Detsky AS. Perioperative assessment and management of risk from coronary artery disease. Ann Intern Med 1997;127:313–28.
25. Bartels C, Bechtel JF, Hossmann V, et al. Cardiac risk stratification for high-risk vascular surgery. Circulation 1997; 95:2473–5.
26. Froehlich JB, Karavite D, Russman PL, et al. American College of Cardiology/American Heart Association preoperative assessment guidelines reduce resource utilization before aortic surgery. J Vasc Surg 2002;36: 758–63.
27. Almanaseer Y, Mukherjee D, Kline-Rogers EM, et al. Implementation of the ACC/AHA guidelines for preoperative cardiac risk assessment in a general medicine preoperative clinic: improving efficiency and preserving outcomes. Cardiology 2005;103:24–9.
28. Halm EA, Browner WS, Tubau JF, et al. Echocardiography for assessing cardiac risk in patients having noncardiac surgery. Study of Perioperative Ischemia Research Group [published erratum appears in Ann Intern Med 1997;126: 494]. Ann Intern Med 1996;125:433–41.
29. Rohde LE, Polanczyk CA, Goldman L, et al. Usefulness of transthoracic echocardiography as a tool for risk stratification of patients undergoing major noncardiac surgery. Am J Cardiol 2001;87:505–9.
30. von Knorring J, Lepantalo M. Prediction of perioperative cardiac complications by electrocardiographic monitoring during treadmill exercise testing before peripheral vascular surgery. Surgery 1986;99:610–3.
31. Arous EJ, Baum PL, Cutler BS. The ischemic exercise test in patients with peripheral vascular disease. Implications for management. Arch Surg 1984;119:780–3.
32. McPhail N, Calvin JE, Shariatmadar A, et al. The use of preoperative exercise testing to predict cardiac complications after arterial reconstruction. J Vasc Surg 1988;7:60–8.
33. Mantha S, Roizen MF, Barnard J, et al. Relative effectiveness of four preoperative tests for predicting adverse cardiac outcomes after vascular surgery: a meta-analysis. Anesth Analg 1994;79:422–33.
34. Rockett JF, Wood WC, Moinuddin M, et al. Intravenous dipyridamole thallium-201 SPECT imaging in patients with left bundle branch block. Clin Nucl Med 1990;15:401–7.
35. O'Keefe JH Jr, Bateman TM, Barnhart CS. Adenosine thallium-201 is superior to exercise thallium-201 for detecting coronary artery disease in patients with left bundle branch block. J Am Coll Cardiol 1993;21:1332–8.
36. Hirzel HO, Senn M, Nuesch K, et al. Thallium-201 scintigraphy in complete left bundle branch block. Am J Cardiol 1984;53:764–9.
37. Tighe DA, Hutchinson HG, Park CH, et al. False-positive reversible perfusion defect during dobutamine-thallium imaging in left bundle branch block. J Nucl Med 1994;35: 1989–91.
38. London MJ. Beta blockers and alpha2 agonists for cardioprotection. Best Pract Res Clin Anaesthesiol. In press 2007.
39. Pasternack PF, Imparato AM, Baumann FG, et al. The hemodynamics of beta-blockade in patients undergoing abdominal aortic aneurysm repair. Circulation 1987;76 (3 Pt 2):III1–7.
40. Stone JG, Foex P, Sear JW, et al. Myocardial ischemia in untreated hypertensive patients: effect of a single small oral dose of a beta-adrenergic blocking agent. Anesthesiology 1988;68:495–500.
41. Devereaux PJ, Yusuf S, Yang H, et al. Are the recommendations to use perioperative beta-blocker therapy in patients undergoing noncardiac surgery based on reliable evidence? CMAJ 2004;171:245–7.
42. Swedberg K, Wedel H. 2-year survival with atenolol administration [letter]. Evid Based Cardiovasc Med 1998;2:33.
43. Yang H, Raymer K, Butler R, et al. The effects of perioperative beta-blockade: results of the Metoprolol after Vascular Surgery (MaVS) study, a randomized controlled trial. Am Heart J 2006;152:983–90.
44. Juul AB, Wetterslev J, Gluud C, et al; DIPOM Trial Group. Effect of perioperative beta blockade in patients with diabetes undergoing major non-cardiac surgery: randomised placebo controlled, blinded multicentre trial. BMJ 2006;332:1482.
45. Lindenauer PK, Pekow P, Wang K, et al. Perioperative beta-blocker therapy and mortality after major noncardiac surgery. N Engl J Med 2005;353:349–61.
46. Devereaux PJ, Beattie WS, Choi PT, et al. How strong is the evidence for the use of perioperative beta blockers in non-cardiac surgery? Systematic review and meta-analysis of randomised controlled trials. BMJ 2005;331:313–21.
47. Feringa HH, Bax JJ, Boersma E, et al. High-dose beta-blockers and tight heart rate control reduce myocardial ischemia and troponin T release in vascular surgery patients. Circulation 2006;114(1 Suppl):I344–9.

48. London MJ, Zaugg M, Schaub MC, et al. Perioperative beta-adrenergic receptor blockade: physiologic foundations and clinical controversies. Anesthesiology 2004;100:170–5.
49. London MJ. Beta-adrenergic-receptor blockade and myocardial ischemia: something old, something new [editorial]. J Cardiothorac Vasc Anesth 2002;16:667–9.
50. Devereaux PJ, Yang H, Guyatt GH, et al; POISE Trial Investigators. Rationale, design, and organization of the PeriOperative ISchemic Evaluation (POISE) trial: a randomized controlled trial of metoprolol versus placebo in patients undergoing noncardiac surgery. Am Heart J 2006; 152:223–30.
51. Redelmeier D, Scales D, Kopp A. Beta blockers for elective surgery in elderly patients: population based, retrospective cohort study. BMJ 2005;331:932.
52. Poldermans D, Bax JJ, Kertai MD, et al. Statins are associated with a reduced incidence of perioperative mortality in patients undergoing major noncardiac vascular surgery. Circulation 2003;107:1848–51.
53. Lindenauer PK, Pekow P, Wang K, et al. Lipid-lowering therapy and in-hospital mortality following major noncardiac surgery. JAMA 2004;291:2092–9.
54. Noordzij PG, Poldermans D, Schouten O, et al. Beta-blockers and statins are individually associated with reduced mortality in patients undergoing noncardiac, nonvascular surgery. Coron Artery Dis 2007;18:67–72.
55. Durazzo AE, Machado FS, Ikeoka DT, et al. Reduction in cardiovascular events after vascular surgery with atorvastatin: a randomized trial. J Vasc Surg 2004;39:967–76.
56. Kapoor AS, Kanji H, Buckingham J, et al. Strength of evidence for perioperative use of statins to reduce cardiovascular risk: systematic review of controlled studies. BMJ 2006;333:1149.
57. Le Manach Y, Godet G, Coriat P, et al. The impact of postoperative discontinuation or continuation of chronic statin therapy on cardiac outcome after major vascular surgery. Anesth Analg 2007;104:1326–33.
58. Schouten O, Kertai MD, Bax JJ, et al. Safety of perioperative statin use in high-risk patients undergoing major vascular surgery. Am J Cardiol 2005;95:658–60.
59. Schouten O, Poldermans D, Visser L, et al. Fluvastatin and bisoprolol for the reduction of perioperative cardiac mortality and morbidity in high-risk patients undergoing noncardiac surgery: rationale and design of the DECREASE-IV study. Am Heart J 2004;148:1047–52.
60. McFalls EO, Ward HB, Moritz TE, et al. Coronary-artery revascularization before elective major vascular surgery. N Engl J Med 2004;351:2795–804.
61. Stone GW, Ellis SG, Cannon L, et al. Comparison of a polymer-based paclitaxel-eluting stent with a bare metal stent in patients with complex coronary artery disease: a randomized controlled trial. JAMA 2005;294:1215–23.
62. Stone GW, Ellis SG, Cox DA, et al; TAXUS-IV Investigators. A polymer-based, paclitaxel-eluting stent in patients with coronary artery disease. N Engl J Med 2004;350:221–31.
63. Reddy PR, Vaitkus PT. Risks of noncardiac surgery after coronary stenting. Am J Cardiol 2005;95:755–7.
64. Wilson SH, Fasseas P, Orford JL, et al. Clinical outcome of patients undergoing non-cardiac surgery in the two months following coronary stenting. J Am Coll Cardiol 2003; 42:234–40.
65. Domanski M, Ellis S, Eagle K. Does preoperative coronary revascularization before noncardiac surgery reduce the risk of coronary events in patients with known coronary artery disease [editorial]? Am J Cardiol 1995;75:829–31.
66. Guidelines and indications for coronary artery bypass graft surgery. A report of the American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Subcommittee on Coronary Artery Bypass Graft Surgery). J Am Coll Cardiol 1991;17:543–89.