Myocardial Ischemia and Postoperative Monitoring

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Introduction

Morbidity and mortality remain associated with coronary artery disease (CAD) in surgical patients, though likely less than in the past. In the US, better chronic medical care appears to be associated with falling rates of myocardial infarction (MI), and reduced mortality after MI, in ambulatory populations. Perioperative myocardial infarction (PMI) may be lethal or compromise a patient's functional status after surgery, and result in additional costs. Less-invasive surgery may lessen these risks. Attempts to improve perioperative outcome of patients at risk for having CAD have focused on 3 approaches: (i) preoperative identification of high-risk patients who might benefit from myocardial revascularization, (ii) improved detection of perioperative myocardial ischemia to allow for prompt therapeutic intervention, and (iii) the prophylactic use of anesthetic and antiischemic techniques to decrease the prevalence and severity of postoperative myocardial ischemia. Many of studies referenced have been undertaken in vascular surgery patients.

Myocardial Ischemia Vs. Myocardial Infarction:

Myocardial ischemia on ECG was a surrogate outcome was most often used in the past in the research reviewed in this lecture. More recent studies have focused on troponin elevations as evidence of ischemia/infarction. Troponin elevations are often higher in prevalence than ECG changes diagnosing infarction, allowing greater statistical power in smaller studies. Despite greater sensitivity, troponin elevations predict subsequent postoperative cardiac morbidity and mortality after cardiac and noncardiac surgery.

Predictors And Prognosis:

Demographic predictors (prior probability). Risk factors may include known CAD, congestive heart failure, valvular heart disease, peripheral vascular disease, advanced age, severely limited exercise tolerance, chronic renal insufficiency, uncontrolled hypertension and left ventricular hypertrophy, impaired glucose tolerance and/or diabetes, and the use of digoxin. Evidence of decompensated heart disease, such as arrhythmias or CHF, appears particularly associated with adverse outcomes. Multifactorial indices, such as the RCRI (revised cardiac risk index), have been proposed to risk-stratify patients. Lee et al determined preoperative predictors of adverse cardiac events after noncardiac surgery in a large cohort; these predictors include previous MI, CHF, cerebrovascular disease, major surgery, and diabetes treated with insulin. The RCRI appears to be less predictive of outcome after vascular surgery compared to other noncardiac surgery. Resting echocardiographic indicators (systolic dysfunction) may also have additive predictive value (above and beyond clinical risk factors) for predicting perioperative myocardial infarction in high-risk vascular surgery patients; recent work suggests that routine preoperative echo may be warranted in vascular surgery patients. The most recent AHA/ACC guidelines have deemphasized the role of preoperative stress testing, after the CARP study showed no benefit to preoperative stress testing and coronary revascularization before vascular surgery.

Recent preoperative MI remains a risk factor for poor postoperative outcome, even in the modern era with sensitive detection with troponins and the use of coronary revascularization and modern medical therapy.

Dynamic postoperative predictors. Factors that may increase the likelihood of postoperative myocardial ischemia that we can address include tachycardia, anemia, hypothermia, shivering, hypoxemia, endotracheal suctioning, and less-than-optimal analgesia. For patients undergoing noncardiac surgery, perioperative MI may be associated with higher postoperative heart rates and higher pain thresholds, but not necessarily angina (most are silent). Other factors, such as postoperative hypercoagulability and platelet reactivity, and REM sleep rebound are more speculative culprits.
**Prognosis.** Postoperative myocardial ischemia confers increased risk to surgical patients. The longer the ischemic episode(s) and the greater the ST segment change, the worse the prognosis. Modern preop preparation, surgery, and anesthesia may be associated with less myocardial ischemia than in the past. We believe that patients with documented severe postoperative myocardial ischemia or troponin release should be referred to a cardiologist, since they are at high risk for adverse long-term cardiac outcomes. PMI is still associated with significant in-hospital mortality (in proportion to troponin elevation), and is a marker for poor prognosis after discharge in those who survive.

**Detection of Myocardial Ischemia and Infarction:**
Patients undergoing vascular surgery are most likely to manifest myocardial ischemia in the immediate postoperative period, usually on the day of surgery or the next. The "silent" nature of postoperative ischemia suggests that frequent ECG monitoring may be useful. Unfortunately, approximately 1/4 of vascular surgery patients will have baseline ECG abnormalities (LBBB, paced rhythm, digoxin effect, LVH with strain) that preclude the detection of myocardial ischemia. The presence of v-waves in the PCWP tracing or decrements in regional wall motion detected with TEE, are less useful after surgery because they are discontinuous, expensive, and relatively invasive. Troponin levels appear more specific in detecting perioperative myocardial infarction than CK-MB isoenzymes; troponin elevations are associated with lower survival after vascular surgery. Routine troponin surveillance appears to be cost effective after traditional AAA surgery.

**Proposed Mechanisms Of Postoperative Myocardial Ischemia:**
Stable ischemic syndromes presumably occur with increased oxygen demand on the myocardium in a setting of fixed coronary plaques. Unstable syndromes are thought to be the result of plaque rupture with local thrombus and vasoreactivity that produce intermittent critical decreases in coronary oxygen supply. Patients with elevated coronary calcium on CT scan have greater rates of perioperative MI after vascular surgery. Endothelial function is impaired in CAD, hypertension, hypercholesterolemia, diabetes, and tobacco abuse, resulting in exaggerated vasoconstriction. Poor endothelial function is also associated with poor outcome after vascular surgery. Treatment to “heal” the endothelium (often with statin drugs) improves perioperative outcome, though effective therapy may have to begin weeks before surgery. Early postoperative ischemia is usually associated with ST segment depression rather than ST elevation. Most perioperative MIs are of the non-Q wave variety.

The postoperative period is characterized by adrenergic stress, which can induce myocardial ischemia in patients with CAD; cause coronary vasoconstriction, and facilitate platelet aggregation. Tachycardia limits diastolic time and coronary perfusion, and it can paradoxically reduce coronary artery diameter. Hypertension and tachycardia in the PACU have been shown in a large study to be associated with increased mortality and unplanned ICU admission (although association does not necessarily mean causation.)

Surgery can induce a hypercoagulable response due to increased platelet number and function, diminished fibrinolysis, decreases in protein C and antithrombin III, and increases in procoagulants (including fibrinogen, factor VIII coagulant, and von Willebrand factor). These postoperative changes may contribute to an increased likelihood of coronary thrombosis in the postoperative period, but their relative importance in predicting postoperative coronary events remains speculative. TEG may identify high-risk patients.

Cardiologists and internists are increasingly undertaking aggressive long-term pharmacologic risk reduction in patients with CAD. These strategies include statins (which stabilize coronary plaques and reduce inflammation), antihypertensive therapy with ACE inhibitors and/or ARBs, and “tighter” glucose control in diabetics. These patients may be more prone to perioperative hypotension, bradycardia, and hypoglycemia.

**Prophylaxis And Treatment Of Postoperative Myocardial Ischemia: Beta Blockers.**
Beta adrenergic blocking drugs, through their ability to suppress perioperative tachycardia, may be efficacious in preventing perioperative myocardial ischemia. They are well tolerated by most surgical patients and may reduce long-term cardiac events. Beta adrenergic blocking drugs have been approved for treatment of hypertension, supraventricular tachycardias, ventricular arrhythmias, angina, and myocardial infarction. They are a cornerstone of
chronic post-MI therapy, as they reduce subsequent reinfarction. Antihypertensive effects of beta blockers are useful during adrenergic activation during events such as endotracheal intubation, extubation, ECT, and sternotomy. They also blunt tachycardia at these times, and this is likely the predominant mechanism of their antiischemic effects. Several trials which document the ability of beta blockers to improve perioperative cardiac outcomes have been published, though several very recent trials have questioned this conclusion. Two trials (MAVS, DIPOM) have questioned the perioperative protective effects of beta blockade. A recent (n=430 very high risk patients) Dutch RCT (DECREASES-V) suggests that HR control to 60 bpm with titrated beta blockade is better than stress testing +/- coronary revascularization. Retrospective work, using propensity adjustment) from a single center (UCSF) in >30,000 patients showed that atenolol might be superior to metoprolol in reducing cardiac death after noncardiac surgery, and that starting or continuing perioperative beta blockade reduces 30 d and 1 yr mortality. Conversely, beta blockade withdrawal increased mortality 2-4 fold.

The larger POISE trial (n= 8351), however, suggests that while fixed-dosed beta blockade with metoprolol lowers rates of myocardial infarction and atrial fibrillation, these improvements come at the cost of increased stroke and death. POISE used a fixed, maximal dose of metoprolol; some have suggested that better outcomes would have followed had the drug been titrated to hemodynamics. The POISE trial may result in the scaling-back of CQI and P4P initiatives aimed at increasing the use of periop beta blockade.

The most recent European Society of Cardiologists guidelines suggest Class I use of beta blockers in preparation for vascular surgery. However, in the US (following POISE), Class I recommendation is limited to continuation of pre-existing chronic beta blockade in the perioperative period per AHA/ACC guidelines. This is a SCIP recommendation (“SCIP-CARD”). De novo beta blockade carries a Class II recommendation by AHA/ACC, and then only in vascular surgery patients with documented CAD.

**Epidural Analgesia.** Epidural anesthetics reduce cardiac preload and afterload, postoperative adrenergic and coagulation responses, and produce coronary vasodilatation (thoracic epidurals only). These effects suggest that they may reduce perioperative myocardial ischemia. However, evidence of benefits in cardiac outcome has been limited in individual trials. Concerns about respiratory depression, neuroaxis hematomas, and the expense of surveillance have limited the use of peridural narcotics in greater numbers of patients.

**Volatile Anesthetics.** Volatile anesthetics reduce myocardial infarct size. The preconditioning effects of volatile anesthetics suggest that they should be incorporated into general anesthetic techniques for patients with known or suspected coronary artery disease, though protection has only been proven in cardiac surgery.

**Non-steroidal anti-inflammatory drugs (NSAIDs)** might be particularly useful in surgical patients with coronary artery disease due to their analgesic effects. However, variable effects on platelets may increase or decrease cardiovascular events. Ketorolac may reduce the stress response to surgery without increasing bleeding times or producing renal insufficiency. However, concerns about increased postoperative hemorrhage make the use of these therapies in surgical patients controversial. A decision analysis has suggested that the benefits of aspirin in vascular surgery patients exceed the risks. COX-2 inhibitors are effective analgesics in the perioperative period. However, their chronic use does not protect the heart as much as do NSAIDs with direct platelet actions, and they may impair preconditioning. COX2 drugs use appears contraindicated in cardiac surgery, and possibly in vascular surgery, due their prothrombotic and vasoconstrictor effects.

**Dual antiplatelet therapy (DAT).** Patients who have drug-eluting coronary stents are at increased risk of acute stent thrombosis in the setting of surgery. This may occur because surgery produces a hypercoagulable state, and because surgeons may wish to stop DAT (aspirin and clopidogrel) before surgery to reduce blood loss. However, stent thrombosis has a high associated mortality. Elective surgery should probably be postponed until after a year of DAT following DES placement. When possible, consideration should be given to continuing DAT through the time of surgery. These patients should probably have at least ASA continued for the rest of their lives, including the perioperative period (with rare exceptions, such as for intracranial surgery). Some work suggests that such patients
should have surgery in locations with the availability of invasive cardiologists and a cardiac catheterization lab should stent thrombosis occur.

**Alpha2 Agonists.** Alpha2 adrenergic agonists decrease noradrenergic central nervous system transmission and produce sedation, anxiolysis, and analgesia. Clonidine premedication reduces hypertension, tachycardia, and norepinephrine levels in patients undergoing aortic reconstruction. Clonidine also suppresses the normal postoperative increase in fibrinogen levels and antagonizes epinephrine-induced platelet aggregation. Our work has shown that clonidine can reduce intraoperative myocardial ischemia. The more specific alpha2 agonists dexmedetomidine and mivazerol may also reduce postoperative myocardial ischemia.

**Statins.** These drugs reduce cholesterol and reduce reinfarction in patients with coronary disease. They can reduce coronary calcium, which may be a predictor of perioperative cardiac events in vascular surgery patients. Several large observation studies, meta-analyses, and randomized trials have correlated statin use with reduced rates of perioperative death and postoperative cardiac events. Recent work from the group in Rotterdam has substantiated their ability to reduce ECG ischemia and troponin release, and work from Paris has shown that stopping chronic statin therapy after surgery is associated with increased cardiovascular complications. Their anti-inflammatory effects may have beneficial effects on numerous other organ systems. As perioperative beta blockade becomes more controversial, statins are becoming that much more popular to prevent cardiovascular complications.

**Hyperglycemia.** Hyperglycemia appears to impair preconditioning mechanisms. It has been shown to be associated with worse outcomes in surgical ICU patients, CABG patients, and after acute myocardial infarction in nonsurgical patients. Impaired glucose tolerance and insulin sensitivity is common in patients with known or suspected coronary disease and is associated with endothelial dysfunction. Many such patients have not been classified as diabetic before surgery, yet manifest perioperative hyperglycemia. Recent perioperative studies have differed on whether “tight control” improves coronary and other outcomes. However, some payers have begun to target tight control of perioperative glucose levels in CQI and P4P initiatives. Currently, recommendations for target range of perioperative glucose have increased.

**Anemia / Hypothermia.** Anemia is associated with an increased prevalence of postoperative myocardial ischemia. Whether more aggressive transfusion lowers this risk is unclear. In high-risk patients and in those who demonstrate myocardial ischemia, we used to routinely transfuse PRBCs to augment hematocrit to 30%. This simple strategy is complicated by studies showing that transfusion (especially of old blood) also increases cardiac risks. The combination of anemia and beta blockade may be particularly problematic. The elusive goal of a blood substitute might allow safer augmentation of oxygen carrying capacity, but to date, the NO scavenging properties of hemoglobin-based preparations may actually be associated with higher rates of perioperative MI than autologous blood. Hypothermia is also associated with postoperative myocardial ischemia; aggressive warming and heat conservation are warranted during and after surgery in high-risk patients.

**Managing Acute MI.** A cardiologist should see patients with suspected MI as soon as possible. Acute care for myocardial infarction may include prompt reperfusion (thrombolysis and DES placement requiring DAT are generally contraindicated after surgery), therapy with statins, aspirin and beta blockers in those who can tolerate them, the avoidance of calcium entry blockers, and the use of ACE inhibitors or ARBs in those with poor LV function. It is not known if these recommendations are necessarily transferable to the perioperative setting. In patients with evolving myocardial infarction, intraaortic balloon pumping (IABP) can improve coronary blood flow while decreasing workload. Anecdotal reports exist of IABP placement as prophylaxis against postoperative coronary events for NCS, but definitive studies are lacking. IABP use may be particularly risky in patients with peripheral vascular disease.
The Future:

Improvements in our management of these patients appear to be reducing perioperative cardiac morbidity to the point where other organ system dysfunction may be responsible for the majority of in-hospital deaths. If this is true, then we are truly making remarkable strides. The key will be to identify cost-effective strategies that improve outcome and to identify patients most likely to benefit.

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Disclosure

This speaker has indicated that he or she has no significant financial relationship with the manufacturer of a commercial product or provider of a commercial service that may be discussed in this presentation.