CARDIOLOGY Rounds®

As presented in the rounds of the Division of Cardiology, St. Michael's Hospital, University of Toronto

The Assessment and Management of Perioperative Cardiac Risk in Patients undergoing Non-cardiac Surgery

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Of the 26 million North Americans undergoing noncardiac surgery every year, between 1% to 5% suffer a major cardiovascular event.[1] Managing this risk is a common challenge encountered by surgeons, anesthetists, internists, and cardiologists and the challenge is augmented by the increasing frequency of older patients with chronic illnesses undergoing major surgery. Although guidelines for the perioperative assessment of patients with coronary artery disease (CAD) undergoing noncardiac surgery exist, choosing an optimal approach may be problematic.[2] This issue of *Cardiology Rounds* describes advances in clinical risk factor stratification and perspectives on management strategies to decrease cardiac risk in patients undergoing non-cardiac surgery.

Case example

An 86-year old man requiring a total hip replacement for osteoarthritis is seen in a preoperative clinic. Five years previously, he underwent angioplasty for a right coronary artery stenosis due to symptoms of angina. He denies symptoms of angina, but has poor functional status due to the osteoarthritis and has not recently undergone noninvasive cardiac testing. He is otherwise well. His medications include aspirin and atenolol. His physical examination is unremarkable and his resting electrocardiogram (ECG) is normal.

This case is similar to others encountered by clinicians and the issues include:

- defining this patient's risk of a perioperative cardiac event
- determining whether further testing can refine risk estimates and impact management strategies
- instituting appropriate therapy for higher-risk patients.

Clinical risk stratification

A cardiac risk assessment is critical for any patient undergoing major non-cardiac surgery. It may be determined simply by paying attention to both the patient's health status and the risk associated with the procedure that will be undertaken. Over the past 25 years, numerous clinical risk indices have been developed to predict perioperative cardiac risk, many employing complicated algorithms or point scoring systems that may be challenging for the busy clinician. Two commonly employed indices are the Goldman Cardiac Risk Index that was initiated in 1977[3] and the Detsky Index initiated in 1986.[4] While popular, these indices are less relevant today, given the advances that have been made in surgical technique, anesthesia, and the management of CAD, as well as the attention to metabolic derangements and need for recognition of valvular abnormalities (eg, aortic stenosis).

To address the shortcomings of these risk indices, Lee and colleagues[5] prospectively followed 4315 patients undergoing major noncardiac surgery (35% orthopedic, 20% vascular, and 12%

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thoracic) at The Brigham and Women's Hospital in Boston in the early 1990s. Major complications, including acute myocardial infarction (MI), pulmonary edema, ventricular fibrillation, and complete heart block occurred in 2.1% of patients in their study cohort. This complication rate was less than half that reported in the previous decade, likely reflecting the advances in patient management mentioned previously. Six independent correlates of major cardiac complications were identified (Table 1) and include:

- high-risk surgery (ie, intra-thoracic, intra-peritoneal, supra-inguinal vascular surgery)
- a history of ischemic heart disease
- a history of congestive heart failure
- a history of cerebrovascular disease
- insulin-dependent diabetes
- renal failure with a serum creatinine >177mmol/L.

Simply assigning 1 point for the presence of each risk factor and reporting the total score allowed an accurate determination of cardiac risk. Individuals with 0 to 1 point were considered to be at low risk with an estimated rate of cardiac events of 0.4% and 1%. Those with ≥2 risk factors were at higher risk, with a complication rate of 7% in those with 2 points and 11% in those with ≥3 points. The simplicity of this risk scoring method does not sacrifice any accuracy. Indeed, when compared to previous risk indices,[3,4] the Lee Index is, in fact, a more accurate method of predicting contemporary perioperative cardiac risk.[5]

Unlike previous risk indices, metabolic problems, abnormal heart rhythms, and critical aortic stenosis were not independent risk factors in the Lee Index, likely due to attention to and correction of these factors prior to referral for elective noncardiac surgery. Interestingly, only 0.2% of Lee's derivation cohort was comprised of patients with significant aortic stenosis. The lack of representation of these patients limits the ability to identify aortic stenosis as an independent risk factor. However, others have continued to demonstrate that moderate to severe aortic stenosis remains a significant risk factor for perioperative cardiac events (odds ratio = 5.2), even after adjusting for other cardiac risk factors.[6] Thus, the presence of significant aortic stenosis should not be ignored.

Noninvasive testing

While clinical assessment is quite predictive of cardiac risk, certain patients with poor functional status or unclear histories may require further testing to ascertain risk. Noninvasive testing (with myocardial perfusion imaging or stress echocardiography) to determine the extent of myocardial ischemia may provide useful information in these situations. The American College of Cardiology (ACC)/American Heart Association (AHA) guidelines[7] have attempted to restrain the widespread use of noninvasive imaging and define specific roles for pre-operative noninvasive imaging in patients with cardiac risk factors and poor functional status undergoing non-low risk procedures, and in those with risk factors undergoing high-risk surgery, regardless of functional status.

Table 1: The Lee Index for assessing perioperative cardiac risk[5]

One point for each of the following:	
High-risk surgery	
History of ischemic heart disease	
Congestive heart failure	
Cerebrovascular disease	
Insulin-dependent diabetes mellitus	
Serum creatinine > 2.0 mg/dL	
TOTAL POINTS	**COMPLICATION**
0	0.4%
1	1%
2	7%
≥3	11%

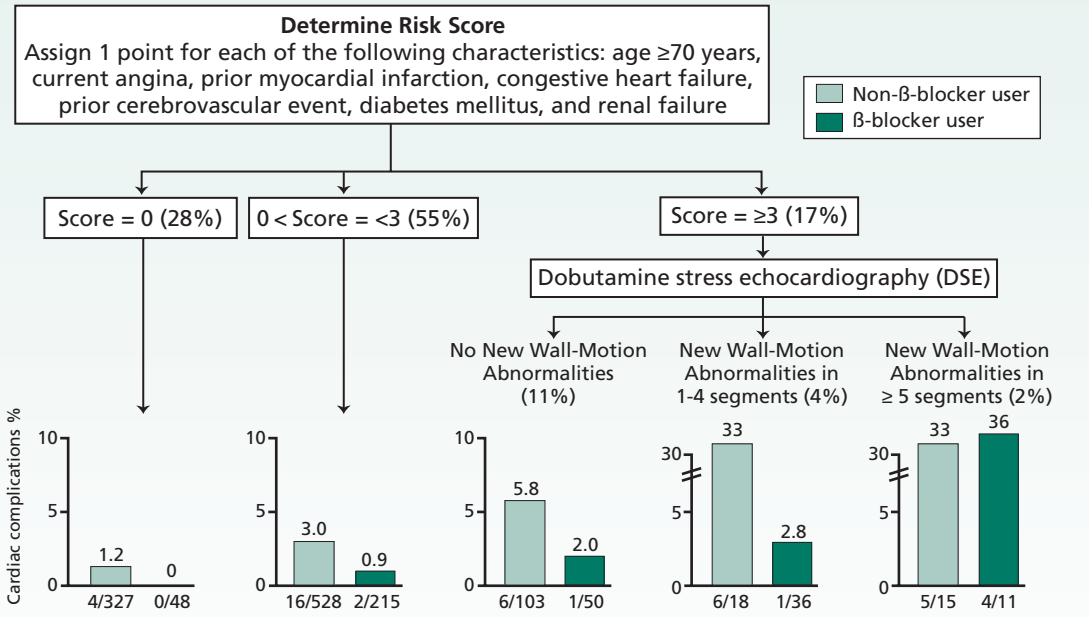
* Myocardial infarction, pulmonary edema, ventricular fibrillation or primary cardiac arrest, complete heart block

Noninvasive imaging is most useful when the testing is negative for ischemia; and the absence of significant ischemia on imaging identifies truly low-risk patients. Boserma and colleagues[8] retrospectively examined the relationship between a patient's score on the Lee Index and findings on dobutamine stress echocardiography in an attempt to define a group of individuals in whom preoperative noninvasive testing would be most informative. As shown in Figure 1, patients at low risk with a score on the Lee Index of 0 to 2, had a low rate of cardiac events (<1%) if they had received beta-blocker therapy, regardless of whether their noninvasive tests were abnormal. Those at high-risk, based on a Lee Index score of ≥3 had an acceptable perioperative cardiac risk (<2%), if they were on beta-blockers and if <4 new segments with abnormal wall motion were noted on dobutamine stress echocardiography. Those with ≥4 areas of new wall motion abnormality were at high risk of perioperative cardiac events, regardless of the use of beta-blockers.

These findings suggest that patients with a score of ≤2 can safely go to the operating room if they are on beta-blockers. Those who score ≥3 points may require further testing, although many may still safely go to the operating room if they are on beta-blockade therapy.

It is possible that the growing body of evidence on the protective effect of beta-blockers, as well as a potential lack of benefit with perioperative coronary artery revascularization (see below), may further limit the role of and future use of perioperative noninvasive testing.

Figure 1: Perioperative cardiac risk of death or MI observed in subpopulations stratified by clinical features[8]



Results are according to the clinical risk score, dobutamine stress echocardiography, and receipt of ß-blockers during surgery. Percentages in parentheses represent the number of patients in the target category as a proportion of the total number of 1351 patients. Numbers underneath the bars represent the actual number of events/patients in the specific category.

Reducing perioperative cardiac risk

Beta-blockers

Beta-blocker therapy was one of the first interventions shown to decrease perioperative cardiac risk. In 1996, Mangano and colleagues[9] randomized 200 patients with known CAD or 2 cardiac risk factors undergoing non-cardiac surgery. They received intravenous atenolol on the day of surgery, followed by oral atenolol as tolerated for the duration of hospitalization. A 55% relative risk reduction in cardiac events was noted during the 2-year follow-up period. This benefit was most pronounced during the first 6 months post-operatively. The number needed to treat (NNT) to prevent 1 death was calculated to be 8.3 patients and the NNT to prevent 1 episode of cardiac ischemia was calculated to be 6.7 patients.

Poldermans and colleagues[10] randomized 112 patients undergoing vascular surgery to bisoprolol or placebo. The medication was initiated 1 week prior to surgery and continued 30 days post-operatively. All patients had known CAD and an abnormal dobutamine stress echocardiogram – a truly high-risk population. The primary endpoint of death or non-fatal MI occurred in 34% of patients in the placebo arm and in 3.4% of patients in the bisoprolol arm. A relative risk reduction of 90% was achieved with 3 patients requiring treatment to prevent either a death or non-fatal MI. The trial was slated to enroll 266 patients, but was halted early by the ethics committee due to these dramatic results.

Based on these findings, the ACC /AHA guidelines[7] state that beta-blockers should be employed in high-risk patients undergoing vascular surgery (Class I) and for those with CAD undergoing other noncardiac surgery (Class II). While the results of these 2 trials are impressive, one needs to recognize that both were small. A recent meta-analysis of 11 perioperative beta-blocker trials that randomized 866 patients demonstrated a 75% relative risk reduction in death from a cardiac event in the perioperative period.[11] Interestingly, when the results from Poldermans' study are removed from the analysis, a non-significant difference is noted with beta-blocker use in the perioperative period.[12]

Recent trials have also failed to demonstrate the benefit of beta-blockers in the perioperative period:

- The Diabetic Post-Operative Morbidity and Mortality (DIPOM)[13] study randomized 921 diabetic patients undergoing major non-cardiac surgery to receive metoprolol or placebo for 1 week post-operatively. A reduction in postoperative cardiac events was not observed. This may be related to the low risk associated with the population being studied (in-hospital rate of events was 1%), and the inconsistent use of the metoprolol in the first 2 postoperative days, which may have resulted in variable drug levels.

• The Metoprolol after Vascular Surgery (MaVS) trial[14] and the Perioperative Beta-Blockade (POBBLE) trial in patients undergoing infrarenal vascular surgery[15] both failed to demonstrate any benefit of perioperative metoprolol therapy in patients undergoing vascular surgery.

• The issue of the presence and magnitude of benefit of perioperative beta-blocker therapy may be settled on completion of the PeriOperative ISchemic Evaluation (POISE) Trial.[12] This large multi-national trial intends to randomize 10,000 patients to receive metoprolol or placebo pre- and 30 days post-operatively.

At the present time, beta-blockers remain the strongest tool in our armamentarium for decreasing perioperative cardiac risk. However, questions remain unanswered about the appropriate length of time that beta-blocker therapy is required pre- and post-operatively; whether all beta-blockers are as effective as bisoprolol; should all patients be started on beta-blockers pre-operatively regardless of previous cardiac risk factors (given their safety record and low cost); what is the actual risk reduction obtained with beta-blockers; and is noninvasive imaging required in patients who are receiving beta-blocker therapy.

Statins

It has recently been suggested that the use of statins may decrease perioperative cardiac risk. An analysis of a large administrative database involving 780,000 patients who underwent non-cardiac surgery in the United States demonstrated that those receiving statins during the perioperative period (9.9% of the cohort) had a 1% absolute reduction in in-hospital mortality after adjusting for other factors.[16] To date, the only randomized controlled trial examining the use of statins perioperatively was performed in 100 patients undergoing vascular surgery in Sao Paolo, Brazil.[17] Patients were randomized to atorvastatin 20 mg daily, initiated 2 weeks prior to the procedure. The medication was continued for a total of 45 days. Half of the patients received beta-blockers. Overall, there was a 31% relative risk reduction in the combined endpoint of death, non-fatal MI, and unstable angina or stroke in the group receiving atorvastatin (P=0.018).

Since the reduction in cardiac risk in patients with stable CAD receiving statin therapy is often not apparent until months after the therapy is initiated, many have called into question the plausibility of benefit with acute statin use in the perioperative period. While the exact mechanism of statins in the perioperative period is unclear, it may be related to decreased inflammation, improved thrombogenic profile, and/or increased endothelial nitric oxide production[18] – factors that all may theoretically decrease the risk and extent of perioperative cardiac ischemia.

The benefit of statin therapy appears to be incremental to that of beta-blockers[19] and without an associated increased risk of myopathy or rhabdomyolysis.[20] Further information about the role of perioperative statin use may be obtained from the Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echo – IV trial (DECREASE IV),[21] a large randomized controlled trial currently enrolling patients that plans to evaluate the benefit of combined therapy with both beta-blockers (bisoprolol) and statins (fluvastatin) in the perioperative period.

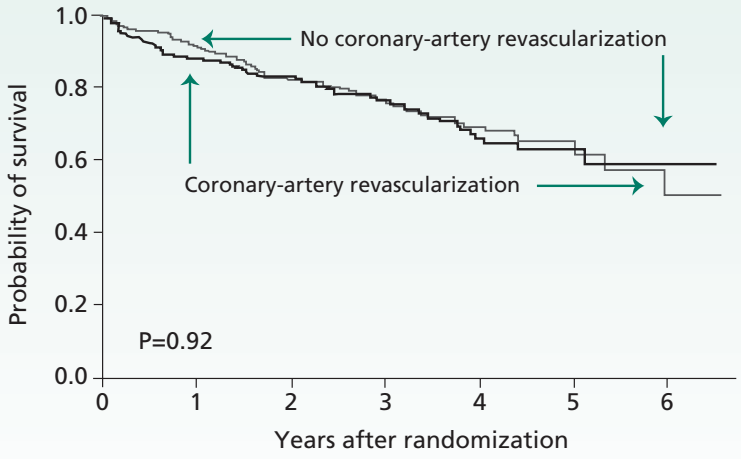
Revascularization

Prior to December 2004, the role of perioperative coronary revascularization had not been studied in a randomized fashion. Retrospective data, including the Coronary Artery Surgery trial,[22] suggested a potential benefit of pre-operative coronary artery revascularization in patients undergoing vascular surgery, especially individuals with 3-vessel CAD. While guidelines[7] recommend conservative management of patients with stable CAD and low-risk coronary anatomy, there is significant practice variation. The results of the recently published Coronary Artery Revascularization Prophylaxis trial (CARP)[23] provide added support for a conservative strategy.

The CARP trial enrolled 510 individuals undergoing vascular surgery. Those with left main disease, severe left ventricular dysfunction, or aortic stenosis were excluded from the trial. Those with residual CAD amenable to percutaneous or surgical revascularization were included. Seventy-four percent of participants in the trial demonstrated moderate to large reversible defects on perfusion imaging or were considered to be at intermediate or high risk based on clinical criteria. More than 80% received beta-blocker therapy and 50% received statin therapy. There was no significant difference in mortality at 30 days (3.1% vs. 3.4%) or at a median follow-up of 2.7 years (22% vs. 23%) between the revascularized versus the non-revascularized groups (Figure 2). Subgroup analysis of high-risk individuals (those with positive stress imaging, large stress defect, 3-vessel disease, and left ventricular dysfunction) also failed to demonstrate a group that would benefit from prophylactic revascularization. Those who underwent revascularization waited an additional 36 days prior to undergoing their vascular procedure.

Although it can be argued that the CARP trial was not adequately powered, had a short follow-up

Figure 2: Survival in patients undering coronary revascularization versus no revascularization prior to undergoing elective major vascular surgery[22]



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

period, and may not be generalizable given the preponderance of males and the exclusion of individuals with left main, severe aortic, and left ventricular disease, the results reassure clinicians and provide evidence against the practice of prophylactic coronary revascularization prior to noncardiac surgery.

Conclusions

Given the findings summarized above, obtaining a thorough history is critical to the appropriate risk stratification of patients undergoing non-cardiac surgery. The use of the Lee Index is a simple and accurate approach to approximate perioperative cardiac risk. Individuals with a history of CAD or ≥2 risk factors should receive beta-blocker therapy pre-operatively. Statin therapy should also be considered.

Patients with unstable coronary syndromes are not appropriate candidates for elective non-cardiac surgery and should be managed the same as other patients with unstable coronary syndromes. The management of individuals with poor functional status or those with a known history of CAD and no recent risk stratification is less clear. These individuals should receive beta-blocker and statin therapy if not contraindicated. The role of noninvasive imaging is less clear given the benefits of beta-blocker therapy demonstrated in Poldermans study[10] and the lack of benefit of perioperative cardiac revascularization.[23] Clinical judgement, medication optimization, attention to intra-operative and post-operative care, and early detection and appropriate management of post-operative ischemia may be all that is necessary.

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Atstract of Interest

Coronary artery revascularization before elective major vascular surgery.

McFalls EO, Ward H, Moritz T, et. al.

Background: The benefit of coronary-artery revascularization before elective major vascular surgery is unclear.

Methods: We randomly assigned patients at increased risk for perioperative cardiac complications and clinically significant coronary artery disease to undergo either revascularization or no revascularization before elective major vascular surgery. The primary end point was long-term mortality.

Results: Of 5859 patients scheduled for vascular operations at 18 Veterans Affairs medical centers, 510 (9 percent) were eligible for the study and were randomly assigned to either coronary-artery revascularization before surgery or no revascularization before surgery. The indications for a vascular operation were an expanding abdominal aortic aneurysm (33 percent) or arterial occlusive disease of the legs (67 percent). Among the patients assigned to preoperative coronary-artery revascularization, percutaneous coronary intervention was performed in 59 percent, and bypass surgery was performed in 41 percent. The median time from randomization to vascular surgery was 54 days in the revascularization group and 18 days in the group not undergoing revascularization (P<0.001). At 2.7 years after randomization, mortality in the revascularization group was 22 percent and in the no-revascularization group 23 percent (relative risk, 0.98; 95 percent confidence interval, 0.70 to 1.37; P=0.92). Within 30 days after the vascular operation, a postoperative myocardial infarction, defined by elevated troponin levels, occurred in 12 percent of the revascularization group and 14 percent of the no- revascularization group (P=0.37).

Conclusions: Coronary-artery revascularization before elective vascular surgery does not significantly alter the long-term outcome. On the basis of these data, a strategy of coronary-artery revascularization before elective vascular surgery among patients with stable cardiac symptoms cannot be recommended.

N Engl J Med 2004;351:2795-804.

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This publication is made possible by an educational grant from

Novartis Pharmaceuticals Canada Inc.