Pre-Operative Evaluation of the Risk of Cardiac Events in Patients Undergoing Non-Cardiac Surgery

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Internists and cardiologists are frequently consulted preoperatively to evaluate the risk of cardiac death or myocardial infarction (MI) in patients undergoing noncardiac surgery. This is a vexing problem because of obvious difficulties in defining the risk that an individual patient will have an event and because of a lack of high quality clinical trials on which to base decision making. Two major position papers on this topic have been published, one by the American College of Cardiology/American Heart Association (ACC/AHA) in 1996 (1) and another two-part paper by the American College of Physicians (ACP) in 1997 (2,3). Since their publication, new data have emerged which prompt reconsideration of the issue, particularly from the standpoint of therapy. This review will cover the primary issues regarding risk stratification as it relates to the pathophysiology and management of perioperative cardiac death or MI.

Magnitude of the Problem

It has been estimated that there are over 27 million noncardiac surgeries performed annually in the United States (4). Of these, approximately 8 million have known coronary artery disease (CAD) or significant risk factors for it. There are roughly 500,000 peripheral vascular surgeries performed annually. These patients have long been considered to have a higher risk of peri-operative cardiac events due to a particularly high prevalence of CAD. Traditional teaching is that the surgical mortality for vascular surgery is around 5% (5). However, more recent data shows that surgical mortality has declined for vascular surgery, particularly for carotid endarterectomy. Table 1 shows the operative mortality for 8 common operations performed in the VA system between 1991 and 1997 (6). Surgical mortality, defined as all-cause 30-day mortality, varies with type of operation and undoubtedly is related to the overall age and health of the patient as well as to the specific operation. The mortality for vascular surgery was less than 5% for AAA repair and only 1.2% for carotid endarterectomy. The rate of MI was only 0.7% for all operations, although it is important to note that this is defined as Q-wave MI. Interestingly, the majority of deaths in this population were noncardiac in origin.

Table 1. Surgical mortality for 8 common operations performed in the VA system (1991-1997).

Operation	Total n	30-day mortality (%)
Abdominal aortic aneurysm repair	3,767	4.7
Infrainguinal vascular reconstruction	12,535	3.1
Carotid endarterectomy	10,173	1.2
Total hip arthroplasty	8,241	1.0
Colectomy	13,310	6.9
Laparoscopic cholecystectomy	8,602	0.5
Open cholecystectomy	7,113	2.8
Lobectomy/pneumonectomy	4,890	5.5
Total	68,631	3.2

Other studies confirm the declining operative mortality in recent years. Brittenden, et al (7) examined the trends in mortality for carotid endarterectomy before (1975-1991) and after (1992-1998) publication of the randomized clinical trials of this procedure. They found that the combined mortality and disabling stroke rates fell from 3.6% to 2.0%. Pearce, et al (8) studied the relation between surgeon caseload and outcome in 3 major vascular surgical procedure in the State of Florida from 1992-1996. The results are shown in table 2. It is now clear that carotid endarterectomy is a low risk surgical procedure.

Table 2. Rates of death and MI in vascular surgery in Florida (1992-1996).

Operation	Number of pts	Mortality (%)	MI (%)
Carotid endarterectomy	45,744	0.8	0.8
Lower extremity bypass	31,172	3.3	1.9
Abdominal aortic aneurysm repair	13,415	5.7	1.8

Technical developments in vascular surgery offer less invasive alternatives to traditionally high-risk procedures. Abdominal aortic aneurysms can now be repaired by endoluminal stent placement with a mortality rate of 0-2% and a myocardial infarction rate of 1-2%, whereas conventional repair carries an operative mortality of 3-5% and a myocardial infarction rate of 3-5% (9,10). Improvements in stent design and deployment techniques are likely to continue to improve in peripheral vascular and aortic surgery as they have done in coronary artery intervention.

Pathophysiology of Perioperative Cardiac Complications

The major cardiac complications of noncardiac surgery are death and nonfatal MI. Angina and heart failure are generally considered soft endpoints because they are subjective and can be confused with other post-operative events such as pulmonary embolism, incisional pain, or volume overload. Arrhythmias may also complicate noncardiac surgery, however; their management is usually straightforward. These "soft" endpoints are often included in small retrospective studies in order to achieve statistical significance. Their definitions very considerably from study to study, making comparisons difficult. Therefore, this review will focus on the more easily defined "hard" endpoints of cardiac death or MI.

The substrate for most postoperative cardiac complications is underlying CAD. However, there are important differences between postoperative MI and that seen in the usual setting of the CCU or emergency room. Most patients presenting to the emergency room with acute coronary syndromes have symptoms caused by plaque rupture with either complete (ST elevation) or incomplete (non-Q MI or unstable angina) thrombosis of the coronary artery. It is well known that the anatomic site of plaque rupture does not correlate with the angiographic severity of coronary obstruction (11). In contrast, patients with perioperative MI are often asymptomatic and the underlying pathophysiology is different.

Despite the well known hemodynamic and adrenergic stress associated with the actual surgical procedure, it has been clearly shown that the amount of intra-operative myocardial ischemia is not different than pre-operative ischemia in patients with coronary artery disease (12-14). However, there is an increase in myocardial ischemia in the post-operative period and most perioperative MI's occur 1-4 days after surgery (12-14). This is related to several factors. Myocardial oxygen demand can be greatly increased by tachycardia and hypertension that may result from post-operative pain or discomfort, withdrawal of anesthesia, or fluid shifts. On the other hand, myocardial oxygen supply can be reduced by anemia or hypotension due to blood loss. These factors tend to cause non-ST elevation MI in patients with underlying coronary artery disease. Abnormal endothelial function related to diabetes, hypertension, or hypercholesterolemia may be a contributing factor. ST elevation MI's occur less frequently in the post-operative period and may be related to increased shear stress and platelet aggregation associated with increased adrenergic tone and a generalized hypercoagulable state with increased fibrinogen levels (15). It follows logically that treatment or prevention of post-operative MI should focus on reducing the hyperadrenergic state with beta-blockade and pain medication.

Issues in Risk Stratification

Risk stratification is used in many professions besides medicine. Insurance companies have developed sophisticated mathematical modeling of risk in order to limit their liability and ensure profitability. Their risk models explain why your automobile insurance rate increases after you have had an accident or if you add a teenager to your policy. In any profession, risk stratification in and of itself is useless. Risk stratification is always done with the goal of reducing risk. The concept of preoperative risk stratification carries important assumptions regarding the reduction of surgical risk (Table 3). First, any parameter used for risk stratification must be able to accurately distinguish low from high risk patients. In other words, the marker of risk stratification must have a high positive and negative predictive value. Second, the marker(s) must result in a significant change in risk compared to the pre-test likelihood (Bayes theorem). In other words, the marker should tell us something that we do not already know (i.e. that CAD is present). Third, the cost/benefit ratio of risk stratification must be favorable. Noninvasive imaging tests are expensive and lead to delays in surgery. If coronary revascularization is considered, the delay of surgery may be prolonged and may not be appropriate for certain cases, such as threatened loss of limb or metastatic spread of a resectable primary tumor. Finally, there is really no reason to perform risk stratification unless it ultimately has an effect on outcome. One needs to ask whether risk stratification would lead to cancellation of surgery or an alternative treatment. If not, would risk stratification mandate a therapy to eliminate or reduce the surgical risk, such as prophylactic coronary revascularization? The corollary to this question is that there are proven therapies to reduce surgical risk.

The remainder of this review will focus on specific clinical and diagnostic tests for risk stratification of patients undergoing noncardiac surgery. The evidence regarding each test will be evaluated as to whether it meets or fails to meet the critical elements in Table 3. Finally, the evidence supporting various therapies to reduce or eliminate risk will be reviewed within the context of the critical elements in Table 3.

Table 3. Critical Elements for Risk Stratification of Patients Undergoing Noncardiac Surgery.

- Risk Assessment Tool Must Be Accurate
  - -High positive and negative predictive value for post-operative events
  - -Results in significant change from pre-test assessment of risk
  - -Favorable cost/benefit ratio
- Risk Assessment Tool Must Influence Outcome
  - -Cancellation of surgery or change to different treatment
  - -Mandates proven therapy for eliminating or reducing risk

Risk Stratification by Clinical Markers

A number of different algorithms have been developed over the years to classify risk of perioperative cardiac events. The original Cardiac Risk Index was described by Goldman in 1977 in a series of 1001 patients undergoing general, orthopedic, and urologic procedures (16). Subsequently, Detsky et al (17) modified this index by adding the presence of angina or remote MI. This Modified Cardiac Risk Index was prospectively validated in blinded fashion in patients undergoing both vascular and general surgery. Patients were stratified into 3 risk groups with event rates of 5% in Class I (low risk), 27% in Class II (intermediate risk), and 60% in Class III (high risk). Eagle, et al (18) proposed a simple clinical risk index in which 1 point was given for each of the following risk factors: age > 70 years, Q waves on ECG, angina, ventricular ectopy, or diabetes. Although this index has been widely used, it has never been properly validated in a large prospective series. Importantly, all of these indexes are more than a decade old and developments in surgical and anesthetic techniques have led to improved surgical risk. Therefore, Lee at al (19) recently published the largest and most current scheme, which is known as the Revised Cardiac Risk Index (Table 4). The study is of high quality because the index was derived in a large series of 2893 patients and then prospectively validated in 1422 patients. Outcomes were assessed in blinded fashion. By receiver-operating characteristic curve analysis, the Revised Cardiac Risk Index performed better than either the other indexes (Table 5).

Table 4. The Revised Cardiac Risk Index (19)

Clinical Variable	Scoring System
High risk surgical procedure*	Class I - 0 risk factors
History of ischemic heart disease†	Class II - 1 risk factor
History of congestive heart failure	Class III - 2 risk factors
History of TIA or stroke	Class IV - 3 or more risk factors
Preoperative insulin therapy	
Preoperative serum creatinine >2.0 mg/dL	

* intraperitoneal, intrathoracic, or suprainguinal vascular; † excludes prior coronary revascularization

Table 5. Major Cardiac Event Rates by Cardiac Risk Index (19).

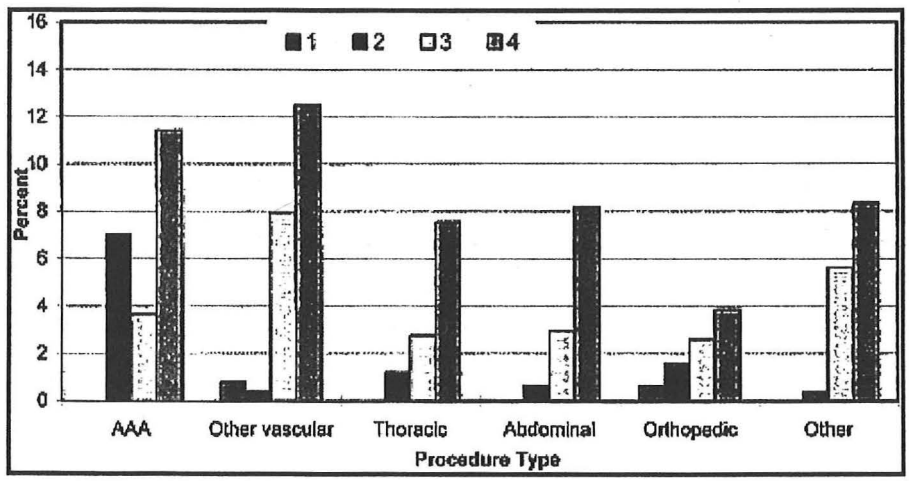
	Events / No. of pts	Event Rate (%)	Event Rate (95% CI)
Original Cardiac Risk Index			
Class I	13/1039	1.3	0.7-2.1
Class II	15/297	5.1	2.9-8.2
Class III	8/84	9.5	4.2-17.9
Class IV	0/2	0	
ROC area	0.701		
Modified Cardiac Risk Index			
Class I	29/1371	2.1	1.4-3.0
Class II	4/44	9.1	2.5-12.8
Class III	3/7	42.9	9.9-82
ROC area	0.582		
Revised Cardiac Risk Index			
Class I	2/488	0.4	0.05-1.5
Class II	5/567	0.9	0.3-2.1
Class III	17/258	6.6	3.9-10.3
Class IV	12/109	11.0	5.8-18.4
ROC area	0.806 *		

* p = 0.034 vs other risk indexes, major cardiac events include MI, cardiac arrest, pulmonary edema, and complete heart block.

Importantly, this study showed an overall in-hospital mortality rate of 0.8% for the derivation group (n=2893) and 1.5% for the validation group (n=1422). This confirms the earlier point that surgical results are improving over time, lessening the need for risk stratification. Based on the strength of the study design and large number of recently studied patients, the Revised Cardiac Risk Index is the recommended clinical index for simple risk evaluation.

Does this clinical risk stratification satisfy the critical elements?

1. Is it accurate? The answer is yes. The ROC area of >0.8 indicates that the Revised Cardiac Index is accurate in distinguishing patient risk groups.
2. Does it add to pre-test knowledge? The answer is yes. The Revised Cardiac Risk Index adds to the pre-test assessment since the latter can only provide the general event rate for a given surgical procedure. Figure 1 shows that for each surgical procedure except aortic aneurysm repair, there is a statistically significant trend toward increased event rates with increased index.
3. Is the cost/benefit ratio favorable? The answer is yes. The Revised Cardiac Risk Index is derived cheaply from the history, physical, and serum creatinine.



Risk Stratification by Diagnostic Tests

A large number of studies have proposed the use of various diagnostic tests for further risk stratification of patients undergoing noncardiac surgery. Such tests are often expensive and can cause unnecessary and even harmful delays in surgery. Unless a diagnostic test can be shown to improve upon clinical risk stratification and lead to proven therapy to reduce risk, there is no logical justification for performing it. Nevertheless, preoperative stress nuclear perfusion imaging is widely used at an estimated cost of around $10 billion dollars annually (20,21). This "irrational exuberance" for preoperative diagnostic testing has been questioned by several authors (20-23). The most common of these tests are briefly reviewed in the following paragraphs, holding them up against the critical elements of a test for risk stratification.

Exercise Stress Testing. The goal of exercise testing is to identify functional capacity and/or myocardial ischemia, both of which are predictors of perioperative mortality. In general, the exercise ECG is only a modest predictor of the presence of obstructive CAD. In a meta-analysis of published studies of exercise ECG for diagnosing CAD, the mean sensitivity and specificity were 68% and 77%, respectively (24). For multivessel CAD, the sensitivity and specificity were 81% and 66%, respectively (25). Table 6 shows the results of exercise ECG testing for preoperative risk stratification in studies of over 100 patients.

Table 6. Studies of Exercise ECG Testing for Risk Stratification.

Study	Type of Surgery	No of Pts	Death/ MI (%)	PPV (%)	NPV (%)	Comments
Cutler (26)	vascular	130	7	16	99	
von Knorring (27)	vascular	105	3	8	99	
McPhail (28)	vascular	100	19	24	93	70% failed to reach target heart rate
Urbinati (29)	vascular	121	0	0	100	
Carliner (30)	mixed	200	32	16	93	ETT not an independent predictor

PPV - positive predictive value for death or MI; NPV - negative predictive value for death or MI

Does this test satisfy the critical elements?

1. Is it accurate? The answer is no. As can be seen in Table 6, the positive predictive value is uniformly low, although the negative predictive value is high.
2. Does it add to pre-test knowledge? The answer is no. The Carliner study (30) showed that exercise stress testing failed to add important information to the clinical risk index.
3. Is the cost/benefit ratio favorable? The answer is no since there is no benefit to preoperative exercise testing. The published guidelines of the ACC/AHA (1) and the ACP (2,3) do not support routine exercise testing for preoperative risk stratification.

Myocardial Perfusion Imaging. As is typically the case with diagnostic tests, early studies show promising results and later studies are less favorable. Earlier studies are often conducting in a single center in highly selected patients, without blinding the physicians to the results. Later studies are applied to larger, broader patient groups and are more likely to be blinded or randomized and to employ statistical methods that adjust for covariates.

The rationale behind myocardial perfusion imaging is that many patients referred for vascular surgery are not fully ambulatory due to claudication. Therefore, the history may not yield an accurate assessment of functional class or exertional angina. Accordingly, myocardial perfusion imaging is performed at rest and during vasodilator stress with dipyridamole or adenosine. Patients with reversible or fixed defects are likely to have underlying coronary artery disease, which is the main risk factor for perioperative cardiac events. A widely held misperception about vasodilator stress imaging is that a reversible defect represents ischemia. This is not the case. The majority of patients do not develop ST depression or chest pain during vasodilator stress (31). Instead, they have impaired maximal vasodilator reserve in areas subtended by a coronary stenosis. This leads to relative differences in radionuclide activity in different myocardial segments. For example, a normal area of myocardium supplied by a normal coronary artery should have a maximal vasodilator reserve of about 4:1 (i.e a four-fold increase from resting flow). A hypothetical region of myocardium supplied by a 40-50% stenosis might have a vasodilator reserve of only 2:1. Although this is only half the normal vasodilator reserve, it still represents twice the flow needed to meet resting metabolic needs. Thus, SPECT nuclear

perfusion imaging during vasodilator stress is very sensitive for the presence of even minor degrees of CAD, but does not necessarily equate to ischemia (32). Table 7 lists large studies (>100 pts) in whom vasodilator stress SPECT imaging has been used to evaluate the risk of perioperative cardiac events.

Table 7. Studies of Vasodilator Stress Nuclear Perfusion Imaging for Risk Stratification.

Study	Type of Surgery	No of Pts	Death/ MI (%)	PPV (%)	NPV (%)	Comments
Eagle (18)	vascular	200	8	16	98	defined clinical risk prior to SPECT
Cutler (33)	abd aortic	116	10	20	100	
Younnis (34)	vascular	111	7	15	100	
Hendel (35)	vascular	327	9	14	99	
Lette (36)	mixed	355	8	17	99	
Brown (37)	vascular	231	5	13	99	
Kresowik (38)	vascular	170	3	4	98	
Baron (39)	abd aortic	457	5	4	96	consecutive series, no benefit of SPECT
Bry (40)	vascular	237	7	11	100	
Coley (41)	general	100	4	8	98	defined clinical risk
Younnis (42)	general	161	9	18	98	intermediate to high risk pts
Vanzetto (43)	abd aortic	134	9	13	98	high clinical risk, blinded to results/outcome
Roghi (44)	vascular	320	4	5	98	randomized medium risk pts, no SPECT benefit

PPV - positive predictive value for death or MI; NPV - negative predictive value for death or MI

Does this test satisfy the critical elements?

1. Is it accurate? The answer is no. As can be seen in Table 6, the positive predictive value is uniformly low, although the negative predictive value is high.
2. Does it add to pre-test knowledge? The answer is no. The early unblinded study by Eagle et al (18) suggested that perfusion imaging added important information to the clinical risk index. Similar findings were reported by Vanzetto (43) who studied only patients selected for a high clinical risk index. However, two subsequent large, prospective, blinded studies showed that SPECT myocardial perfusion imaging had no independent predictive value (39,44).
3. Is the cost/benefit ratio favorable? The answer is no. Although quality cost analysis studies are not available, SPECT nuclear imaging is expensive and has low positive predictive value. Thus, patients with positive test results may be subjected to further evaluation such as coronary arteriography and even revascularization. Such a strategy is costly and may cause an unnecessary delay in surgery.

Dobutamine stress echocardiography (DSE). DSE uses visual grading of regional wall motion at rest and during intravenous dobutamine infusion. It offers some theoretical advantages over nuclear imaging. Dobutamine provides an adrenergic stimulus that is more physiologically similar to the stress of the perioperative period than vasodilator stress agents. It is able to identify stress-induced wall motion abnormalities, which are indicative of myocardial ischemia. Moreover, DSE is widely available, portable, and does not involve radiation exposure. Its major limitation is that an adequate hemodynamic workload is not always achieved with dobutamine. Therefore, atropine or handgrip exercise are commonly used along with dobutamine to ensure an adequate heart rate and blood pressure response (45,46).

Several studies have evaluated the ability of DSE to risk stratify patients undergoing noncardiac surgery (Table 8). Overall, the results are similar to myocardial perfusion imaging with a low positive predictive value and a high negative predictive value.

Table 8. Studies of Dobutamine Stress Echocardiography for Risk Stratification.

Study	Type of Surgery	No of Pts	Death/ MI (%)	PPV (%)	NPV (%)	Comments
Lane (47)	mixed	38	8	16	100	
Lalka (48)	abd aortic	60	15	23	93	multivariate analysis
Eichelberger (49)	vascular	75	3	7	100	
Langan (50)	abd aortic	74	4	17	100	
Poldermans (51)	vascular	131	4	14	100	
Poldermans (52)	vascular	300	6	24	100	blinded, ischemic threshold helpful
Davila-Roman (53)	vascular	88	2	10	100	
Das (54)	general	530	6	15	100	not blinded, added increment to risk index
Boersma (55)	vascular	1097	4	14	98	consecutive pts, added value to Revised Cardiac Risk Index only in high risk pts

PPV - positive predictive value for death or MI; NPV - negative predictive value for death or MI

Does this test satisfy the critical elements?

1. Is it accurate? The answer is no. As with nuclear perfusion imaging, studies consistently show a low positive predictive value and the negative predictive value is high.
2. Does it add to pre-test knowledge? The answer is not usually. The recent large, consecutive series by Boersma, et al (55) showed that DSE did not add any incremental value to low or medium risk patients (Score of 0-2 on the Revised Cardiac Risk Index). This cohort comprised over 80% of the patients undergoing major vascular surgery. In the relatively small subset of patients with a high clinical risk, dobutamine added incremental value.
3. Is the cost/benefit ratio favorable? The answer is no. Although quality cost analysis studies are not available, DSE is relatively expensive and has low positive predictive value. Thus, patients with positive test results may be subjected to further evaluation such as coronary arteriography and even revascularization. Such a strategy is costly and may cause an unnecessary delay in surgery. The Boersma study (55) does suggest that it may be beneficial to do DSE in patients with high clinical risk in order to determine whether they will benefit from β-blocker therapy (see later section on therapy).

Resting Echocardiography or Radionuclide Angiography. The concept underlying the use of these tests is that estimation of global left ventricular function would identify patients at high risk for noncardiac surgery. Left ventricular ejection fraction by radionuclide angiography has shown poor positive and negative predictive values for perioperative cardiac complications in a large consecutive series (39). Similarly, echocardiographic assessment of left ventricular systolic function shows poor receiver-operator curve characteristics and does not add substantially to the clinical estimation of risk (56,57). Accordingly, the clinical guidelines published by the ACC/AHA (1) and the ACP (2) do not recommend the use of either echocrdiography or redionuclide angiography for preoperative risk stratification. However, echocardiography may be useful in selected patients if the clinical evaluation suggests significant valvular heart disease such as aortic stenosis, congestive heart failure, or left ventricular hypertrophy (58).

Do these tests satisfy the critical elements?

1. Is it accurate? The answer is no. Although both radionuclide angiography and echocardiography can accurately assess LV function, this does not translate into accurate prediction of surgical risk.
2. Does it add to pre-test knowledge? The answer is no. There is no evidence that these tests add any incremental value to the Revised Cardiac Risk Index.
3. Is the cost/benefit ratio favorable? This point is moot since there is no benefit.

Ambulatory ECG Monitoring. Since the amount of intraoperative ischemia is no different than preoperative ischemia (12-14), it would follow that measuring the latter by ambulatory ECG monitoring may help predict the risk of perioperative complications. However, several studies have examined this hypothesis and found poor positive and negative predictive values. Accordingly, ambulatory ECG monitoring is not recommended for risk stratification of patients undergoing noncardiac surgery (1-3).

Coronary Angiography. Routine coronary angiography is not recommended for risk stratification of patients undergoing noncardiac surgery (1-3). However, patients considered for noncardiac surgery who already have an indication for cardiac catheterization should undergo this procedure. Such patients include those with acute coronary syndromes or angina refractory to medical therapy. ACC/AHA guidelines also recommend coronary angiography for patients with high risk results of noninvasive testing preoperatively. This recommendation is illogical since there is no evidence that a strategy of coronary angiography followed by revascularization is beneficial. In fact, there is some evidence that such a strategy is harmful, as will be discussed subsequently.

Therapies to Reduce Perioperative Risk of Cardiac Complications

Coronary Artery Bypass Grafting (CABG). No randomized, controlled, or prospective trials have been done to evaluate the potential benefit of CABG prior to noncardiac surgery. However, several studies have shown that patients with previous CABG have very low rates of cardiac complications after noncardiac surgery (59-62). In the best of these studies, Eagle et al (62), reviewed the CASS Registry data and found 3368 patients who subsequently underwent noncardiac surgery after either prior CABG (n=1961) or medical therapy (1297). Those with prior CABG had fewer deaths (1.7% vs 3.3%, p=0.03) or MI's (0.8% vs 2.7%, p=0.002) compared to those receiving medical therapy. The benefit of CABG was limited to patients undergoing major vascular, abdominal, thoracic, or head and neck surgery. Those undergoing orthopedic, urologic, breast, or skin operations and a very low complication rate regardless of prior CABG. Based on these data, the ACC/AHA and ACP guidelines do not recommend noninvasive testing for risk stratification in patients who have undergone CABG within the past 5 years (1,2), unless there are recurrent symptoms.

It is an entirely different matter to recommend CABG to a patient referred for evaluation of the risk of planned noncardiac surgery. If the patient has symptoms and coronary anatomy that would mandate surgery anyway (such as left main disease or multivessel disease and impaired LV function), CABG is indicated. However, CABG is never indicated solely for the purpose of protecting an asymptomatic patients from possible complications of noncardiac

surgery. The primary reason for this is the CABG itself exposes the patient to a substantial risk of death, nonfatal MI, stroke, and measurable cognitive dysfunction (Table 9). In addition, the recovery period after CABG results in a delay in the planned noncardiac surgery, which then carries its own risks. Two decision-analysis models have examined the risk/benefit ratio of prophylactic CABG prior to planned vascular surgery. Mason et al (63) found that in patients with an abnormal dipyridamole thallium scan, a strategy of coronary angiography and CABG, if appropriate coronary anatomy was found) led to worse results than just proceeding to noncardiac surgery. Similarly, Fleisher et al (64) examined whether a strategy of preoperative dipyridamole thallium testing with subsequent coronary angiography and possible CABG was superior to proceeding to noncardiac surgery with testing. They also found that the more aggressive strategy led to worse outcomes. These findings lead to the obvious conclusion that prophylactic CABG is more likely to harm than benefit most patients undergoing vascular surgery.

Table 9. Risks Associated with CABG.

Study	Study Type	No of Pts - CABG	Death (%)	MI (%)
RITA '93 (65)	CABG vs PTCA	501	1.2	2.4 *
CABRI '95 (66)	CABG vs PTCA	513	1.3	NR
BARI '96 (67)	CABG vs PTCA	914	1.3	4.6 *
ARTS '01 (68)	CABG vs stent	605	2.8	4.8†
HCFA Medicare '96 (69)	All CABG >65yrs	>180,000	5.4%	NR

* Q-wave MI only, † 12.6% had CK >5 x normal, NR- not reported

Percutaneous Coronary Intervention. As with CABG, there are no randomized, controlled trials showing the percutaneous coronary intervention is beneficial as prophylactic therapy for patients undergoing noncardiac surgery. A couple of small retrospective studies indicated that PCI might possible offer benefit. Huber et al (70) reported the results of balloon coronary angioplasty in 55 patients with a high preoperative cardiac risk for noncardiac surgery. Angioplasty was successful in 50 of these patients with a perioperative rate of death or MI of 1.9% and 5.6%, respectively. Gottlieb, et al (71) analyzed 194 patients who underwent noncardiac surgery within 3 months after coronary angioplasty. The perioperative event rate was very low with only 1 death and 1 MI. On the other hand, a recent study by Kaluza, et al (72) indicates that caution must be used in performing noncardiac surgery soon after coronary stenting. They report that in 40 patients who underwent noncardiac surgery within 6 weeks of coronary stent placement, there were 8 deaths (20%), 7 nonfatal MI's (18%), and 11 major bleeding episodes (28%). All of the deaths and MI's occurred within 2 weeks of the stent placement. The general practice was to withhold antiplatelet drugs 1-2 days prior to noncardiac surgery. The authors suggest that this may have led to stent thrombosis. It is also evident that this practice did not avoid postoperative bleeding complications. Currently, there is no evidence to support the use of prophylactic coronary angioplasty or stent placement prior to noncardiac surgery. These procedures should be reserved for those patients who require them anyway for management of acute coronary syndromes or stable angina refractory to medical therapy. It would seem prudent in such patients to defer any elective noncardiac surgery for at least 6 weeks.

Beta-Adrenergic Blockade. Since the publication of the ACC/AHA and ACP guidelines on risk stratification for noncardiac surgery, there have been two randomized, controlled trials and one large nonrandomized report of beta-blocker therapy to reduce the risk of perioperative cardiac complications in patients undergoing noncardiac surgery. Perioperative beta-blockade is quite

logical since the pathophysiology of perioperative cardiac events is related to catecholamine stress as discussed previously.

Mangano, et al (73) performed a randomized, double-blind, placebo-controlled trial of atenolol in 200 patients undergoing noncardiac surgery at the San Francisco VA Medical Center. All patients had either known CAD or significant risk factors for it. Exclusion criteria were heart rate < 55 min^{-1}, systolic blood pressure <100 mmHg, congestive heart failure, third degree heart block, or bronchospasm. Atenolol (or placebo) was given prior to induction of anesthesia as a 5mg intravenous infusion over 5 minutes. After 5 minutes, a second infusion was given unless the exclusion criteria were met. The patients then received 50 -100 mg of atenolol daily for up to 7 days postoperatively. The primary end-point of the study was two-year mortality. There were no perioperative deaths in the atenolol group and only 1 in the placebo group (a patient who died 19 days after surgery). However, by 6 months, there were 8 deaths in the placebo group and none in the atenolol group ($p<0.001$). Figure 2 shows the Kaplan-Meier survival curves from the patients in this study.

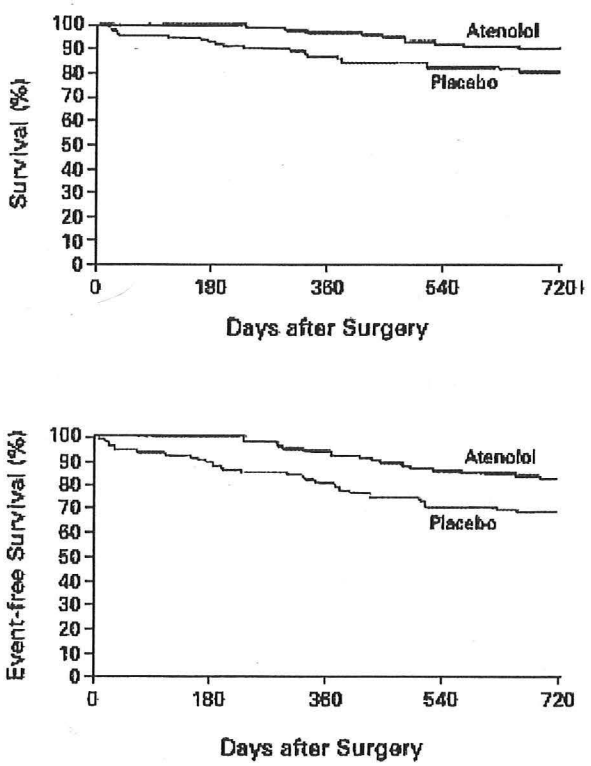


Fig. 2. Kaplan-Meier curves showing survival (top) and event-free survival for 2 years after preoperative randomization to atenolol or placebo (73).

Poldermans, et al (74) performed a randomized trial of bisoprolol in high risk patients undergoing either abdominal aortic aneurysm repair or infrainguinal arterial reconstruction. A total of 1351 patients were screened for the study, of which 846 had at least one clinical risk factor. Of these, 173 had ischemia by DSE and were considered eligible for the study. Fifty-nine patients were randomized to bisoprolol and 53 to standard care. The other patients were excluded because they were already on a beta-blocker or had severe LV dysfunction. Bisoprolol was started orally at 5mg daily at least one week prior to surgery. It was increased to 10 mg daily, if tolerated, and continued for 30 days postoperatively. The study was stopped early by a monitoring committee because of the strong beneficial effect of bisoprolol (Table 10).

Table 10. Effects of bisoprolol on cardiac death and MI perioperatively.

	Death (30 days)	MI (30 days)	P value
Bisoprolol	2 (3.4%)	0 (0%)	0.02
Standard Care	9 (17%)	9 (17%)	<0.001

Boersma et al (55) subsequently published the results of the entire cohort of 1351 patients who were screened for the above study. By multivariate analysis, they analyzed the relationship between clinical risk stratification by the Revised Cardiac Risk Index, DSE, and beta-blocker therapy. DSE was performed in 1097 patients (81%) and beta-blockers were given to 360 patients (27%). The overall rate of death or nonfatal MI was only 3.3%. In the 83% of patients determined to be at low or intermediate risk by the Revised Cardiac Risk Index (<3 risk factors), the rate of cardiac complications was 0.8% in patients taking beta-blockers compared to 2.3% in patients not taking a beta-blocker. In this large subgroup of patients, DSE added no significant incremental value as a marker of risk stratification. In patients with 3 or more risk factors, DSE added additional information. For example, patients receiving beta-blockers without ischemia by DSE had a 2.0% (1/50) event rate compared to 10.6% (5/47) if DSE showed ischemia. Moreover, if the ischemia by DSE were limited to 1-4 myocardial segments, the event rate remained low (2.8%, 1/36) compared to patients with ischemia in > 5 segments (36%, 4/11). Unfortunately, this subgroup analysis is limited by small sample sizes.

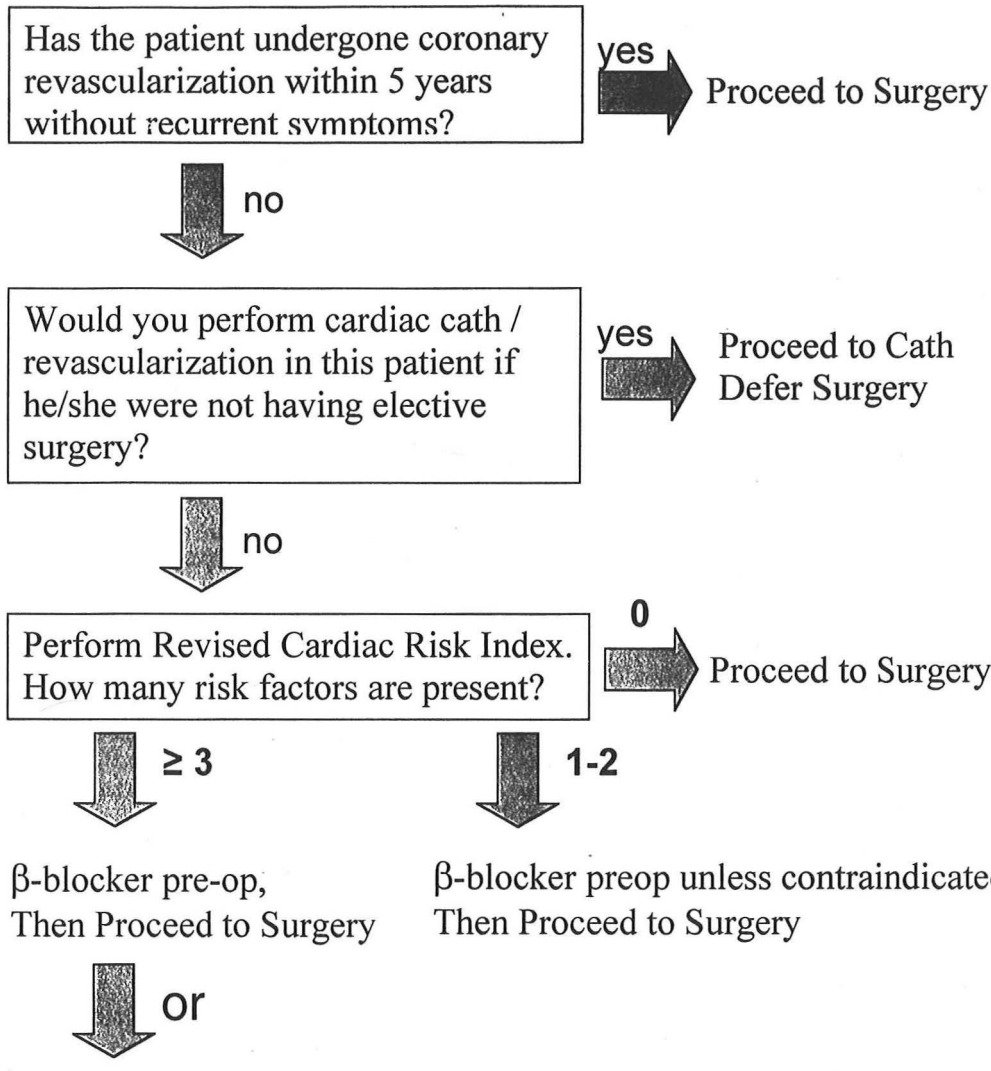
Several important conclusions can be drawn regarding the use of β-blocker therapy in noncardiac surgery. First, β-blockade is the only therapy that has proven to be beneficial in reducing perioperative complications. Second, β-blockers reduce the risk of cardiac events in patients at low, intermediate, and high risk groups as defined by the Revised Cardiac Risk Index. Third, β-blocker therapy is effective even in patients with inducible ischemia by DSE. Finally, β-blockers are inexpensive.

Several questions remain unanswered regarding β-blocker therapy in noncardiac surgery. In the studies done to date, patients with severe LV dysfunction have been excluded. It is not clear how these patients should be treated. Second, the duration of β-blocker therapy is not clear. Given that the risk of cardiac complications of noncardiac surgery is related to the presence of CAD, it would seem prudent that life-long β-blocker therapy may be needed. However, this is a hypothesis that has not been tested. Third, it is not clear whether this is a class effect or due to specific properties of atenolol or bisoprolol.

Other Medical Therapies. A few small studies have examined the use of nitroglycerin or calcium blockers in perioperative management of patients undegoing noncardiac surgery. These have been summarized in the ACC/AHA guidelines (1) and are inconclusive. Since aspirin and other antiplatelet agents are known to reduce cardiac events in patients after acute coronary syndromes (75), it would seem reasonable to use them in the perioperative period. However, no data exist regarding this important issue and aspirin use has to be balanced against the risk of postoperative bleeding. Similarly, it is well established that HMG-CoA reductase inhibitors are beneficial in primary and secondary prevention of cardiac events in patients with known CAD or significant risk factors for it (76). Therefore, it is possible that these agents could reduce perioperative risk, especially since they may have plaque-stabilizing properties (77). Finally, ACE inhibitors have been shown to prevent death and nonfatal MI in patients with CAD (78). Again, no studies have examined the effect of these important drugs on the risk of perioperative cardiac events. However, it is well recognized that hypertension and blood sugar should be well controlled prior to elective surgery. In the VA surgery database (6), a blood sugar > 200 mg/dL was a better predictor of outcome than the presence of diabetes.

Proposed Clinical Algorithm for Preoperative Risk Stratification

Based on the above considerations, the approach to preoperative risk stratification can be greatly simplified (fig 3). The following questions should be asked. First, has the patient undergone coronary revascularization within the past 5 years without recurrent symptoms. If yes, then the patient can go to surgery because the risk is very low. Second, would you perform cardiac catheterization and possible revascularization in the patient irrespective of the proposed surgery? If yes, then proceed to cardiac catheterization and defer surgery until the issue has been resolved. If CABG or coronary artery stent placement is performed, surgery should be deferred for at least 6 weeks. Next, perform the Revised Cardiac Risk Index. If there are no risk factors, surgery can proceed without delay. If there are 1 or 2 risk factors, a β-blocker should be used in the perioperative period. If a β-blocker is contraindicated, the surgery can proceed without it since the risk in these patients is only mildly increased. If there are 3 or more risk factors, a β-blocker should be used in the perioperative period. According to the Poldermans paper, this reduces risk from very high (34%) to very low levels (3%). However, if a β-blocker is contraindicated or the surgical risk is deemed excessively high, one should consider canceling or deferring the surgery. Alternatively, Boermsa, et al (55) propose performing DSE in patients at high risk by the Revised Cardiac Risk Index. If it shows no ischemia, the risk is low and surgery can proceed. If it shows ischemia, the risk of death or MI is about 35% (55,74). Unfortunately, there is no evidence that prophylactic revascularization of such patients has any benefit. A trial is underway to assess this question (79), but it is currently on probation for lack of enough randomizable patients. As of this writing, there is no evidence that high risk patients who cannot take a β-blocker would benefit from coronary revascularization.



If b-blocker contraindicated, consider one of the following: cancel/defer surgery or preop DSE (if no ischemia, risk is low)

Conclusions

Risk stratification for noncardiac surgery remains an important clinical issue. However, the era of performing expensive noninvasive tests has come to an end. Myocardial perfusion imaging and dobutamine echocardiography do not add significantly to the clinical defined risk index in most patients, nor do they determine therapy. The role of coronary angiography and revascularization is limited to patients who require them anyway for clinical reasons. Patients considered to be at risk for cardiac events during noncardiac surgery should be treated with a β-blocker, which is the only therapy proven to reduce the risk of perioperative cardiac events.

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