Editorial Comment

Risk Stratification for Noncardiac Surgery
How (and Why)?

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Although the occurrence of life-threatening cardiac complications during and after noncardiac surgery has long been recognized, this problem has gained increasing attention over the past 15 years. In part, this new interest reflects the growing numbers of complex operations in an aging population and increased scrutiny of what were once considered expected events. However, it is also clear that this trend is to a significant extent driven by technology. As methods such as multilead ST segment monitoring and transesophageal echocardiography have made their way into the operating and recovery areas, there has been a greater appreciation of the association of myocardial ischemia with adverse cardiac events. More importantly, improvements and increased availability of noninvasive imaging techniques have made it possible to detect and quantify ischemia before surgery. Not surprisingly, the occurrence of preoperative, intraoperative, and especially postoperative ischemia has proved to be a predictor or marker of cardiac morbidity and mortality.

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These trends and observations, however, have not clarified either how to best assess perioperative risk or, more importantly, why and when such assessments are necessary.

Perioperative Cardiac Morbidity: The Problem

Nearly 25 million patients undergo noncardiac surgical procedures each year in the United States. Of these, 1 million are known to have coronary artery disease, another 2–3 million have multiple risk factors, and an additional 4 million are at risk by virtue of being >65 years old. These groups account for approximately 80% of the 1 million patients who suffer perioperative cardiac morbidity and mortality, with its accompanying in-hospital cost of over $12 billion annually. The 400,000 patients undergoing vascular surgery represent the highest risk group, both because they have a high incidence of coronary disease and because the operative procedures are particularly stressful.

Death, nonfatal myocardial infarction, unstable angina pectoris, and congestive heart failure or pulmonary edema are the most important cardiac complications of noncardiac surgery. Mortality rates from cardiac causes range from negligible to 5% or higher for major vascular procedures. Although the incidence of perioperative myocardial infarction is <1% in the general population, it rises to 2–8% in patients with previous myocardial infarction and ranges from 1% to 15% in patients undergoing vascular surgery. The incidence of unstable angina and congestive heart failure are less well defined, primarily because criteria remain more subjective, but these complications generally occur in 1–5% of patients. Coronary artery disease and/or significant left ventricular dysfunction are the underlying substrates for most of these complications.

Myocardial infarction and unstable angina differ in the perioperative period from other settings in that these conditions are silent in the majority of cases and that the pathophysiology associated with the postoperative period is unique. Myocardial oxygen requirements may be markedly increased as a result of tachycardia, hypertension, and left ventricular dilatation. Blood oxygen-carrying capacity is often substantially reduced because of anemia and the less optimal characteristics of transfused blood. Marked changes in the neurohormonal milieu may increase coronary vascular tone. All of these factors have the potential to precipitate ischemia and infarction without complete coronary occlusion, but other perioperative changes may also facilitate coronary thrombosis. These potential factors include 1) increased coronary artery shear stresses resulting from alterations in contractility, blood pressure, coronary flow, and coronary tone; 2) enhanced platelet aggregation as a result of high levels of circulating catecholamines, thrombocytosis, and changes in blood viscosity and coronary flow; 3) a generalized hypercoagulable state resulting from increased fibrinogen levels and other alterations in hemostasis; and 4) a precipitating role of vasospasm induced by neurohormonal factors. As is the case for myocardial infarction in nonsurgical patients, it is quite likely that thrombotic occlusions occur frequently in vessels that initially were not severely obstructed. Thus, the presence of coronary disease but not necessarily preexisting critical stenosis is the substrate for perioperative ischemic events.

Postoperative congestive heart failure and pulmonary edema are multifactorial in origin. Although they may be precipitated by myocardial ischemia, other factors play a role, such as hypertension, hypoxemia, mobilization of extravascular volume, removal of positive-pres-
sure ventilation, and the effect of withdrawal of previous medical therapy, which all tend to occur on postoperative days 1–3, when the incidence of heart failure is greatest. Many of these patients have reduced left ventricular ejection fractions, but impaired left ventricular diastolic function, most commonly caused by left ventricular hypertrophy or diabetes mellitus, is also an important substrate for pulmonary edema.

Perioperative Cardiac Risk: How Should It Be Assessed?

Because of the magnitude of the problem of perioperative cardiac morbidity, clinicians and investigators have sought to identify patients at greatest risk preoperatively. In this regard, a number of clinical factors have been identified, including 1) clinical evidence of coronary artery disease from prior myocardial infarction or angina pectoris; 2) severe left ventricular dysfunction as evidenced by a history of heart failure, a third heart sound, or elevated jugular venous pressure; 3) factors that increase the likelihood of these conditions such as advanced age, severe hypertension, diabetes mellitus, and cardiac arrhythmias; and 4) instability or progression of cardiac disease (e.g., recent myocardial infarction, unstable angina, or refractory heart failure). Several multifactorial indexes have incorporated these markers and have proved quite helpful in identifying patients at high and low risk for noncardiac procedures.3,4,11–14

However, when the population under evaluation has a high prevalence of coronary artery disease, whether apparent or silent, such as patients undergoing abdominal aorta or peripheral vascular surgery, even individuals at apparently low risk may have a 5–10% incidence of cardiac complications.3–6,13 Therefore, a number of additional diagnostic tests have been evaluated for their potential to further stratify risk. Approaches that have been used are resting and exercise ECG, measurements of left ventricular ejection fraction at rest or with exercise, ambulatory ECG assessments of arrhythmias and ischemia, exercise and pharmacological stress myocardial scintigraphy, and stress echocardiography. Results with most of these procedures have been reviewed in recent articles.3,4

Several comments concerning this extensive literature are warranted. First, since underlying coronary artery disease and left ventricular dysfunction are major factors in perioperative cardiac morbidity, any test for these conditions is likely to have prognostic value. Second, although positive results are to be expected, the initial reports with each of these tests have been remarkably favorable.3,4 Virtually all of the complications in each of these series have occurred in the minority of patients with positive tests. This is, perhaps, to be expected in studies that generally have included only small numbers of patients and events and have been conducted retrospectively, often without investigator blinding. Such uniformly favorable results are also to be expected from a publication process that is biased in favor of positive studies and new techniques. Third, more realistic appraisals of earlier approaches are often provided when the previous techniques are compared with newer or different ones. Eventually, if more widespread experience does not confirm the initial enthusiasm for a given technique, less favorable results may be published and some tests may be used less frequently. A recent example of this trend has been the recognition that the results of dipyridamole–thallium scintigraphy may not be as predictive as was once thought.15–17

The article by Poldermans et al.18 in this issue of Circulation provides strong evidence that dobutamine stress echocardiography is useful in assessing perioperative cardiac risk. It has a number of strengths. The study population was relatively large (136 patients) and was limited to patients undergoing elective major vascular surgery. The testing protocol was well defined, and results and follow-up were obtained in nearly all patients. The number of cardiac events was substantial (11%) and included five fatal myocardial infarctions and nine patients with unstable angina. Most importantly, the data were collected prospectively, the results of the tests were not available to the physicians managing the patients, the echocardiograms were interpreted by observers blinded to the patient’s clinical presentation, and complications were assessed by observers unaware of the echocardiographic results. Echocardiograms in 35 of the 131 patients with analyzable studies were positive, as defined by a new or worsening wall-motion abnormality during dobutamine infusion. All 15 postoperative cardiac complications occurred in these 35 individuals, so that the predictive value of a negative test for the absence of complications was 100% and that of a positive test for subsequent events was 43%. These results are in accord with the findings of two additional studies with this technique.19,20

Is dobutamine stress echocardiography now the test of choice for risk stratification? There are several reasons why this test may be advantageous. Unlike measurements of ejection fraction or scintigraphic or ECG measures of ischemia, this test is able to assess both left ventricular function and the potential for myocardial ischemia, the two major factors responsible for most cardiac complications. Furthermore, the indicator of ischemia, regional left ventricular dysfunction induced by increased myocardial oxygen demand, is specifically relevant to the circumstances underlying perioperative ischemia. Additional information that may be helpful can be generated by echocardiography, including recognition of valvular abnormalities, left ventricular hypertrophy, and diastolic dysfunction.

However, it is unlikely that the nearly perfect results in this study will be obtainable in all patient populations and in every laboratory. The proportion of inadequate studies varies considerably among laboratories, although those with a higher incidence of poor-quality studies rarely publish their results. Interpretation of the echocardiographic results is highly subjective, and many laboratories either do not perform dobutamine stress echocardiograms or have very limited experience with this procedure. The potential for serious complications with high doses of dobutamine and with the addition of intravenous atropine is not trivial, as evidenced by the occurrence of ventricular fibrillation in one patient in the present study. Although the authors emphasize the potentially lower costs of stress echocardiography than of scintigraphic techniques, this procedure is quite costly in the United States. Thus, a great deal more experience will be needed to determine stress echocardiography in this setting can be determined, and eventually the choice of test will de-
pend not only on the relative accuracy of the procedures but also on availability and experience in individual laboratories.

**Perioperative Risk Stratification: Why or Why Not?**

Although experience with approaches to perioperative risk stratification continues to evolve, relatively little thought has been given to the rationale for such assessments. The costs of performing one noninvasive test in only the subgroup of patients undergoing vascular surgery would range from $200 to $400 million annually in the United States. The fiscal impact would increase substantially if more patients at risk were studied or multiple tests were performed. In addition, the results of these tests are likely to lead to additional procedures, morbidity, and mortality. It is possible that these costs and risks are warranted, if they result in improved long-term outcomes for patients undergoing noncardiac surgery. Unfortunately, there is no convincing evidence that this is the case. There are three potential circumstances under which risk stratification makes sense: 1) if the results would alter the surgical plan, leading either to cancellation of surgery or to an alternative procedure, such as amputation instead of peripheral arterial bypass; 2) if the results indicate a need for coronary revascularization before noncardiac surgery, either by coronary artery bypass grafting or percutaneous transluminal angioplasty; and 3) if the results would alter perioperative management. Each of these potential applications warrants careful scrutiny because even if preoperative testing does lead to these interventions, as is now often the case, are there data to justify these approaches?

Perhaps the clearest application of risk stratification is the first of these three interventions. However, cancellation of surgery or the selection of a different procedure are decisions that are usually based on clinical factors. Age, comorbidity and general poor condition, and unstable or refractory cardiac disease are the usual reasons, rather than the results of additional diagnostic tests.

Prophylactic coronary artery revascularization to reduce perioperative cardiac morbidity is the most controversial intervention. Three pieces of data are usually cited to support this practice: 1) the high risk of the identified patients; 2) the low risk of surgery in patients who have undergone prior revascularization\(^1\); and 3) the high incidence of myocardial infarction and death during long-term postoperative follow-up in patients undergoing major vascular operations or in patients with evidence of perioperative myocardial ischemia.\(^2\) However, these data are difficult to interpret and must be considered critically, because they reflect retrospective analyses based on selected patients. The risk of coronary revascularization in these patients is not cited. Those at highest risk for noncardiac surgery are also often at very high risk for coronary bypass surgery. Many surgeons would be circumspect in undertaking coronary revascularization in individuals with diffuse vascular disease, poor left ventricular function, multiple associated diseases, and no potential for symptomatic benefit, with the sole goal being to reduce the risk of a subsequent surgical procedure. Angioplasty is a more attractive approach, but given the physiology of perioperative ischemic events and the often-cited goal of long-term improvement in prognosis, it is difficult to infer a benefit from a procedure that improves only one or several stenoses, in many cases only temporarily, without providing complete revascularization.

These questions can be answered only by a prospective randomized trial in which patients identified as being at high risk for perioperative cardiac events are assigned to undergo elective noncardiac surgery with optimal monitoring and medical management, either with or without prophylactic coronary revascularization. The end point would be total mortality and morbidity over a period of 1–3 years, and ideally, both bypass surgery and coronary angioplasty would be examined. Unless or until this information is available, preoperative coronary revascularization should be reserved for patients with the usual indications for this procedure—those symptom-limited on medical therapy, those with unstable angina, or patients with manifest coronary disease and significant left ventricular dysfunction in whom extensive ischemia is present.

The third potential application for risk stratification is to use the results to modify perioperative management. Careful intraoperative and postoperative monitoring are standard procedures for patients undergoing major vascular operations and for those with important clinical risk factors. The ability of additional monitoring by transesophageal echocardiography or prolonged intensive care unit observation to prevent complications remains unproven. Whether additional risk stratification would lead to safer or more cost-effective perioperative care is a hypothesis that requires testing. Given our understanding of the pathophysiology of perioperative cardiac events, several medical interventions are potentially attractive. These include the use of \(\beta\)-blockers to minimize hemodynamic fluctuations and the effect of excess catecholamines, central sympatholytic agents for much the same objectives, antithrombotic therapy, and other investigational agents that increase myocardial adenosine levels. However, each of these therapies has the potential to increase complications as well as to reduce them. Therefore, the use of these approaches is also not an adequate justification for risk stratification until trials demonstrating their efficacy have been performed.

**Conclusions**

The considerable attention that has been devoted to the characterization of cardiac complications of noncardiac surgery is certainly justified. Patients at greatest risk can be identified by clinical assessment, but in patients with intermediate risk by clinical assessment, additional noninvasive tests for ischemia and measurements of left ventricular function can further stratify risk, albeit probably not as well as might be assumed from the highly favorable results that predominate in the literature. Based on our understanding of the mechanisms of perioperative cardiac events and the initial experience with dobutamine stress echocardiography, including the article by Poldermans et al in this issue, this test is likely to be useful in appropriately selected patients. However, until additional studies confirm that interventions dictated by this and other tests can alter long-term outcome, preoperative risk assessment should be based primarily on clinical evaluation rather than the
routine use of additional modalities of noninvasive testing.

References

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