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Editorial Comment

Cardiac Risk for Vascular Surgery*

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Patients undergoing major vascular surgery often represent a special challenge for cardiologists, vascular surgeons and anesthesiologists. Such patients are commonly at higher risk for cardiac complications than those undergoing other types of operation (1), and they may be more difficult to evaluate, especially if they are unable to exercise. Because functional status appears to be an important predictor of major complications with noncardiac surgery, the inability to exercise because of peripheral vascular disease has led cardiologists to seek alternative diagnostic methods to assess cardiac risk. In this issue of the Journal, an original research article (2) and a meta-analysis (3) use sophisticated methods to assess the ability of clinical data and test results to predict cardiac complications after vascular surgery.

The Bayesian model for perioperative assessment of vascular surgery candidates (2) uses several readily available preoperative clinical characteristics to estimate a patient's risk for major cardiac complications. The Bayesian approach assumes that a patient's pretest, or "prior," probability of complications can be assessed on a clinical basis and that this probability can then be modified by adding incremental, independent information provided by a diagnostic test. In this particular model, the authors begin by using the rate of complications for a given type of procedure. They then modify this probability according to patient age and history of diabetes, angina, congestive heart failure, myocardial infarction or prior coronary artery bypass graft surgery. Finally, this second probability is further modified on the basis of the results of dipyridamole–thallium scintigraphy. Although this sequential approach is an ideal way to assess the independent incremental impact of a diagnostic test, several methodologic questions are raised: 1) The higher initial probability of complications for peripheral vascular procedures than for more formidable aortic procedures is unlikely to be an independent characteristic of the operation itself; most likely, the higher rate of complications with peripheral vascular procedures relates to other higher risk characteristics of these patients. If so, the subsequent clinical characteristics probably are not truly independent of this prior estimate. 2) The authors weighted individual factors on the basis of logistic regression coefficients regardless of their statistical significance. Although each of these clinical factors might be suspected to correlate with cardiac complication rates, inclusion of factors in a multivariate model regardless of their statistical significance runs counter to the usual approach.

The sequential approach is an important strength of the analysis. It is critical that tests be viewed in terms of their true incremental information rather than on whether they simply substitute for other, more easily obtainable factors. The authors are also to be congratulated for their careful statistical analysis using receiver operating characteristic (ROC) curves and C statistics, as well as their reliance on the more reliable end points of myocardial infarction and cardiac death. Nevertheless, the authors are appropriate in carefully acknowledging three important limitations: 1) All patients included in the analyses were referred for dipyridamole–thallium testing and hence are almost certainly at significantly higher risk than other patients who were not referred for testing (1). 2) The physicians were aware of the dipyridamole–thallium results, and these results may have influenced postoperative observation and diagnosis of complications, such as acute myocardial infarction in patients with known positive test results. 3) The gathering of data by chart review is far different from a physician prospectively recording clinical data preoperatively for risk assessment. Regardless of any theoretic, methodologic issues, the sequential model worked well on the independent validation sets of patients in whom they were tested, with ROC areas ranging from 0.72 to 0.76. These figures are far more relevant than the 0.81 ROC area reported for the set of patients from whom the model was derived. Although it is beyond the scope of this editorial to describe such statistical analyses in detail. ROC values between 0.7 and 0.8 in prospective validation testing are generally considered to be very good, whereas values >0.8 would be excellent. Figure 4 of L'Italien et al. (2) clearly demonstrates how dipyridamole–thallium scintigraphy adds important incremental information in patients who are at moderate risk on the basis of clinical assessment alone, but little if any information in those at low or high risk on the basis of clinical assessment. It emphasizes a common-sense approach to dipyridamole–thallium scintigraphy and risk stratification.

To put these findings in perspective, the original cardiac risk index (4), which has shortcomings when applied to vascular surgery candidates (1,5), had ROC areas of 0.81 and 0.77 when tested in two large-scale validation studies of the same types of patients from whom it was originally derived (1,6,7): unselected, consecutive patients undergoing a variety of major noncardiac operations. Thus, the authors' sequential clinical and thallium approach to assessing the risk of major cardiac complications after vascular surgery was, in prospective validation testing in vascular candidates similar to those in whom it was derived, not quite as good as the original cardiac risk index without supplemental testing is when applied to a broad

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range of general surgical patients. The utility of each of these two approaches for their respective types of patients is therefore relatively similar.

Meta-analysis of dipyridamole–thallium scintigraphy and dobutamine echocardiography. Meta-analysis represents a quantitative approach to analyzing pooled data from various studies. Most commonly, meta-analysis has been used to combine data from randomized control trials to increase sample size and reduce uncertainty. The method is most helpful when multiple small studies indicate a consistent trend favoring one therapy or another, and then the pooled analysis of data from all studies has an adequate sample size to demonstrate statistical significance.

As noted many years ago (8), pooled analyses are subject to a variety of methodologic issues, most notably whether or not the studies being pooled are truly comparable. For studies of preoperative dipyridamole–thallium scintigraphy, a key problem relates to whether patients who have been referred for testing are similar to "all comers" undergoing similar procedures (1). The current meta-analysis of dypiridamole–thallium scintigraphy suggests that the accuracy of the test varies depending on the prevalence of coronary artery disease in the cohort being tested (3). Although this is certainly a reasonable interpretation, the accuracy of the test may depend more on the severity of coronary disease than on its simple presence or absence. Regardless, it is clear that a transient defect on dipyridamole–thallium scintigraphy is associated with about a ninefold increase in the relative risk for major cardiac complications among patients referred for testing (1), but does not appear to be significantly related to risk when used in unselected, consecutive vascular candidates (1,9).

Studies of stress echocardiography, using either dobutamine or dipyridamole, have shown (1,10) that a positive result on this test is associated with even more of an increase in risk than is found with a positive result on thallium scintigraphy. In fact, the largest single study of stress echocardiography (10) reported that all major cardiac complications occurred in patients with a positive result on the stress echocardiogram. Once again, as noted in other studies, the incremental impact of stress echocardiography was most impressive in patients who were at intermediate risk on the basis of clinical characteristics alone.

I am not nearly as certain as the authors (3) that a positive result on the dipyridamole thallium scintigram in an intermediate likelihood patient is a definitive indication for preoperative coronary revascularization. Certainly, the cardiac complication rate is low among patients who have vascular surgery after surviving coronary artery bypass grafting, but the overall risk of myocardial infarction and cardiac death using this strategy appears to be no lower than that found overall when patients are managed medically (11,12). Although coronary revascularization in such patients is not at all unreasonable, I believe that it is premature to be influenced by a cost-effectiveness analysis that is still in abstract form.

Clinical decision making in the face of uncertainty. My own interpretation is that the three alternative modalities for preoperative testing in vascular surgery candidates who cannot exercise (dipyridamole–thallium scintigraphy, stress echocardiography, ambulatory ischemia monitoring [11]) all add incremental information for risk assessment in patients who are at intermediate risk on the basis of clinical criteria. These criteria can be those put forward by L'Italien et al. (2) or other reasonable approaches (1). In patients who are at low risk on the basis of clinical criteria, the test results are infrequently positive and, even when positive, still do not imply high risk status. In patients who are at high risk on the basis of clinical criteria, even a negative test result is not reassuring.

In my opinion, existing data are insufficient to make definitive recommendations regarding the preferred perioperative management strategies for patients who are known to be at high risk on the basis of clinical factors alone or whose results on a diagnostic test (be it an exercise electrocardiogram, stress scintigram, stress echocardiogram or ambulatory ischemia monitoring) have converted them from a patient at medium risk on the basis of clinical criteria alone to a patient at high risk after inclusion of the test result. One approach is to recommend coronary arteriography followed by revascularization of important stenoses. This approach is based on the favorable outcome of noncardiac surgery among patients who remain candidates for it after successful coronary revascularization (12), as well as the general recognition that higher risk patients who are reasonable candidates for coronary artery revascularization tend to obtain the most benefit from this procedure. However, on the basis of the rates of hard end points, such as myocardial infarction and cardiac death, at leading centers with aggressive perioperative medical management (13), the rate of short-term events with a more aggressive strategy (12,14) has not been shown to be lower with one or the other approaches. For example, although the rate of death was reduced from 2.4% to 0.9% in patients in the Coronary Artery Surgery Study (12) who had had coronary revascularization before their noncoronary surgery compared with patients who had not, the *combined* death rate from the sequence of coronary artery bypass grafting and noncardiac surgery was virtually identical to that with noncardiac surgery itself (12). Furthermore, there was no difference in the rate of nonfatal myocardial infarctions with the noncardiac surgery, suggesting that any nonfatal myocardial infarctions sustained during coronary bypass grafting were incremental. Large series of consecutive patients at leading medical centers treated medically with very modest rates of preoperative testing or coronary revascularization (13) have had outcomes virtually identical to those reported from centers using more aggressive preoperative diagnostic and surgical strategies (14).

In light of the paucity of data, it is not surprising that different analyses have yielded varying recommendations regarding preoperative coronary angiography and revascularization (15–17). I believe that it is still reasonable to consider one of three options in higher risk patients: 1) coronary arteriography followed by coronary revascularization, as indicated; 2) aggressive augmentation of preoperative medications in an attempt to improve functional status or the results of the

preoperative ischemia test, or both—coronary arteriography and revascularization are then reserved for those who do not improve; 3) aggressive preoperative augmentation of medications combined with aggressive use of beta-adrenergic blocking agents and nitrates (18) to control pulse and blood pressure, perhaps combined with postoperative ischemia monitoring to detect transient asymptomatic ischemia, which is the primary predictor of a symptomatic postoperative event (19) and which may be effectively treated by short-term changes in medications guided by such findings.

Because the major incremental benefit of coronary revascularization in vascular surgery candidates may be more for long-term outcome than perioperative survival, it is critical that patients who survive vascular surgery be reassessed for their possible benefit from coronary revascularization. In many patients, the peripheral vascular status may be sufficiently improved by operation to unmask more symptomatic coronary disease. It must be remembered that the major cause of subsequent death in patients with peripheral vascular disease is coronary events (20). If there is reasonable fear, because of logistic or other reasons, that such a postoperative evaluation followed by appropriate treatment will not take place, then more aggressive preoperative measures are warranted.

In considering preoperative revascularization, two caveats should be kept in mind: 1) Successful percutaneous transluminal coronary angioplasty will result in a delay in noncardiac surgery of only several days, whereas coronary bypass grafting may result in considerable delay. Nevertheless, recurrences in stenosis after coronary angioplasty may be problematic, and multiple randomized trials suggest that coronary artery bypass grafting is associated with lower postprocedural rates of angina and better functional status. Despite some early enthusiasm, the morbidity and mortality rates of coronary artery bypass grafting under the same anesthetic as major vascular surgery are sufficiently high that it is hard to be enthusiastic about such an approach. 2) Q wave myocardial infarctions are thought to be caused by rupture of a plaque, commonly at the site of a stenosis that previously was not critical. If such a hypothesis also holds for perioperative Q wave infarctions, then the abnormalities found by most preoperative diagnostic tests may reflect existing lesions that serve as markers for another lesion that commonly is not yet critical enough to yield a positive test result. The limited benefit of coronary angioplasty and perhaps coronary bypass grafting as well in such circumstances must be considered. If the lesions detected by preoperative tests are of major hemodynamic significance and hence serve primarily to increase the risk of acute supply–demand imbalances, such as might be found when patients develop ischemia on a treadmill test but cannot stop the test before persistent ischemia begets subendocardial infarction and other complications, then postoperative detection of ischemia and its rapid treatment may be as good as preoperative coronary artery revascularization. For either type of infarction, postoperative aspirin or heparin, or both, in the doses used to prevent postoperative deep venous thrombosis may be useful.

It is not uncommon for there to be times in the evolution of our knowledge when our ability to predict risk precedes definitive knowledge regarding what to do in high risk patients. The standard recommendation in such situations is to conduct a large-scale randomized trial to answer the question. In this circumstance, it might be a trial of various therapeutic options in patients who are either at high risk clinically or who are at intermediate risk clinically and then had positive results on any of a variety of ischemia tests, provided that there was standardized and reproducible approach to screening and selecting patients for the trial. Given issues regarding long-term outcome, any conservative perioperative strategy would be combined with postoperative evaluation to determine whether coronary revascularization is now indicated. Because of the small expected differences between the various competing strategies, thousands of patients would be required. Although such a study would have the potential for guiding the clinical practice for an important issue, it is understandable why such a massive undertaking has not been at the top of the priority list for funding agencies. Nevertheless, until such a study is completed, it is unlikely that the debate among therapeutic choices for demonstrably high risk patients will be settled.

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